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# A Study of Genetic and Environmental Effects on the Co-Occurrence of Problem Behaviors in Three-Year-Old Twins

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The authors examined the genetic and environmental causes of the co-occurrence of problem behaviors in children. The analyses involved mother and father ratings of Oppositional, Withdrawn/Depressed, Aggressive, Anxious, Overactive, and Sleep Problems in 446 monozygotic and 912 dizygotic pairs of 3-year-old twins. Genetic factors contributed on average .150 (37.3%), shared environment .206 (51.2%), and nonshared environment .046 (11.4%) to the phenotypic correlations between the syndromes. Genetic and environmental factors caused different groupings. Internalizing and Externalizing groupings were indicative of nonshared environmental factors; clusters of problem behaviors with either the Aggressive or Anxious symptoms were most suggestive of genetic factors, and high scores on all syndromes indicated shared environmental influences.

Many disordered children show multiple problems (Caron & Rutter, 1991). Artifacts such as overlapping diagnostic criteria, the fact that referral may be more likely when a child is causing concern in more than one way, or an incorrect subdivision of syndromes can sometimes provide an explanation. However, in many instances real genetic and environmental effects seem to be involved. For example, a number of family studies have shown that relatives of affected individuals are not only at higher risk for the same disorder but also for a wider range of other psychosocial problems (Faraone et al., 1995; Rende et al., 1997; Wozniak, Biederman, Mundy, Mennin, & Faroane, 1995). Generally, the co-occurrence of problem behaviors may therefore perhaps better be viewed as one of the complexities of child psychopathology.

The presence of multiple problems does not necessarily imply that the child suffers from two or more truly distinct and unrelated disorders. An indication for this is that problem behaviors often co-occur in specific patterns or groupings. Such groupings of problem behaviors have frequently been studied with higher order factor analyses (Achenbach, 1991, p. 63). In these analyses, several syndrome scales that measure different types of behavioral and emotional problems are simultaneously subjected to a factor analysis. Results often indicate a grouping of anxious or inhibited behaviors on the one hand and a grouping of aggressive or antisocial behaviors on the other hand. In the clinical literature, these two groupings have been designed with terms such as Internalizing versus Externalizing, Inhibition versus Aggression, or Overcontrolled versus Undercontrolled. These groupings suggests that comorbid disorders could be different manifestations of the same underlying factors and reflect higher order clinical syndromes that may be distinguishable from other syndromes with respect to prognoses, course, or response to clinical interventions (Verhulst & Van der Ende, 1993).

Using twin data, it is possible to go one step further and study groupings of problem behavior at the level of etiology rather than symptomatology (Plomin, Rende, & Rutter, 1991). That is, instead of explaining groupings of problem behavior on the basis of higher order clinical syndromes, it is possible to examine whether different problem behaviors may be variable expressions of the same genetic or environmental causes. An example of this approach is a study by Kendler et al. (1995) that examined the multivariate genetic and environmental structure of psychiatric disorders in women. Their results suggested for instance that phobia, panic disorder, and bulimia may for an important part be different expressions of the same genes. Thus, these syndromes tended to co-occur at the symptom level because they were genetically speaking very similar.

In this article the same type of approach was applied to a broad spectrum of problems behaviors in 3-year-old twins. There were three main aims. The first aim was to determine the relative importance of genetic and environmental factors for the co-occurrence of problem behaviors. More specifically, we appor-

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tioned the correlations between syndrome scores of preschool twins to the three theoretical components: heredity, shared environment, and nonshared environment. The shared-environment component involves those environmental influences that operate to make twins alike and is estimated from the resemblance of the twins' syndrome scores. For example, if extreme poverty was characteristic of some families but not others, then it should induce similarity between twin pairs. It is important to realize that shared environment does not necessarily pertain to the home environment. For instance, a recent study showed that shared-environmental effects on academic achievement were equal for cousins and siblings (Van den Oord & Rowe, 1998). This implies that the shared-environment components as studied in behavior genetic studies can also reflect the wider community in which families are embedded (Bronfenbrenner, 1979; Harris, 1995; Parke & Kellam, 1994, p. 3). Nonshared environment refers to environmental effects that are unique to a particular child and uncorrelated across pairs of twins. By this definition, nonshared environment always operates to make twins dissimilar in a trait. Examples of nonshared-environmental effects for preschoolers are diseases, differential parental treatment or the experience of being treated differently (Reiss et al. 1995), and developmental variation such as when small initial differences magnify because siblings follow different developmental pathways (Molenaar, Boomsma, & Dolan, 1993).

Groupings of problem behaviors are usually studied by performing higher order phenotypic factor analyses on a broad range of problem behaviors. In this case the correlations between syndrome scores are ascribed to latent phenotypic or psychometric factors. The natural extension of this model in a genetically informative design is to estimate the relative importance of genetic and environmental effects on the latent psychometric factor. This extension shows that an implicit assumption made by higher order phenotypic factor analyses is that genetic and environmental factors cause similar patterns of problem behavior. That is, because genetic and environmental factors affect the syndrome scores via the latent psychometric factor, the groupings are necessarily constrained to be identical and defined by the loadings from the syndromes on the latent psychometric factor. However, in reality this does not have to be the case. For instance, it has been speculated that genetic factors mainly determine a general vulnerability for psychopathology and that environment could work in a much more specific way by coding for separate symptoms (Tyrer, 1985). In such a scenario, genetic and environmental effects could easily result in very different patterns of problem behavior. Thus, the same set of genes would affect all problem behaviors, whereas the effects of a specific set of environmental influences would be limited to a small subset of the symptoms. To gain insight into the mode in which multiple problems are caused, the second aim of our study was to examine whether genetic and environmental influences cause similar or distinct patterns of problem behaviors.

The previous aims involve the quantification of the genetic and environmental effects and the identification of the general mechanism underlying the occurrence of multiple problems. Our third aim was to determine the specific structure of the genetic and environmental contributions. One issue involves the number of common genetic and environmental effects that are necessary to explain the phenotypic correlations. For instance, there could be multiple sets of genes causing co-morbidity. If so, a next step would be to determine the type of co-morbid disorders those genes code for. In addition to genes and environmental factors that affect multiple syndromes, there will be factors that are disorder specific. We therefore also examined the nature of these specific effects. Comparisons with the common effects could then for instance reveal whether certain types of genetic and environmental risk factors tend to cause a clustering of syndromes or are specific in their impact.

## Method

### *Sample*

In the Netherlands, about 85% of the parents of all newborns are paid a home visit by a commercial organization. During this visit parents of twins are asked to participate in the Netherlands Twin Register (NTR; Boomsma, Orlebeke, & Van Baal, 1992) kept by the department of Biological Psychology of the Free University of Amsterdam. It is estimated that about 40 to 50% of all multiple births in the Netherlands are registered. For this study questionnaires were mailed to 1,792 parents of 3-year-old twins. Nonresponders were sent reminders, and when still no response was obtained, they were contacted by phone. Completed questionnaires were returned by 1,377 parents (77%).

For 374 same-sex twin pairs, results from a blood test were available to determine the zygosity of the twins. This test was based on an analysis of 26 blood group polymorphisms. For the remainder of the same sex twin pairs, information about zygosity was obtained from a questionnaire completed by parents when the twins were about 2 years old. In this questionnaire parents are asked to indicate the twins' zygosity on the basis of their physical similarity (e.g., hair, eyes, face). The parents of 31 twin pairs who indicated that they were insecure were contacted by phone to identify as yet the zygosity. Nineteen twin pairs had to be discarded because their parents remained uncertain. This left a sample of 446 monozygotic (MZ) and 912 dizygotic (DZ) twin pairs (236 MZ girls, 210 MZ boys, 238 DZ girls, 265 DZ boys, and 409 opposite-sex pairs). The twins' mean age was 42.12 months ($SD$ = 3.94). Mother and father ratings were available for 99% and 82% of the twin pairs, respectively.

To establish the reliability of the parental questionnaire, the zygosity indicated on the questionnaire was compared with the zygosity as determined using the blood test. For the 327 same-sex twin pairs for whom both blood test and questionnaire results were available, the agreement was 81%. This agreement is somewhat lower compared with reliabilities reported by other authors (Bonnelykke, Hauge, Holm, Kristoffersen, & Gurtler, 1989). Additional analyses showed that particularly MZ twins tended to be misclassified as DZ twins. One explanation could therefore be that parents applied the criteria mentioned in the questionnaire very strictly and concluded that their children were DZ even in the case of minor physical differences. Another explanation is that parents who were uncertain about their twins' zygosity were more likely to consent with the blood test. Thus, the twins for whom it was easy to tell whether they were MZ or DZ may not have been included in this comparison. The agreement of 81% may therefore perhaps better be viewed as the lower bound of the reliability of the questionnaire. Finally, we want to mention that for only 41% (556 pairs) of the twin pairs, zygosity was determined using the questionnaire (the remainder consisted of opposite-sex twins and twins classified with the blood test). Thus, possible effects of classification errors on our results were limited because of the fact that only a subgroup of twins was at risk of being misclassified.

### *Assessment Instrument*

Fathers' and mothers' ratings of problem behaviors in their twins were obtained with the Child Behavior Checklist for children aged 2 to 3

(CBCL/2–3; Achenbach, 1992). Dutch syndromes for the CBCL/2–3 were derived through a series of exploratory and confirmatory factor analyses on a clinical sample, a community sample, and the twin sample from the present study (Koot, Van den Oord, Verhulst, & Boomsma, 1997). The syndromes were labeled Oppositional, Withdrawn/Depressed, Aggressive, Anxious, Overactive, and Sleep Problems. In addition, by subjecting the syndrome scales to higher order factor analyses, Externalizing and Internalizing groupings were derived. The Externalizing grouping was composed of the Oppositional, Aggressive, and Overactive syndromes. The Internalizing grouping was composed of the Anxious and Withdrawn/Depressed syndromes. Comparisons with a community sample showed that syndrome scores were quite similar for twins and singletons (Van den Oord, Koot, Boomsma, Verhulst, & Orlebeke, 1995). This supported the representativeness of our twin sample with respect to problem behaviors.

### *Multivariate Genetic Models*

In univariate genetic analyses, the phenotypic variance of a variable is usually decomposed into a contribution of the additive effects of many genes, environmental influences that are shared by twins, and environmental influences that are not shared by twins (Falconer, 1989; Neale & Cardon, 1992; Plomin, DeFries, & McClearn, 1990). Estimates of the importance of these three variance components can be derived on the basis of the resemblance between MZ twins who are genetically identical and DZ twins who share only a proportion of their genes. That is, genetic effects are indicated when the MZ twin correlation $r_{MZ}$ is higher than the DZ twin correlation $r_{DZ}$; shared-environmental effects are indicated if the twin correlations are larger than zero after the genetic effects are partialled out; and nonshared-environmental effects are indicated if the sum of the genetic and shared environmental effects does not explain the total phenotypic variance. More precisely, the proportion of variance explained by each component is genetic variance $= 2 \times (r_{MZ} - R_{DZ})$, shared-environmental variance $= 2 \times r_{DZ} - r_{MZ}$, and nonshared-environmental variance $= 1 -$ genetic variance $-$ shared-environmental variance.

Similar to the decomposition of the phenotypic variance of a variable, phenotypic correlations between variables can also be decomposed into additive genetic, shared-environmental, and nonshared-environmental contributions. This decomposition can again be made by comparing the resemblance of MZ twins versus DZ twins. However, instead of using the twin correlations for the same variables (the same-variable twin correlation between Variable A in Twin 1 and Variable A in Twin 2), the comparison now involves twin correlations for different variables (the cross-variable twin correlation between Variable A in Twin 1 and Variable B in Twin 2). Genetic effects are indicated when the cross-variable twin correlation is higher for MZ twins compared with DZ twins; shared-environmental effects are indicated if the cross-variable twin correlations are larger than zero after the genetic effects have been partialled out; and a nonshared-environmental contribution is indicated when the sum of the genetic and shared-environmental effects does not explain the total phenotypic correlation between Variables A and B. Similar formulas to the ones discussed above for the variances can again be used to compute the contribution of each component to the phenotypic correlation: genetic contribution $= 2 \times (r_{MZ\text{-}cross} - r_{DZ\text{-}cross})$, shared-environmental contribution $= 2 \times r_{DZ\text{-}cross} - r_{MZ\text{-}cross}$, and nonshared-environmental contribution = phenotypic correlation $-$ genetic contribution $-$ shared-environmental contribution.

The above discussed formulas show that in the case of multiple variables, the whole phenotypic variance–covariance matrix can be decomposed into a matrix of genetic variances and covariances, a matrix of shared-environmental variances and covariances, and a matrix of nonshared-environmental variances and covariances. Instead of decomposing each variance and covariance separately, it is preferable to make such a decomposition by fitting multivariate genetic models. A multivariate genetic analysis can perhaps best be viewed as a simultaneous factor analysis on the genetic and environmental variances and covariances. Just like ordinary factor analyses, these models make a distinction between common factors that influence all problem behaviors and factors that are unique for a certain syndrome scale (Boomsma & Molenaar, 1986; Martin & Eaves, 1977). The common genetic and environmental factors explain the covariances between the problem behaviors and determine the groupings. The unique genetic and environmental factors explain the remainder of the variance that is not shared by the different problem behaviors and do not result in a clustering of syndromes.

Two classes of multivariate genetic models can be distinguished (McArdle & Goldsmith, 1990; Neale & Cardon, 1992, pp. 231–259). The two classes differ in the way the common factors are assumed to influence the different problem behaviors. The way the unique factors influence the syndrome scales is identical in both classes. The first class of models is usually referred to as *psychometric* or *common pathway* models. An example is depicted in Figure 1. In multivariate genetic models, the number of latent variables is usually large. For sake of simplicity, we therefore only

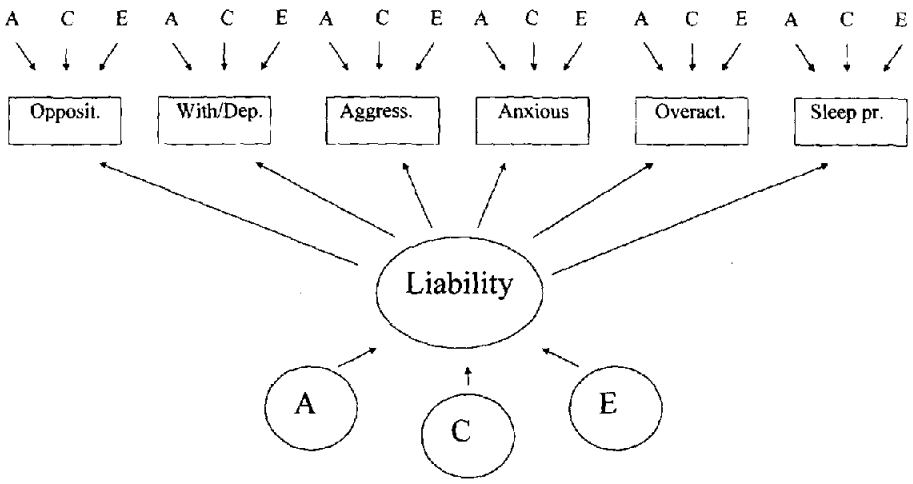


*Figure 1.* A one-factor psychometric model. *A* refers to additive genetic factors, *C* to shared environmental factors, and *E* to nonshared environmental factors. Opposit. = oppositional; With/Dep. = withdrawn/depressed; Aggress. = aggressive; Overact. = overactive; Sleep pr. = sleep problems.

depicted the path diagram for one twin. However, a complete path diagram for the whole twin pair can easily be obtained by specifying the same model for the co-twin. In this complete path diagram, the correlations between the shared-environmental factors of the two twins would need to be fixed to 1, and the correlations between the genetic factors of the two twins would need to be fixed to 1 for MZ twins and .5 for DZ twins.

Figure 1 shows that the common genetic and environmental factors influence the different problem behaviors via a psychometric factor. This factor could be interpreted as a general liability to problem behavior. In this example there is only one such factor, and we therefore called it an one factor psychometric model. However, models with multiple psychometric factors are also possible. These psychometric factor(s) are identical to the factor(s) derived from higher order phenotypic factor analyses that have repeatedly been used to study groupings of problem behavior in samples that are not genetically informative. Both types of analyses would therefore yield the same groupings of problem behaviors. The difference is that with genetically informative data it is also possible to estimate the relative importance of genetic and environmental factors for these groupings.

The second class of models is usually referred to as biometric or independent pathway models. Figure 2 depicts an example. For reasons discussed in relation to Figure 1, the path diagram applies to one twin only. The figure shows that the common genetic and environmental factors influence the different problem behaviors directly, and there is no intervening higher order factor. We labeled this model a *one-factor* biometric model because there was only one set of common genetic and environmental factors. Biometric models with more than one set of common genetic and environmental factors are also possible. The most important difference with Figure 1 is that there are no psychometric factors that mediate the genetic and environmental effects. As a result, the common genetic and environmental factors do not necessarily cause similar groupings of problem behaviors. Thus, it can occur that one group of problems behaviors may cluster because they share the same environmental causes, whereas another group of problems behaviors may cluster because they are affected by the same set of genes. For this reason biometric models can also yield different results compared with those obtained with higher order phenotypic factor analyses. That is, the phenotypic factor models implicitly assume that genetic and environmental effects cause identical groupings, whereas a biometric model may indicate that such a constraint is incorrect and suggest different groupings for genetic and environmental factors.

## *Model Fitting*

A number of different multivariate genetic models were fitted. First, a baseline model was fitted that specified only variances and implied covariances of zero between the syndromes. This model was mainly used to obtain a baseline for assessing the improvement in fit obtained with the other models. The second model was the saturated unconstrained model, also known as Cholesky or triangular decomposition, for the genetic and environmental contributions to the phenotypic variances and covariances. In contrast to psychometric and biometric models that account for the covariances using a few common genetic and environmental factors, this model does not impose any restrictions on the genetic and environmental contributions to the covariances. Fit indices for the saturated model therefore give the best possible fit and can be used to assess the fit of psychometric and biometric models that do impose restrictions. Finally, one- and two-factor biometric and psychometric models were fitted to the data. For two-factor biometric and psychometric models, the issue of rotation arises. Similar to the way this is dealt with in exploratory factor analysis, we first obtained an initial solution and then rotated this solution to improve the interpretability. We obtained the initial solution by leaving the two factors uncorrelated and fixing one-factor loading to zero (technically speaking this is an orthogonal rotation with a reference variable; see Jöreskog, 1971). Next, we performed a varimax rotation to improve the interpretation.

To select the best fitting parsimonious model, we used the chi-square difference test, the Tucker–Lewis Index (TLI), and Akaike's Information Criterion (AIC). An elaborate discussion of these fit indices is given by Marsh, Balla, and McDonald (1988). We used the chi-square difference test to test whether in comparison to the saturated model, a target model (i.e., the different biometric and psychometric models) fitted significantly poorer. The test statistic equals the difference between the chi-squares of the saturated model and target model and is chi-square distributed with the degrees of freedom equal to the difference in degrees of freedom of both models. The TLI and AIC are both based on the chi-square fit index. They incorporate a penalty function so that they can be poorer if the use of more parameters results in little improvement in fit. The TLI reflects the improvement in fit of the target model compared with the baseline model. It ranges from 0 to 1, and because higher values imply a better fit, we selected the model with the highest TLI. AIC is frequently used in genetic research. Smaller values of AIC indicate a better fit, and we therefore selected the model with the lowest AIC.

The correlations between mother and father ratings for Oppositional, Withdrawn/Depressed, Aggressive Behavior, Anxious, Overactive, and Sleep Problems were .71, .57, .70, .70, .69, and .72, respectively. Although their ratings did not seem to be completely interchangeable, these correlations suggested a substantial agreement between both parents. To study the (dis)agreement between mothers and fathers, we fitted three models

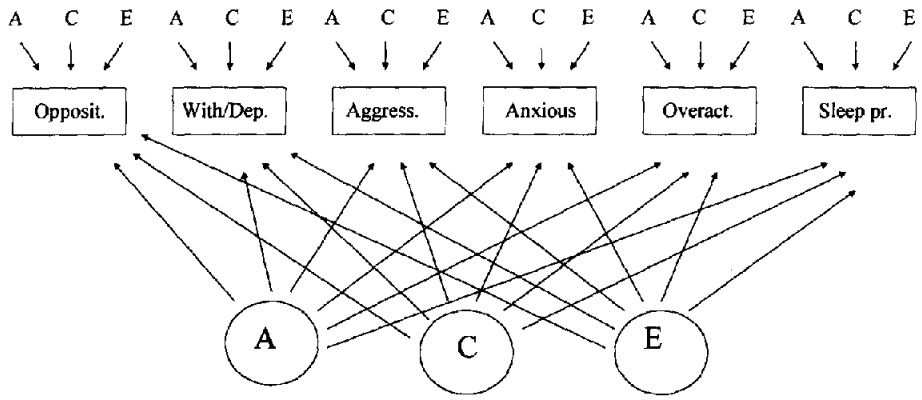


*Figure 2.* A one-factor biometric model. *A* refers to additive genetic factors, *C* to shared environmental factors, and *E* to nonshared environmental factors. Opposit. = oppositional; With/Dep. = withdrawn/depressed; Aggress. = aggressive; Overact. = overactive; Sleep pr. = sleep problems.

discussed by Hewitt, Silberg, Neale, Eaves, and Erickson (1992) to our data (Van den Oord, 1993; Van den Oord, Verhulst, & Boomsma, 1996). Results showed that mother and father ratings could best be viewed as two indicators of the same trait and that disagreement was for an important part caused by measurement error and rater bias (the tendency of an individual rater to overestimate or underestimate scores consistently as a result of, for instance, response styles or different normative standards). This finding justified analyzing the mean of both parents' ratings, which has the advantage that the multivariate models become much simpler. Univariate genetic analyses (Van den Oord et al., 1996) showed no evidence for sex differences in three of the six syndromes. Sex differences for the other syndromes were small and never involved more than one parameter. This result suggested that data of boys and girls could be combined into a single analysis.

We used the LISREL 7.20 (Jöreskog & Sörbom, 1989) to fit the models. The syndrome scores that consisted of the mean of both parents' ratings displayed some skewness and kurtosis. For this reason, we performed the model fitting by using an asymptotically distribution free estimation procedure that did not assume normal distributions.

## Results

The phenotypic correlations among the six syndrome scales are shown in Table 1. To study the higher order factor structure for the CBCL/2–3 reported by Koot et al. (1997), we extracted two factors with an exploratory factor analysis. The total amount of variance explained by these factors was 56.2%, and after a varimax rotation both factors explained nearly equal proportions of variance. The factor loadings for Oppositional, Withdrawn/Depressed, Aggressive Behavior, Anxious, Overactive, and Sleep Problems were .77, .44, .79, .19, .66, and .36, respectively, on the first factor and .35, .42, .11, .98, .18, and .24, respectively, on the second factor. Thus, on the Externalizing factor the highest factor loadings were for the Oppositional, Aggressive, and Overactive syndromes. On the Internalizing factor, the highest factor loadings were found for the Withdrawn/Depressed and Anxious syndromes. However, the substantial cross-loading of Oppositional as well as the fact that the loading from Withdrawn/Depressed on the Externalizing factor was even larger than on the Internalizing factor suggested that this subdivision into Internalizing and Externalizing was not clear-cut.

Table 2 shows the MZ and DZ twin correlations. The same-variable twin correlations on the diagonal are important for decomposing the variances and the off-diagonal cross-variable twin correlations are important for decomposing the correlations between syndrome scores into genetic and environmental contributions. When the decomposition is done using the simple formulas discussed above, Table 3 is obtained. The same-variable twin correlations suggest substantial genetic influences, small shared-environmental influences, and moderate amounts of nonshared-environmental influences. For instance, the formulas discussed above indicate that for Aggressive the proportion of genetic variance equals $2 \times (.77 - .45) = .64$, the proportion shared-environmental variance equals $2 \times .45 - .77 = .13$, and the proportion nonshared-environmental variance equals $1 - .64 - .13 = .23$. We also want to note that in particular for Overactive and Anxious these formulas yield negative estimates of the proportion of shared-environmental variance. Negative estimates can be the result of sample fluctuations (which are likely in situations where the real effect is close to zero) or indicate that the assumptions used to make the decomposition are too restrictive.

Table 1
*Phenotypic Correlations Among Syndrome Scales*

| Scale | 1 | 2 | 3 | 4 | 5 | 6 |
|---|---|---|---|---|---|---|
| 1. Oppositional | — | | | | | |
| 2. Withdrawn/Depressed | .47 | — | | | | |
| 3. Aggressive | .64 | .40 | — | | | |
| 4. Anxious | .49 | .49 | .25 | — | | |
| 5. Overactive | .57 | .37 | .54 | .31 | — | |
| 6. Sleep Problems | .39 | .25 | .29 | .30 | .26 | — |

Table 2
*MZ and DZ Twin Correlations*

| | Twin 2 | | | | | |
|---|---|---|---|---|---|---|
| Twin 1 | 1 | 2 | 3 | 4 | 5 | 6 |
| MZ twins | | | | | | |
| 1. Oppositional | .78 | — | | | | |
| 2. Withdrawn/Depressed | .44 | .71 | — | | | |
| 3. Aggressive | .58 | .33 | .77 | — | | |
| 4. Anxious | .47 | .37 | .26 | .67 | — | |
| 5. Overactive | .48 | .36 | .44 | .30 | .50 | — |
| 6. Sleep Problems | .40 | .20 | .21 | .32 | .21 | .69 |
| DZ twins | | | | | | |
| 1. Oppositional | .47 | — | | | | |
| 2. Withdrawn/Depressed | .31 | .33 | — | | | |
| 3. Aggressive | .44 | .30 | .45 | — | | |
| 4. Anxious | .35 | .22 | .28 | .28 | — | |
| 5. Overactive | .32 | .27 | .23 | .30 | .07 | — |
| 6. Sleep Problems | .29 | .20 | .28 | .25 | .17 | .34 |

*Note.* MZ = monozygotic; DZ = dizygotic.

The cross-variable twin correlations suggest very different results with respect to the relative importance of genetic and environmental effects on the phenotypic correlations. For instance, Table 1 shows that the phenotypic correlation between Aggressive and Withdrawn/Depressed equals .40. A decomposition of this correlation using the formulas discussed above indicates a genetic contribution of $2 \times (.33 - .30) = .06$, a shared-environmental contribution of $2 \times .30 - .33 = .27$, and a nonshared-environmental contribution of $.40 - .06 - .27 = .07$. On average genetic factors contribute .155, shared environment .203, and nonshared environment .044 to the phenotypic correlations between six syndromes. In terms of percentages or proportions of the correlations, this result corresponds with 38.6%, 50.5%, and 10.9%. This suggested that with respect to the phenotypic correlations between the syndrome scales, shared-environmental effects were more important than genetic effects, and genetic effects were more important than nonshared-environmental effects.

Table 4 presents indices for the multivariate genetic models fitted to the covariance matrices in groups of MZ and DZ twins. Note that the input matrices for these analyses are not only composed of cross-twin statistics such as reported in Table 2 but also phenotypic statistics such as reported in Table 1 that pertain to the same child. All chi-squares were significant, which implies that none of the models fitted. Biometric models fitted better than

Table 3
*Univariate Decomposition of Phenotypic Statistics Into Genetic and Environmental Effects*

| | Genetic | | | | | | Shared environment | | | | | | Nonshared environment | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Scale | 1 | 2 | 3 | 4 | 5 | 6 | 1 | 2 | 3 | 4 | 5 | 6 | 1 | 2 | 3 | 4 | 5 | 6 |
| 1. Oppositional | .62 | | | | | | .16 | | | | | | .22 | | | | | |
| 2. Withdrawn/Depressed | .26 | .76 | | | | | .18 | −.05 | | | | | .03 | .29 | | | | |
| 3. Aggressive | .28 | .06 | .64 | | | | .30 | .27 | .13 | | | | .06 | .07 | .23 | | | |
| 4. Anxious | .24 | .30 | −.04 | .78 | | | .23 | .07 | .30 | −.11 | | | .02 | .12 | −.01 | .33 | | |
| 5. Overactive | .32 | .18 | .42 | .00 | .86 | | .16 | .18 | .02 | .30 | −.36 | | .09 | .01 | .10 | .01 | .50 | |
| 6. Sleep Problems | .22 | .00 | −.14 | .14 | .08 | .70 | .18 | .20 | .35 | .18 | .13 | −.01 | −.01 | .05 | .08 | −.02 | .05 | .31 |

psychometric models. This result suggested that genetic and environmental factors caused different groupings of problem behaviors. The chi-square difference test showed that in comparison to the saturated model, only the two-factor biometric model did not result in a significant decrease in fit. Thus, the biometric two-factor model accounted for the covariances between the syndromes as well as the model that simply decomposed all observed covariances between the syndromes into genetic, shared-environmental contributions, and nonshared-environmental contributions. In addition, the biometric two-factor model had the highest TLI and the lowest AIC. This outcome confirmed the results from the chi-square difference test and showed that the biometric two-factor model was the best fitting parsimonious model.

Next we tested whether the biometric two-factor model could be simplified by successively eliminating one genetic, one shared-environmental factor, or one nonshared-environmental factor. We fixed all loadings on the second common factor at zero. Then we used the chi-square difference test to test the simplified model against the full biometric two-factor model. For the second genetic factor, $\chi^2_5 = 18.92$, $p < .05$, and the second nonshared environmental factor, $\chi^2_5 = 59.61$, $p < .05$, the decrease in fit was significant. This result indicated that patterns of groupings of problem behavior involve two different sets of genes and nonshared-environmental influences. However, the decrease in fit was not significant when one shared-environmental factor was eliminated, $\chi^2_5 = 4.12$, $p > .05$. This result suggested that to explain groupings of problem behaviors, one set of shared-environmental influences is sufficient. This simplification resulted in a biometric model with two common genetic, one common shared-environmental factor, and two common nonshared-environmental factors. For this simplified model, the TLI was .804 and AIC was 73.47. A comparison with the values reported in Table 3 for the full two-factor biometric model showed that also on the basis of these fit indices the simplified model had to be preferred.

The varimax rotated solution for our best fitting model is shown in Table 5. The completely standardized solution is given in which all latent and observed variables have variances of one. This solution has the advantage that the parameter estimates can be compared with each other and are directly related to the importance of that factor for the phenotypic variances and correlations.[1] Computations showed that genetic factors made on average a contribution of .150, shared environment made a contribution of .206, and nonshared environment made a contribution of .046 to the phenotypic correlations between the six syndromes. In terms of percentages or proportions of the correlations, this result corresponds with 37.3%, 51.2%, and 11.4%. This result showed that genetic and shared-environmental influences were most important and that nonshared-environmental influences were least important for groupings of problem behavior. In contrast, for the variances that were unique to each syndrome, there were no shared-environmental influences at all, and nonshared-environmental influences were relatively much more important. This result indicated that nonshared environment was most specific and shared environment least specific in their effects.

Table 5 shows the highest factor loadings on the first common genetic factor for the Oppositional, Withdrawn/Depressed, Overactive, and Aggressive syndromes. This result implies that this set of genes causes a grouping of these syndromes. The second common genetic factor seemed to affect the same variables except that the Aggressive syndrome was replaced by the Anxious syndrome. Particularly, the Oppositional, Aggressive, and Overactive syndromes loaded on the first common nonshared-environmental factor. This result suggested a so-called Externalizing pattern of problem behaviors. The second common nonshared-environmental factor seemed largely defined by the loading from Anxious. The next highest loading involved Withdrawn/Depressed so that to a certain extent this nonshared environmental factor tended to cause an Internalizing grouping of problem behavior. All syndromes loaded on the common shared-environmental factor. This result indicated that the common shared-environmental influences resulted in a grouping of all syndromes.

To determine which syndromes are indicators of which common factors, in ordinary phenotypic factor analyses a (arbitrary) cut-off factor loading is usually specified. Indicators with factor loadings

[1] The proportion of variance explained by a factor can be computed by squaring the path coefficient and the total proportion of variance explained by genetic and environmental factors by summing the squared effects. For instance, the syndrome Aggressive is affected by two common genetic factors, $A_1$ and $A_2$ plus an unique genetic factor A. The total proportion of genetic variance therefore equals $(.56)^2 + (.09)^2 + (.43)^2 = .51$. The contribution of a common factor to the phenotypic correlation can be computed by multiplying the relevant factor loadings and the total contribution of genetic and environmental factors by summing the multiplied factor loadings. For instance, the genetic contribution to the correlation between Aggressive and Withdrawn/Depressed is composed of effects $A_1$ and $A_2$ and equals $.25 \times 56 + 43 \times .09 = .18$.

Table 4
*Fit Indices for Multivariate Genetic Models*

| Model | Sets of common factors | Overall model fit | | | | | Chi-square difference test (target vs. saturated model) | | |
|---|---|---|---|---|---|---|---|---|---|
| | | *df* | $\chi^2$ | *p* | TLI | AIC | *df* | $\chi^2$ | *p* |
| Baseline | 0 | 138 | 1311.73 | .0 | n.a. | 1035.73 | 45 | 1039.53 | .00 |
| Saturated unconstrained | n.a. | 93 | 272.19 | .00 | .77 | 86.19 | | n.a. | |
| Biometric | 1 | 120 | 373.42 | .00 | .75 | 133.42 | 27 | 101.23 | .00 |
| Psychometric | 1 | 130 | 605.77 | .00 | .57 | 345.77 | 37 | 333.58 | .00 |
| Biometric model[a] | 2 | 105 | 289.35 | .00 | .79 | 79.35 | 12 | 17.16 | .14 |
| Psychometric | 2 | 123 | 527.00 | .00 | .61 | 281.00 | 30 | 254.81 | .00 |

*Note.* n.a. = not applicable. TLI = Tucker–Lewis Index; AIC = Akaike's Information Criterion.
[a] Denotes preferred model.

above this cutoff are subsequently viewed as indicators and used to interpret the factor. We used a similar approach in this article as well. The cut-off factor loadings used in phenotypic factor analyses apply to situations where correlation matrices are analyzed. For this reason, we first calculated the genetic, shared-environmental, and nonshared-environmental correlation matrices on the basis of our final model. Next, these genetic and environmental correlation matrices were subjected to factor analyses with varimax rotations to find the syndromes with loadings larger than our cutoff that was .3. This procedure resulted in very similar groupings of problem behavior as discussed in relation to the completely standardized solution shown in Table 5. Thus, Oppositional, Withdrawn/Depressed, Overactive, and Aggressive syndromes had loadings larger than .3 on first but not on the second common genetic factor, and Oppositional, Withdrawn/Depressed, Overactive, and Anxious syndromes had loadings larger than .3 on second but not on the first common genetic factor. The analyses on the nonshared-environmental correlation matrix suggested again Internalizing and Externalizing groupings. That is, the syndromes within the groupings had loadings larger than .3 on their own factor but not on the common factor affecting the syndromes in the other group. The only exception involved the factor loading from Withdrawn/Depressed on the Internalizing nonshared-environmental factor that was .26. Given the fact that Withdrawn/Depressed had the second largest factor loading on the Internalizing factor and that because of sampling error it can always happen that some criteria and not perfectly met, it still seems reasonable to conclude that nonshared environment tended to cause Internalizing and Externalizing groupings of problem behavior. Because there was only one common shared-environmental factor and no unique shared-environmental contributions, all shared-environmental influences on the syndromes could be explained by that common factor. This result implies that the factor loadings, which measure the amount of shared-environmental variance that the common factor explains in the indicators, obtained from analyzing the shared-environmental correlation matrix are by definition equal to one. It may be important to mention that even in the solution reported in Table 5 that is not based on the shared-environmental correlations but on the shared-environmental contributions to the phenotypic correlations, the loadings already exceeded .3. This result suggested that all syndromes were indicators of the same shared-environmental factor.

In addition to the orthogonal varimax rotation shown in Table 5, we also performed an oblique promax rotation in which the common factors were not assumed to be uncorrelated. For the nonshared-environmental factors, the promax rotation yielded very similar results as the varimax rotation. The explanation was the very low correlation of .08 between the two nonshared-environmental factors in the promax rotation. This result implied that nonshared-environmental effects that cause Internalizing pat-

Table 5
*Parameter Estimates for Preferred Multivariate Genetic Model*

| Scale | First set common factors | | | Second set common factors | | | Unique factors | | |
|---|---|---|---|---|---|---|---|---|---|
| | A | C | E | A | C | E | A | C | E |
| 1. Oppositional | .34 | .65 | .33 | .25 | — | 0.12 | .30 | .00 | .43 |
| 2. Withdrawn/Depressed | .25 | .34 | .05 | .43 | — | 0.13 | .62 | .00 | .48 |
| 3. Aggressive | .56 | .52 | .34 | .09 | — | −0.03 | .43 | .00 | .32 |
| 4. Anxious | .03 | .42 | −.06 | .53 | — | 0.63 | .36 | .00 | .00 |
| 5. Overactive | .26 | .40 | .50 | .39 | — | 0.01 | .00 | .00 | .61 |
| 6. Sleep Problems | .09 | .41 | .07 | .17 | — | 0.03 | .72 | .00 | .53 |

*Note.* *A* refers to additive genetic factors, *C* to shared environmental factors, and *E* to nonshared environmental factors. The varimax rotated completely standardized solution is shown where all latent and observed variables have a variance of one. Dashes indicate parameters that are fixed to zero.

terns are distinct from nonshared-environmental effects that cause Externalizing patterns. For the genetic factors, the promax solution was not as easy to interpret as the solution obtained with the varimax rotation. A salient feature was, however, the estimated correlation of .47, suggesting a substantial overlap between the two sets of genes. In addition, Aggressive had the highest factor loading on the first factor and the lowest factor loading on the second factor, whereas Anxious had the highest factor loading on the second factor and the lowest factor loading on first factor. This result confirmed the results from the varimax rotation, suggesting that genetically speaking Aggressive and Anxious were distinct syndromes. Instead of using the mean parental rating, we repeated the analysis by specifying a multivariate model for both parents separately. Results turned out, however, to be very similar. To avoid unnecessary complexities, we therefore confined the discussion of the results to those obtained using the mean parental rating.

## Discussion

Multivariate genetic models were fitted to a broad spectrum of problem behaviors in 3-year-old twins. We now summarize our findings with respect to our three main aims.

### *Relative Importance of Genetic and Environmental Effects*

The best fitting model indicated that on average genetic factors contributed .150, shared environment .206, and nonshared environment .046 to the phenotypic correlations between the syndromes. In terms of percentages or proportions of the correlations, this result corresponds with 37.3%, 51.2%, and 11.4%, an outcome which indicated that genetic and shared-environmental influences were most important and that nonshared-environmental influences were least important for groupings of problem behavior.

Our finding that shared-environmental influences may be relatively important for groupings of problem behaviors seems to be consistent with another CBCL study in young twins (Schmitz, Cherny, Fulker, & Mrazek, 1994). One explanation could be that preschool twins are too young to have different friends or teachers so that they still share many of their experiences. However, evidence has been found for shared environmental effects on the co-occurrence of depressive and antisocial behavior in adolescents (O'Connor, McGuire, Reiss, Hetherington, & Plomin, 1998). In addition, a number of CBCL studies in older children have shown larger shared-environmental influences for total problem scores than for the separate syndrome scales (Edelbrock, Rende, Plomin, & Thompson, 1995; Van den Oord, Boomsma, & Verhulst, 1994; Van den Oord et al., 1996; Van den Oord & Rowe, 1997). The reason why this pattern of results may suggest that shared-environmental influences are especially important for the co-occurrence of problem behaviors is that the variance of total problem scores consists of the variances of separate syndrome scores plus two times all the correlations between the syndrome scores. The shared-environmental effects on the correlations between syndromes will therefore be reflected when total problem scores are analyzed but not when separate syndrome scores are analyzed.

Among behavior geneticists, it is generally acknowledged that for most traits the environmental influences are mainly of the nonshared type and that shared-environmental influences are usually rather small (Plomin & Daniels, 1987; Rowe, 1994). We should stress that this observation is not inconsistent with our results that point to a possible role of shared family environment for groupings of problem behaviors. The reason is that the traditional behavior genetic analysis focuses on a single variable, whereas this article pertains to correlations between syndromes. For instance, suppose that shared environment contributes .15 to a phenotypic correlation between two variables that equals .3. Because shared environment explains half of the phenotypic correlation, it seems fair to say that it is important for the correlation between the variables. However, if we assume that there are no other shared-environmental influences and that these influences are equally large for both variables, shared environment would still explain merely 15% of the total phenotypic variance. Thus, the fact that shared environment may be important for groupings of problem behavior does not necessarily mean that it is important in the univariate sense as well.

Rater bias is the tendency of an individual rater to overestimate or underestimate scores consistently compared with the mean of all raters (e.g., as a result of different normative standards or response tendencies see Hewitt et al., 1992). Because rater bias increases the twin correlations, it could offer a methodological explanation for the substantial shared-environmental effects in our study. There are, however, two reasons that would have reduced the possible confounding of shared environment by rater bias. The most important reason is that we analyzed the mean of both parents. Thus, rater bias could only be a problem to the extent that it was correlated for both parents. The second reason is that rater bias could be more influential in a univariate analysis in which both twins are rater on the same scale than a multivariate analysis that involves sibling correlations for different scales. For instance, because of a different normative standard, a rater could judge certain behaviors as more aggressive than other raters so that rater bias inflates the twin correlations for aggression. However, it may not necessarily be the case that normative standards are correlated for different behaviors. Thus, the fact that a rater overestimates the severity of aggression may not imply that the same rater would also overestimate the severity of depression.

### *Distinct Instead of Similar Patterns*

Genetic and environmental factors appeared to cause their own unique patterns of comorbidity. More specifically, Internalizing/Externalizing patterns were indicative of nonshared-environmental factors; clusters of problem behaviors with either the Aggressive or Anxious syndrome were most suggestive of genetic factors; and high scores on all syndromes indicated shared-environmental influences. Because of a lack of similar studies in children, it is unclear whether our finding that genetic and environmental factors cause different patterns may be associated with unique features of this study, such as the use of the CBCL or the young age of our twins. However, it may be relevant to mention two multivariate genetic studies in adult psychiatry that also involved a variety of syndromes (Kendler, Heath, Martin, & Eaves, 1987; Kendler et al., 1995). Although the age range, assessment procedure, and the nature of the disorders were quite different compared with those in the present study, in both cases the data also showed that genetic

and environmental factors cause different groupings. This result suggested that the independent pathway model might have a more general validity.

Phenotypic factor analyses assume that genetic and environmental factors result in similar patterns. Our evidence for independent pathways therefore implies that the higher order clinical syndromes obtained from phenotypic factor analyses are difficult to interpret because they do not represent clear-cut etiological entities. This conclusion seems indirectly also indicated by phenotypic factor analyses. That is, confirmatory phenotypic factor analyses showed in three independent Dutch samples that a phenotypic factor model composed of an Internalizing/Externalizing factor did not fit (Koot et al., 1997). In addition, exploratory phenotypic factor analyses performed on American samples yielded for the Withdrawn scale of the CBCL/2–3 equal loadings on both the Internalizing and Externalizing factors (Achenbach, 1992; Achenbach, Edelbrock, & Howell, 1987). This result suggested the absence of a sharp distinction between Internalizing and Externalizing syndromes. Thus, the lack of the fit of the phenotypic factor model as well as difficulties in making a clear subdivision seem to provide indirect evidence for our finding that genetic and shared-environmental influences may result in different groupings and that the Internalizing/Externalizing distinction may not indicate clear-cut etiological components.

The fact that genetic and environmental factors cause different patterns might be useful to obtain a better understanding and control of child psychiatric disorders. On the basis of the specific patterns, a differential diagnosis at the level of etiology could be made by subdividing problem children into subgroups with high genetic or high environmental scores (Boomsma, Molenaar, & Orlebeke, 1990). These etiologically different groups could then, for instance, be compared with respect to response to treatment, which could be valuable to optimize clinical interventions.

### *Structure of Genetic and Environmental Contributions*

The genetic effects on the co-occurrence of problem behaviors seemed to involve two sets of genes. Whereas most syndromes were affected by both sets of genes, Aggressive was exclusively affected by the first set, and Anxious was exclusively affected by the second set. Thus, genetically speaking Aggressive and Anxious were completely distinct syndromes. Furthermore, Aggressive showed the highest factor loading on the first set, and Anxious showed that highest factor loading on the second set, indicating that these syndromes gave the best characterization of the type of problems the two sets of genes code for. The interpretation is that in 3-year-olds an Aggressive and an Anxious genetic–comorbid syndrome can be distinguished.

These results do not confirm the hypothesis that genetic factors mainly determine the vulnerability for psychopathology and that environment codes for the specific symptoms (Tyrer, 1985). It is true that for the genetic contribution to patterns of problem behavior only two sets of genes were involved that affected the majority of problem behaviors. Thus, to a certain extent one could say that the various problem behaviors were merely different expressions of the same genetic liability. However, genes also seemed important for differentiation. The first indication involves the above mentioned differentiation between Aggressive and Anxious comorbid syndromes. A second indication is that Sleep Problems was not affected by common genetic factors at all. This result implied that Sleep Problems was genetically unrelated to all other syndromes. A final indication is that in addition to the two common sets of genes, most syndromes were also affected by genes that were specific for each syndrome. Thus, genetic factors did not merely determine a general vulnerability for psychopathology but were important for differentiation as well.

Our finding that shared environment may be represented by a single general factor replicates results from genetic studies of correlations between Wechsler Intelligence Scale for Children—Revised subscales (Casto, DeFries, & Fulker, 1995) as well as relationships among measures of cognitive ability, temperament, and scholastic achievement (Petrill & Thompson, 1993). Interestingly, it also seems to correspond with results found in a number of developmental behavior genetic studies of behavior problems and IQ showing that a single set of shared-environmental factors may be important for stability across time (Cardon, Fulker, DeFries, & Plomin, 1992; Cherny et al., 1994; Van den Oord & Rowe, 1997). This pattern of results seems to suggest that shared-environmental effects may be very pervasive and disrupt the child's functioning in many domains and at multiple time points.

In sharp contrast with shared-environmental effects, nonshared-environmental influences appeared to be specific in their effects. First, the effects of the common nonshared-environmental factors were relatively much less important than the effects of the unique nonshared-environmental factors. This result indicated that nonshared-environmental factors tend to cause pure syndromes instead of a clustering of syndromes. Second, the groupings that were caused by nonshared-environmental effects were relatively more refined. That is, the common shared-environmental factors affected all six syndromes, whereas the common nonshared-environmental factors affected only two or three syndromes.

### *Other Issues*

There were clear indications that our final multivariate genetic model accounted very well for the phenotypic correlations. First, the decomposition of the separate phenotypic correlations using simple formulas suggested that on average genetic factors contributed .155, shared environment .203, and nonshared environment .044. Our model suggested very similar contributions of .150, .206, and .046, respectively. Second, a chi-square difference test showed that our final model did not fit significantly poorer than the saturated model. These two points indicate that it was possible to explain the groupings of problem behavior using a very limited number of common genetic and environmental factors and support the validity of our conclusions with respect to the causes underlying patterns of problem behaviors. It is important to realize that it is not necessarily the case that a genetic model accounts so well for the phenotypic correlations. The reason is that besides a misspecification of the number of common factors, the mechanism underlying the groupings of problem behavior can be different as well (Caron & Rutter, 1991; Klein & Riso, 1995). For instance, instead of being different expressions of the same set of genes or environmental factors, one disorder could be the cause of the other disorder. Thus, sleep problems could be the result of anxiety instead of both disorders being indicators of the same underlying

disturbance. Such mechanisms imply a pattern of correlations between syndromes that are not necessarily consistent with patterns implied by a common factor model (Neale & Kendler, 1995). The fact that our model accounted so well for the phenotypic correlation therefore supported the validity of the assumed mechanism.

In contrast to the correlations between the syndromes, our model did not account very well for the genetic and environmental contributions to the phenotypic variances. The reason involves the different patterns of same-variable (that are relevant for the variances) and cross-variable twin correlations (that are relevant for the covariances). For the variances the difference between the MZ twin correlations and DZ twin correlations was large, and the DZ twin correlations were about half the MZ twin correlations. Assuming a model with additive genetic (A), shared-environmental effects (C), and nonshared-environmental effects (E), this result implies large genetic effects and no shared-environmental effects. For the phenotypic correlations, the difference between the MZ twin correlations and DZ twin correlations was much smaller, and the DZ twin correlations were generally larger than half the MZ twin correlations. Assuming an ACE model, this result implies relatively smaller genetic effects and larger shared-environmental effects. The estimates we obtained by using the multivariate model mainly reflected the results as indicated by the cross-variable twin correlations. The explanation seems to be that there are much more cross-variable twin correlations than same-variable twin correlations, so that the pattern of cross-variable twin correlations is more influential for obtaining parameter estimates.

Different patterns for same-variable and cross-variable twin correlations can be the result of sampling error. Another explanation is that for the variances an ACE model might be too restrictive. In this case, caution would be required to interpret our results with respect to the genetic and environmental contributions to the variances. An indication is that for some syndromes (particularly Overactive and Anxious), the ACE model implied negative estimates of the proportion of shared-environmental variance. Another indication involves the chi-square test, suggesting that the saturated model did not fit. Given the fact that the cross-variable twin correlations were consistent with an ACE model and that modeling the correlations with an ACE model did not yield a significantly poorer fit than the one obtained with the saturated model, the lack of fit seems to point to a failure of the ACE model to account for the pattern of same-variable twin correlations.

This latter explanation raises questions about possible factors that may have caused this failure. One possibility is contrast effects. Our univariate analyses did indeed show evidence for such effects (Van den Oord et al., 1996). Contrast effects may be caused by sibling interaction or parental rating bias. Sibling interaction involves true behavioral changes as a result of twins trying to accentuate existing differences or when the behavior of one twin evokes the opposing behavior in the other (Carey, 1986; Eaves, 1976). Contrast effects due to bias may result from a lack of an age-standardized view of "normal" behavior so that parents are inclined to compare and contrast the twins with each other (Simonoff et al., 1998). In addition, because it also seems possible that contrast effects mainly involve similar behaviors and are less important for correlations between different syndromes, it might explain the failure of the ACE model for the variances but not the covariances.

Because of the lack of a different type of rater, with our data it is not possible to distinguish empirically between sibling interaction and parental bias and to draw firm conclusions. However, a number of points are noteworthy. First, Simonoff et al. (1998) studied contrast effects in maternal and teacher reports of hyperactivity in adolescents. These authors argued that because teachers can compare the behavior of a child to many same-age peers rather than just the co-twin, contrast effects due to bias are less likely. Because they found contrast effects for maternal but not for teacher ratings, these authors favored the parental bias explanation. Second, the twins in our study were 3 years old. Although it seems reasonable to assume that age is irrelevant to the parental bias explanation, it is not clear whether this is true for sibling interaction as well. For instance, it could be argued that the desire to accentuate existing differences to strengthen individuality (Schacter, Shore, Feldman-Rotman, Marquis, & Campbell, 1976) is more likely to occur later in life. Third, the clearest evidence for contrast effects was found for Overactive and Anxious. Such a syndrome-specific pattern seems conformable with the parental-bias explanation predicting that contrast effects are stronger in syndromes where the definition and norms are less clear cut. It seems more difficult to imagine why sibling-contrast effects would result in such a syndrome-specific pattern.

To the extent that it does not affect the cross-variable twin correlations, another explanation for the different patterns for same-variable and cross-variable twin correlations could be parental zygosity bias. Zygosity bias consists of a tendency to overstate the similarity of MZ twins and understate the similarity of DZ twins. The plausibility of this explanation can be assessed by comparing twin correlations in correctly classified and misclassified twins. Goodman and Stevenson (1989) argued that MZ twins misclassified as DZ twins are more useful for this purpose than DZ twins misclassified as MZ twins. The reason is that DZ twin pairs differ from each other with respect to the proportion of relevant genes they share. So if the more similar DZ twin pairs have an increased risk of being misclassified as MZ, then twin correlations will be larger for misclassified DZ twins because of true genetic effects instead of zygosity bias. It may be important to add that caution may even be required to interpret differences between misclassified and correctly classified MZ twins as zygosity bias because there could be real nonshared-environmental effects that make MZ twins less alike and increase the chance of misclassification. In the present study, blood test results indicated that 43 MZ twins were, according to the parental response on the questionnaire, mistakenly thought of as DZ twins. The average same-variable/cross-variable twin correlation for the six syndromes were .56/.30 in the group of MZ twins misclassified as DZ. For the 137 MZ twins who were according to the blood test correctly classified as MZ twins, the average same-variable/cross-variable twin correlation were .72/.39. Although the twin correlations tended to be somewhat higher for the correctly classified MZ twins, the difference was not statistically significant. In addition, the same trend was present for same-variable and cross-variable twin correlations. Thus, even if we assume that zygosity bias caused this difference, it would still not explain why the ACE model failed for the variances and not the covariances.

Although there were substantial phenotypic correlations among the syndromes, it is important to realize that there were also substantial unique genetic and environmental effects that explained about half of the total variation of the syndromes. Because of the possibility of contrast effects for Overactive and Anxious, some caution is required to interpret the unique effects of these syndromes. Results, however, seemed to suggest that mainly the genetic and nonshared-environmental influences code for the specific disorders. The specific effects were particularly large for Sleep Problems and Withdrawn/Depressed, suggesting that these syndromes tended to be affected by somewhat more distinct etiological factors than the other syndromes.

The twins in our study were all 3 years of age, so the conclusions from this article are necessarily limited to the age range being studied. For instance, it could be that when children grow older, the genetic and shared-environmental effects will become more differentiated. Another issue is whether the children were too young to show many of the problem behaviors being studied. For instance, most early studies concerning the factor structure of standardized ratings for preschoolers have only reported syndromes comparable to the broad-band Internalizing and Externalizing dimensions (Behar & Stringfield, 1974; Kohn & Rosman, 1972; McGuire & Richman, 1986). However, there are now clear indications that further differentiation between preschoolers' behavior problems is possible. That is, through factor analyses, separate syndromes can be identified; these syndromes can be assessed reliably; and the different correlations with variables such as referral status, sex, and socioeconomic status support the discriminative validity of the syndromes (Achenbach, 1992; Achenbach et al., 1987; Koot et al., 1997). Furthermore, problem behavior in preschoolers appear to be a powerful predictor for later maladjustment where the stability coefficients tend to be higher for similar than for different syndromes (Campbell, 1994; Koot, 1993; Lavigne et al. 1998a, 1998b; Van der Valk, personal communication). These studies suggest that for syndromes found in older children, specific precursors that can be discriminated in preschoolers. Thus, although children in our study may be too young to obtain clinical diagnoses for the majority of problem behaviors being studied, just as in older children it seems possible to study liabilities for specific problem behaviors that are clinically meaningful.

### *Conclusions*

Findings such as that syndromes defined at the symptom level may share common etiological factors and that patterns of problem behavior may be informative of the underlying cause may be helpful for a better understanding and control of child psychiatric disorders. For instance, scientists are presently searching for genes underlying childhood disorders. Although this field is quite new, results already seem to suggest that genes found for one phenotype may be relevant for other phenotypes as well. So, the dopamine receptor 4 gene DRD4 may not only be important for novelty seeking (Benjamin, Patterson, Greenburg, Murphy, & Hamer, 1996; Ebstein et al., 1996) but also for hyperactivity/attention problems (LaHoste et al., 1996; Smalley et al., 1998; Swanson et al., 1998), and the dopamine transporter gene DAT1 may not only be important for hyperactivity/attention problems (Cook et al., 1995; Gill, Daly, Heron, Hawi, & Fitzgerald, 1997; Waldman et al., 1998) but also for Internalizing disorders (Rowe et al., 1998). It therefore seems reasonable to assume that once genes are found for one disorder, knowledge about the genetic–comorbid structure of behavior problems might be helpful to identify other disorders for which the gene could be relevant as well. Insight into the etiological structure underlying groupings of problem behaviors may not only be important for scientific reasons but also for clinical issues. An example is the above mentioned result that especially children who continue to experience adverse shared environments may be at risk for later maladjustment (Van den Oord & Rowe, 1997). The clinical implication is that for these children a wait-and-see policy may be inappropriate, and an active intervention could be required. Results from the present study suggest that an examination of patterns of problem behaviors may be helpful to make the crucial differential diagnosis.

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