The Genetic and Environmental Contributions to Children's Problem Behaviors:

A Developmental Approach

Jolande van der Valk

The study reported in this thesis was a combined project of the Department of Child and Adolescent Psychiatry, University Hospital Rotterdam-Sophia / Erasmus University Rotterdam, the Netherlands, and the Department of Biological Psychology, Vrije Universiteit Amsterdam, the Netherlands. The Sophia Foundation for Medical Research is gratefully acknowledged for funding this project, grant number 165.

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The Genetic and Environmental Contributions to Children's Problem Behaviors: A Developmental Approach

De Genetische Bijdrage en Omgevingsbijdrage aan Gedragsproblemen bij Kinderen: een Ontwikkelingsbenadering

PROEFSCHRIFT

ter verkrijging van de graad van doctor
aan de Erasmus Universiteit Rotterdam
op gezag van de Rector Magnificus

Prof.dr.ir. J.H. van Bemmel

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Paranimfen: Tony Kerklaan
Edith van der Valk

"I've such a short time to tell you so much,
words come second best to a kiss or a touch.
Far thicker than water this blood we all share,
so please never think that for you I don't care.
Fate may have driven us all separate ways,
but can't sever ancestry - splice DNA.
If life seems a road that's uneven and long,
to know where you're going,
just look who you came from."

'No Deposit, No Return' - Skyclad
lyrics written by Martin Walkyier

Being a Ph.D.-student, running a boarding stable, and training & showing young performance horses all at the same time requires excellent time management and does not leave much room for anything else.

I would like to dedicate this thesis to the ones who supported me the most:

Tony Kerklaan

Lisette van der Valk - De Jonghe

Cor van der Valk

Edith van derValk

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1

Studying the Development of Children's Problem Behaviors Using Quantitative Genetic Techniques

Van der Valk JC[1,2], *Verhulst FC*[1], *and Boomsma DI*[2]

This chapter is a slightly revised version of a publication in HM Koot, AAM Crijnen, & RF Ferdinand (Eds.), *Child psychiatric epidemiology: Accomplishments and future directions*, 1999, pp. 116-141. Assen: Van Gorcum.

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Problem behaviors in children: a general health problem worthy of investigation

The last three decades have shown problem behaviors in children to be quite prevalent. Of preschool children, Richman et al. (1975, 1982) using parental reports, identified 6-7% of 3-year-old children as moderately or severely disturbed. They found no significant differences between the sexes in overall scores, but the individual items showed boys to be significantly more likely to be overactive and girls to be more likely to be fearful. In middle childhood, Rutter et al. (1976) using parental interviews, diagnosed 12.7% boys versus 10.9% girls of 10-year-old children and 13.2% boys versus 12.5% girls of 14- and 15-year-old children to have a psychiatric disorder. Rutter concluded that although psychiatric conditions were probably a little commoner during adolescence than during middle childhood, the difference was not a large one. Verhulst and Koot (1992b), in a review of 38 studies (using different techniques, sample sizes, age ranges, assessment methods, informants and case definitions) calculated the median prevalence rate for general psychiatric dysfunction to be 13%. The majority of studies were consistent in their reports of sex differences with regard to types of disorders. Girls tended to show more internalizing or emotional problems, whereas boys were more inclined to show externalizing or disruptive behavior problems. The studies showed conflicting results as far as overall level of deviance was concerned.

Longitudinal studies have shown problem behaviors to be persistent. The Dunedin study (Caspi *et al.*, 1995, 1996) found that temperamental qualities observed by examiners at ages 3 and 5, predicted specific behavior problems rated by parents at ages 9, 11, 13 and 15 and even DSM-III-R diagnoses of adult psychiatric disorders at age 21. Undercontrolled 3-year-olds were more likely at 21 years of age to meet diagnostic criteria for antisocial personality disorder and to be involved in crime, while inhibited 3-year-olds were more likely at 21 years of age to meet diagnostic criteria for depression. The best predictor of good outcome was the absence of early behavior problems, indicating that high levels of problem behaviors at a young age were not just a normal developmental aspect. Hofstra et al. (in press) conducted a longitudinal follow-up of a Dutch general population sample. Of the 1615 4-16 year-olds

initially classified deviant, 41% still classified themselves as deviant 14 years later and 29% were still classified deviant according to their parents. Koot (1995) concluded in his review of longitudinal studies of general population and community samples that, across studies, one-third to one-half of children with initial deviant scores maintain deviant scores across 2- to 6-year intervals. Although most children showed fluctuations over time in their level of deviant behavior, extreme changes were rare.

Taken together, the demonstration that high levels of problem behaviors are not just a normal developmental aspect, the median prevalence rate for general psychiatric dysfunction of 13%, and the fact that children do not simply grow out of their behavior problems indicate that problem behaviors in children are a general health problem worthy of investigation.

Outline of this chapter

For purposes of prevention and treatment of problem behaviors in children, it is important to understand their etiology. During the last decade, quantitative genetic studies have begun to disentangle the genetic and environmental influences on the interindividual differences in problem behaviors during childhood, adolescence and young adulthood.

In this chapter, quantitative genetic techniques and studies exploring the development of children's problem behaviors will be presented. First, the continuous distribution that most problem behaviors are assumed to show is discussed. Second, three different designs for examining the role of genetic and environmental influences on problem behaviors, that is family, twin and adoption studies, and their underlying assumptions are introduced. Third, various effects that might be incorporated in the theoretical model, like sex limited gene expression, gene-environment interaction and correlation, longitudinal effects and multivariate modelling, are outlined. Fourth, three issues pertaining to the measurement of children's problem behaviors, namely developmental changes, rater bias and sibling interactions, are discussed. Fifth, studies exploring the genetic and environmental influences on children's problem behaviors are presented. Sixth, the need for longitudinal behavior genetic studies is addressed, followed by a description of the Dutch twin study of problem behaviors. This study examines the genetic and environmental influences on the development

of problem behaviors in children, by conducting a longitudinal follow-up of a large sample of twins. Finally, several research questions that are still in need of exploration are discussed.

Multiple genetic and environmental influences on continuously distributed problem behaviors

Most problem behaviors of children, such as aggression or anxiety, generally do not fall into distinct categories of behaviors that are either present or absent, but involve quantitative variations of behaviors that most children display to some degree.

These continuous variations in problem behaviors are hypothesized to be caused by multiple genes and environmental influences. The polymorphic genes (each possibly with a small effect) are assumed to combine to produce, together with various environmental influences, the observable differences among individuals in a population. In twin and other genetic epidemiologic studies, the influences of the genetic and environmental components are estimated in terms of the amount of variance they explain of this underlying continuous distribution.

Different quantitative genetic designs

Different genetically informative designs can be used to examine the contributions of genetic and environmental factors, the three basic designs being: family, twin and adoption studies. No design is ideal for every purpose. For each research question a certain genetically informative design is best suited to answer it.

Faraone and Santangelo (1992) summarized a sequence of questions which tend to follow in a logical progression when doing genetic epidemiologic research. The first reasonable question to be asked is whether a disorder is familial, in other words: "Does it run in families?". Family studies are best suited to answer this question and detect familial transmission. The next logical question is: "What is the relative magnitude of genetic and environmental contributions to disease etiology and expression?". Twin and adoption studies are quite appropriate for this kind of research. Twin studies give direct and powerful tests of

genetic and environmental effects and adoption studies are excellent for the detection of cultural effects. The third question in the sequence is: "How is the disease transmitted from generation to generation?". Segregation analyses, employing family data (pedigrees) can be used to study this issue. The fourth question in the sequence is: "If genes mediate this transmission, where are they located?". To be able to search for disease genes on the human genome, chromosomal material (DNA) has to be collected from the subjects that are to be studied. Linkage analysis requires DNA from the members of a family, for instance from sib pairs, to be able to assess the co-inheritance of a disease with a marker. Association studies test whether a particular allele is associated with a disease and therefore do not require information on family members, obtaining sufficient data from, for example, samples of unrelated patients and controls (if issues of population stratification can be assumed to be not important). The last logical question when doing genetic epidemiologic research is: "What are the genetic and environmental mechanisms of disease?". In other words what kind of function does the gene have and are there any kinds of environmental influences that have some effect on the gene's (in)activation? To answer this question, the identity of the gene has to be known so its biochemical activities can be studied, possibly in interaction with various environmental influences.

The three basic genetically informative designs: family, twin and adoption studies and their underlying assumptions will be explained next. Because the most often used design is the twin study, some assumptions (like assortative mating) are described under that subheading even though they are also of importance for the other designs.

Family studies

Family studies are useful to answer the first question to be asked: whether or not there is familial resemblance for the behaviors being investigated. The idea behind the family study is that if a behavior has a genetic etiology, then the relatives of probands (individuals displaying the behavior) should have greater risk for demonstrating the behavior than the relatives of controls (individuals not showing the behavior). Also, the chance that relatives of probands display the behavior should be correlated with the degree of relationship the relative has to the proband. The risk should be greater for first-degree relatives (parents, siblings, children),

who share on average 50% of their genetic material with the proband, than for second-degree relatives (grandparents, half-siblings, nephews, etc.), who share on average 25% of their genes with the proband. Thus, a genetic hypothesis predicts that the risk for relatives of probands is higher than the risk for relatives of controls, and that the risk for relatives of probands increases as the amount of genes shared increases (Faraone & Tsuang, 1995). Familiality has been found for family studies of depression, attention deficit / hyperactivity disorder, antisocial behavior, alcohol and drug problems, schizophrenia and autism, among others (Rutter *et al.*, 1999b). However, results of family studies can only provide initial hints that a behavior might have a genetic etiology. The conclusion that the familial resemblance is caused by genes can not be made, because problem behaviors can also 'run in families' for nongenetic reasons such as shared environmental adversity, viral transmission, and social learning (Faraone & Tsuang, 1995). Twin or adoption studies are necessary to examine the relative magnitude of genetic and environmental contributions to the etiology and expression of the problem behaviors.

Twin studies

The second question in the chain of genetic epidemiologic research: "What is the relative magnitude of genetic and environmental contributions to the etiology and expression of behavior problems?" can be studied using twin or adoption studies. In twin studies, monozygotic twins, who are genetically identical and thus share 100% of all their genes, are compared with dizygotic twins, who share on average 50% of their segregating genes. Because both types of twins usually grow up in the same family, they are assumed to share on average the same kind of familial environment. A certain behavior is influenced by genes if monozygotic twins resemble each other to a greater extent than dizygotic twins, because the only difference between the two groups is in genetic relatedness. By comparing the correlation of problem behaviors between monozygotic twins with the correlation of problem behaviors between dizygotic twins, the magnitude of genetic and environmental influences can be estimated. Two kinds of environmental influences can be distinguished: shared environmental influences and nonshared environmental influences. Shared environmental influences denote life experiences affecting twins growing up in the same family similarly,

for instance socioeconomic level, religion, or style of parenting. Nonshared environmental influences denote the impact of all environmental factors influencing only one of the subjects being studied, such as an illness, disease, trauma, experiences at school, relationships with peers or the way one perceives the world.

For each problem behavior under investigation, the following situations can apply:

1. Only nonshared environmental influences are of importance. In this case, the correlation of problem behaviors between monozygotic twin pairs and the correlation of problem behaviors between dizygotic twin pairs are both zero, because the twins neither share genetic nor environmental influences. (For sake of brevity, the correlation of problem behaviors between monozygotic (dizygotic) twin pairs is often called the correlation between monozygotic (dizygotic) twins).

2. In addition to the nonshared environmental influences, genetic effects are also of importance. Monozygotic twins, who have a genetic relatedness of 100%, are now expected to show a correlation that is twice as large as the correlation between the dizygotic twins, who share on average 50% of their genetic inheritance.

3. Shared environmental influences and nonshared environmental influences are of importance, but there are no genetic effects. In this case the correlation between monozygotic twins will be bigger than zero and equal to the correlation between the dizygotic twins. Because genetic effects are absent, the correlation between monozygotic twins is not expected to be larger than the correlation between dizygotic twins. Individuals only resemble each other because of environmental influences, which monozygotic and dizygotic twins share to the same extent.

4. All three influences are of importance to explain the variances between individuals in a population. In this situation the correlation between monozygotic twins will be bigger than the correlation between dizygotic twins but less than twice its size, because in addition to genetic influences shared environmental influences also cause twins to resemble each other.

5. Genetic effects do not sum up (additive genetic effects) but interact with each other at the same locus (genetic dominance) or at different loci (epistatic influences). In this case the correlation between monozygotic twins, who have an identical genetic make-up, will be much larger than twice the correlation between dizygotic twins, because dizygotic twins do

not share identical genes at the same loci.

To estimate the magnitude of the genetic and environmental influences, a theoretical model incorporating these possible correlational effects is fitted to the observed data which are summarized in variance-covariance matrices. The model describes the observed data to a satisfactory extent if the theoretical model can not be statistically rejected. Of course, the collected sample size should be large enough to enable rejection. A small sample size may result in a model being accepted that actually has a poor fit to the observed data (Marsh *et al.*, 1988). The magnitude of the genetic and environmental influences are estimated in this theoretical model, regardless of the modes of action or the number of genes or environmental factors involved. Confidence intervals of the estimated influences can be obtained as a guide to their significance and precision, and goodness-of-fit tests show if the model is indeed consistent with the observed data within the limits of precision imposed by the sampling variation (Eaves, 1982).

Assumptions when studying twins

When twins are used to study the etiology of problem behaviors in children, at least three assumptions are made which must be fulfilled in order to obtain valid results.

First, as explained above, quantitative genetic techniques assume that monozygotic and dizygotic twins experience on average the same shared environmental influences, the so-called equal environments assumption. The fulfilment of this assumption is crucial because, if the equal environments assumption is incorrect, excess resemblance of monozygotic twins compared with dizygotic twins ascribed to genetic factors could be partly or entirely due to environmental effects. The equal environments assumption has lead to at least two different concerns. One concern has been that parents are more likely to treat monozygotic twin pairs more similarly than dizygotic twin pairs because of their knowledge that they are identical. Kendler (1993a) summarized five different ways in which the equal environments assumption can be tested, among others the effects on reported twin resemblance when parents are either correctly informed or misinformed about their twins' true zygosity. He concludes that available empirical evidence suggests that the assumption is probably at least approximately correct for the psychiatric disorders he studied, which included major

depression, generalized anxiety disorder, phobia, and alcoholism in adult females. Another concern has been that parents and others are more likely to treat monozygotic twins, who look alike, more similarly than dizygotic twins. Fitting a structural equation model to examine the impact of physical similarity on phenotypic resemblance, Hettema et al. (1995) concluded that for the disorders mentioned by Kendler (1993a), the equal environments assumption is supported. People do not seem to treat children who look alike more similarly than children who show less physical similarity.

The second assumption made when studying twins is that the level of problem behaviors reported for twins are comparable to those of singletons. The validity of this assumption is necessary in order to generalize the results of twin studies to singleton populations. Studies comparing twin and general population samples found few differences between the two groups. Van den Oord et al. (1995) compared preschool twins and singletons and concluded that the general level of problem behaviors in twins was broadly comparable to that in singletons. Gjone and Növik (1995) examined the impact of pre- and perinatal factors on parental reports of behavior problems and found that birth weight and birth order did not contribute significantly to differences between twins and a general population sample. When differences between twins and singletons were found, twins tended to have somewhat higher levels of externalizing behaviors than children from the general population (Gau *et al.*, 1992; Simonoff, 1992). A possible reason for this result is sibling effects (Carey, 1986). Twins, always from a sibship of size 2, might show sibling interactions (imitation or cooperation) that are absent in singleton populations if the subjects grow up without siblings. Sibling interactions may also have caused the increased variance found for twins' externalizing behaviors by Gjone and Növik (1995). Nevertheless, differences found between twin and singleton populations were usually small.

The third assumption in classical twin designs (as in other designs) is that there has been no assortative mating between the (twins') parents. Assortative mating denotes the nonrandom selection of a mate on basis of either similarities or differences between the spouses. For instance, spouses can select each other on the ground of similar psychiatric disorders, or on the basis of cross-assortment between disorders: alcoholism in husbands with depression in wives. Effects of assortative mating may be confounded with shared

environmental factors (Neale & Cardon, 1992) because both assortative mating and shared environmental influences act to increase the variance and covariance between monozygotic and dizygotic twins equally. Therefore, without adjustment for significant levels of assortment, estimates of genetic influences on the liability of a certain trait will be biased downwards. Still, if effects of assortative mating exist, they will probably not be large because when spousal correlations are found they are mostly small, in the region of 0.1 to 0.3 (Simonoff *et al.*, 1994). Meas et al. (1998) tested directly whether a significant association could be found for psychiatric diagnoses (alcoholism, generalized anxiety disorder, major depressive disorder, panic disorder and phobias) between husbands and wives in two population-based samples. They found significant but moderate assortment for psychiatric disorders and concluded that the bias in twin studies that have ignored the small amount of assortment is negligible.

Adoption studies

The advantage of adoption studies is that genetic and shared environmental influences are separated. Adoption studies can correlate traits measured in subjects from within the family or outside the family. Within the family, adopted children can either be compared with their nonadopted siblings or with their adoptive parents. With both family relations they only share the same environmental influences, because the adoptees have no genes in common with their adoptive parents. Thus, if the adoptees' behavior is correlated with the behavior of either their adoptive parents or their nonadopted siblings, only the shared environmental influences can be responsible for the phenotypic resemblance. Outside the family, adopted children can be compared with their biological parents or their biological siblings, with whom they share on average 50% of their genetic make-up. Because the adopted children and their biological parents or biological siblings do not share the same environment, similarities between adoptees and their biological parents or biological siblings must be effected by genetic influences.

A number of factors might cause the genetic and environmental influences in adoption studies to be not completely dissociated, thereby distorting the results. First, selective placement can cause the biological and adoptive parents to be correlated for the studied

behavior or for characteristics which may affect the studied behavior. Second, the more the adoptive parents know regarding the biological parents, the more they could be biased in their expectations of and behavior towards their adopted children. Adopted children might also differ from nonadopted, biological children. First, the 'status of being adopted' could be an adversity which predisposes to problem behaviors. Second, biological parents who give up their child for adoption might differ from the general population and adoptive parents may also form a non-random sample from the population.

In a special kind of adoption study, using siblings that are both adopted as subjects, one can correct for the possible distortion of results by differences between adopted and biological children because in this case all subjects are adopted. Also, possible correlations between genotype and environment, that might occur when studying parents and their biological children, can not distort the results. Prerequisite is that large enough samples of adopted siblings can be collected. Van den Oord et al. (1994) compared two groups of adopted siblings: a group of siblings who were biologically related and both adopted into the same home, with another group of siblings who were not biologically related but also adopted into the same family. Biologically related adoptees shared on average 50% of their segregating genes (assuming they were full siblings), while nonbiologically related adoptees had no genetic resemblance. The adoptees shared the same environmental influences because both groups grew up in the same adopted family. Therefore, the correlations between the biologically related siblings can be compared with the correlations between the nonbiologically related siblings, the same way as the correlations of monozygotic and dizygotic twins can be compared. If the biologically related adoptees resemble each other to the same degree as the nonbiologically related adoptees do, only environmental factors are of importance in explaining sibling resemblance. However, when the biologically related adoptees resemble each other more than the nonbiologically related adoptees do, genetic factors are of importance, since the only difference between the two groups is in their genetic relatedness. In contrast to twin studies, genetic dominance or epistasis cannot be detected, because biologically related adoptees do not share identical genes at the same loci as monozygotic twins do. Later in this chapter we will present some of the longitudinal results found using this adoption design (Van der Valk *et al.*, 1998a).

Various effects that might be incorporated in the theoretical model

Depending on the elaborateness of the collected data and the inspiration of the investigator all kinds of genetic models can be tested. For instance, the genetic model can be extended to test not only for genetic and environmental influences, but also for effects of sex differences, gene - environment correlation or interaction, longitudinal effects or incorporating multiple variables simultaneously.

Sex-limited gene expression

When data are available from opposite-sex twin pairs (boy-girl pairs), it is interesting to test whether different genes are expressed in males and females. Two basic types of sex-limited gene expression can be distinguished (Neale & Cardon, 1992). One is called scalar sex limitation and points to those situations when the same genes affect both males and females, but their effects differ by some constant multiple over all the genes involved. The other is called non-scalar sex-limitation and concerns those cases when the genetic effects are not just a constant multiple of their effects in the other sex. In this case, different genes control the expression in the two sexes, like for instance in chest-girth. Correlations of dizygotic opposite-sex twins (boy-girl pairs) in comparison with correlations of same-sex twins (boy-boy or girl-girl pairs) indicate if similar genes are active in both sexes. For if one gender has different genetic influences than the other, correlations between opposite-sex dizygotic twin pairs are expected to be either higher or lower than the correlations between same-sex twin pairs. Several studies have found differences in observed behaviors for boys and girls (girls tend to show more internalizing or emotional problems, and boys display more externalizing or disruptive behavior problems) making the inclusion of sex-limited gene expression in the model sensible.

Genotype-environment interaction and correlation

Problem behaviors are thought to develop as a result of interactions between genetic vulnerability and environmental risk factors. Genes might increase the risk for certain problem behaviors by making individuals more sensitive to environmental risk factors

(genotype-environment interaction), or by making individuals more likely to select high-risk environments (genotype-environment correlation). Genotype-environmental interaction refers to the sensitivity of genes to differences in the environment. It relates to the way genes and environment ultimately affect the phenotype (Neale & Cardon, 1992). As an example of genotype-environment interaction one can consider an environment which is changed by introducing a pathogen. This will have a different impact on susceptible individuals than on resistant ones. Resistant individuals will be free of the disease even in a pathogenic environment. Genetically susceptible individuals however will be free of disease only as long as the environment does not contain the pathogen but they will get sick when the pathogen is introduced. For gene-environmental interactions to be studied specific hypothesis must be proposed, discriminating measures of the environmental risk factors must be made, appropriate samples must be used and statistical techniques must be employed that are well adapted to detect and test the postulated variety of genetic sensitivity (Kendler & Eaves, 1986). Both twin and adoption studies can be used to study possible gene-environment interactions. Essential is that the genetic risk can be measured directly, so molecular genetic findings with strong effects will help tremendously (Plomin & Rutter, 1998). Genotype-environmental correlation reflects a non-random distribution of environments among different phenotypes (Neale & Cardon, 1992). It can either be passive (for instance, parents who pass on their genes to their children are the same parents who provide their rearing experiences) or active / evocative (for example, children actively select their environments based on their genetic make-up and other people (parents) evocatively react on the behavior shown by the child). As Rose (1995, p.648) has stated, "We inherit dispositions, not destinies. Life outcomes are consequences of lifetimes of behavior choices. The choices are guided by our dispositional tendencies, and the tendencies find expression within environmental opportunities that we actively create." Both twin and adoption studies provide ways of studying possible gene-environment correlations. To examine the effects of gene-environment correlations it is essential to differentiate parental effects on children from children's effects on parents. In order to do this, genes and environmental factors must be identified and their mutual behaving must be determined (Rutter *et al.*, 1999a). Again, molecular genetic findings with strong effects will probably be of tremendous help.

Longitudinal genetic models

When data have been collected on different assessment points, the genetic and environmental influences can be estimated at each time interval separately. However, using a longitudinal model one can also estimate how genes and environmental influences operate throughout development. For example, is an increase in heritability due to new, additional, genetic factors being expressed as children grow older, or is there an amplification of existing genetic influences? Such a longitudinal model can address the question to what extent the stability of showing a certain problem behavior is due to the same genes being expressed at different ages and to what extent the stability is due to the same environmental influences being of importance. Contrary to popular points of view, genetically determined characters need not be stable, nor are longitudinally stable characters always influenced by heredity (Molenaar *et al.*, 1991).

Multivariate genetic models

Another important class of models are multivariate genetic models. Like ordinary factor analyses, multivariate models make a distinction between a (genetic or environmental) factor that influences only one, specific behavior problem, called a unique factor, and a (genetic or environmental) factor that influences all the different behavior problems, called a common factor (Martin & Eaves, 1977; Boomsma & Molenaar, 1986). The common genetic and environmental factors explain the covariances between the problem behaviors, while the unique genetic and environmental factors explain the remainder of the variance that is not shared by the different problem behaviors. In this way, multivariate models can construct a picture of the causes of the relationships between the several problem behaviors. The multivariate approach is more powerful than the univariate approach, but its unambiguous interpretation often requires that univariate results are already known.

Issues of concern when measuring problem behaviors during development

To study the etiology of problem behaviors during development, children have to be followed over time. In order to tap developmental changes in the level and type of children's

problem behaviors, assessment instruments should be sensitive to these variations. The instruments should also allow different responders, like parents, parent surrogates or teachers, to report on the child's behavior, because young children are unable to reflect on their own behaviors.

The Child Behavior Checklist (CBCL)

The Child Behavior Checklist (CBCL) developed by Achenbach (1991a, 1992) is a standardized questionnaire for parents to report on the frequency of problem behaviors shown by the child. Responders rate each behavior on a three-point scale: zero when the child never exhibits the behavior, one if the child sometimes shows the behavior and two when the behavior is frequently seen. Depending on the age of the child either the CBCL for 2- and 3-year-old children (CBCL2/3; Achenbach, 1992) or the CBCL for 4- to 18-year-old children (CBCL/4-18; Achenbach, 1991a) can be filled out. The 118 behaviors of the CBCL/4-18 have been summarized into eight empirically validated syndrome scales. The eight syndrome scales were named: Withdrawn, Somatic Complaints, Anxious/Depressed, Social Problems, Thought Problems, Attention Problems, Delinquent Behavior, and Aggressive Behavior. The first three syndrome scales can be summed to form a broad-band grouping, called Internalizing. The last two syndrome scales can be summed to form a broad-band grouping called Externalizing. A Total Problem score is derived by summing all the individual item scores. The psychometric stability of the CBCL/4-18 is well established (Achenbach, 1991a) and replicated for a Dutch clinical sample (De Groot *et al.*, 1994).

The CBCL/2-3 (Achenbach, 1992) was modelled after the CBCL/4-18 and measures similar syndrome scales. Several scales of the CBCL/2-3 are fairly comparable to scales of the CBCL/4-18. However, their precise content differs in accord with the age differences and findings on the covariation among items from the different instruments (Achenbach, 1992). The CBCL/2-3 scales that have the clearest counterparts on the CBCL/4-18 are: Anxious/Depressed, Withdrawn, Somatic Problems, Aggressive Behavior, Internalizing, Externalizing, and Total Problem score. The American factor solution for the CBCL/2-3 is not replicated for Dutch samples, so for the CBCL/2-3 Dutch syndrome scales are developed (Koot *et al.*, 1997). Koot showed that the Dutch syndrome scales are comparable to those

developed by Achenbach. The broad-band grouping Internalizing is composed of the syndrome scales Anxious and Withdrawn/Depressed, while the broad-band grouping Externalizing consists of the syndrome scales Aggressive, Oppositional and Overactive.

Using the CBCL, the child's problem behaviors can be rated at different assessment points during development and can be compared with norm groups of similar age and sex. By comparing the child's score with the scores obtained from a norm sample, one can determine whether the child shows significantly more problems than children of a similar age.

Rater bias

Especially for children up to age 12, parents (or other kinds of informants) are needed to report on possible problem behaviors shown by the child. However, informants might have their own rater biases (Van der Ende, 1999). For example, some might judge behaviors more severely than others and the child might show different problem behaviors depending on the kind of relationship it has with the informant. Disentangling the child's phenotype from that of the rater becomes and important methodological problem when relying on ratings of the child by an observer. Using a rater bias model, the variance in the parental ratings can be partitioned into their components due to reliable trait variance, due to parental bias, and due to unreliability or error in the particular rating of a particular child. The reliable trait variance can then be decomposed into its components due to genetic influences, shared environmental influences, and nonshared environmental influences (Neale & Cardon, 1992). Rater bias models can only be fitted when data from more than one kind of informant, for instance from both parents, are available.

Sibling interactions

Sibling interactions are a special type of gene - environment correlation, referring to the fact that children might influence each other to either express or suppress certain behaviors. For example, aggressive behaviors in one twin might evoke the same kind of behaviors in the other twin. Especially when studying twins (who are of similar age) the effects of sibling interactions, when not taken along in the analyses, might bias the obtained genetic and environmental estimates (Eaves, 1976; Hewitt *et al.*, 1992).

Sibling interactions might either involve cooperation (imitation) effects, when the behavior of one twin tends to evoke the same kind of behavior in the other twin, or the interactions may produce competition (contrast) effects, when a certain behavior of one twin causes the opposite behavior in the other twin. Effects of sibling interactions depend on the degree of biological relationship between the socially interacting siblings. Monozygotic twins are reared with a cotwin of identical genotype. If there are cooperation (imitation) effects, the total variance of monozygotic twins is expected to be greater than that of dizygotic twins (which in turn would exceed that of singletons) (Eaves, 1976). Apart from the effects in variances, both the correlations between monozygotic and between dizygotic twins will be inflated in case of cooperation effects, thereby mimicking the effects of shared environment. Competition (contrast) effects are expected to make the total variance of monozygotic twins smaller than that of dizygotic twins (which again would be smaller than that of singletons). In twin data competition effects can also reduce the correlation between the dizygotic twins to very low values, thereby inflating the estimates of (non-additive) genetic variance.

Of course, the process of having informants report on the behavior of the children might also implicitly lead to "sibling" effects, for informants may unconsciously compare one twin with the other in rating the children. In order to get less biased estimates, the effects of sibling interactions and of rater biases need to be incorporated in the theoretical model that is to be fitted to the observed data.

Studies exploring the etiology of children's problem behaviors using the CBCL

Twin studies

To obtain sufficient statistical power to fit a theoretical model to the observed data that incorporates not only genetic and environmental influences on variations in problem behaviors, but also the effects of rater biases and sibling interactions, large samples of related individuals are needed. For this reason, twin registries in various countries have, during the last two decades, started to enlist large samples of twins and their parents for participation in their studies.

Table 1.1 *Quantitative genetic studies of behavior problems during childhood, using the Child Behavior Checklist Internalizing and Externalizing Problems (Achenbach, 1991, 1992)*

Twin Registry / Project	Author	Instrument	Responder	N (pairs)		Age (years)	Sex differ.?	Genetic Influences		Shared envi. Influences	
				MZ	DZ			Exter	Inter	Exter	Inter
Western Reserve Twin Project	Edelbrock, et al. (1995)	CBCL/4_18	mother (91.5)	99	82	7-15	--	.51	.50	.28	.25
Oregon Twin Project	Leve, et al. (1998)	CBCL/4_18 (among others)	mother	77	77	6-11	--	.44	.56	.41	--
Colorado Twin Registry	Schmitz, et al. (1995)	CBCL/2_3 CBCL/4_18 longitudinal	mother	77 66 30	183 137 65	2.8 7.6	-- --	.34 .57	.17 .37	.32 .22	.45 .26
								early childhood mostly shared environment, middle childhood mostly genetic influences.			
	Zahn-Waxler, et al. (1996)	CBCL/4_18 (among others)	mother father (teacher and observations)	184 139		5	No (with CBR: yes)	.57 .48	.56 --	.30 .35	-- .57
Norway Twin Registry	Gjone, et al. (1996)	CBCL/4_18	pooled together: mother (77.3) father (6.6) joint (16.1)	526	389	5-15	No	.52	.33	.38	.41
								logtransformed variables showed no changes in heritability with increasing level of severity of problem behaviors.			
	Gjone, et al. (1997)	CBCL/4_18	pooled together: mother (77.3) father (6.6) joint (16.1)	526	389	5- 9 12-15	No	genetic factors were most influential for separate Externalizing and Internalizing, shared environmental factors explained most of the variance for comorbid conditions.			
Virginia Twin Registry	Silberg, et al. (1994)	CBCL/4_18	mother	515	749	8-11 boys 8-11 girls 12-16	Yes (only for: External. young group)	.38 .13 .24	.23	.46 .62 .57	.36
	Eaves, et al. (1997) Hewitt, et al. (1997)	questionnaires and interviews	mother father	689	666	8-16	No	all measures of Internalizing and Externalizing Problems showed moderate genetic effects.			
Netherlands Twin Registry	van den Oord, et al. (1996)	CBCL/2_3	average rating of mother father	446	912	3	No	.60	.77	.20	--
	van der Valk, et al. (1998)	CBCL/2_3	mother	1328	2292	3 boys 3 girls	Yes (only for: External.)	.50 .74	.68	.22 --	--

N.B. MZ = monozygotic twins, DZ = dizygotic twins, differ.? = differences, Shared envi. = shared environmental influences, Exter = Externalizing Problems, Inter = Internalizing Problems.
Nonshared environmental influences= 1 - genetic influences - shared environmental influences.

With the help of these registries a large number of twin and adoption studies of behavioral disorders have been conducted. In this chapter, for sake of comparability, we only consider behavioral genetic studies of children and adolescents using the CBCL (see Table 1.1: Internalizing and Externalizing Problems). Zahn-Waxler et al. (1996) collected mother, father and teacher ratings on 5-year-old twin pairs from Colorado. Their largest sample of informants (although still relatively small) were mothers who rated the twins (184 pairs) on the CBCL. For these ratings they found significant genetic influences, explaining more than half of the variance for Internalizing, Externalizing and Attention/Activity problems. An effect of shared environmental influences was found only for Externalizing Problems. Edelbrock et al. (1995) collected mostly mother ratings on the CBCL for a (also relatively small) sample of 181 pairs of same-sex twins, aged 7-15 years, of the Western Reserve Twin Project. They found significant genetic influences for all areas of problem behaviors. Shared environmental influence was detected for Anxiety/Depression and Delinquent behavior, but was negligible for most other areas of problem behaviors. Leve et al. (1998) collected mother ratings on the CBCL (and observational data) on 154 twin pairs, aged 6-11 years. Their results indicated that genetic variation accounted for the majority of the variance in child reported maladaptive behaviors (average = 62%). Silberg et al. (1994) collected mother ratings on the CBCL on 1264 twin pairs, aged 8-16 years, residing in the state of Virginia. They found that genetic, shared, and nonshared environmental factors all played a significant role in explaining individual differences in maternal ratings of Externalizing and Internalizing behaviors in boys and girls. The shared environmental factor had the largest influence, accounting for 36% of the variance of the Internalizing scale and around 57% of the variance of the Externalizing scale. Externalizing behaviors showed a sex difference for 8- to 11-year-olds, but not for 12- to 16-year-olds. The data for boys showed larger genetic influences, while the data for girls showed larger environmental influences. For Internalizing behaviors neither a sex difference nor an age effect was found.

Van den Oord et al. (1996) collected mother and father ratings on the CBCL on 1358 3-year-old twin pairs from the Netherlands Twin Registry (NTR). They found that genetic influences accounted on average for about 64% of the variance of various problem behaviors. Shared environmental influences were smaller than nonshared environmental influences,

accounting for 9% and 27% of the variance, respectively. Genetic influences for Internalizing Problems were somewhat larger than for Externalizing Problems. For most problem behaviors no sex differences were found at this young age. Van der Valk et al. (1998b) used the same 1358 twin pairs, enlarged with an additional sample from the NTR of 2658 twin pairs, giving a total same of 4016 3-year-old twin pairs. For 3620 twin pairs complete CBCL's were filled out by the mothers. Using this larger sample of twin pairs, which provided a higher statistical power to detect influences of small size, evidence for sex differences and for sibling interactions was found. These effects were only detected for Externalizing Problems and not for Internalizing Problems. One twin's behavior stimulated the expression of the same behavior in the other twin. Since only maternal ratings were analysed, these cooperation (imitation) effects might also have been caused by informants unconsciously comparing one twin's behavior with the behavior of the other twin. For boys, genetic factors explained 50% of the variance of Externalizing Problems, while shared environmental factors explained 22% of the variance. For girls, genetic factors explained 74% of the variance and no shared environmental influences were found. The correlations of same-sex (boy-boy or girl-girl pairs) and the correlations of opposite-sex dizygotic twin pairs (boy-girl pairs) were quite similar, indicating that the same genes seemed to be responsible for the genetic influence in both sexes. In the same sample, no sex differences or sibling interactions were found for Internalizing Problems. Genetic and nonshared environmental factors accounted for all of the variance, genetic factors explaining 68%. For both Internalizing and Externalizing Problems, nonshared environmental factors explained 25 to 32% of the variance.

The Virginia Twin Study (Hewitt *et al.*, 1997; Eaves *et al.*, 1997) did not employ the CBCL but used various other instruments and interviews to assess behavioral development and psychopathology. We still mention this study because it collected a population-based, unselected sample of 1412 twin pairs. Most twin studies use twins who are part of a twin registry, but this study ascertained twins through Virginia schools. Using a sequential cohort design, twins from 8 through 16 years of age and their parents, were followed longitudinally. The first wave of data showed that across informants, questionnaire scales provided as good a prediction of symptoms as clinical interviews did. All the measures of Internalizing and

Externalizing behavior showed moderate genetic effects. No sex differences in genetic or environmental factors were seen, which (as noted by the authors) could have been caused by their relatively low power to detect sex-limited gene expression for moderately heritable traits. Attention Deficit Hyperactivity Disorder showed, apart from genetic influences, also contrast effects. However, having only parents and the twins themselves to rate the behaviors, it was not possible to determine whether these effects reflected social interaction between the twins themselves or whether they were artifacts of asking parents to rate their children. Simonoff et al. (1998), using ratings from mothers and teachers for 1644 twin pairs in the Virginia Twin Study, concluded that the contrast effects found for maternal hyperactivity ratings were a form of rater bias and did not reflect social interaction between the twins themselves.

Gjone et al. (1996) conducted a cross-sectional twin study in Norway, using five birth cohorts (aged 5-6, 8-9, 12-13, 13-14, and 14-15 years) giving a total of 915 twin pairs. For most twins, the mother's ratings on the CBCL were collected. Results indicated significant heritability for Internalizing and Externalizing Problems. Logtransformed variables showed no changes in heritability with increasing level of severity of problem behaviors. Using the same sample, Gjone and Stevenson (1997a) found that genetic factors were most influential for separate Internalizing and Externalizing behaviors, while shared environmental factors were more influential for comorbid conditions, meaning for disorders which co-occur. Silberg et al. (1996) studied the genetic and environmental influences on the covariation between hyperactivity and conduct disturbance, rated with the Rutter Parent 'A' scale (Rutter *et al.*, 1970). Using the same sample of twin pairs from Virginia, they found that for the 557 younger twin pairs (8-11 years) the covariation could be attributed to a common set of genetic influences, whereas for the 640 older twin pairs (12-16 years) a different set of genes contributed to the two behaviors independently. O'Connor et al. (1998a) used a national sample of 720 same-sex adolescent siblings between 10 and 18 years of age, consisting of monozygotic and dizygotic twins, and full, half and unrelated siblings. They employed different observational measures and adolescent and parent reports, one of them being the Behavior Problem Index (Zill, 1985), a 32 item questionnaire adopted from the CBCL and another the Child Depression Inventory (Kovacs, 1981). Using composite scores, results

showed that 45% of the observed correlation between depressive and antisocial symptoms could be explained by a common genetic liability. In their conclusions, the authors make a plea for research using longitudinal methods to examine genetic influences on change and stability of depressive and antisocial symptoms. Longitudinal studies may possibly provide evidence for genetic risks for co-occurring dimensions of psychopathology.

We know of only three twin studies which have examined the etiology of problem behaviors longitudinally. O'Conner et al. (1998b) approached the same adolescent siblings again three years later and collected longitudinal data on 405 families. The central findings were that genetic influences explained 54% of the stability of antisocial symptoms and 64% of the stability of depressive symptoms. Half of the phenotypic correlation between wave 1 antisocial symptoms and wave 2 depressive symptoms were mediated by genetic influences. The second longitudinal twin study is a two year follow-up of 759 Norwegian same-sex twin pairs, aged 7 through 17 (Gjone & Stevenson, 1997b). CBCL ratings were collected from one of the parents, preferably the mother. Results showed temperament, particularly negative emotionality, to be an important factor in the development of behavior problems. The third is a study of Schmitz et al. (1995). For a small longitudinal sample of 95 twin pairs from Colorado, measured at the age of 2 years and 10 months and followed-up at the age of 7 years and 7 months, they collected (mostly) mother ratings on the CBCL. Results suggested that shared environmental influences were more important in early childhood than in middle childhood, while the reverse held for genetic influences. However, as also pointed out by the authors themselves, these results need to be replicated by larger samples of genetically informative data.

The Dutch twin study of problem behaviors (described later in this chapter) is currently collecting longitudinal CBCL data on a large sample of young twins (4016 3-year-old twin pairs and 1926 7-year-old twin pairs). The contributions of genetic and environmental factors to the covariation of behavior across time will be examined using this sample.

A longitudinal adoption study

In a sample of adolescents who were all adopted before their second birthday, we collected longitudinal data (Van der Valk *et al.*, 1998a). These siblings were either biologically related

and adopted into the same family (111 pairs) or nonbiologically related but also adopted into the same family (221 pairs).

The adoptees were first assessed at 10 to 15 years of age (95.9% of the sample was between 11-14 years) (Van den Oord *et al.*, 1994) and followed up three years later. At the second assessment, usable CBCL/4-18 questionnaires were obtained from 75 biologically related and 154 nonbiologically related pairs. The longitudinal correlations, which were mostly around .60, pointed to a considerable stability of the problem behaviors during the three-year interval. At both assessments, most of the variance for Externalizing Problems and Aggressive Behavior was explained by genetic factors, while nonshared environmental factors were most important for Internalizing Problems, Thought Problems and Delinquent Behavior. Structural equation models showed that the stability of Externalizing Problems over time was caused mostly by genetic factors. The stability of Internalizing Problems was caused mostly by nonshared environmental factors, suggesting that idiosyncratic experiences were largely responsible for the stability of Internalizing Problems over a three-year interval.

Unfortunately, rater biases could not be studied in this sample of adoptees because only one of the parents had been asked to complete a CBCL. Also sex differences were not examined because the obtained longitudinal sample size was too small to be divided into boys and girls.

The need for longitudinal studies

As shown by the twin study of O'Conner et al. (1998b) and the results of the adoption study, longitudinal data enable the researcher to examine the contributions of genetic and environmental factors to the covariation of behavior across time. In this way, one can determine if the relative importance of genetic versus environmental factors change over time. When a child shows the same behavior at various points in time, this phenotypic stability might be caused by the same genes or the same environmental influences operating throughout development. Also, longitudinal studies can reveal if the same or different genetic and environmental factors exert their influence during development. For example, is an increase in heritability due to new, additional, genetic factors being expressed as children

grow older, or is there an amplification of existing genetic influences? As already mentioned, genetically determined characters need not be stable, nor are longitudinally stable characters always influenced by heredity (Molenaar *et al.*, 1991). Longitudinal studies (using appropriate longitudinal models) are essential to understand the etiology of children's problem behaviors.

Conducting a sound prospective longitudinal study

During this last decade, behavior genetic studies (see also Table 1.1) have examined the genetic and environmental influences on children's problem behaviors. To our awareness, only three twin studies have examined the etiology of problem behaviors longitudinally. However, both the study of O'Connor et al. (1998b) and the study of Gjone et al. (1997b) used twins of a very wide age range (13-21 years and 7-17 years, respectively) who were all of same-sex, and both the study of O'Connor et al. (1998b) and the study of Schmitz et al. (1995) used relatively small longitudinal samples (405 families and 95 twin pairs, respectively). To conduct a sound longitudinal study on the etiology of problem behaviors in children, the study should:

- collect samples of (twin) pairs that are large enough to match most of the demands of statistical power required for the genetic analysis of kinship data (Martin *et al.*, 1978),
- use samples of children measured at more or less similar developmental stages, like for instance: preschool, middle childhood, and adolescence,
- use assessment instruments that are sensitive to developmental changes,
- collect data of same-sex and opposite-sex (twin) pairs to be able to study possible sex differences in the etiology of problem behaviors,
- use multiple informants:
    - ask both mothers and fathers to fill out a questionnaire (for example the CBCL/2-3 or CBCL/4-18 (Achenbach 1991a, 1992)). This will also enable the analyses to correct for possible rater biases,
    - if the children are going to school, ask their teachers to fill out a questionnaire, for instance the Teacher's Report Form (TRF) (Achenbach, 1991b). This extra source of information can be compared with the information collected on the CBCL by using

the cross-informant syndrome constructs (Achenbach, 1991d),

- if subjects in the sample are 11 years or older, ask them to either fill out a questionnaire about themselves, for instance the Youth Self-Report (YSR) questionnaire (Achenbach, 1991c) (which also has cross-informant syndrome constructs with the CBCL and the TRF), or ask them to rate each others behaviors or the relationship they have with their sibling(s). At this age, they might also be able to fill out a life-events questionnaire, providing information about their nonshared environmental influences,

- use statistical techniques that can deal with missing data.

The Dutch twin study of problem behaviors

In an effort to conduct a sound prospective longitudinal study examining the etiology of problem behaviors during development, we have collected CBCL/2-3 questionnaires on 3-year-old twin pairs and four years later CBCL/4-18 questionnaires when the children reached their 7th birthday. The twins are members of the Netherlands Twin Registry (NTR), which registers 40-50% of all multiple births in the Netherlands. Data from all twin pairs from the NTR and born between 1987 and 1991 have been used to investigate the genetic and environmental influences on problem behaviors. At this moment, questionnaires on 4016 3-year-old twin pairs and 1926 7-year-old twin pairs are available, giving a group of preschool children and a group of schoolaged children (middle childhood) that are both large enough to fulfill most demands of statistical power.

We have chosen to start collecting longitudinal data on preschool and subsequently on schoolage children because, with the exception of the relatively small sample of the Colorado Twin Registry, no other behavior genetic study has been conducted using preschool children. Analysing these longitudinal data, we will not only get a better understanding of the genetic and environmental influences on various problem behaviors during these young ages, but also of age-related changes in the contribution of genes and environment over time. At these young years, children experience many developmental transitions that might cause the etiology of problem behaviors to change during this period. Preschool children spend most of their time at home with their parents or care-takers. They are largely passive recipients of

their social worlds. Shared environmental influences will probably be largest during this period. Schoolage children are away from home for at least half the day and therefore have more freedom to choose their own network of friends and activities. Genetic influences might be more expressed in these schoolage children, because they are better able to follow their own genetically induced interests and potentials (Kendler, 1995).

We have collected data on twin pairs of similar sexes and of opposite sexes, to enable the exploration of sex differences in genetic and environmental influences on various problem behaviors. Both mothers and fathers have been asked to fill out a CBCL at both assessment points, enabling us to estimate the effects of rater biases in the theoretical model. Also the effects of sibling interactions can be incorporated in the model because questionnaires have been filled out by each parent for each child.

Future intentions and possible research questions

The longitudinal results of the twin sample (all children) will be complemented with the longitudinal results of the adoption sample (all adolescents). Hopefully the results will give a clearer picture of the etiology of problem behaviors during childhood.

Future studies (if funds can be found) will follow-up the same twins again during adolescence and young adulthood. Currently, the oldest of the twins are being assessed again at the age of 12. By following the twins during their development, the operation of genes and environmental influences throughout development can be estimated. Also the genetic and environmental effects on comorbidity, the tendency of some problem behaviors to co-occur, can be explored. Over time, some distinct problem behaviors might be the different expressions of the same underlying genetic or environmental influence. Knowing the underlying etiology of the behaviors that tend to co-occur might help in developing distinct diagnoses and effective treatments.

Once it is known what the relative contributions of genes and environmental influences for the different problem behaviors at specific ages are, and how these influences change during development, the last three questions in the sequence of genetic epidemiologic research can be addressed: "What is the mode of transmission, where are the gene(s) located on the

chromosome, and what are the genetic and environmental mechanisms of disease?". Although we are a long way of answering these questions, some techniques enabling this kind of research have been developed.

The mechanism of transmission from parent to child (Is a single gene responsible, multiple genes or are environmental factors implicated? Is the gene dominant or recessive?) can be studied using segregation analysis. This technique allows one to detect the contribution of individual genes of large effect against the background of other genetic and environmental effects. Using a theoretical model of familial transmission, assumptions about the genetic and environmental causes are translated into mathematical equations. These equations are then used to predict the distribution of a disorder in pedigrees. The theoretical model is accepted when the pattern of a disorder predicted by the model is close to what is observed (when the model cannot be statistically rejected) (Faraone & Tsuang, 1995). When studying the mode of transmission of children's problem behaviors, family studies have the difficulty of collecting accurate information not only from the child but also from adult family members about their behavior problems when they were children (Simonoff *et al.*, 1994).

To answer the fourth question in the chain: "Where is (are) the gene(s) located?" sib-pair strategies have been developed (Haseman & Elston, 1972). Complex traits are multifactorial in nature, involving a number of genes, each with relatively small effect (Cardon, 1995). These multiple genetic loci that are thought to influence continuous traits are known as 'quantitative trait loci' or QTL's (Gelderman, 1975). In sib-pair strategies, trait and marker data are obtained from siblings and (optimally) their parents in a number of different families. The methods do not involve any assumptions concerning the mode of transmission and are robust with respect to genetic heterogeneity (meaning the same phenotype resulting from the expression of different genes or gene combinations) (Cardon, 1995). The idea behind the Haseman and Elston approach for continuous traits is that under linkage between a trait and a QTL, differences between siblings in their phenotypes will decrease in accordance with greater similarity at the marker locus. Haseman and Elston employ the proportion of alleles that siblings share identical-by-descent (IBD) as their measure of QTL resemblance. Extensions of this approach have been developed to take multiple markers or multiple traits simultaneously into account, which strengthens the statistical power of the method (Fulker *et*

al., 1991, Fulker & Cardon, 1994; Cardon & Fulker, 1994, Boomsma, 1996, Boomsma & Dolan, 1998b, Dolan *et al.*, 1999). The sib-pair design for QTL linkage analysis corresponds well to the classical twin study. Except for the collected data on different phenotypes, all that is needed are DNA samples drawn from blood samples or buccal swaps, because dizygotic twins are full siblings.

When a gene is localised its function must be explored. For instance, what proteins does the gene code for and are there any environmental effects that influence the workings of this gene? This of course is the last question in the chain of genetic epidemiologic research: "What are the genetic and environmental mechanisms of the behavior?" but to answer this question genes and environmental influences must be identified first.

2

Quantitative Genetic Analysis of Internalizing and Externalizing Problems in a Large Sample of 3-Year-Old Twins

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Abstract

For a quantitative genetic study of preschool problem behaviors, we have collected data with the Child Behavior Checklist for 2 and 3 year old children (CBCL 2/3). Questionnaires were completed by mothers of 3620 twin pairs: 633 monozygotic males, 581 dizygotic males, 695 monozygotic females, 519 dizygotic females and 1192 dizygotic opposite sex twin pairs. The genetic and environmental influences on the Externalizing and Internalizing scales were estimated, simultaneously with sex differences and sibling interaction effects. Genetic factors explained most of the observed variance for both Externalizing and Internalizing Problems. Cooperative sibling interactions were found for Externalizing Problems, indicating that twins reinforce each other's behavior. Sex differences in genetic architecture were found for Externalizing Problems. Genetic factors explained 75% of the variance in girls and 50% in boys. Shared environmental influences were only of importance in boys. For both Problem scales, nonshared environmental factors accounted for 25 to 32% of the variance. The observed variances of Internalizing Problems could be adequately explained by genetic and nonshared environmental factors, with genetic factors accounting for 68% of the variance.

Keywords

preschool children, problem behavior, Child Behavior Checklist, twins, behavior genetics.

Introduction

A number of studies indicate that roughly 10 to 15% of preschool children show problem behaviors (Campbell, 1995; Richman *et al.*, 1982). Despite the fact that problem behaviors in preschool children may cause suffering for both the child and his family as well as put the child at risk for later malfunctioning, relatively few studies have looked at the etiology of problem behaviors in preschool children. Most problem behaviors in young children generally involve quantitative variations in behavior that most children display to some degree. These continuous variations in behavioral problems are hypothesized to be caused by multiple genes and environmental influences. A better understanding of the etiology of individual differences in preschool problem behaviors is important, for it may guide clinical interventions and provide ideas for future research.

By carrying out quantitative genetic studies, the relative influences of genetic and environmental factors on the continuous variations in problem behaviors can be estimated. In order to determine what the genetic and environmental effects on variation in behavior are, genetically informative subjects (such as twins) are needed. Their observed, i.e. phenotypic, variance can be partitioned into a genetic part, an environmental part that is shared between children growing up in the same family and an environmental part that is not shared with other family members (idiosyncratic experiences). A way to quantify preschool children's problem behaviors is by asking their parents to score their children's behavioral and emotional problems on the Child Behavior Checklist for 2 and 3 year old children (CBCL 2/3) (Achenbach, 1992). The CBCL 2/3 is a standardized questionnaire consisting of 99 problem items which are scored by the parents on a 3-point scale, based on the occurrence of the behavior during the preceding 2 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. With factor analysis different problem scales have been derived, which can be computed by summing the items belonging to that scale. For instance, the scale Aggressive Behavior is composed of items like: demands must be met, disobedient, easily frustrated, jealous, fights, hits others, screams, moody, etc. Different scales can be combined to form two broad band scales: Internalizing Problems and Externalizing Problems. The broad band scale

Internalizing Problems reflects anxious, depressed and withdrawn behaviors, while the broad band scale Externalizing Problems is characterized by 'acting out'- oppositional and aggressive behaviors. Finally, a Total Problem Score can be computed by summing all 99 items.

Studies disentangling the influence of nature and nurture on the etiology of differences among preschoolers in problem behaviors are rare. We know of only two quantitative genetic studies of preschool children's problem behaviors, each using 3-year-old twins. Both studies employed the CBCL 2/3. Schmitz et al. (1995) studied 260 twin pairs from Colorado and Van den Oord et al. (1996) used 1358 Dutch twin pairs. Overall, genetic influences appeared to be most important for explaining the observed phenotypic variance, while shared environmental influences had only a minor influence. For most scales sex differences in the magnitude of the genetic and environmental influences were not found. A limitation however, especially of the first study, is the sample size used. To evaluate genetic models, which do not only test for genetic and environmental influences but also for possible sex differences, large sample sizes are needed.

Social interactions between siblings may also influence problem behaviors. Especially for behaviors which are easily observable for the other sibling, like aggressive behaviors, one can expect siblings to influence each other. Interactions can either be in a cooperative manner, through imitation or mutual reinforcement, or in a competitive manner, when the behavior of one sibling evokes the opposite reaction in the other sibling (Eaves, 1976). The incorporation of sibling interaction into a model can dramatically change estimates of genetic factors and especially of shared environmental factors. For a sample of juvenile twins, aged 8 through 16 years (Hewitt *et al.*, 1992), mothers' ratings for Externalizing Behavior were obtained. Because the pooled individual phenotypic variances of the monozygotic twins were greater than those of the dizygotic twins, a model with sibling interactions was tried as a way of illustrating a sibling interaction model (Neale & Cardon, 1992). Incorporating sibling interaction into the model caused the shared environmental factor to decrease from a large influence to zero. This indicated that the obtained shared environmental effect could totally be explained by sibling interactions. The boys proved to stimulate each other in showing Externalizing Behaviors.

To enable a quantitative genetic study of preschool problem behaviors with a reasonable power to detect sex differences and social interactions between the twins, we have supplemented the original Dutch sample of 1358 3-year-old twin pairs (Van den Oord *et al.*, 1996), with an additional sample of 2658 3-year-old twin pairs. For all these twins, we have collected the CBCL 2/3 (Achenbach, 1992), a standardized questionnaire, when the twins just reached their third birthday. With this sample of twin pairs, we have estimated the genetic and environmental influences on the two broad band groupings of the CBCL 2/3: Internalizing Problems and Externalizing Problems, while at the same time testing for possible sex differences and sibling interactions.

Methods

Subjects

This study is part of a project in which the genetic and environmental influences on the development of problem behaviors in 3 to 7 year old children are studied. All participants were members of the Netherlands Twin Registry (NTR), kept by the Department of Psychonomics at the Free University in Amsterdam. Of all multiple births in The Netherlands, 40 to 50% are registered by the NTR (Boomsma *et al.*, 1992). For this study, all twins from the birth cohorts 1987 to 1991 were used. Questionnaires were mailed to 5103 families, within three months of the twins' third birthday. After two to three months, reminders were sent and four months after the initial mailing persistent nonresponders were contacted by phone. A response rate of 78.7% was obtained, giving data on a total of 4016 families of twins; 60 twin pairs were excluded from the analyses because either one or both of the children had a disease or handicap that interfered severely with daily functioning. Another 183 twin pairs were excluded because the questionnaires of either one or both of the children were not filled in by the mother. Zygosity was determined for 686 twin pairs by either blood group polymorphisms or DNA analyses. For all other twin pairs, zygosity was determined by discriminant analysis, using questionnaire items which the parents had completed when the children were about five years of age. Parents were asked how much the twins resembled each other in hair color, eye color, facial structure, and whether they were

ever mistaken for each other by family, friends or the parents themselves. The discriminant analysis resulted in a 92.71% correct classification, suggesting that at most 4% of the twins' zygosity was wrongly classified ((7.29% * (4016-686-1122(dizygotic opposite sex twins not included in group with blood/DNA data)))/4016). For 153 twin pairs zygosity could not be determined because the questionnaire with zygosity information was missing. These twin pairs were excluded from this study. This procedure left a sample of 633 monozygotic males (MZM), 581 dizygotic males (DZM), 695 monozygotic females (MZF), 519 dizygotic females (DZF) and 1192 dizygotic opposite sex (DOS). Children were rated by both parents in 45% of cases. In this paper we report maternal ratings.

Measures

The CBCL 2/3 is a standardized questionnaire, developed for parents to score the behavioral and emotional problems of their 2 and 3 year old children (Achenbach, 1992). It was modeled after a similar questionnaire for children of 4 to 18 years of age. Dutch syndrome scales for the CBCL 2/3 were derived by exploratory, followed by confirmatory, factor analyses across three independent samples: 426 children referred to mental health services, 420 children from the general population and 1306 twin pairs from the present study (Koot *et al.*, 1997). Koot et al. (1997) showed that the Dutch syndrome scales are comparable to the scales developed by Achenbach (1992). The Dutch scale Oppositional showed a high correlation with the American scale Aggressive Behavior (.94), while the Dutch scale Aggressive showed a high correlation with the American scale Destructive Behavior (.82) and the scale Aggressive Behavior (.80). All other scales obtained similar names: correlation between Dutch Withdrawn/Depressed and American Withdrawn was .88, Dutch Anxious and American Anxious/Depressed was .84, Dutch Internalizing and American Internalizing was .90 and Dutch Externalizing and American Externalizing was .97. All these correlations were significantly higher than those between any other combinations of Dutch and American syndrome scales (except Internalizing and Externalizing). In contrast to the Dutch version, there is no Overactive scale in the American version.

The syndrome scales used in this study were composed according to this Dutch version. The broad band scale Internalizing Problems was composed of the items of the Anxious and

Withdrawn/Depressed subscales (in contrast to the composition of the Anxious scale reported by Koot et al. (1997), item 32 was not included because it lowered Cronbach's α (Koot, 1993)). The broad band scale Externalizing Problems was composed of the items of the Aggressive, Oppositional and Overactive subscales.

The data were subjected to square-root transformation before the analyses were performed, because most children showed no or just little problem behaviors, causing a skewed distribution. The distribution of Externalizing Problems and Internalizing Problems after transformation is shown in Figures 2.1 and 2.2, respectively.

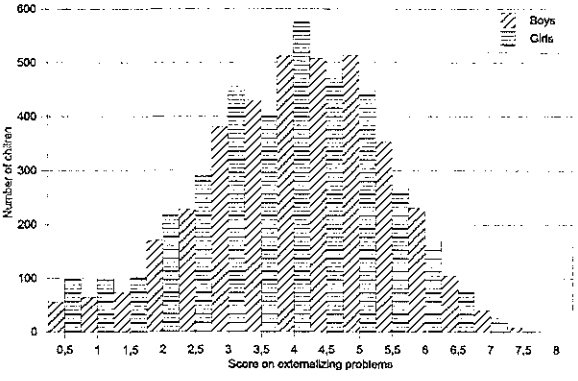

Figure 2.1 *Distribution of the broad band scale Externalizing Problems after square-root transformation.*

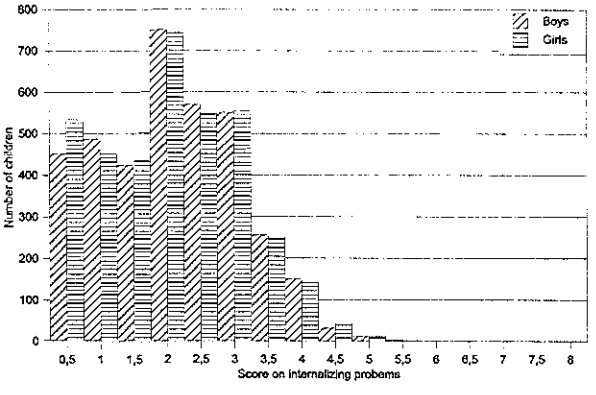

Figure 2.2 *Distribution of the broad band scale Internalizing Problems after square-root transformation.*

For the scale Internalizing Problems, the kurtosis of the total twin sample was -.415 (range of all different zygosity-by-sex groups -.568 - .021) and the skewness was -.101 (range of all different zygosity by sex groups -.324 - .047). The scale Externalizing Problems showed a smaller kurtosis for the total twin sample of -.038 (range of all different zygosity by sex groups -.404 - .007) and a slightly larger skewness of -.326 (range of all different zygosity by sex groups -.404 - -.197). All absolute values of kurtosis and skewness were smaller than .6, suggesting that after transformation the distribution of both scales approached normality.

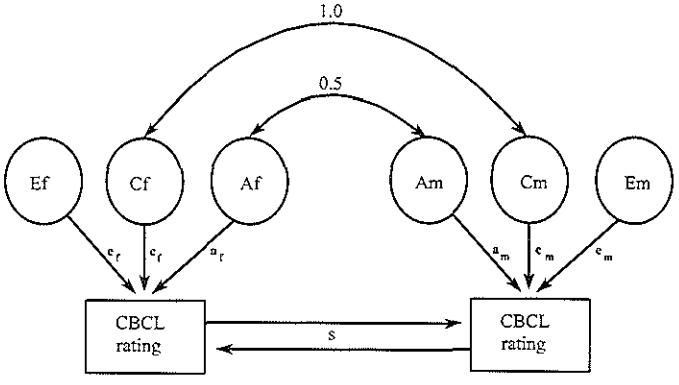

Figure 2.3 *ACE model allowing for sex differences and sibling interactions.*

Models

A twin model, composed to test for genetic and environmental influences on the CBCL 2/3 broad band scales, was fitted to the data. Monozygotic twins, who are genetically identical, were compared with dizygotic twins, who share on average 50% of their segregating genes. Both type of twins grow up in a family. They are assumed to share the same kind of familial environment. By comparing the similarity between the monozygotic twins with the similarity between the dizygotic twins, identification of the model to estimate the contributions of genotype (A), shared environment (C), and nonshared environment (E) is achieved (ACE model). If the monozygotic twins resemble each other to the same degree as

the dizygotic twins, only environmental influences can be of importance. However, when the monozygotic twins resemble each other more than the dizygotic twins, genetic factors are supposed to be of importance, since the only difference between the two groups is in genetic relatedness.

In order to estimate the genetic and environmental influences on preschool problem behaviors, while testing for possible sex differences and sibling interactions, the model shown in Figure 2.3 was fitted to the observed variance-covariance matrices of the 5 different twin groups (MZM, DZM, MZF, DZF, DOS). Monozygotic twin covariances and dizygotic twin covariances are compared, assuming a correlation between the twins' shared environmental influences of 1.0, regardless of twin type, and a genotypic correlation of 1.0 for monozygotic twins and 0.5 for dizygotic twins. The model decomposes the observed variance of the maternal ratings into three latent factors, that may have a different influence for females (i.e. A_f, C_f, E_f) and for males (i.e. A_m, C_m, E_m). Sibling interaction is incorporated in the model by allowing the behavior of the twins to influence each other (s).

Model fitting

Structural equation modeling was used, in which the observed variance-covariance matrices of the 5 different twin groups are compared with the expected variance-covariance matrices of the theoretical model. A good model describes the observed variance-covariance matrices to such an extent that the residual variance-covariance matrices are trivially small. In this case one can say that the theoretical model describes the observed data adequately, which is also indicated by the χ^2 test statistic. So, the χ^2 test statistic provides a test of whether the residual differences between the observed and the expected variance-covariance matrices converge in probability to zero as the sample size approaches infinity (Cudeck & Browne, 1983). However, because theoretical models are never able to describe the real world perfectly, any model can be rejected if the sample size is large enough. Because of this influence of sample size, a poor fit based on a small sample size may result in a model being accepted, whereas a good fit based on a large sample size may result in a model being rejected (Marsch *et al.*, 1988). Using a large sample of twins to test the fit of the model to the observed variance-covariance matrices, we have not only taken the χ^2 test statistic as

measures of how well the model described the observed data, but also looked at the differences between the observed and predicted variance-covariance matrices.

Using Mx, a structural equation modeling program (Neale, 1997b), we have first fitted an ACE model to the observed data, that allowed for sex differences and sibling interactions. Next we tested whether a model without either sibling interactions or without sex differences or without both interactions and sex differences fitted the observed data as well as the full ACE model. This test was accomplished by subtracting the model's χ^2 test statistic from the χ^2 test statistic of a less constrained model. The degree of freedoms for this test statistic are the number of parameters in the model, subtracted from the number of parameters in the less constrained model. The most simplified model was then retained to analyze the causes of variation in preschool problem behaviors.

Results

Table 2.1 gives the untransformed mean problem scores and standard deviations of the twin sample and those of a Dutch community sample (Koot, 1993) of 420 singleton children. For all CBCL 2/3 broad band and subscales, the two samples showed comparable means and standard deviations.

Table 2.1 *Means and standard deviations of community sample and twin sample for Dutch CBCL/2-3 broad band and subscales.*

CBCL/2-3 profiles	Community Sample	Twins
Sample size	420	3773 x 2
Externalizing Scale	17.0 (9.2)	16.0 (10.1)
Aggressive	3.2 (2.6)	3.3 (2.8)
Oppositional	10.7 (6.0)	10.0 (6.6)
Overactive	3.1 (2.4)	2.7 (2.2)
Internalizing Scale	4.4 (4.0)	4.6 (4.1)
Anxious	3.3 (2.9)	3.5 (3.1)
Withdrawn/Depressed	1.1 (1.8)	1.1 (1.6)

The sample sizes of the different zygosity by sex groups and their means and standard deviations for oldest and youngest twins (male and female twins in the opposite sex group) are given in Table 2.2. The scales were subjected to square-root transformation. There were no mean differences between the sexes for the broad band scale Internalizing Problems, but for the scale Externalizing Problems females obtained lower mean scores than males. For the Externalizing scale, the standard deviations shown by the monozygotic twins were larger than the standard deviations shown by the dizygotic twins, both for males and females.

Table 2.2 *Sample size, means and standard deviations (oldest and youngest twin) for each zygosity by sex group for CBCL/2-3 broad band scales. Order of DOS twins: male, female.*

CBCL/2-3 profiles	MZM	DZM	MZF	DZF	DOS
Twin Pairs	633	581	695	519	1192
Broad band scales:					
Externalizing Problems	4.03 (1.37) 3.92 (1.38)	3.97 (1.24) 3.83 (1.33)	3.70 (1.43) 3.61 (1.45)	3.73 (1.35) 3.54 (1.36)	3.76 (1.36) 3.47 (1.38)
Internalizing Problems	1.93 (1.00) 1.84 (1.04)	1.94 (.99) 1.77 (1.10)	1.96 (1.06) 1.86 (1.12)	1.96 (1.04) 1.88 (1.01)	1.86 (1.04) 1.68 (1.06)

MZM/F = monozygotic males/females, DZM/F = dizygotic males/females, DOS = dizygotic opposite sex.
Note. Scales have been subjected to square-root transformation.

Table 2.3 shows this result in more detail by giving the variance-covariance matrices of the observed data, for both broad band scales per zygosity by sex group. For Externalizing Problems, monozygotic twins showed larger variances and covariances than dizygotic twins, both for males and females. A larger variance of monozygotic twins than for dizygotic twins, indicates the possibility of sibling interaction. Cooperative interactions between siblings causes the variances of the monozygotic twins, who are genetically identical, to be larger than the variances of the dizygotic twins, who share on average only half of their segregating genes (Neale & Cardon, 1992).

Table 2.3 *Observed variance-covariance matrix for Externalizing Problems and Internalizing Problems per zygosity by sex group.*

Zygosity	Externalizing Problems observed (cov-)variance		Internalizing Problems observed (cov-)variance	
MZM	1.8748		1.0000	
	1.4746	1.8914	0.6652	1.0839
DZM	1.5396		0.9730	
	0.9542	1.7731	0.4021	1.2103
MZF	2.0419		1.1256	
	1.6715	2.0960	0.8433	1.2517
DZF	1.8260		1.0816	
	0.9502	1.8457	0.3911	1.0245
DOS	1.8533		1.0886	
	0.9506	1.9115	0.3948	1.1278

MZM/F = monozygotic males/females, DZM/F = dizygotic males/females, DOS = dizygotic opposite sex.

The Internalizing scale did not show these systematic differences in variances between monozygotic and dizygotic twins, so the siblings probably do not influence each other with respect to internalizing behaviors.

Table 2.4 *Twin correlations per zygosity by sex group for CBCL/2-3 broad band scales.*

CBCL/2-3 profiles	MZM	DZM	MZF	DZF	DOS
Broad band scales:					
Externalizing Problems	.78	.58	.81	.52	.51
Internalizing Problems	.64	.37	.71	.37	.36

MZM/F = monozygotic males/females, DZM/F = dizygotic males/females, DOS = dizygotic opposite sex.

The correlations between the twins, given per zygosity by sex group and for each broad band scale, are shown in Table 2.4. For the Externalizing scale, the correlation between the monozygotic males was higher than the correlation between the dizygotic males. However, it did not approach twice the size of the correlation between the dizygotic males. This suggests that apart from genetic influences, shared and nonshared environmental influences are also important for explaining the males' externalizing behaviors. The correlation between the female twins showed the same pattern, suggesting that also for female twins genetic

influences, shared environmental influences and nonshared environmental influences will be necessary to explain their externalizing behaviors.

For the Internalizing scale, the correlations between the monozygotic males were almost twice the size of the correlations between the dizygotic males. In order to explain internalizing behaviors of the males, we expect genetic and nonshared environmental influences to be important but not shared environmental influences. Again, female twin correlations showed comparable results, suggesting that also for the female twins genetic and nonshared environmental influences will be important.

For both scales, dizygotic opposite sex twins' correlations had the same size as those of the same-sex twins' correlations. This suggests that the same genes are expressed in males as in females.

Table 2.5 *Fittings of the different models for CBCL 2/3 Externalizing and Internalizing Problems.*

	Externalizing Problems			Internalizing Problems		
Model	χ^2	df	p	χ^2	df	p
ACE + sex diffs. + sibl. int.	**9.716**	**8**	**0.286**	17.938	8	0.022
ACE + sex diffs.	14.313	9	0.112	18.549	9	0.029
ACE + sibl. int.	23.970	11	0.013	22.182	11	0.023
ACE	28.094	12	0.005	22.491	12	0.032
AE + sex diffs. + sibl. int.	18.507	10	0.047	18.262	10	0.051
AE + sex diffs.	96.063	11	0.000	21.028	11	0.033
AE + sibl. int.	23.970	12	0.021	22.182	12	0.036
AE	101.321	13	0.000	**24.735**	**13**	**0.025**

Note. Sex diffs. = sex differences; sibl. int. = sibling interactions.

We have fitted a twin model with genetic, shared environmental and nonshared environmental factors to the observed data. The model allowed for possible sex differences and sibling interactions. The fit of the full model and its submodels are given in Table 2.5.

For the Externalizing scale, the full model described the observed variance-covariance matrices adequately and better than the more parsimonious models. The χ^2 of the full model

proved to have a good fit with a p-value of .29. All residual variance-covariance matrices were trivially small, indicating that almost all of the observed variances and covariances were explained by the theoretical model.

The different model-fits of the Internalizing scale showed that the submodel with only genetic influences and nonshared environmental influences described the observed data adequately and not significantly worse than a more complex model. The residual variance-covariance matrices were trivially small, indicating that although the model's obtained p-value was low (0.03), it described the observed data satisfactorily.

Table 2.6 *Percentage of variance explained by genetic, shared and nonshared environmental factors for best-fitting models and path estimate for sibling interaction.*

		Environment		path estimate
CBCL 2/3 scales	Genetic	Shared	Nonshared	Sibl. interac.
Externalizing Problems				
Monozygotic males	51%	22%	27%	.102
Dizygotic males	49%	22%	29%	.102
Monozygotic females	75%	-	25%	.102
Dizygotic females	74%	-	26%	.102
Internalizing Problems	68%	-	32%	-

The percentage of variance explained by the genetic, shared environmental and nonshared environmental factors is given in Table 2.6. Because the model of Externalizing Problems contained sex differences and sibling interactions, the estimates for monozygotic males and females and dizygotic males and females differed (Neale & Cardon, 1992). The path allowing for sibling interactions was constrained to be equal for male and female twins (which did not lead to a worse fit than the model in which it differed for males and females). For males, genetic factors explained half of the percentage of variance. Shared and nonshared environmental factors had almost equal influences, explaining between 22% and 29% of the variance. For females, shared environmental factors were nonexistent. Most of their variance, between 74% and 75%, was explained by genetic factors, while the nonshared environmental factors explained the rest of the variance.

The best fitting model for Internalizing Problems only allowed for genetic and nonshared

environmental factors, without sex differences or sibling interactions. The genetic factors explained 68% of the variance, while the nonshared environmental factors explained 32% of the variance. Genetic factors were, for males and females, more important for explaining the observed data.

Discussion

In the present study, the CBCL 2/3 was used to assess the genetic and environmental influences on two broad band scales Externalizing Problems and Internalizing Problems, scored for 3620 twin pairs. For both scales, genetic factors explained most of the observed variances. Nonshared environmental factors accounted for 25% to 32%. These results are consistent with the estimates Van den Oord et al. (1996) found, for the previously collected smaller sample of 1358 Dutch twin pairs. However, in contrast to the former study (Van den Oord *et al.*, 1996), using an effective sample size of 3620 twins, we now also found sibling interactions and sex differences in the estimates of the scale Externalizing Problems. Genetic factors accounted for 74% to 75% of the variance for females, versus 49% to 51% for males. Shared environmental influences were only present in males, explaining 22% of the variance. Overall, these results indicate that differences in Externalizing Problems in preschool children are caused predominantly by genetic differences. Although genetic influences are stronger for females than for males, the same genes seem to be responsible for this influence in both sexes, as was shown by the similarity between the correlations of the same-sex and opposite sex dizygotic twin pairs. The finding that shared environmental influences are present only in males but not in females is difficult to interpret without the help of further studies. It could be an indication that boys, even as young as 3 years of age, are more sensitive to the morals and values the family attach to externalizing behaviors, or it could indicate that families are more directive and controlling over externalizing behaviors in young boys.

For the broad band scale Internalizing Problems we did not find any evidence for sex differences or the effects of shared environment. All the observed variance of this scale could be explained by genetic and nonshared environmental factors, with genetic factors accounting

for 68% of the variance. Finding this simple model in such a large sample of twins gives strong evidence that Internalizing Problems in 3-year-old children, regardless of sex, are largely influenced by genes and, for a lesser degree, by idiosyncratic experiences that are not shared by other children in the family. This result is in contrast with the estimates reported by Schmitz et al. (1995). In a small sample of 3-year-old twins from Colorado, Schmitz et al. (1995) found that the scale Internalizing Problems was more strongly influenced by shared and nonshared environmental factors than by genetic factors.

Using the large effective sample size of 3620 twins, we now also found evidence of sibling interactions for the scale Externalizing Problems. The interactions proved to be in a cooperative manner, with twins reinforcing each other's behavior. We are not aware of any other study investigating sibling interactions in preschool children. However, the results are consistent with the interactions Hewitt et al (1992). found for a sample of 8 to 16-year-old twins. These schoolaged and adolescent children also reinforced each other's externalizing behaviors (Neale & Cardon, 1992). For the scale Internalizing Problems no sibling interactions were found. It appears that preschool children, who show Internalizing Problems such as anxiety and depression, do not influence their twin in showing either the same or opposite behaviors.

Nonshared environmental influences were, apart from genetic influences, the only other factor of importance for females, accounting for both broad band scales between 25% to 32% of the observed variance. For males, the nonshared environmental factor was just as important as it was for females. This result indicates that, for both scales and for both sexes, idiosyncratic experiences are of importance in the rate of problem behaviors shown by preschool children. However, errors of measurement are also part of the estimate of the nonshared environmental factors. Maybe by including the ratings of other raters, like fathers and caretakers other than the parents, possible errors of measurement can be reduced, thereby decreasing the estimates of the nonshared environmental factors. Rater bias, another possible error of measurement, caused by raters consistently scoring their children as having either more or fewer problems, was probably not very large in this data set. If rater bias had occurred, the estimates of the shared environmental factors would have been increased. Considering the fact that we only found evidence of shared environmental factors for the

scale Externalizing Problems in males, and not for the female ratings or for the ratings of the scale Internalizing Problems, rater bias probably did not play an important role. Van den Oord et al. (1996) addressed this issue in the sample of 1358 Dutch twin pairs and found that rater bias did not influence the estimates of genetic and environmental factors. Rater bias thus does not seem to be a large problem in this sample.

Fitting the most simplified model for the scale Internalizing Problems, the obtained p-value of the χ^2 test was low. Nevertheless, the residual variance-covariance matrices were trivially small. So probably this poor fit of the model was caused by the large sample size of twin pairs used (Marsch *et al.*, 1988).

The model used assumed that there were no interactions between genes and the environment. However, one cannot be certain that this is true in real life. It could be that the kind of environmental influences that the child experiences, depends on the genotype of the child himself. As Campbell (1995) suggests in her review article of recent studies "it seems likely that biological propensities in the child interact with salient aspects of the caregiving environment to produce either adaptive or maladaptive outcomes..." (p. 141). If this interaction occurs with the nonshared environmental influences, the estimate of the nonshared environmental factor increases. Probably this was not the case in this study, because the estimate of the nonshared environmental factor was quite small, between 25% and 32%. If the kind of shared environmental influences that the child experiences depends on its genotype, the estimate of the genetic factor will increase. Because we found quite large estimates of genetic influences, interactions between shared environment and genotype could have inflated the genetic estimate. However, in case the kind of shared environmental influences that the child experiences depends on its genotype, then the influence of this interaction actually also belongs to the estimate of the genetic factor.

The estimates found are not applicable to the individual. Quantitative genetic studies estimate average differences between individuals in a certain population. For other populations or for specific individuals different estimates might be applicable. This study used a nonclinical sample of twin pairs, showing problem behaviors in the normal range. Whether the results also apply to a clinical population, showing problem behaviors in an extreme range, will have to be tested by further studies.

3

Using Parental Ratings to Study the Etiology of 3-Year-Old Twins' Problem Behaviors: Different Views or Rater Bias?

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Abstract

Child Behavior Checklist questionnaires (Achenbach, 1992), filled out separately by mothers and fathers, were collected for an effective sample of 3501 Dutch 3-year-old twin pairs. To disentangle the child's phenotype from that of the rater two contrasting models were fitted to the data. One model, called a Rater Bias model, is based on the assumption that both parents assess exactly the same behaviors in the child. A weaker alternative of this model, called a Psychometric model, assumes that apart from these common behavioral views, each parent also assesses an unique aspect of the child's behavior. A Psychometric model fitted the data of both Internalizing and Externalizing scales significantly better than a Rater Bias model. This implied that each parent provided unique information from his or her own perspective, apart from the common behavioral view. Using this best fitting model, the etiology of both the Internalizing and Externalizing scales was studied. Common factors (influencing behaviors similarly assessed by both parents) were more important than unique factors (influencing behaviors uniquely assessed by one parent). Common genetic factors explained about 50% of the variance of both scales, indicating a possible inborn vulnerability to childhood psychopathology. Common environmental factors not shared between twins (free of unreliability and error) explained around 14% of both scales, suggesting the importance of pure idiosyncratic experiences even for children as young as 3 years. Common environmental factors shared between twins (unconfounded by rater bias) were only found for the Externalizing scale, explaining 18% of the variance. Rater bias and unreliability, if present in the data, were included in the estimates of the unique factors. Unique genetic, shared and nonshared environmental factors each explained around 8% of the variance for both scales. These small effects could be detected because of the large sample of twin pairs used.

Keywords

behavior genetics, children, Child Behavior Checklist, problem behavior, rater bias, twins.

Introduction

To study children's behaviors parental descriptions are often used. Parents observe the child in natural situations at home and in the playground and so are a useful source of information. However, parents do not generally agree in detail about a given child's behavior (Achenbach *et al.*, 1987). There are very good reasons why this should be so. Ratings obtained via the assessment of children by their parents are a function of both parent and child. As noticed by Neale and Cardon (1992) each parent has a different situational exposure, a different degree of insight, and a different perception, evaluation and normative standard that may create rater differences of various kinds in reporting behaviors. Therefore, when using parental ratings disentangling the child's phenotype from that of the parent becomes an important methodological problem. For the analysis of genetic and environmental contributions to children's behavior, solutions to this are available when multiple raters, e.g., two parents, rate multiple children, e.g., twins (Neale & Cardon, 1992). To disentangle the child's phenotype from that of the rater two contrasting models have been developed. One model, called the Rater Bias model (Neale & Stevenson, 1989; Hewitt *et al.*, 1992), is based on the assumption that both parents are rating the same behaviors in their children. A weaker alternative of this model, called the Psychometric model (Hewitt *et al.*, 1992) assumes that parents are rating correlated behaviors in their children.

A Rater Bias model may apply when both parents are equally confronted with the behaviors shown by the child (for instance at home). In this case the parents may have a common behavioral view (assess exactly the same behaviors in the child) and share a common understanding of the behavioral descriptions. Disagreement between the raters is regarded as error, resulting from rater bias and/or unreliability. Rater bias in this context is considered to be the tendency of an individual rater to overestimate or underestimate scores consistently. Sources of rater bias are stereotyping, employing different normative standards, or having certain response styles, i.e. judging problem behaviors more or less severely. Because these types of bias may differ between raters, they may also lead to disagreement between raters. Unreliability can become an important source of disagreement when raters cannot give an accurate description of relevant behaviors. For instance, evidence is found that

parents may be relatively insensitive to affective disturbances in children (Angold *et al.*, 1987). Using the Rater Bias model it becomes possible to partition the variance in the parental ratings into their components due to reliable trait variance, due to parental bias, and due to unreliability or error in the particular rating of a particular child. Only the reliable trait variance will then be decomposed into its components due to genetic and environmental influences (Neale & Cardon, 1992).

A Psychometric model may apply when, in addition to the common behavioral view and shared understanding of the behavioral descriptions, parents also assess an unique aspect of their child's behavior. Unique behavioral views will occur when the parent also observes the child in distinct situations where they are exposed to different samples of the behavior. For instance, the parent who usually brings the child to a day care center may also be more familiar with the child's behavior outside the home. Moreover, each parent may interact differently with the child (Achenbach *et al.*, 1987). 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. Disagreement in this model does not merely arise due to rater bias and/or unreliability, but also because each parent contributes, from his own perspective, different but valid information on the child's functioning. Using the Psychometric model it becomes possible to partition the variance in the parental ratings into their components due to trait variance shared between parents and due to trait variance unique to one parent. Genetic and environmental influences can then be estimated apart for the trait variance shared between parents and the trait variance unique to one parent. For the trait variance shared between parents genetic and environmental influences contain only reliable variance. Possible rater bias and/or unreliability can, in this model, only confound the environmental influences estimated for the trait variance unique to one parent. When genetic factors are estimated to influence the behaviors uniquely rated by one parent, the parent must have been assessing "real" unique behavioral views. For error and/or unreliability cannot cause the systematic effects necessary for the model to estimate genetic influences.

Several quantitative genetic studies have collected parental ratings using the Child Behavior Checklist (CBCL) (Achenbach, 1991a, 1992) to examine the etiology of children's

problem behaviors (Silberg *et al.*, 1994; Edelbrock *et al.*, 1995; Schmitz *et al.*, 1995; Van den Oord *et al.*, 1996; Zahn-Waxler *et al.*, 1996; Gjone, & Stevenson, 1997a; Leve *et al.*, 1998; Van der Valk *et al.*, 1998a; Van der Valk *et al.*, 1998b). Yet, only a few studies employed models that incorporated rater differences. Rowe and Kandel (1997) collected the CBCL completed by mothers and fathers for their oldest two offspring (aged 9 to 17) in 76 families. They did not fit either Psychometric or Rater Bias models. Still, their results showed that the parental ratings contained a substantial shared behavioral view. Simonoff et al. (1995), in a study of 282 twin pairs aged 8 to 16, also found evidence in favor of a shared behavioral view for antisocial behaviors. However, from their analyses they could not determine what underlay the shared parental view and described it as due to a shared set of expectations of the parents against which both twins were rated. Hewitt et al. (1992) applied both the Rater Bias and Psychometric model on parental ratings of the Internalizing scale (CBCL) for 983 twin pairs. They found that both for their prepubertal cohort (8 to 11 years) and for their pubertal cohort (12 to 16 years) the Psychometric model fitted the data better than the Rater Bias model. Hewitt et al. (1992) concluded that for the Internalizing scale, mothers and fathers rate the same phenotype in their children (i.e. have a shared behavioral view). However, unique genetic influences were also found, implying that the rater differences reflected the existence of real unique behavioral views and not just error and/or rater bias.

In the present study we fitted Rater Bias and Psychometric models to the Internalizing and Externalizing scale of 3501 Dutch 3-year-old twin pairs to examine whether disagreement was caused by rater bias and unreliability, or also involved the fact that parents provide unique and complementary information about their children's functioning. A correct representation is not only important from a substantive point of view, but also to obtain accurate estimates of genetic and environmental effects. If a quantitative genetic model does not take rater bias into account, it's presence will cause environmental influences shared between twins to be overestimated. Similarly, possible measurement errors will magnify the estimates of idiosyncratic environmental influences. Moreover, it may be incorrect to assume similar heritabilities when parents are actually exposed to different samples of behavior. Thus, using a model that takes possible rater bias and/or unreliability into account allows to estimate accurate genetic and environmental influences on the behaviors studied. The large

sample of twin pairs used in this study provided the power necessary to be able to detect possible small effects.

In short, the processes underlying parental disagreement were examined in a sample of 3-year-old twin pairs and, using a model that best fitted the data, the etiology of Internalizing and Externalizing Problems was studied.

Method

Subjects

All participants were members of 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 *et al.*, 1992; Boomsma, 1998a). For this study, data from all twins from the birth cohorts 1987 - 1991 were used. Questionnaires were mailed to 5103 families within three months of the twins' third birthday. After two to three months reminders were sent and four months after the initial mailing persistent non-responders were contacted by phone. Families whose address was not available were included in the nonresponse group. A response rate of 78.7 % was obtained (N = 4016 families). 60 twin pairs were excluded from the analyses because either one or both of the children had a disease or handicap that interfered severely with daily functioning. Another 303 twin pairs were excluded because questionnaire items of either one or both of the children were missing.

Zygosity was determined for 880 same-sex twin pairs by DNA analyses or blood group polymorphisms (tests were administered for 719 twin pairs by the NTR, and for 161 twin pairs (of whom the NTR had no zygosity data available) by their parents). For all other same-sex twin pairs zygosity was determined by discriminant analysis, using questionnaire items. The discriminant function was created using 784 same-sex twin pairs, for which both DNA/blood results and questionnaire items were available. Around the twins' fifth birthday mothers, and around their seventh birthday both mothers and fathers, completed a zygosity questionnaire. 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, by family, or by 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. The discriminant analysis resulted in a 93.5 % correct classification, suggesting that at most 3 % of the twins' zygosity was wrongly classified ((6.5 % × (4016 - 880 - 1284)) (dizygotic opposite sex twins not included in group with DNA/blood data or in discriminant analysis) / 4016). Zygosity could not be determined for 152 twin pairs because neither the results from DNA/blood analyses, nor the zygosity questionnaires were available. These twin pairs were excluded from the study.

This left a sample of 567 monozygotic males (MZM), 596 dizygotic males (DZM), 654 monozygotic females (MZF), 521 dizygotic females (DZF), and 1163 dizygotic opposite sex (DOS) twin pairs. For half of the sample both mothers and fathers had been asked to complete a CBCL, and for the other half of the sample only mothers had been asked to reply. Therefore data could be further divided into twin pairs for which both mothers and fathers had replied (293 MZM, 303 DZM, 333 MZF, 261 DZF, 547 DOS) and twin pairs for which only mothers had replied (274 MZM, 293 DZM, 321 MZF, 260 DZF, 616 DOS).

Measures

The Child Behavior Checklist (CBCL 2/3) (Achenbach, 1992) was developed for parents to score the behavioral and emotional problems of their 2- and 3-year-old children. It consists of 100 problem items that are scored by the parents on a 3-point scale based on the occurrence of the behavior during the preceding 2 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. Dutch syndrome scales and comparability with the syndrome scales as developed by Achenbach (1992) are reported by Koot et al. (1997). In this paper the two broad-band scales Internalizing and Externalizing are analyzed. The Internalizing scale consists of the Anxious and Withdrawn/Depressed subscales. The Externalizing scale consists of the Aggressive, Oppositional, and Overactive subscales. For the Internalizing scale subjects were only included if not more than 1 item was missing for the Anxious, and not more than 2 items were missing for the Withdrawn/Depressed scale. For the Externalizing scale the inclusion

criterion was not more than 1 item missing for the Aggressive and the Overactive and not more than 3 items for the Oppositional scale. This ensured that the two syndrome scales were always composed of all problem behaviors loading on that scale.

The data were square-root transformated 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 & Kaplan, 1985).

The twin method

Data from monozygotic and dizygotic twins were used to decompose the scores on the Internalizing and Externalizing scales into a contribution of the additive effects of many genes, environmental influences that are shared by twins (like style of parenting, socioeconomic level, or religion) and environmental influences that are not shared by twins (such as an illness, relationships with peers, or measurement errors). For a summary of the twin method, the various assumptions, and the plausibility of these assumptions see Eaves (1982); Falconer (1989); Kendler and Eaves (1986); Martin and Eaves (1977); Neale and Cardon (1992); Plomin et al. (1990); for a short explanation in relation to children's problem behaviors see Van der Valk et al. (1999).

The relative importance of the additive genetic, shared environmental, and nonshared environmental variance components can be derived from the resemblance between MZ twins who are genetically identical and DZ twins who share on average half of their genes. 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 correlation between MZ twins is smaller than 1. Assuming additive genetic variance so that the genotypic correlation is .5 for DZ twins, the proportion of variance explained by each component can be calculated as follows: genetic variance = $2 \times (r_{mz} - r_{dz})$, shared environmental variance = $2 \times r_{dz} - r_{mz}$, and nonshared environmental variance = $1 - r_{mz}$.

To decompose the variance shared by both parents, the correlation between the twins rated by different raters (cross-correlation) has to be used. This way, the variance is decomposed

into additive genetic, shared environmental, and nonshared environmental contributions for which both parents agree. The decomposition can again be made by comparing the resemblance of MZ twins versus DZ twins. Genetic effects are indicated when the cross-correlation is higher for MZ twins compared to DZ twins. Shared environmental effects are indicated if the cross-correlations are larger than zero after the genetic effects have been partialled out, and a nonshared environmental contribution is indicated when the cross-correlations for MZ twins is smaller than the interparent correlation. Similar formulas to the ones discussed above for the variances can again be used to compute the contributions of each component: 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 = interparent correlation - $r_{mz\text{-}cross}$.

The above discussed formulas indicate that the whole 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. For this purpose Hewitt et al. (1992) proposed a Rater Bias (see Figure 3.1) and Psychometric model (see Figure 3.2).

Structural equation modeling of twin data rated by more than one rater

In the Rater Bias model (Hewitt *et al.*, 1992) the phenotypes of the twins are a function of three common factors underlying the ratings of both mothers and fathers: a genetic factor (A), a shared environmental factor (C), and a nonshared environmental factor (E). In addition to these three common factors unique factors are modeled: a maternal rater bias factor, a paternal rater bias factor, and residual (unreliability) factors affecting each rating. The influence of the common factors (A, C, and E) is assumed to be independent of the maternal and paternal rater bias and unreliability factors.

The Psychometric model (Hewitt *et al.*, 1992) also estimates for the behavioral view common to both parents the influence of a common genetic (A), a common shared environmental (C), and a common nonshared environmental factor (E). These three common

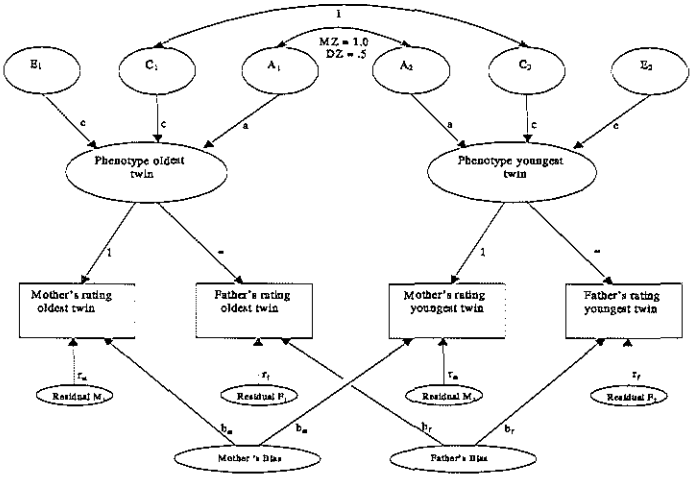

Figure 3.1 *Rater bias model.*
Rater Bias model for ratings of a pair of twins (oldest and youngest twin) by their parents. Mother's and Father's observed ratings (in squares) are linear functions of the latent phenotypes of the twins, mother's and father's bias, and residual errors (M = mother, F = father). Latent phenotypes of the twins are influenced by A, C, and E, representing genetic, shared environmental, and nonshared environmental factors.

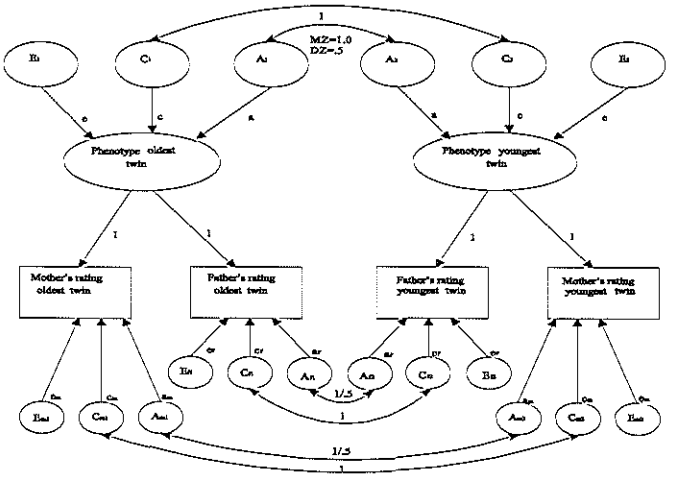

Figure 3.2 *Psychometric model.*
Psychometric model for ratings of a pair of twins (oldest and youngest twin) by their parents. Mother's and Father's observed ratings (in squares) are linear functions of the latent phenotypes of the twins, and rater specific variance. Latent phenotypes of the twins are influenced by common (i.e. across both parents) A, C, and E, representing common genetic, common shared environmental, and common nonshared environmental factors. Rater specific variance is made up of unique (i.e. to each parent) A, C, and E, representing unique genetic, unique shared environmental, and unique nonshared environmental factors.

factors loading on the twins' phenotypes contain only reliable trait variance, causing the common nonshared environmental factor to contain only pure idiosyncratic environmental effects (McArdle & Goldsmith, 1990) and the common shared environmental factor to contain only pure shared familial environmental effects. In addition the model estimates for the behavioral view unique to one parent three unique factors, a unique genetic ($A_{m/f}$), a unique shared environmental ($C_{m/f}$), and a unique nonshared environmental factor ($E_{m/f}$). In this model disagreement between parents can either be caused by parent's unique behavioral views, leading to different but valid information of each rater, or by rater bias and/or unreliability. Rater bias will confound the unique shared environmental effects, while unreliability will confound the unique nonshared environmental effects.

Model fitting

The program Mx (Neale, 1997b) was used to analyze the data through a simultaneous analysis of the 4 × 4 variance-covariance matrices of the five zygosity by sex twin groups (MZM, DZM, MZF, DZF, DOS) where both mother and father ratings were available, and the 2 × 2 variance-covariance matrices of the five zygosity by sex twin groups with only mother ratings. The model describes the observed variance-covariance matrices adequately when the residual variance-covariance matrices are trivially small. A good model is indicated by a low non-significant χ^2 test statistic ($P > .05$). Apart from the χ^2 test statistic, Akaike's Information Criterion (AIC = χ^2 - 2 × degrees of freedom) was computed. The lower the AIC the better the fit of the model to the observed data. Although the Rater Bias model and the Psychometric model do not form a nested pair, they may be compared in terms of parsimony and goodness of fit because they represent alternative sets of constraints on a more general model (Neale & Cardon, 1992).

Fitting the Rater Bias and Psychometric model of Hewitt et al. (1992) to the data showed which model described the processes involved in either agreement or disagreement between the parental ratings best. Monozygotic twin covariances and dizygotic twin covariances were modeled, assuming a correlation between the twins' shared environmental factors of 1.0, regardless of twin type, and a genotypic correlation of 1.0 for monozygotic twins and 0.5 for dizygotic twins. Estimates for male and female twins were allowed to differ. This model was

further examined for possible simplifications. It was tested whether the common and/or unique factors could be removed from the model, whether estimates for boys and girls could be constrained to be the same, and if the unique factors for mothers and fathers could be constrained to be equal. The only factor that was never dropped from the model was the unique nonshared environmental factor, because apart from the influences of idiosyncratic experiences, measurement errors are also estimated in this factor.

Results

Description of the data

For half of the sample both mothers and fathers, and for the other half of the sample only mothers were asked to complete a CBCL. Oneway ANOVA indicated that the ratings for the "mothers only" group did not differ from the mothers in the "mothers and fathers" group. Thus in the analyses, no differences had to be made between mothers who were asked to complete a CBCL alone and mothers who were asked to complete a CBCL while the fathers also filled out a questionnaire. When calculating the means, standard deviations and correlations both types of mothers were taken as one group. During model fitting, estimates of the "mothers only" group were constrained to be equal to the estimates of the mothers in the "mothers and fathers" group.

The untransformed mean problem scores and standard deviations of the twin sample and those of a Dutch community sample of 2- and 3-year-old children (Koot, 1993) are given in Table 3.1. For both the Internalizing and Externalizing scale, the ratings given to the twins were quite similar to the ratings given to the Dutch community sample. In a previous study, a comparable level of problem behaviors between 2- and 3-year-old twins and singletons was also found for the subscales of the CBCL and for the Total Problem score (Van den Oord *et al.*, 1995). Within the twin group, Oneway ANOVA showed no significant mean differences between MZ and DZ twin pairs for boys (MZM vs DZM) or for girls (MZF vs DZF), neither for maternal nor for paternal ratings. Comparing boys and girls (MZM vs MZF, and DZM vs DZF), both mothers and fathers gave significantly higher ratings to the boys for the Externalizing scale (MZ: Mothers: F=30.383, df=1, 2512, p=.000; Fathers: F=19.413 df=1,

Table 3.1 *Means (standard deviations) and sample sizes for the Internalizing and Externalizing scale, in a 3-year-old twin (per zygosity) and a 2- and 3-year-old Dutch community sample.*

	MALES				FEMALES			
	Twins			Commun.	Twins			Commun.
	MZM	DZM	DOS		MZF	DZF	DOS	
Internalizing								
Mothers	4.66 (4.05)	4.51 (4.00)	4.59 (4.02)	4.5 (4.4)	4.85 (4.22)	4.74 (4.00)	3.97 (3.88)	4.3 (3.6)
Fathers	4.38 (3.69)	4.53 (4.09)	4.50 (3.93)		4.55 (3.94)	4.81 (4.08)	3.74 (3.75)	
N children M/F	1168 / 657	1212 / 672	1193 / 628	215	1347 / 744	1072 / 591	1196 / 617	205
Externalizing								
Mothers	17.82 (10.50)	16.69 (9.79)	16.00 (10.05)	17.5 (9.5)	15.55 (10.16)	15.02 (9.73)	13.93 (9.49)	16.5 (8.8)
Fathers	16.95 (10.24)	15.94 (9.54)	15.05 (9.79)		14.65 (9.36)	14.44 (9.43)	13.61 (9.19)	
N children M/F	1167 / 657	1211 / 669	1195 / 628	215	1347 / 744	1072 / 592	1198 / 617	205

Note. MZM/DZM = Monozygotic/Dizygotic males, MZF/DZF = Monozygotic/Dizygotic females, DOS = Dizygotic opposite sex, Commun.= Dutch community sample, N children M/F = number of children for Mothers (M) and Fathers (F).

1399, p=.000; DZ: Mothers: F=16.618, df=1, 2281, p=.000; Fathers: F=7.867, df=1, 1259, p=.005). For the Internalizing scale ratings for boys and girls did not differ. Comparing mother and father ratings, a paired T-Test showed that the ratings for the Externalizing scale given by mothers were significantly higher than ratings given by fathers for both boys and girls (boys: T=4.997 df=1823, p=.000; girls: T=4.848, df=1817, p=.000). For the Internalizing scale no differences were found. Thus, MZ and DZ twin pairs were not rated differently, allowing to use the twin data for genetic analyses. Boys did receive higher ratings than girls for the Externalizing scale. For this same scale, Mothers gave higher ratings to their twin children than fathers did, implying possible rater differences. For the Internalizing scale no differences between boys and girls or between mothers and fathers were found.

The homogeneity of the variance was tested with Mx (Neale, 1997b). No differences could be found in the variances and covariances of MZM, DZM, MZF, DZF, and DOS, neither for the Externalizing scale nor for the Internalizing scale. Because the variances did not differ depending on zygosity, siblings were not expected to influence each others behaviors (sibling interactions).

Table 3.2 *Correlations (ratings given by the same rater), and cross-correlations (ratings given by different raters) between the twins and the interparent correlations, per zygosity, for 3-year-olds and sample sizes.*

	Internalizing scale						Externalizing scale							
	same rater		different raters				same rater		different raters					
	Twins		Twins		Interparent		Twins		Twins		Interparent		sample sizes[a]	
	M/M	F/F	M/F	F/M	O	Y	M/M	F/F	M/F	F/M	O	Y	M	M+F
MZM	.65	.65	.49	.49	.63	.61	.79	.75	.61	.59	.71	.66	274	293
DZM	.37	.39	.27	.24	.69	.65	.58	.49	.38	.38	.72	.74	293	303
MZF	.73	.71	.55	.52	.66	.67	.81	.78	.61	.63	.71	.72	321	333
DZF	.35	.43	.27	.22	.70	.64	.53	.41	.26	.35	.67	.71	260	261
DOS	.36	.39	.29	.26	.63	.64	.51	.49	.38	.33	.67	.69	616	547

Note. MZM/DZM = monozygotic/dizygotic males, MZF/DZF = monozygotic/dizygotic females, DOS = dizygotic opposite sex twins. Same rater Twins = correlation between the oldest and youngest twin, rated by M/M = mothers or F/F = fathers. Different raters Twins = cross-correlation: either oldest twin rated by mothers and youngest by fathers (M/F) or the other way around (F/M). Different raters Interparent: O = correlation between mother and father ratings for the oldest child; Y = idem for the Youngest child. Sample sizes[a]: M = number of twin pairs rated by mothers only, sample sizes M+F = number of twin pairs rated by both mothers and fathers.

Twin correlations

Table 3.2 shows, for both the Internalizing and Externalizing scale, in the first and second column the correlations between the twins rated by the same rater (mother *or* father rated both children), and in the third and fourth column the cross-correlations between the twins each rated by a different rater (mother *and* father each rated one child). In the fifth and sixth column the interparent correlations between mothers and fathers is given, both for oldest and youngest twin. The interparent correlations were comparable for both oldest and youngest twin for all zygosity by sex groups.

The correlations between the oldest and youngest twins both rated by mothers (M/M; first column) and those both rated by fathers (F/F; second column) can be used to obtain a first estimate of the genetic influences (h^2), the shared environmental influences (c^2), and the nonshared environmental influences (e^2) on the total variance. For instance, if we take for the Internalizing scale the first column "M/M": the genetic influences for boys can be estimated as $(r_{MZM} - r_{DZM}) \times 2 = (.65 - .37) \times 2 = .56$. Nonshared environmental influences for boys can be estimated as $(1 - r_{MZM}) = (1 - .65) = .35$. Following the shared environmental influences for boys can be estimated as $(2 \times r_{DZM}) - r_{MZM} = (2 \times .37) - .65 = .09$. For girls, father ratings of the Internalizing scale, and mother and father ratings of the Externalizing scale, the correlations between the MZ and DZ twin pairs can be compared in similar ways to obtain a first impression of the genetic and environmental influences.

Table 3.3 *Univariate estimates of genetic and environmental influences on Internalizing and Externalizing Problems rated for 3-year-old twins.*

	Internalizing Problems		Externalizing Problems	
	Mothers	Fathers	Mothers	Fathers
Genetic	69 %	59 %	52 %	56 %
Shared		10 %	27 %	19 %
Nonshared	31 %	31 %	21 %	25 %

Fitting univariate models (one for mother ratings of Internalizing, one for father ratings of Internalizing, one for mother ratings of Externalizing, and one for father ratings of Externalizing) that estimated three factors: A, C, and E and possible sex differences, the obtained results were comparable to those calculated by comparing the MZ and DZ

correlations. Take for example the Internalizing scale rated by mothers. As shown in Table 3.3, no differences between boys and girls were found. The genetic factor explained 69% of the variance and the nonshared environmental factor explained 31%. Using a model fitting approach, no significant shared environmental influences were found.

Univariate analyses make a decomposition of the total variance in genetic, shared environmental, and nonshared environmental factors. To take rater differences into account, the information from the twin's cross-correlations has to be used. By calculating cross-correlations between mother ratings of oldest twins with father ratings of youngest twins (M/F; third column of Table 3.2) or the other way around (F/M; fourth column), one can make a decomposition of the variance on which both kinds of raters agree. The difference between the decomposition of the variance shared between raters (i.e. common view) and the decomposition of the total variance can be used to estimate the genetic, shared environmental, and nonshared environmental influences on the variance uniquely rated by one particular rater (i.e. unique view). Take for instance for the Internalizing scale: the cross-correlations between mother ratings of oldest twins and father ratings of youngest twins (M/F) for boys. The same comparisons between the r_{MZ} and r_{DZ} can be made to estimate the genetic influences on the variance shared by raters, namely $2 \times (r_{MZM\text{-}cross} - r_{DZM\text{-}cross}) = (.49 - .27) \times 2 = .44$. Thus we can conclude that the total genetic variance of 56% can be divided into a genetic influence for behaviors that are similarly rated by the parents of 44% and a genetic influence for behaviors that are uniquely rated by mothers of 12%. This shows that genes of the child affect the unique part of the maternal ratings, implying that the parental disagreement is not merely caused by measurement errors but that mothers in addition to the common view also assess a valid unique part of the child's behavior. Finding genetic influences for behaviors that are differently rated by mothers and fathers does not seem to be a chance finding, but arises systematically in the data. Also for the father ratings of boys and for the mother and father ratings of girls, both for the Internalizing and Externalizing scale, similar unique genetic effects are found.

To estimate the environmental influences on the variance shared by raters the interparent correlations (fifth and sixth columns for oldest and youngest twin, respectively) have to be used. Table 3.2 shows that for the Internalizing scale the interparent correlation (between

mothers and fathers of the same child) in the MZM group was .63 for the oldest twin. The cross-correlation (between mothers and fathers of different children) was .49, indicating a nonshared environmental contribution on the variance shared by raters of: interparent correlation - $r_{mzm\text{-}cross}$ = .63 - .49 = .14. Thus the nonshared environmental influences can be divided into an influence for behaviors that are similarly rated by both parents of 14% and an influence for behaviors that are uniquely rated by mothers of 21% (i.e. 35% - 14%). Shared environmental influences on the variance shared by raters can be estimated as (2 × r_{DZM}) - r_{MZM} = (2 × .27) - .49 = .05. Taking rater differences into account the shared environmental influences can be divided into an influence for behaviors that are similarly rated by the parents of 5% and an influence for behaviors that are differently rated by mothers of 4% (i.e. 9% - 5%). For the cross-correlations of father ratings for boys, mother and father ratings for girls, and all ratings of the Externalizing scale, similar comparisons can be made.

Table 3.4 *Model fitting statistics for Psychometric and Rater Bias model and simplification of best fitting (Psychometric) model, for 3-year-old twins' Internalizing and Externalizing Problems.*

	Internalizing Problems							Externalizing Problems						
	χ^2	df	p	AIC	χ^2diff.	df	p	χ^2	df	p	AIC	χ^2diff.	df	p
Overall model:														
Psychometric model	**58.295**	**47**	**.125**	**-35.71**				**56.616**	**47**	**.159**	**-37.38**			
Rater Bias model	81.761	49	.002	-16.24				85.607	49	.001	-12.39			
Simplification of overall model:														
Factor estimates:														
No common genetic effects	235.911	49	.000	137.91	177.616	2	.000	284.837	49	.000	186.84	228.221	2	.000
No unique genetic effects	84.26	51	.002	-17.74	25.965	4	.000	87.722	51	.001	-14.28	31.106	4	.000
No common shared environment	**58.845**	**49**	**.158**	**-39.16**	**0.55**	**2**	**.760**	89.651	49	.000	-8.35	33.035	2	.000
No unique shared environment	72.67	51	.025	-29.33	14.375	4	.006	108.344	51	.000	6.34	51.728	4	.000
No common nonshared environment	378.837	49	.000	280.84	320.542	2	.000	471.444	49	.000	373.44	414.828	2	.000
Sex differences:														
No sex differences common effects	59.928	50	.159	-40.07	1.633	3	.652	59.751	50	.163	-40.25	3.135	3	.371
No sex differences unique effects	65.825	53	.111	-40.18	7.53	6	.275	63.253	53	.158	-42.75	6.637	6	.356
No sex differences common + unique	**71.032**	**56**	**.085**	**-40.97**	**12.737**	**9**	**.175**	**69.166**	**56**	**.111**	**-42.83**	**12.55**	**9**	**.184**
Rater differences:														
Unique rater effect: mother-father identical	**66.587**	**53**	**.099**	**-39.41**	**8.292**	**6**	**.217**	**67.635**	**53**	**.085**	**-38.37**	**11.019**	**6**	**.088**
Simplified model:	**78.852**	**60**	**.052**	**-41.15**				**78.766**	**59**	**.044**	**-39.23**			

Rater models

As indicated by the lower χ^2 test statistic and the lower AIC in Table 3.4, the Psychometric model fitted the data better than the Rater Bias model both for the Internalizing and the Externalizing scale. This signified that although both parents partially assessed the same behaviors, there also was a component which was unique to each rater. For sake of

comparison we also performed a Cholesky or triangular decomposition (also called a Biometric model). This model can be viewed as a psychologically less informative rotation of the Psychometric model (Hewitt *et al.*, 1992). It assumes that each parent only assesses on unique aspects of the child's behavior. Parental ratings may be correlated but for unspecified reasons. This view may be appropriate if mothers and fathers only report on behaviors observed in distinct situations, or if they do not share a common understanding of the behavioral descriptions. Neither for the Internalizing scale nor for the Externalizing scale did this saturated model fit the data any better than the Psychometric model. The high p-values obtained for the Psychometric model of both problem scales were remarkable, especially when considering the large sample size used (Neale, 1997b). This indicated a very good fit of the model to the data.

The Psychometric model was further examined for possible simplifications. Only the common shared environmental factor could be omitted from the model for the Internalizing scale. For the Externalizing scale none of the common or unique factors could be omitted. Other model simplifications worked for both scales. Between boys and girls, the estimates of the common and the unique factors could be constrained to be equal. Between mother and father ratings of a sibling only the estimates of the unique factors could be constrained to be equal. The fit of the most simplified model is given in Table 3.4.

Table 3.5 *Genetic and environmental influences, estimated using best fitting Psychometric model, for Internalizing and Externalizing Problems rated for 3-year-old twins.*

	Internalizing	Externalizing
Genetic factor:		
common genetic factor	57 %	47 %
unique genetic factor	9 %	7 %
Shared environmental factor:		
common shared environment		18 %
unique shared environment	5 %	8 %
Nonshared environmental factor:		
common nonshared evironment	16 %	12 %
unique nonshared environment	13 %	8 %

The percentages of variance explained by the common and unique genetic, shared, and nonshared environmental factors are given in Table 3.5. A major part of the variance was explained by common factors. For both the Internalizing and the Externalizing scale the

largest part of the variance was explained by the common genetic factor, explaining 57% and 47% respectively. The common nonshared environmental factor explained 16% of the variance for the Internalizing scale and 12% for the Externalizing scale. The common shared environmental factor only had an influence on the Externalizing scale, explaining 18% of the variance. The unique factors explained a relatively small part of the variance. For the Internalizing scale unique genetic factors explained 9%, unique shared environmental factors explained 5%, and unique nonshared environmental explained 13% of the variance. For the Externalizing scale unique factors also explained relatively small parts of the variance, of respectively 7% genetic influence, 8% shared, and 8% nonshared environmental influences.

Discussion

We examined the processes underlying agreement and disagreement between maternal and paternal ratings and, using a model that best fitted the data, studied the etiology of the Internalizing and Externalizing scale, employing a sample of 3501 Dutch 3-year-old twin pairs. The Psychometric model (Hewitt *et al.*, 1992) fitted the data significantly better than the Rater Bias model, implying that although both parents partially assessed the same behaviors in their children, there also was a component which was unique to each rater. These results are in agreement with the results of Hewitt et al. (1992), who also found a good fitting of the Psychometric model for both their prepubertal (8 to 11 years) and their pubertal (12 to 16 years) cohort of twin pairs. Also Rowe and Kandel (1997), although not fitting Psychometric and Rater Bias models, found that mother and father ratings contained a component that was unique to one rater in addition to a shared behavioral view.

When a Psychometric model fits genetically informative data better than a Rater Bias model, unique genetic factors can be estimated for behaviors that are differently assessed by the diverse raters. If unique genetic factors are estimated in a model, systematic effects must exist in the data that are not expected when differences between parental ratings are only caused by rater bias and unreliability. Thus, because unique genetic factors were estimated in the present study the conclusion must be that the observed rater differences are the result of the fact that raters really do assess different aspects of the child's behavior. As was already

suggested by Achenbach, et al. (1987) unique interactions between a certain parent and the child might allow each parent to provide additional information about the child's behavior, apart from the information on which they both agree. It thus seems important to collect data from multiple informants. As outlined by Achenbach (1992) "because any reports by any informants may be affected by characteristics of the informants, as well as by their own particular knowledge of the child's behavior, no single informant's reports can provide a complete picture".

The genetic and environmental influences were estimated while the underlying processes causing agreement or disagreement between the individual raters were taken into account. By taking these effects along in the model, more accurate estimates of genetic and environmental influences were obtained. The common genetic, shared and nonshared environmental factors, influencing behaviors similarly assessed by both parents, explained the largest part of the variance (around 75%). Thus, although each parent does assess unique aspects of the children's behaviors, most of the behaviors are similarly assessed by both parents. Common genetic factors explained about 50% of the variance of both the Internalizing and Externalizing scale, implying a possible inborn vulnerability.

Decomposing the genetic, shared, and nonshared environmental influences into common and unique factors allowed to estimate the common shared and nonshared environmental factors apart from rater bias and unreliability. The common nonshared environmental factor explained 14% of the variance, indicating a pure independent environmental effect on the Internalizing and Externalizing scales that cannot be explained by measurement error or unreliability. Thus, already for children as young as three years of age, idiosyncratic experiences seem to be influencing their behaviors. The common shared environmental factor explained 18% of the variance, suggesting that for the Externalizing scale there is a pure shared environmental influence that is not confounded by rater bias. The importance of shared environmental influences for externalizing behaviors have been demonstrated by various epidemiological studies. Family discord and disruption, lack of affection and poor supervision all predispose to conduct disturbance and antisocial behavior (Rutter, 1985). However, often it is not family adversity as such but its persistence that predicts chronic problems (Campbell, 1995). To detect shared environmental effects for 3-year-old children

thus seems a remarkable finding. An alternative explanation might be that the siblings have been imitating each others behaviors. Even though the variances and covariances were found to be the same for all five twin groups (MZM, DZM, MZF, DZF, DOS), in a previous study we did find a small influence of sibling interactions (Van der Valk *et al.*, 1998b). Sibling interactions for externalizing behaviors have also been found by Hewitt et al. (Neale & Cardon, 1992) for a sample of 8 to 16-year-old twins. If siblings imitate each other's externalizing behaviors, the estimates of the common shared environmental factor for the Externalizing scale might be inflated. Another explanation might be correlated rater bias, like for instance parents copying each others answers. However, this explanation seems not very likely. For if this would have been the case, the same common shared environmental influence should also have been found for the Internalizing scale, because the items of the Internalizing and Externalizing scales were mixed on the CBCL.

Unique genetic, shared, and nonshared environmental factors, influencing behaviors differently rated by the parents, each explained around 8% of the variance for both scales. Rater bias and unreliability, if present, were included in the estimates of these unique factors. Probably these small unique effects were only detected because this study used a large sample of 3501 twin pairs. Rater bias may have confounded the estimates of the unique shared environmental factors. Nevertheless, considering the modest influence of the unique shared environmental factors of 5% and 8% for the Internalizing and Externalizing scale, respectively, these possible effects of rater bias were small. This result contrasts with the findings of Neale and Stevenson (1989) and Simonoff et al. (1998). These two studies tested for the possible influence of rater bias and found this influence to be significant. Maybe this difference emerged because of the subject studied. Neale and Stevenson (1989) investigated temperament in 3.5-year-old twins and Simonoff et al. (1998) examined hyperactivity in 8- to 16-year-old twins. For temperament and activity measures, it is common to find DZ twin correlations that are too low. Simonoff et al. (1998) examined this phenomenon and found that these too low DZ correlations were not caused by siblings influencing each other, but by parental rater bias (parents contrasting the twins when rating their hyperactivity). Possibly for the Internalizing and Externalizing scale parents do not contrast their children's behaviors. However, the difference may also have emerged because the various questionnaires used

possibly differed in their sensitivity for rater bias. The current study used the CBCL (Achenbach, 1992), while Neale and Stevenson (1989) used EASI temperament scales (Buss & Plomin, 1975), and Simonoff et al. (1998) used three hyperactivity items from the Rutter A questionnaire (Rutter *et al.*, 1970).

Unreliability and measurement error may have confounded the estimates of the unique nonshared environmental factors. Nevertheless, considering the small size of these estimates of 13% and 8% for the Internalizing and Externalizing scale, respectively, also these effects cannot have been strong. Possibly measurement error and unreliability were low because of the high internal consistency shown by the Dutch factor solution of the CBCL (Koot *et al.*, 1997). Cronbach's alphas are for the Externalizing scales: Aggressive .82, Oppositional .91, Overactive .78, and for the Internalizing scales: Withdrawn/Depressed .64, Anxious .83.

Neither sex differences, nor distinct estimates for mothers and fathers for the unique factors were needed. The behaviors of 3-year-old children are predominantly influenced by the child's genotype. Parental guidance in this case may not be so much dependent on the parents own values and ideas, but may be much more directed by the child's genotype. Maybe parents can only then guide the child's behavior, when the child is somewhat older, able to understand other peoples values and can direct its behavior accordingly. This could mean that at such a young age, the genotype of the child determines what kind of environmental influences the child experiences. In the literature there is cumulating evidence that genotype-environment correlations are important for children's development. For example, a number of studies have shown that when environmental measures (such as parenting behaviors) are used as the dependent variable in a behavior genetic analysis, the correlations between environmental measures of relatives increases with the degree of genetic relatedness (Braungart *et al.*, 1992; Goodman & Stevenson, 1991; Plomin *et al.*, 1994; Rende *et al.*, 1992). This suggests that environmental measures tend to reflect the differential genetic resemblance of relatives and that they are dependent on the genetic propensities of individuals. A correlation between genotype of the child and environmental influences was not incorporated in the model and thus could have inflated the genetic estimates.

If at a young age the genotype of the child determines the environmental influences the child experiences, a relatively high genetic estimate with smaller shared and nonshared

environmental estimates would be expected. Subsequently, when the child matures, parental guidance may become less directed by the child's genotype and more by the parent's own values and ideas. If this is correct, estimates of environmental influences will then increase for schoolaged children compared with preschool children.

This paper used a nonclinical sample of twin pairs, showing problem behaviors in the normal range. Whether similar results apply to clinical populations, showing problem behaviors in an extreme range, remains to be explored. Also, estimates found using quantitative genetic techniques do not pertain to the individual but involve average differences between individuals in the population. For other populations, or for specific individuals, different estimates might be applicable. Even though large genetic influences were found for both problem scales, implying a possible inborn vulnerability for children with problem behaviors, this does not mean that those behaviors are unchangeable. The finding of genetic effects implies hereditary propensities, not predestination (Plomin & Daniels, 1986).

4

Using Common and Unique Parental Views to Study the Etiology of 7-Year-Old Twins' Internalizing and Externalizing Problems

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This chapter is a slightly revised version of an article which is currently in review.

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Abstract

In a sample of 1940 Dutch 7-year-old twin pairs we studied the etiology of Internalizing and Externalizing Problems, while taking account of the processes underlying agreement and disagreement between maternal and paternal ratings. For both scales the Psychometric model fitted the data better than the Rater Bias model. This implied that rater differences did not merely reflect measurement errors, but were also the result of parents assessing different aspects of the child's behavior. Common factors (influencing behaviors similarly assessed by both parents) were more important than unique factors (influencing behaviors uniquely assessed by one parent). Genetic factors were most important for the Externalizing scale, explaining over 50% of the variance. For the Internalizing scale genetic factors explained around 35% of the variance. Shared environmental factors explained around 32% of the variance of the Externalizing scale and around 34% of the variance of the Internalizing scale. Rater bias and unreliability, if present in the data, were included in the estimates of the unique factors, which explained between 4% and 14% of the variance.

Keywords

behavior genetics, children, Child Behavior Checklist, problem behavior, multiple informants, twins.

Introduction

Research conducted during the last three decades has shown the medium prevalence for problem behaviors in children to be 13% (Verhulst & Koot, 1992a). The majority of studies have reported that girls tend to show more internalizing or emotional problems, whereas boys are more inclined to show externalizing or disruptive behavior problems. To get a better understanding of the etiology of children's problem behaviors quantitative genetic studies can be carried out. Comprehending the etiology of individual differences in children's problem behaviors is important, for it may guide clinical interventions and provide ideas for future research. Also, knowing the relative genetic and environmental influences can help future gene finding studies.

To study children's behaviors parental descriptions are often used. Parents observe the child in natural situations at home and in the playground and so are a useful source of information. However, although ratings of mothers and fathers are usually correlated, they may not be completely interchangeable (Achenbach *et al.*, 1987). Rater differences occur because parental reports of children's behaviors are a function of both the parent and the child. As noticed by Neale and Cardon (1992) each parent has a different situational exposure, a different degree of insight, and a different perception, evaluation and normative standard that may create rater differences of various kinds in reporting behaviors. Therefore, when using parental ratings disentangling the child's phenotype from that of the parent becomes an important methodological problem. For the analysis of genetic and environmental contributions to children's behavior, solutions to this are available when multiple raters, e.g., two parents, rate multiple children, e.g., twins (Neale & Cardon, 1992). To disentangle the child's phenotype from that of the rater Hewitt et al. (1992) proposed so called Rater Bias and Psychometric models.

The Rater Bias model (shown in Figure 4.1) assumes that parents assess exactly the same behaviors in the child and share a common understanding of the behavioral descriptions. Disagreement between the raters is regarded as error, resulting from rater bias and/or unreliability. The Psychometric model (shown in Figure 4.2) assumes that, in addition to the common view, parents assess a unique aspect of their child's behavior. For instance, the

parent who usually brings the child to school may also be familiar with the quality of the child's relations with classmates, which appears to be related to behavior problems such as depression and aggression (Newcomb *et al.*, 1993; Parker & Asher, 1987). Moreover, each parent may interact differently with the child (Achenbach *et al.*, 1987). In the Psychometric model, disagreement between the parents arises therefore not only because of error but also because each informant provides from his own perspective different but valid information on the child's functioning.

With genetically informative twin data it is possible to discriminate between these two models of rater (dis)agreement. For in the Rater Bias model the unique aspect of each parent's assessment is a function of rater errors only, whereas in the Psychometric model genetic effects can influence the unique aspects of parental assessment as well. Because errors cannot cause the systematic effects necessary for a model to estimate genetic effects, behaviors uniquely observed by only one parent must reliably exist when genetic influences for unique aspects of parental assessment are found.

Several studies have investigated the etiology of problem behaviors in children using the Child Behavior Checklist (CBCL) (Silberg *et al.*, 1994; Edelbrock *et al.*, 1995; Schmitz *et al.*, 1995; Van den Oord *et al.*, 1996; Zahn-Waxler *et al.*, 1996; Gjone & Stevenson, 1997b; Leve *et al.*, 1998; Van der Valk *et al.*, 1998a; Van der Valk *et al.*, 1998b) but only a few have taken the processes underlying parental disagreement into account. Hewitt et al. (1992) fitted Rater Bias and Psychometric models to the ratings of the Internalizing scale of the Child Behavior Checklist (CBCL; Achenbach, 1991a) of 983 twin pairs. The Psychometric model fitted the data best, both for the prepubertal (8 to 11 years) and pubertal cohort (12 to 16 years). In a previous study (Van der Valk *et al.*, in press), both models were fitted to the CBCL ratings of Internalizing and Externalizing Problems in 4016 Dutch 3-year-old twin pairs. Again, the Psychometric model fitted the data best. Thus, results from both studies implied that mothers and fathers partially assessed the same behaviors, and that in addition, each parent provided his or her own unique information.

In this study we fitted Rater Bias and Psychometric models to mother and father ratings of the CBCL (Achenbach, 1991a) in a large sample of 1940 Dutch 7-year-old twin pairs. The best fitting model was used to estimate the genetic and environmental influences on the

Internalizing and Externalizing scales. An advantage of this procedure is that in the Rater Bias and Psychometric model the part of the child's behavior assessed by both parents cannot be affected by rater bias and measurement error. Thus, whereas rater bias normally inflates estimates of shared environment and measurement error inflates estimates of nonshared environment, by fitting these models accurate estimates can be obtained of the genetic and environmental influences on the Internalizing and Externalizing problem scales. Also, for behaviors differently assessed by mothers and fathers, unique genetic influences can be estimated, allowing heritabilities to vary depending on assessment source.

While growing up, children may show developmental changes and it seems likely that the etiology of problem behaviors changes. Therefore, in order to obtain estimates of genetic and environmental influences on problem behaviors of schoolage children that are not biased by age effects, we studied a homogeneous group of children who were all 7 years of age.

Method

Subjects

All participants were members of 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 *et al.*, 1992; Boomsma, 1998a). For this study, data from all twins from the birth cohorts 1987, 1988 and 1989 were used. Questionnaires were mailed to 2855 families within three months of the twins' seventh birthday. After two to three months reminders were sent and four months after the initial mailing persistent non-responders were contacted by phone. Families whose address was not available were included in the nonresponse group. A response rate of 68% was obtained (N = 1940 families). For 27 twin pairs either one or both of the children had a disease or handicap that interfered severely with daily functioning. These twins were excluded from the analyses. Another 28 twin pairs were omitted because questionnaire items of either one or both of the children were missing.

Zygosity was determined for 639 same-sex twin pairs by DNA or blood group polymorphisms. For the remaining 720 same-sex twin pairs zygosity was determined by

discriminant analysis, using questionnaire items filled out by the mothers. The discriminant function was created using data from 595 twin pairs for which both DNA/blood results and questionnaire items were available. Mothers 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, by family, or by 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. The discriminant analysis resulted in 6% misclassifications. This implied that merely two percent of the total number of twin pairs was wrongly classified: ((6% × 720) / 1940) = 2%. One twin pair had to be excluded from the study because both the DNA/blood results and the questionnaire on zygosity information were missing.

This procedure left a sample of 342 monozygotic males (MZM), 316 dizygotic males (DZM), 360 monozygotic females (MZF), 300 dizygotic females (DZF), and 566 dizygotic opposite sex (DOS) twin pairs. Data were further divided into twin pairs for which both mothers and fathers had completed the CBCL (267 MZM, 233 DZM, 280 MZF, 230, DZF, 421 DOS) and twin pairs for which only mothers had responded (75 MZM, 83 DZM, 80 MZF, 70 DZF, 145 DOS).

Measures

The Child Behavior Checklist (CBCL) (Achenbach, 1991a) is developed for parents to rate the behavioral and emotional problems of their 4- to 18-year-old children. It consists of 20 competence items and 120 problem items. Only the problem items are used in this study. They were scored by the 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.

In this paper the two broad-band syndrome scales Internalizing Problems and Externalizing Problems are analyzed. The syndrome scales were composed according to the 1991 profile (Achenbach, 1991a). The Internalizing scale consists of the Withdrawn, Somatic Complaints, and Anxious/Depressed syndrome scales. The Externalizing scale consists of the Delinquent and Aggressive Behavior syndrome scales. For the Internalizing scale subjects

were only included if not more than 2 items were missing for the Withdrawn and Somatic Complaints scale, and not more than 3 items were missing for the Anxious/Depressed scale. For the Externalizing scale the inclusion criterion was not more than 3 items missing for both the Delinquent and Aggressive Behavior scales. This ensured that the two broad-band syndrome scales were always composed of all syndrome scales loading on that scale.

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

Statistical Analyses

Sample characteristics are presented through means and standard deviations. Oneway ANOVA was used to test for mean differences between monozygotic (MZ) and dizygotic (DZ) twins, between boys and girls, and between ratings of mothers and fathers. The homogeneity of the variance among the five different zygosity by sex twin groups (MZM, DZM, MZF, DZF, DOS) was tested with Mx (Neale, 1997b). Interparent correlations are given, both for the oldest and youngest twin, to indicate agreement between mothers and fathers. Cross-rater twin correlations (mother rating the oldest twin and father rating the youngest twin, or the other way around) are given to indicate the similarity between the twins' problem behaviors upon which both parents agree (common parental view). Intra-rater twin correlations (mother rating both twins or father rating both twins) are given to indicate the association between the twins' problem behaviors as rated by one particular rater. The difference between the intra-rater twin correlation and the cross-rater twin correlation denotes the part which is rated by one particular rater only, also called the unique parental view.

Structural equation modeling (Neale & Cardon, 1992) was used to test for genetic and environmental influences on the Internalizing and Externalizing scale, while taking the effects of rater differences into account. The Rater Bias model (shown in Figure 4.1) and Psychometric model (shown in Figure 4.2) of Hewitt et al. (1992) were fitted to the observed variance-covariance matrices of the five different zygosity by sex twin groups which were

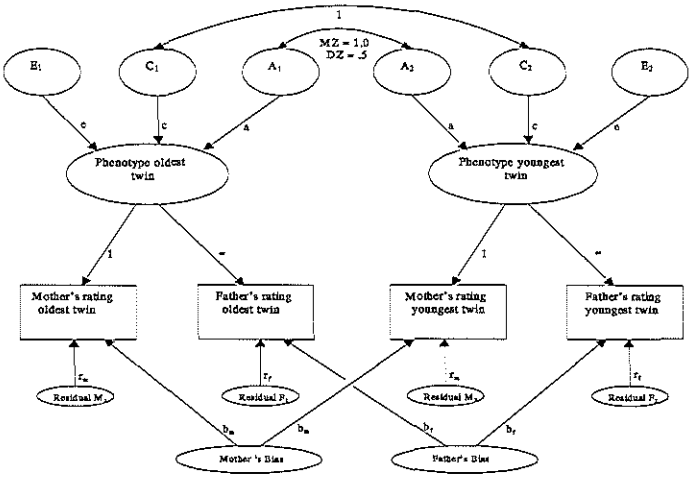

Figure 4.1 *Rater bias model.*
Rater Bias model for ratings of a pair of twins (oldest and youngest twin) by their parents. Mother's and Father's observed ratings (in squares) are linear functions of the latent phenotypes of the twins, mother's and father's bias, and residual errors (M = mother, F = father). Latent phenotypes of the twins are influenced by A, C, and E, representing genetic, shared environmental, and nonshared environmental factors.

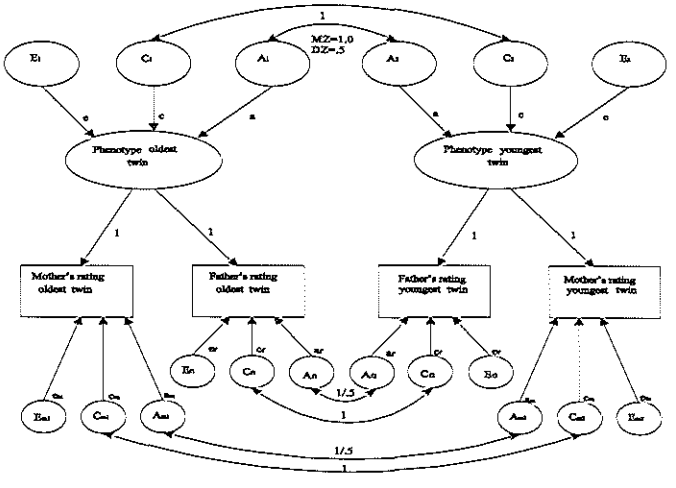

Figure 4.2 *Psychometric model.*
Psychometric model for ratings of a pair of twins (oldest and youngest twin) by their parents. Mother's and Father's observed ratings (in squares) are linear functions of the latent phenotypes of the twins, and rater specific variance. Latent phenotypes of the twins are influenced by common (i.e. across both parents) A, C, and E, representing common genetic, common shared environmental, and common nonshared environmental factors. Rater specific variance is made up of unique (i.e. to each parent) A, C, and E, representing unique genetic, unique shared environmental, and unique nonshared environmental factors.

rated by both mothers and fathers, and simultaneously to the observed variance-covariance matrices of the five different zygosity by sex twin groups which were rated by mothers only. Goodness of fit was assessed by the χ^2 test statistic and Akaike's Information Criterion (AIC). The best fitting model was further examined for possible simplifications by testing if the common and/or unique factors could be removed from the model, if estimates for boys and girls could be constrained to be the same, and if the unique factors for mothers and fathers could be constrained to be equal. For a more detailed description of the models used see Hewitt et al. (1992).

Results

Equating the variances of the ratings of Internalizing and Externalizing Problems in the "mothers only" group and the ratings of the mothers in the "mothers and fathers" group with Mx did not result in a significantly poorer fit. Thus, in the analyses no distinction was made between twins where only the mothers responded and twins where both parents responded. While calculating the means, standard deviations and correlations both types of mothers were treated as one group. During model fitting, estimates of the "mothers only" group were constrained to be equal to the estimates of the mothers in the "mothers and fathers" group.

The untransformed mean problem scores and standard deviations of the twin sample and those of a Dutch norm group (Verhulst *et al.*, 1996) are given in Table 4.1. For both the Internalizing and Externalizing scale, the means in the twins were quite similar to those in the Dutch norm group. Within the twin group, Oneway ANOVA showed no significant mean differences between MZ and DZ twin pairs for boys (MZM vs DZM) or for girls (MZF vs DZF), neither for maternal nor for paternal ratings. Comparing boys and girls (MZM vs MZF and DZM vs DZF), both mothers and fathers gave significantly higher ratings to boys for the Externalizing scale (MZ: Mothers: F=34.794, df=1, 1424, p=.000; Fathers: F=31.73, df=1, 1168, p=.000; DZ: Mothers: F=28.505, df=1, 1243, p=.000; Fathers: F=31.52, df=1, 1000, p=.000). Girls tended to get higher scores than boys for the Internalizing scale, but only for

Table 4.1 *Means (standard deviations) and sample sizes for the Internalizing and Externalizing scale, in a 7-year-old twin group (per zygosity; both for mother's and father's ratings) and a 4- to 11-year-old Dutch norm group (mother's ratings).*

	MALES				FEMALES			
	Twins			Norm group	Twins			Norm group
	MZM	DZM	DOS		MZF	DZF	DOS	
Internalizing								
Mothers	4.39 (4.24)	4.88 (4.86)	4.04 (3.91)	4.52 (4.27)	5.46 (4.92)	5.42 (4.83)	4.25 (4.38)	5.16 (5.02)
Fathers	3.54 (3.76)	3.95 (4.22)	3.18 (3.29)		3.83 (3.77)	4.23 (4.37)	3.40 (3.71)	
N children M/F	686 / 571	625 / 503	567 / 448	579	723 / 584	585 / 483	569 / 446	593
Externalizing								
Mothers	9.42 (7.07)	8.72 (7.05)	8.66 (7.05)	8.26 (6.36)	7.35 (6.21)	6.76 (5.81)	6.06 (5.72)	6.04 (5.57)
Fathers	8.37 (6.80)	8.15 (6.71)	7.53 (6.52)		6.34 (5.50)	5.96 (5.58)	5.00 (5.07)	
N children M/F	694 / 580	643 / 510	575 / 448	579	732 / 590	602 / 492	576 / 446	593

Note. MZM/DZM = Monozygotic/Dizygotic males, MZF/DZF = Monozygotic/Dizygotic females, DOS = Dizygotic opposite sex, N children M/F = Number of children rated by Mothers (M) and Fathers (F).

maternal ratings of MZ twins (MZM vs MZF) did this difference reach significance (F=19.000, df=1, 1407, p=.000). Monozygotic and dizygotic females differed from opposite sex twin pairs in getting higher scores for Internalizing Problems, both for maternal and paternal ratings (MZF vs DOS: Mothers: F=38.458, df=1,1857, p=.000; Fathers: F=7.484, df=1,1483, p=.006; DZF vs DOS: Mothers: F=32.596, df=1,1719, p=.000; Fathers: F=18.364, df=1,1382, p=.000). Monozygotic and dizygotic males differed from opposite sex twin pairs in getting higher scores for Externalizing Problems, both for maternal and paternal ratings (MZM vs DOS: Mothers: F=40.603, df=1,1843, p=.000; Fathers: F=39.341, df=1,1480, p=.000; DZM vs DOS: Mothers: F=16.98, df=1,1792, p=.000; Fathers: F=29.632, df=1,1410, p=.000). It seems that being a member of an opposite sex twin pair buffers against getting high ratings for problem behaviors. Comparing maternal and paternal ratings, a paired T-Test showed that for both the Internalizing and Externalizing scale, maternal ratings were significantly higher than paternal ratings for both boys and girls (Internalizing: boys: T=10.271, df=1479, p=.000; girls: T=12.646, df=1476, p=.000; Externalizing: boys: T=6.960, df=1514, p=.000; girls: T=7.508, df=1508, p=.000). Although a difference between maternal and paternal ratings was not reported for the Dutch norm group (Verhulst *et al.*, 1996), we did find similar differences in a sample of adopted children (Van der Valk, *et al.*, 1998a) (both for the Internalizing and Externalizing scale) and in a sample of preschool twin pairs (Van der Valk, *et al.*, in press) (for the Externalizing scale). In summary, MZ and DZ twins pairs were not rated differently, allowing the twin data to be used for genetic analyses. Boys received higher ratings than girls for the Externalizing scale, whereas girls tended to get higher scores than boys for the Internalizing scale. Mothers scored their children higher than fathers, implying possible rater differences.

The homogeneity of the variance was tested with Mx (Neale, 1997b). For maternal and paternal ratings of both the Internalizing and Externalizing scale, the variances of MZM, DZM, MZF, and DZF but not of DOS twins could be constrained to be equal. Thus little or no indication for sibling interactions was found. Because otherwise cooperative (competitive) interactions between siblings would have caused the variances of the MZ twin pairs, who are genetically identical, to be larger (smaller) than the variances of the DZ twin pairs, who share on average half of their segregating genes.

Table 4.2 *Correlations (ratings from the same rater), and cross-rater twin correlations (ratings from different raters) between the twins and the interparent correlations, per zygosity, for 7-year-olds and sample sizes.*

	Internalizing scale						Externalizing scale							
	same rater		different raters				same rater		different raters					
	Twins		Twins		interparent		Twins		Twins		interparent		sample sizes[a]	
	M/M	F/F	M/F	F/M	O	Y	M/M	F/F	M/F	F/M	O	Y	M	M+F
MZM	.69	.68	.42	.45	.60	.65	.85	.87	.66	.66	.75	.73	75	267
DZM	.49	.44	.27	.39	.73	.68	.54	.55	.41	.38	.76	.67	83	233
MZF	.71	.67	.42	.45	.65	.65	.84	.86	.72	.65	.78	.75	80	280
DZF	.54	.55	.30	.35	.65	.64	.55	.61	.43	.44	.77	.74	70	230
DOS	.51	.54	.26	.29	.61	.60	.62	.57	.42	.41	.76	.64	145	421

Note. MZM/DZM = monozygotic/dizygotic males, MZF/DZF = monozygotic/dizygotic females, DOS = dizygotic opposite sex twins.
Same rater Twins = correlation between the oldest and youngest twin, rated by M/M = mothers or F/F = fathers. Different raters Twins = cross-correlation: either oldest twin rated by mothers and youngest by fathers (M/F) or the other way around (F/M). Different raters interparent: O = correlation between mother and father ratings for the oldest child; Y = correlation between mother and father ratings for the youngest child. [a] Sample sizes M = number of twin pairs rated by mothers only, sample sizes M+F = number of twin pairs rated by both mothers and fathers.

Twin correlations

Table 4.2 shows for the Internalizing and Externalizing scale in the first and second column the intra-rater twin correlations between the twins where *one* parent rated both children, in the third and fourth column the cross-rater twin correlations between the twins where mother *and* father each rated one child, and in the fifth and sixth column the interparent correlations where mothers and fathers either rated the oldest or the youngest twin. The interparent correlations were comparable for the oldest and youngest twin in all zygosity by sex groups. On average, the interparent correlations for the Internalizing scale were .66, and for the Externalizing scale .75. This resembled the interparent correlations obtained in the Dutch norm group (Verhulst *et al.*, 1996). Correlations of opposite sex and like sex dizygotic twin pairs were quite comparable, suggesting that there are no large differences between the genetic and environmental influences for boys and girls.

The intra-rater twin correlations between oldest and youngest twins were higher for MZ than for DZ twins, suggesting that genetic factors could play a role in the etiology of these problem behaviors. Especially for the Externalizing scale was the MZ correlation larger than

the DZ correlation, implying higher genetic influences for the Externalizing versus the Internalizing scale. The MZ twin correlations, being smaller than 1, also reflected nonshared environmental influences, especially for the Internalizing scale. Shared environmental influences were also suggested since no correlation for MZ twins was twice as large as the correlation for DZ twins.

Table 4.3 *Univariate estimates of genetic and environmental influences on the Internalizing and Externalizing scale rated for 7-year-old twins.*

	Internalizing scale		Externalizing scale	
	Mothers	Fathers	Mothers	Fathers
Sex differences	No	No	Yes	Yes
Genetic	38 %	35 %	52 %	56 %
Shared	32 %	33 %	32 %	30 %
Nonshared	30 %	32 %	16 %	14 %

Sex differences = boys and girls obtained different estimates for the unique genetic, shared environmental, and nonshared environmental factors.

Table 4.3 shows the genetic, shared and nonshared environmental influences estimated by fitting univariate models with possible sex differences. For both the Internalizing (first two columns) and Externalizing (last two columns) scale, parameter estimates for mothers' and fathers' ratings were comparable. The genetic and environmental influences for boys and girls only differed for the Externalizing scale. For the Internalizing scale no significant sex differences were found. Genetic influences (second row) were largest for the Externalizing scale, explaining more than half of the variance in the behavioral ratings. For the Internalizing scale genetic factors explained around 36% of the variance in the behavioral ratings. Shared environmental influences (third row) were similar for both the Internalizing and the Externalizing scale, explaining around 32% of the variance in the behavioral ratings. Nonshared environmental influences (last row) were most important for the Internalizing scale, explaining around 31% of the variance in the behavioral ratings, while for the Externalizing scale this factor explained around 15% of the variance in the behavioral ratings.

The above presented univariate analyses yield a decomposition of the total phenotypic variance and no distinction is made between the variance that is shared and unique to mothers and fathers. To make a separate decomposition of these two parts, the correlations between

raters are required. To compute the contributions of the genetic and environmental influences to the variance shared by both raters, MZ and DZ correlations can be compared as in the univariate case. However, now the cross-rater twin correlations (see, for each scale, third and fourth column in Table 4.2) have to be compared.

For both scales the cross-rater twin correlations were higher for MZ than for DZ twins, suggesting that genetic factors could also play a role in the etiology of problem behaviors which both raters agree upon. Again, genetic influences seemed to be larger for the Externalizing than for the Internalizing scale. The genetic contribution to the variance in the behavioral ratings shared by parents can be subtracted from the genetic contribution to the total variance in the behavioral ratings, to estimate the genetic effects on the unique variance in the behavioral ratings by mothers or fathers. For instance, for mother's ratings of the Internalizing scale of males: the genetic influence on the variance in the behavioral ratings shared by raters, i.e. $(r_{MZM\text{-}cross} - r_{DZM\text{-}cross}) \times 2 = (.42 - .27) \times 2 = .30$, can be subtracted from the genetic contribution to the total variance in the behavioral ratings $(r_{MZM} - r_{DZM}) \times 2 = (.69 - .49) \times 2 = .40$, to estimate the genetic influence on the unique variance in the behavioral ratings by mothers, i.e. .40 - .30 = .10. The other twin correlations also indicated genetic effects on behaviors uniquely rated by mothers or fathers. This suggested that the parental disagreement was not merely caused by measurement errors, but that mothers also assessed different aspects of the child's behavior than fathers.

To estimate the nonshared environmental influences on the variance in the behavioral ratings shared by raters, the interparent correlations had to be used. Table 4.2 shows that for Internalizing Problems in the MZM group the interparent correlation was .60 for the oldest twin. However, the MZM cross-rater twin correlation (M/F) of .42 was lower. This suggested a nonshared environmental contribution of .60 - .42 = .18. Shared environmental influences on the variance in the behavioral ratings shared by raters can be estimated as: $(2 \times r_{DZM\text{-}cross}) - r_{MZM\text{-}cross} = (2 \times .27) - .42 = .12$. The shared (or nonshared) environmental influence for the decomposition of the variance in the behavioral ratings uniquely rated by one particular rater can now be estimated as the difference between the shared (or nonshared) environmental influence estimated for the decomposition of the total variance in the behavioral ratings and

the shared (or nonshared) environmental influence estimated for the decomposition of the variance in the behavioral ratings shared by raters.

Genetic rater models

Fit indices of the Rater Bias and Psychometric model are presented in Table 4.4. As indicated by the lower χ^2 test statistic and AIC, the Psychometric model fitted better than the Rater Bias model for both the Internalizing and Externalizing scale. This implied that although both parents partially assessed the same behaviors (estimated by the common factors in the model), there also was a component which was unique to each rater (estimated by the unique factors in the model). A Cholesky decomposition (labeled Biometric model by Hewitt *et al.*, 1992) was also performed. The Psychometric model is a constrained rotation of this Biometric model. Both models thus have the same degrees of freedom but a Biometric model can be viewed as a psychologically less informative rotation of the Psychometric model (Hewitt *et al.*, 1992). Neither for the Internalizing, nor for the Externalizing scale did this model fit the data any better than the Psychometric model. Considering the large sample size used, the high p-values obtained for the Psychometric model of both problem scales were quite good (Neale, 1997b). Also the AIC for both scales was low, indicating a good fit of the model.

Table 4.4 *Model fitting statistics for Psychometric and Rater Bias Model and simplification of best fitting (Psychometric) model, for the Internalizing and Externalizing scale of 7-year-old twin pairs.*

	Internalizing scale							Externalizing scale						
	χ^2	df	p	AIC	χ^2diff.	df	p	χ^2	df	p	AIC	χ^2diff.	df	p
Overall model:														
Psychometric model	**53.6**	**47**	**.235**	**-40.38**				**68.8**	**47**	**.021**	**-25.18**			
Rater Bias model	73.0	49	.015	-24.99				129.1	49	0	31.13			
Simplification of overall model:														
Factor estimates:														
No common genetic effects	87.3	49	.001	-10.66	33.7	2	0	238.7	49	0	140.68	169.9	2	0
No unique genetic effects	79.8	51	.006	-22.25	26.1	4	0	129.7	51	0	27.71	60.9	4	0
No common shared environment	80.0	49	.003	-18.02	26.4	2	0	100.2	49	0	2.20	31.4	2	0
No unique shared environment	114.7	51	0	12.68	61.1	4	0	148.0	51	0	46.03	79.2	4	0
No common nonshared environment	509.9	49	0	411.86	456.2	2	0	358.4	49	0	260.45	289.6	2	0
Sex differences:														
No sex differences common effects	55.9	50	.263	-44.09	2.3	3	.514	81.2	50	.003	-18.76	12.4	3	.006
No sex differences unique effects	60.4	53	.226	-45.60	6.8	6	.341	**77.7**	**53**	**.015**	**-28.34**	**8.8**	**6**	**.183**
No sex differences common + unique	**63.1**	**56**	**.241**	**-48.95**	**9.4**	**9**	**.399**	92.4	56	.002	-19.58	23.6	9	.005
Rater differences:														
Unique rater effect: mother-father identical	86.6	53	.002	-19.40	33.0	6	0	**78.4**	**53**	**.013**	**-27.59**	**9.6**	**6**	**.143**
Simplified model:	**63.1**	**56**	**.241**	**-48.95**				**86.3**	**56**	**.006**	**-25.74**			

The Psychometric model was further examined for possible simplifications. Neither for the Internalizing, nor for the Externalizing scale could any of the common or unique factors be removed from the model. For the Internalizing scale the estimates for boys and girls could be constrained to be equal, but the estimates for the unique factors of mothers and fathers differed. For the Externalizing scale the estimates for the unique factors of mothers and fathers could be constrained to be equal, but sex differences were found for the common effects. The fit of the most simplified model is given in Table 4.4.

Table 4.5 *Standardized genetic and environmental influences, estimated using best fitting Psychometric model, for the Internalizing scale of 7-year-old twins.*

	Internalizing scale	
	Age 7	
	Mothers	Fathers
Genetic factor:		
common genetic factor	24 %	28 %
unique genetic factor	14 %	4 %
Shared environmental factor:		
common shared environment	19 %	23 %
unique shared environment	13 %	13 %
Nonshared environmental factor:		
common nonshared evironment	19 %	22 %
unique nonshared environment	11 %	10 %

The parameter estimates for the Internalizing scale, calculated using the best fitting Psychometric model, are given in Table 4.5. Summarizing the common and unique estimates per factor, one can see that the multivariate results are comparable to the univariate results (Table 4.3). Common genetic factors explained 24% of the variance in the behavioral ratings by mothers, and 28% of the variance in the behavioral ratings by fathers. Unique genetic factors explained 14% of the variance in the behavioral ratings by mothers, and 4% of the variance in the behavioral ratings by fathers. Estimating unique genetic factors implied that parental disagreement was not merely caused by measurement errors but that each rater assessed, from his or her own perspective, different but valid aspects of the child's behavior.

By decomposing the observed variance in the behavioral ratings in common and unique factors, common shared and nonshared environmental factors could be estimated without the influence of possible rater bias, unreliability, and measurement errors. Common shared

environmental factors explained 19% of the variance in the behavioral ratings by mothers, and 23% of the variance in the behavioral ratings by fathers. These estimates pointed to a pure shared environmental effect unaffected by possible rater bias. Unique shared environmental factors explained 13%, both of the variance in the behavioral ratings uniquely rated by mothers and of the variance in the behavioral ratings uniquely rated by fathers. Thus, if rater bias existed in the data, it could not have explained more than 13% of the variance. Common nonshared environmental factors explained 19% of the variance in the behavioral ratings by mothers, and 22% of the variance in the behavioral ratings by fathers. These estimated influences suggested that for schoolage children idiosyncratic experiences, unconfounded by possible unreliability and measurement errors, were of importance. Unique nonshared environmental factors explained 11% of the variance in the behavioral ratings uniquely rated by mothers and 10% of the variance in the behavioral ratings uniquely rated by fathers, suggesting that possible unreliability and measurement errors could not have explained more than 11% of the variance.

Table 4.6 *Standardized genetic and environmental influences, estimated using best fitting Psychometric model, for the Externalizing scale of 7-year-old twins.*

	Externalizing scale	
	Age 7	
	Boys	Girls
Genetic factor:		
common genetic factor	44 %	41 %
unique genetic factor	9 %	10 %
Shared environmental factor:		
common shared environment	22 %	21 %
unique shared environment	10 %	12 %
Nonshared environmental factor:		
common nonshared evironment	10 %	10 %
unique nonshared environment	5 %	6 %

The parameter estimates (expressed as percentages of the variance) for the Externalizing scale, calculated using the best fitting Psychometric model, are summarized in Table 4.6. Again, multivariate results were comparable to the univariate results (Table 4.3). The common factors, explaining variance in the behavioral ratings that was shared between the raters, were most important for both boys and girls. Common genetic factors explained 44%

of the variance in the behavioral ratings for boys, and 41% of the variance in the behavioral ratings for girls. Unique factors, explaining variances in the behavioral ratings uniquely rated by one particular rater, explained relatively small parts of the observed variance. Unique genetic factors explained 9% of the variance in the behavioral ratings uniquely rated for boys, and 10% of the variance in the behavioral ratings uniquely rated for girls. Again, estimating unique genetic factors suggested that rater differences reflected valid distinct views. Almost half of the observed variance in the behavioral ratings of the Externalizing scale, for both sexes, was explained by genetic factors. This suggested a possible inborn vulnerability for a child to show Externalizing Problems.

Common shared environmental factors explained 22% of the variance in the behavioral ratings for boys, and 21% of the variance in the behavioral ratings for girls. This implied that there were pure shared environmental effects on the Externalizing scale. Unique shared environmental factors explained 10% of the variance in the behavioral ratings uniquely rated for boys, and 12% of the variance in the behavioral ratings uniquely rated for girls, indicating that if rater bias existed in the data it could at most have explained 12% of the variance. Common nonshared environmental factors explained 10%, both of the variance in the behavioral ratings for boys and girls. Thus idiosyncratic experiences, unaugmented by possible unreliability and measurement errors, seemed to be of importance for both sexes. Unique nonshared environmental factors explained 5% of the variance in the behavioral ratings uniquely rated for boys, and 6% of the variance in the behavioral ratings uniquely rated for girls, suggesting small effects of possible unreliability and measurement errors.

Discussion

In a sample of 1940 Dutch 7-year-old twin pairs we studied the etiology of Internalizing and Externalizing Problems, while taking account of the processes underlying agreement and disagreement between maternal and paternal ratings. The Psychometric model fitted the data better than the Rater Bias model for both scales. Thus rater differences did not merely reflect measurement errors, but were also the result of parents assessing different aspects of the child's behavior. These results are in accordance with previous studies (Hewitt *et al.*, 1992;

Van der Valk *et al.*, in press). As was also suggested by Achenbach et al. (1987) unique interactions seem to allow each parent to provide additional information about the child's behavior. The implication being that it is important to collect data from multiple informants because no single rater may be able to provide a complete picture of the child's behavior.

Genetic factors were most important for the Externalizing scale, explaining over 50% of the variance in the behavioral ratings. Heritabilities of the same size were found for 3-year-old twin pairs (Van der Valk *et al.*, in press). Zahn-Waxler et al. (1996) studying 5-year-old twin pairs, Gjone et al. (1996) examining 5- to 15-year-old twin pairs, and Edelbrock et al. (1995) studying 7- to 15-year-old twin pairs also found that genetic influences explained about half of the variance of the Externalizing scale. These findings suggest that genetic influences remain strong throughout childhood. Shared environmental influences explained 32% of the variance in the behavioral ratings for the Externalizing scale. Again, this was in accordance with the shared environmental influences observed for the 3-year-old twin pairs (Van der Valk *et al.*, in press) and the results found in the studies of Edelbrock et al. (1995), Gjone et al. (1996), and Zahn-Waxler et al. (1996). Apart from quantitative genetic studies, various epidemiological studies have also demonstrated the importance of shared environmental factors in the etiology of externalizing behaviors. Family discord and disruption, lack of affection and poor supervision all predispose to conduct problems and antisocial behavior (Rutter, 1985).

Genetic influences for the Internalizing scale explained about 35% of the variance in the behavioral ratings for 7-year-old twin pairs, which is in accordance with the results found by Gjone et al. (1996) for a sample of 5- to 15-year-old twin pairs. In contrast, for 3-year-old twin pairs (Van der Valk, *et al.*, in press) we found that the Internalizing scale was predominantly influenced by the genetic influences, explaining around 60% of the variance in the behavioral ratings. For a sample of 5-year-old twin pairs Zahn-Waxler et al. (1996) also found that the genetic influences explained more than half of the variance for the Internalizing scale. It may be that the heritability for internalizing behaviors changes with age. Shared environmental influences showed a complementary increase in influences over time, having almost no influence on the Internalizing scale of 3-year-old twin pairs (Van der

Valk *et al.*, in press) and explaining around 34% of the variance in the behavioral ratings of the Internalizing scale for 7-year-old twin pairs.

A differential genetic influence for internalizing behaviors of older versus younger children was also found in other studies. Gjone et al. (1996), examining a sample of twin pairs aged 5-9 and 12-15 years, found a near-significant effect of age on the genetic influence for internalizing behaviors in terms of a decreasing genetic influence with increasing age. Also O'Connor et al. (1998b), studying a sample of 720 siblings initially aged 10 to 18 years, found a decrease in heritability and a complementary increase in environmental influences over a three year interval for a composite score of depressive symptoms. Possibly this remarkable result is caused by developmental differences between older and younger children. Behaviors of preschool children may be predominantly influenced by the child's genotype, while in schoolage children shared environmental influences may become relatively more important. One possible explanation is that parents are only able to guide the child's behavior when he/she is able to understand other people's values and can direct its behavior accordingly. Consequently genetic influences will be higher in preschool children, while shared environmental influences are more likely to be found in older children. Thus even though for 3-year-old twins genetic influences explain most of the variance in the behavioral ratings for Internalizing Problems (Van der Valk *et al.*, in press), it is in the line of expectation to find larger shared environmental influences for problem behaviors of older children, because these children are old enough to be able to direct their behaviors according to their parents' values and ideas.

It may be important, however, to realize that the shared environment is 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 & Rowe, 1998; 1999). This suggests that shared environment reflects the wider community in which families are embedded as well (Bronfenbrenner, 1979; Parke & Kellam, 1994, p.3). This point has also been stressed by Harris (1995) who argues that we should think about environmental effects on development in terms of group processes where peers play an important role. That is, phenomena such as within-group assimilation and between-group contrast that increase the homogeneity of behaviors within groups and widen differences

between social groups could show as shared environment in a behavior genetic analysis. Thus, the possible larger shared environmental effects in schoolage versus preschool children could also reflect a developmental shift due to socialization experiences outside the home which become increasingly important as children grow older.

Although sex differences were found for the Externalizing scale, parameter estimates for boys and girls were very similar. The sex differences were neither scalar sex differences, nor could they be pin-pointed to a specific factor. However, a model without sex differences fitted the data significantly worse. Most likely, the sex differences were a multivariate effect, caused by small effects on various factors. For the Internalizing scale, girls tended to get higher scores than boys. However, no sex differences emerged in genetic and environmental estimates. Also for 3-year-old twin pairs (Van der Valk *et al.*, in press) no sex differences were found, neither for the Internalizing scale nor for the Externalizing scale.

Both for the Internalizing and Externalizing scales, estimates of the common and unique nonshared environmental factors for 7-year-old twin pairs remained almost the same to those for 3-year-old twin pairs (Van der Valk *et al.*, in press). For both ages these factors explained around 18% and 12%, respectively, of the variance in the behavioral ratings for the Internalizing scale and about 11% and 7%, respectively, of the variance in the behavioral ratings for the Externalizing scale. This indicated that parents seem to be able to rate problem behaviors of preschool children just as well as problem behaviors of schoolage children.

Fitting models to the observed data that explicitly incorporate rater bias and unreliability ensured that these effects could not distort estimates of the shared and nonshared environmental factors. Parameters obtained thus reflected more accurate estimates. Measurement errors and unreliability were estimated in the unique nonshared environmental factor. However, neither for the Externalizing scale nor for the Internalizing scale did this factor account for more than 11% of the variance in the behavioral ratings, indicating a small influence. Possible rater bias was included in the estimate of the unique shared environmental factor, accounting for at most 13% of the variance in the behavioral ratings both for the Internalizing and Externalizing scale. Common nonshared environmental influences (undistorted by error or unreliability) were found both for the 7-year-old twin pairs and for the 3-year-old twin pairs (Van der Valk *et al.*, in press). Thus idiosyncratic experiences seem

to be of importance to explain both preschool and schoolage children's problem behaviors. Common shared environmental influences were also found, showing larger estimates for 7-year-old twins compared with 3-year-old twins (Van der Valk *et al.*, in press). Theoretically, estimates of the common shared environmental factor could have been inflated if raters copied each others answers. The models used assumed independence of maternal and paternal rater bias and thus did not correct for this effect. However, it doesn't seem likely that the increase in shared environmental influences over time was caused by parents copying each others answers when their children were age 7, while they did not copy each others answers when their children were age 3. Otherwise the cross-rater twin correlations between mothers and fathers should have been much larger at age 7 compared with age 3, which was not the case.

Estimates found using quantitative genetic studies do not pertain to the individual but involve average differences between individuals in the population. For other populations, or for specific individuals, other estimates may apply. This study used a nonclinical sample of Dutch twin pairs, showing problem behaviors in the normal range. Whether similar results will be obtained in clinical populations, showing more extreme problem behaviors, remains to be explored. Although this study found large genetic influences for both broad-band scales these results should not lead to a sense of fatalism or genetic determinism for parents or for clinicians. As was also pointed out by Pike and Plomin (1996), even if genetic differences completely explain differences in problem behaviors - and this is not the case - does this by no means rule out the possibility of effective treatment, because environmental factors not widely represented at present in the population could have a major impact on these problem behaviors.

5

Genetic and Environmental Contributions to Continuity and Change of Internalizing and Externalizing Problems During Childhood

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This chapter is a slightly revised version of an article which is currently review.

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Abstract

Objective: *A two wave behavior genetic model was used to estimate genetic, shared environmental (between twins), and nonshared environmental (idiosyncratic) contributions to stability and change of Internalizing and Externalizing Problems at ages 3 and 7 years.* ***Method:*** *Maternal ratings of Child Behavior Checklist questionnaires were collected for 3873 twin pairs at age 3, and four years later for 1924 twin pairs at age 7.* ***Results:*** *For Externalizing Problems the estimated influences of genetic, shared, and nonshared environmental factors remained relatively the same at ages 3 and 7. Across sexes, these factors explained 51%, 30%, and 19%, respectively, at age 3, and 52%, 32%, and 17%, respectively, at age 7. The phenotypic stability of r = .54 was explained for 55% by genetic factors, for 37% by shared environmental factors, and for 8% by nonshared environmental factors. At both ages, half of the genetic influences were stable over time and half were age specific. Shared environmental influences were mostly stable, while nonshared environmental influences were mostly age specific. For Internalizing Problems genetic influences decreased while shared environmental influences increased over time. Across sexes, the genetic, shared, and nonshared environmental factors explained 59%, 10%, and 31%, respectively, at age 3, and 40%, 31%, and 29%, respectively, at age 7. The phenotypic stability of r = .38 was explained for 66% by genetic factors, for 23% by shared environmental influences, and for 11% by nonshared environmental influences. Again at both ages, half of the genetic influences were stable and half were age specific. Influences of both shared and nonshared environmental factors were mostly age specific.* ***Conclusions:*** *The stability of Internalizing and Externalizing Problems over a 4-year period is explained mostly by genetic factors. The underlying causes of problem behaviors change over time, suggesting the contribution of different genes to variation in problem behaviors from preschool to schoolage. The family environment becomes more important to regulate problem behaviors as children grow up.*

Keywords

problem behaviors, continuity, change, twins, Child Behavior Checklist.

Introduction

Research conducted during the last three decades have shown problem behaviors in children to be quite prevalent and persistent. Verhulst and Koot (1992a), in a review of 38 studies (using different techniques, sample sizes, age ranges, assessment methods, informants and case definitions) calculated the median prevalence rate for problem behaviors in children to be 13%. The majority of studies were consistent in their reports of sex differences with regard to types of disorders. Girls tended to show more internalizing or emotional problems, whereas boys were more inclined to show externalizing or disruptive behaviors. Longitudinal studies have shown that children do not simply grow out of their behavior problems. Temperamental qualities observed by examiners at ages 3 and 5, have been shown to predict specific behavior problems rated by parents at ages 9, 11, 13 and 15 and even DSM-III diagnoses of adult psychiatric disorders at age 21 (Caspi *et al.*, 1995, 1996). Koot (1995) concluded in his review of longitudinal studies of general population and community samples that, across studies, one-third to one-half of children with initial deviant scores maintain deviant scores across 2- to 6-year intervals. Although most children showed fluctuations over time in their level of deviant behavior, extreme changes were rare.

To get a better understanding of the etiology of children's problem behaviors quantitative genetic studies can be carried out, estimating the genetic and environmental influences on the continuous variations in children's problem behaviors. Environmental factors are further subdivided into influences that have an impact on all children growing up in the same family and into influences that affect children within a family differently. Parental rearing practices or the family's socioeconomic status are examples of possible shared environmental influences. Accidents, differential parental treatment, or peer group influences are examples of possible nonshared environmental influences. Longitudinal behavior genetic studies are able to examine the causes of continuity and change of problem behaviors. In order to treat and possibly even prevent problem behaviors in children, it is necessary to understand their etiology. For instance, an active intervention may be required for causes that affect continuity, whereas for causes that have temporary effects a "wait and see" policy may be justified. To assess the contributions of genetic and environmental factors to the covariation

of behavior across time longitudinal studies of genetically informative groups, such as twins, are needed. This makes it possible to determine whether behaviors are influenced by continuing or by age specific genetic and environmental factors. Continuing factors have effects on all assessments and thus influence stability of problem behaviors. Age specific factors are the residual influences at each assessment after the continuing influences have been partialed out. The age specific factors only influence behaviors at a certain assessment, having no longitudinal influences (i.e. these factors affect change in the etiology of problem behaviors).

Only four studies have examined the genetic and environmental influences to continuity and change in children's problem behaviors. Kendler et al. (1993b) studied the 1-year prevalence of major depression in 938 adult female-female twin pairs. They found a heritability of 41% to 46%, the rest of the variance being explained by nonshared environmental factors. Over a 1-year period, the genetic effects were entirely stable while the shared environmental effects showed only age specific effects. Schmitz et al. (1995) conducted the second study, examining a small longitudinal sample of 95 twin pairs, assessed at ages 2 and 7 years, using the Child Behavior Checklist (CBCL) (Achenbach, 1991a; Achenbach, 1992). Results indicated that for Internalizing Problems continuing shared environmental factors had an effect both in early and middle childhood, while genetic influences had mostly age specific effects. For Externalizing Problems the opposite effect was found, showing continuing genetic and age specific shared environmental effects. However, as suggested by the authors, these results need to be replicated in larger samples of genetically informative data. The third is a study conducted by Van den Oord and Rowe (1997). They studied maternal ratings of The Behavior Problems Index (Peterson & Zill, 1986) of 436 pairs of full siblings, 119 pairs of half siblings, and 122 pairs of cousins assessed at ages 4-6, 6-8, and 8-10. In their study, the continuity of problem behaviors was entirely explained by genetic and shared environmental factors. Nonshared environmental factors only showed age specific effects, influencing changes in children's problem behaviors. The last is a study of O'Connor et al. (1998b), following 405 families over a three year interval. Subjects consisted of monozygotic and dizygotic twins, and full, half & unrelated siblings (all of same-sex) between 10 and 18 years of age at the first assessment.

Results showed that the phenotypic stability of antisocial symptoms of r = .63 was explained for 54% by continuing genetic influences and for 30% by continuing shared environmental influences. For depressive symptoms, the phenotypic stability of r = .59 was explained for 64% by continuing genetic influences and for 36% by continuing nonshared environmental influences. In short, even though each study investigated subjects at a different age interval, most studies showed large influences for genetic factors on the stability of problem behaviors. Effects of shared and nonshared environmental factors are less clear, showing continuing influences for some studies and only age specific effects for others.

To examine the etiology of problem behaviors during development, we have collected mothers' ratings of CBCL/2-3 questionnaires (Achenbach, 1992) for 3-year-old twin pairs and CBCL/4-18 questionnaires (Achenbach, 1991a) when the children reached their 7th birthday. We studied the age interval of 3 to 7 years because it includes many developmental transitions, i.e. on physic, cognitive, social, and emotional levels. For instance, in contrast to preschool children 7-year-old children start going to school. During this transition they must cope with many new demands like meeting academic challenges, learning school and teacher expectations, adjusting to the daily routine of a school class and gaining acceptance in a new peer group (Barth & Parke, 1993; Cowan *et al.*, 1994; Ladd & Price, 1987). Because of these new environmental demands, and the interactions between these changing environmental influences and the biological make-up of the child, the etiology of problem behaviors may change during this period. We focussed on two broad groupings of problem behaviors, reflecting a distinction between anxious, inhibited behavior (Internalizing Problems) and aggressive, antisocial behavior (Externalizing Problems). An advantage of using these broad groupings as level of analyses, is that they are relatively unsensitive to population and/or age specific questionnaire differences because they are composed of a large number of similar items. Furthermore, several studies have found support for the validity of the internalizing - externalizing distinction (Achenbach, 1991a; Achenbach, 1992; De Groot, 1994; Koot *et al.*, 1997). In order to obtain sufficient statistical power to conduct the behavior genetic analyses, we have collected a large sample of twin pairs: 3873 3-year-old and 1924 7-year-old twin pairs.

Previous analyses at age 3 (Van der Valk *et al.*, 1998b; Van der Valk *et al.*, in press) showed that for Externalizing Problems genetic factors were most important, explaining 52% of the variance, while shared environmental influences accounted for 27% of the variance. For 7-year-old twin pairs (Van der Valk *et al.*, submitted) the genetic and environmental estimates for Externalizing Problems had not changed. For a longitudinal study we might thus expect that the behavioral continuity of Externalizing Problems will be influenced by both genetic and shared environmental factors. This would also be in accordance to the results found by O'Connor et al. (1998b) for antisocial symptoms. For Internalizing Problems at age 3 genetic factors also had large effects, explaining 69% of the variance, however no shared environmental influences were found. Over time clear age differences were found. Estimates of genetic factors for Internalizing Problems decreased to explaining 38% of the variance, while estimates of shared environmental factors increased to explaining 32% of the variance at age 7. In a longitudinal study we might thus expect that the stability of showing Internalizing Problems will be influenced by continuing genetic influences, but the shared environmental influences will probably also have some age specific effects.

Method

Samples

All participating twin families belong to the Netherlands Twin Registry (NTR) (Boomsma *et al.*, 1992; Boomsma 1998a). The accuracy of zygosity determination by questionnaire items is described in Rietveld et al. (2000). A detailed description of sample collection, zygosity determination, means and standard deviations for age 3 can be found in Van der Valk et al. (1998b) and Van der Valk et al. (in press), and for age 7 in Van der Valk et al. (submitted). Of all 3-year-old twin pairs 54% had reached the age of 7 at the second assessment. From these we obtained a 86% longitudinal response, resulting in a sample of 292 monozygotic males (MZM), 288 dizygotic males (DZM), 311 monozygotic females (MZF), 252 dizygotic females (DZF), and 495 dizygotic opposite sex (DOS) twin pairs. In addition to this longitudinal data, questionnaires were collected for 322 MZM, 335 DZM,

386 MZF, 299 DZF, 739 DOS twin pairs at age 3 and 57 MZM, 37 DZM, 56 MZF, 49 DZF, 86 DOS twin pairs at age 7.

Measures

The Child Behavior Checklist is developed for parents to rate the behavioral and emotional problems of their 2- and 3-year-old (CBCL/2-3; Achenbach, 1992) or 4- to 18-year-old (CBCL/4-18; Achenbach, 1991a) children. For CBCL/2-3 Dutch syndrome scales and comparability with the syndrome scales as developed by Achenbach (1992) are reported by Koot et al., (1997). CBCL/4-18 syndrome scales could be composed according to the 1991 profile (Achenbach, 1991a), because De Groot et al., (1994) showed that the American factor solution fitted a Dutch normative sample well.

Data Analysis

To estimate the genetic, shared environmental, and nonshared environmental contributions to continuity and change in Internalizing and Externalizing Problems at ages 3 and 7 we used the model outlined in Figure 5.1. This Figure employs the standard assumptions and principles of twin studies (Falconer, 1989; Plomin *et al.*, 1990; Neale & Cardon, 1992). The As refer to the additive genetic factors, the Cs to the shared environmental factors, and the Es to the nonshared environmental factors. The genetic and environmental factors that act at both ages are not subscripted (i.e., A, C, and E). These are the continuing factors that contribute to the stability of problem behaviors. The components subscripted 3 or 7 are the age specific factors that account for change (i.e., A_3, C_3, E_3, A_7, C_7, E_7). Monozygotic twins (MZ) are genetically identical and dizygotic twins (DZ) share on average 50% of their genetic variance. Consequently, the genetic correlation r_g between the additive genetic values of twin 1 and twin 2 (A) equal 1 for MZ and .5 for DZ twins. Shared environment (C) is defined as those environmental influences that are identical for both twins. A correlation of 1 was therefore specified between the Cs of twin 1 and twin 2. Nonshared environmental effects (E) are by definition unique for each twin, so no correlation was specified between the E components. The effects of genetic and environmental factors that pertain to the same twin are assumed to be additive and independent.

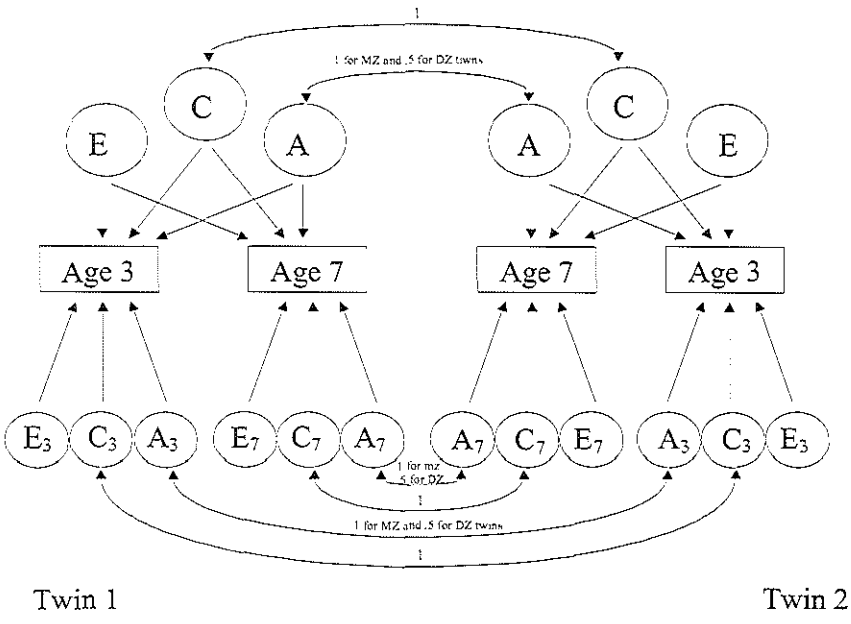

Figure 5.1 Twin model for estimating genetic and environmental contributions to stability and change in problem behaviors at ages 3 and 7. Latent (unobserved) factors are in circles, observed variables are in squares. A, C, and E represent additive genetic, shared environmental and nonshared environmental factors that influence the behavior of the child (either Internalizing or Externalizing Problems) at both ages 3 and 7. A_3, C_3, E_3 and A_7, C_7, E_7 represent these same factors, but restricts their influence to only age 3 or age 7, respectively. The arrows represent the causal influences of the latent factors on the phenotype and all paths have fixed values of 1. The variance of the latent factors is estimated.

We fitted the model with Mx (Neale *et al.*, 1999), using a maximum likelihood estimation procedure for raw data (Lange *et al.*, 1976). This estimation technique can handle incomplete data, and allowed us to retain twin pairs who had not reached the age of 7 yet or had missing assessments. Raw maximum likelihood yields an index, called log-likelihood, that cannot be interpreted itself. However, minus twice the difference between the log-likelihood of the full model versus the log-likelihood of a submodel in which parameters are fixed to zero or

constrained to be equal is chi-square distributed with the difference in the number of estimated parameters as the degrees of freedom.

This χ^2 test was used to examine if the genetic and environmental contributions differed significantly from zero, whether there were sex differences, and if the relative importance of genetic and environmental effects differed at ages 3 and 7. To study possible sex differences the analyses were performed on the five zygosity by sex twin groups (MZM, DZM, MZF, DZF, DOS). In all tests, a model that estimated all variance components in boys and girls separately was used as the baseline. Tests were performed for the continuing factors and age specific factors separately. There were two exceptions. First, age specific nonshared environmental effects are confounded with measurement error, so that it does not make sense to test whether these effects are zero. Second, because not the paths but the variances of the latent factors are estimated in the model, the test that equates the relative importance of genetic and environmental effects to be equal at ages 3 and 7 can only be performed for the age specific effects. Because there are three age specific components for boys as well as for girls this latter test implies six constraints. However, because the assessment instruments differ at ages 3 and 7 (e.g. the number of items) it is incorrect to assume equal phenotypic variances. To account for these scale differences an additional parameter was estimated so that the total number of restrictions or degrees of freedom became 6 - 1 = 5.

The data were square-root transformated 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 in our test statistics (Muthén & Kaplan, 1985).

Results

Table 5.1 shows the within person correlations, the twin correlations, and the twin cross-correlations between ages 3 and 7 for boys and girls. First we discuss the results that apply to the continuity of problem behaviors over time. The within person correlations between ages 3 and 7 (stability coefficients) were on average lower for Internalizing Problems (boys r = .35;

Table 5.1 *Within person correlations (phenotypic stabilities), twin correlations and twin cross-correlations between ages 3 and 7 for Internalizing and Externalizing Problems*

	Within Person Correlation				MZ		MZ		DZ		DZ		Opposite	
	boys		girls		boys		girls		boys		girls		sex	
Age	3.	7.	3.	7.	3.	7.	3.	7.	3.	7.	3.	7.	3.	7.
Internalizing Problems														
3.	1		1		.664		.739		.375		.346		.367	
7.	.345	1	.405	1	.233	.706	.418	.713	.213	.483	.226	.546	.214	.522
Externalizing Problems														
3.	1		1		.805		.826		.579		.533		.512	
7.	.552	1	.527	1	.487	.833	.536	.844	.357	.530	.299	.552	.302	.616

Note. MZ = Monozygotic twins, DZ = Dizygotic twins

girls r = .41) than for Externalizing Problems (boys r = .55; girls r = .53). However, all 4-year stability coefficients were comparable to the 2-year stability coefficients between CBCL/2-3 scale scores at ages 2-3 years and CBCL/4-18 scale scores at ages 4-5 years found for a Dutch community sample (i.e., Internalizing r = .40; Externalizing r = .54) (Koot, 1993). To compute the twin cross-correlations between ages 3 and 7 we used each twin pair twice. That is, the first data record for each pair involved twin 1 assessed at age 3 with twin 2 assessed at age 7, and the second data record included twin 1 assessed at age 7 with twin 2 assessed at age 3. All twin cross-correlations between ages 3 and 7 were larger for MZ than for DZ twins, implying genetic contributions to stability. However, MZ cross-correlations were never twice as large as DZ cross-correlations, implying also shared environmental contributions to stability. In general the MZ twin cross-correlations were only slightly smaller than the within person correlations between ages 3 and 7. This implied that nonshared environmental contributions to stability were rather small.

At each age, an overall estimate of genetic and shared environmental influences can be obtained by comparing MZ twin correlations with DZ twin correlations. At both ages and for both problem behaviors MZ twin correlations were larger than DZ twin correlations,

implying overall genetic influences. By subtracting the continuing genetic estimate discussed above from this overall estimate of genetic variance at a certain age, one can determine the contribution of genes that are specific to that certain age (age specific). In this study, age specific genetic influences seemed to be important for both problem behaviors at both ages. The same technique can be used to estimate the age specific shared and nonshared environmental influences. For the nonshared environmental factors age specific effects seemed to be more important than continuing effects.

Table 5.2 χ^2 *test statistics for significance and equality of genetic and environmental contributions to continuity and age specific effects*

	Internalizing			Externalizing		
	χ^2	*df.*	*p.*	χ^2	*df.*	*p.*
Genetic effects equal to zero						
continuity	50.218	2	0	105.450	2	0
age specific	75.299	4	0	97.975	4	0
Shared environmental effects equal to zero						
continuity	8.728	2	.013	43.115	2	0
age specific	24.884	4	0	20.885	4	0
Nonshared environmental effects equal to zero						
continuity	11.215	2	.004	35.565	2	0
Sex differences						
continuity	1.450	3	.484	2.531	3	.282
age specific	81.890	6	0	18.114	6	0
Genetic and environmental effects equal age 3 and 7						
age specific	30.259	5	0	23.180	5	0

The results from the χ^2 tests are shown in Table 5.2. A large χ^2 test statistic and $p < .05$ implies that the constraints imposed by the model result in a significant deterioration in fit compared with the unconstrained model. The estimates for continuing and age specific genetic, shared environmental, and nonshared environmental factors were all significant, implying that all variance components were larger than zero and thus necessary in the model. The sex differences were non-significant for continuity and significant for the age specific effects. Thus, the size of genetic and environmental effects for boys and girls was equal for the continuing factors, but differed for the age specific factors. Constraining the relative

importance of genetic and environmental effects to be equal at ages 3 and 7 also resulted in a significant poorer fit. In sum, the best fitting parsimonious model estimated the influences of all continuing and age specific genetic, shared, and nonshared environmental factors, had no sex differences in genetic and environmental effects on continuing factors, and did have sex differences in genetic and environmental effects on age specific factors. Further, estimates at ages 3 and 7 had to be allowed to be different.

Unstandardized estimates of the genetic and environmental contributions, obtained using the best fitting model, are reported in Table 5.3. Genetic, shared, and nonshared environmental influences on stability can be estimated by dividing each (continuing) factor estimate by the sum of all (continuing) factor estimates. The phenotypic stability of Internalizing Problems (boys r = .35; girls r = .41) was for 66% genetically based, for 23% accounted for by shared environmental factors, and for 11% explained by nonshared environmental effects. The phenotypic stability of Externalizing Problems (boys r = .55; girls r = .53) was for 55% explained by genetical factors, for 37% by shared environmental factors, and for 8% by nonshared environmental effects.

Table 5.3 *Estimates from the best fitting model of the relative importance of genetic, shared environmental and nonshared environmental components for continuity and age specific effects (change)*

	Internalizing Problems			Externalizing Problems		
	Genetic	Shared	Nonshared	Genetic	Shared	Nonshared
Boys						
continuity	.1736	.0605	.0278	.3981	.2749	.0570
specific age 3	.1964	.0273	.2013	.2718	.3040	.2647
specific age 7	.1641	.1350	.1764	.2396	.0887	.1498
Girls						
continuity	.1736	.0605	.0278	.3981	.2749	.0570
specific age 3	.2581	.0000	.1689	.5699	.1053	.2436
specific age 7	.0850	.2076	.2023	.1585	.0994	.1168

By standardizing the estimates of Table 5.3 we obtained the genetic and environmental influences reported in Table 5.4. The standardized estimates are, both for boys and for girls, expressed either as proportions of the total variance at age 3 or as proportions of the total variance at age 7. In Table 5.4 total influences are reported, both for boys and girls for each factor and at each age. These total influences are further divided into the part that was explained by continuing factors and the part that was accounted for by age specific factors, given behind the total estimate in brackets.

The relative importance of continuing versus age specific effects for a given component can be quantified by computing the genetic and environmental correlation coefficients. This is achieved in the standard way by dividing the covariance or shared variance by the product of the standard deviations at each age. For Internalizing/Externalizing Problems the correlations were .505/.567 for genetic influences, .468/.664 for shared environmental influences, and .130/.235 for nonshared environment. These correlations implied that over 50% of the genetic and shared environmental factors for both scales are active at both ages. Age specific shared environmental factors will only be of importance for Internalizing Problems. Nonshared environmental factors will largely show age specific effects for both scales.

For Externalizing Problems the estimated influences of genetic, shared, and nonshared environmental factors remained relatively the same at ages 3 and 7. For boys, these factors explained 43%, 37%, and 20%, respectively, at age 3, and 53%, 30%, and 17%, respectively, at age 7. For girls, the estimated influences were 59%, 23%, and 18%, respectively, at age 3, and 50%, 34%, and 16%, respectively, at age 7. For both boys and girls at both ages, about half of the genetic influences were stable over time and half were age specific. Thus, apart from finding continuing genetic factors influencing stability, we also obtained genetic influences that were independent of the continuing genetic factors. Indeed, about half of the genetic variance on Externalizing Problems at both ages was independent of the continuing genetic variance, influencing change. Shared environmental factors mostly showed continuing influences, contributing to stability of Externalizing Problems. Nonshared environmental factors on the other hand mostly showed age specific effects, influencing change.

Table 5.4

Standardized estimates from the best fitting model of the relative importance of genetic (continuity + age specific), shared environmental (continuity + age specific) and nonshared environmental (continuity + age specific) components, for boys and girls at ages 3 and 7

	Internalizing Problems			Externalizing Problems		
Boys	Genetic	Shared	Nonshared	Genetic	Shared	Nonshared
Age 3	54 (25 + 29)	13 (9 + 4)	33 (4 + 29)	43 (26 + 17)	37 (18 + 19)	20 (4 + 16)
Age 7	46 (24 + 22)	26 (8 + 18)	28 (4 + 24)	53 (33 + 20)	30 (23 + 7)	17 (5 + 12)
Girls						
Age 3	63 (25 + 38)	8 (8 + 0)	29 (4 + 25)	59 (24 + 35)	23 (17 + 6)	18 (4 + 4)
Age 7	34 (23 + 11)	35 (8 + 27)	31 (4 + 27)	50 (36 + 14)	34 (25 + 9)	16 (5 + 11)

For Internalizing Problems genetic influences decreased while shared environmental influences increased over time. For boys, the genetic, shared, and nonshared environmental factors explained 54%, 13%, and 33%, respectively, at age 3, and 46%, 26%, and 28%, respectively, at age 7. For girls, the factors explained 63%, 8%, and 29%, respectively, at age 3, and 34%, 35%, and 31%, respectively, at age 7. Again both for boys and girls at both ages, half of the genetic influences were stable and half were age specific. Thus also for Internalizing Problems, apart from finding continuing genetic factors influencing stability, we also obtained genetic influences that were independent of the continuing genetic factors, influencing change. Influences of both the shared and nonshared environmental factors showed mostly age specific effects, influencing change.

Discussion

A two wave behavior genetic model was fitted to the data of 3873 twin pairs of age 3 and 1924 twin pairs of age 7 to estimate the genetic, shared environmental, and nonshared environmental contributions to continuity and change of Internalizing and Externalizing Problems. The central findings of this study were that genetic influences underlie the stability of problem behaviors over a 4-year period. For Internalizing Problems the phenotypic stability ($r = .38$) was accounted for 66% by genetic factors, while for Externalizing Problems the phenotypic stability ($r = .54$) was explained for 55% by genetic factors. Comparable results were found by Kendler et al. (1993b), Van den Oord and Rowe (1997), and O'Connor et al. (1998b). Some inborn vulnerability thus appears to exist for showing problem behaviors that persists during childhood. Shared environmental influences also influenced the stability, accounting for 23% of the covariance for Internalizing Problems and 37% of the covariance for Externalizing Problems. Similar results were obtained in studies of Van den Oord and Rowe (1997), and O'Connor et al. (1998b). Finding continuing influences of shared environmental factors is also in accordance to results of epidemiological studies showing that, even though factors like family discord and disruption, lack of affection and poor supervision all predispose to problem behaviors (Rutter, 1985), it is often the persistence of these factors that predict chronic problems (Campbell, 1995).

Just as important as the finding of genetic continuity is the finding of genetic change for both problem behaviors during this 4-year period. That is, significant genetic effects were obtained for both problem behaviors at both ages that were independent of the continuing genetic influences. Indeed, about half of the genetic variance for both problem scales at both ages was independent of the continuing genetic variance, influencing change. In other words, if genes are eventually found that account for genetic influences on Internalizing and/or Externalizing Problems during childhood, these results suggest that different genes may contribute to variation of the problem behaviors from preschool to schoolage. Part of the explanation for this change in etiology could be the many developmental transitions, i.e. on physic, cognitive, social, and emotional levels, that children experience between ages 3 and 7. Schoolage children, in comparison with preschool children, experience many new environmental demands. These changing environmental influences, together with the accompanying changes in interactions between these new environmental influences and the biological make-up of the child, may change the etiology of children's problem behaviors during this period.

For Internalizing Problems at age 3 clear age differences were found. Internalizing Problems of preschool children were predominantly influenced by the child's genotype, while in schoolage children shared environmental influences became relatively more important. One explanation might be that at a young age the genotype of the child determines the environmental influences the child experiences, and thus a relatively high genetic estimate with smaller shared and nonshared environmental estimates will be found. Subsequently, when the child matures, it may have had the cognitive development to understand other people's values and be able to direct its behavior accordingly. Parental guidance for these older children then, may become less directed by the child's genotype and more by the parent's own values and ideas. If correct, estimates of environmental influences will then increase for schoolage children compared with preschool children. However, it may be important to realize that 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 & Rowe, 1998; 1999). This suggests that shared environment reflects the wider community in which families are

embedded as well (Bronfenbrenner, 1979; Parke & Kellam, 1994, p.3). This point has also been stressed by Harris (1995) who argues that we should think about environmental effects on development in terms of group processes where peers play an important role. That is, phenomena such as within-group assimilation and between-group contrast that increase the homogeneity of behaviors within groups and widen differences between social groups could show as shared environment in a behavior genetic analysis. Thus, the possible larger shared environmental effects in schoolage versus preschool children could also reflect a developmental shift due to socialization experiences outside the home which become increasingly important as children grow older.

Nonshared environmental factors largely had age specific effects, explaining 18% and 30% of Externalizing and Internalizing Problems, respectively. At both ages 3 and 7 these effects remained relatively the same. Comparable findings were obtained by Van den Oord and Rowe (1997). Although these results do not imply that nonshared environmental experiences, like illnesses or a possible trauma, are unimportant to children, they do suggest that these factors might be of a transient nature and that children appear to "recover" from them.

Limitations

No rater bias (a tendency of an individual rater to overestimate or underestimate scores consistently) was incorporated in the model. By using the same rater at both assessment points the observed behavior problems could have been influenced by rater biases, thereby inflating the estimates of the shared environmental factors. However, previous studies at age 3 (Van der Valk *et al.*, in press) and at age 7 (Van der Valk *et al.*, submitted) have shown the effects of rater bias to be small, thus possible distortions are probably small. In these previous studies also the effects of measurement errors at both ages were estimated to be small, suggesting that both the CBCL/2-3 and the CBCL/4-18 assessed problem behaviors satisfactorily.

The quantitative genetic analyses done in this study assume an underlying continuous liability for problem behaviors, meaning that active genes which are not pathological in themselves are still associated with an increased (or decreased) risk for showing these

behaviors. Individuals showing extreme problem behaviors were thus not assumed to be qualitatively different, but to be variations of this particular behavior on a quantitative continuum. An underlying continuous liability for problem behaviors was found by Van den Oord & Rowe (1997) for a non-clinical population. However, whether this assumption holds for clinical populations needs to be examined by further studies. If, for instance, clinical depressions are affected by other genes or other environmental factors than "mood" differences between children in the general population, genetic and environmental etiologies may be different for clinical and non-clinical populations.

Clinical Implications

For Externalizing Problems continuing genetic and shared environmental effects were most important to explain stability. Thus children who continue to experience adverse shared environmental influences and have a genetic risk may persist in showing maladjustment. For these children a 'wait and see' policy may be inappropriate and an active intervention would be required. For Internalizing Problems, although genetic factors had a continuing influence from ages 3 to 7, the total genetic influence decreased while age specific shared environmental factors increased over time. Possibly a 'wait and see' policy might sometimes be justified for these kind of problem behaviors because age specific influences only have temporary effects. Nevertheless future research should try to identify these age specific risk factors to enable the development of effective interventions. Also, more research is needed to explore the ways in which genes interact with each other and with the environmental factors to influence an individual's susceptibility to showing problem behaviors.

Although large continuing and age specific genetic influences were found in the present study, these results should not lead to a sense of fatalism or genetic determinism for parents or for clinicians. As pointed out by Pike and Plomin (1996), even if genetic differences completely explain differences in problem behaviors - and this is not the case - does this by no means rule out the possibility of effective treatment, because environmental factors not widely represented at present in the population could have a major impact on these problem behaviors. Also, estimates found using quantitative genetic studies do not pertain to the

individual but involve average differences between individuals in the population. For other populations, or for specific individuals, other estimates may apply.

6

Longitudinal Genetic Analysis of Problem Behaviors in Biologically Related and Unrelated Adoptees

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Abstract

The genetic and environmental influences on problem behaviors at two assessment points, three years apart, and their stability were studied in a sample of international adoptees, initially aged 10 to 15 years. Parents of 111 pairs of adopted biological siblings, 221 pairs of adopted nonbiological siblings and 1484 adopted singletons completed the Child Behavior Checklist (75 pairs, 154 pairs and 1080 singletons respectively at second assessment). At first assessment, genetic factors accounted for more than 50% of the variance in the Externalizing, Aggressive Behavior, Attention Problems and Social Problems scales. Shared environmental influences explained 40% of the variance in the Total Problem scale and less for all other scales. Nonshared environmental influences were most important for the Internalizing scale and its subscales, and for the Thought Problems and Delinquent Behavior scales. At the second assessment, genetic factors explained most of the variance in the Total Problem, Externalizing and Aggressive Behavior scales, while nonshared environmental influences explained most of the variance in all other scales. Shared environmental influences explained 33% of the variance in the Internalizing scale and less for the other scales. The stability of the Externalizing scale over time was caused mostly by genetic factors, while nonshared environmental factors mostly caused the stability of the Internalizing scale.

Keywords

problem behaviors, longitudinal analysis, adolescent psychopathology, Child Behavior Checklist, international adoptees, behavior genetics.

Introduction

Prospective studies showed high stability of behavioral and emotional problems during childhood, adolescence and early adulthood. Across studies, one-third to one-half of children with initial deviant scores maintain deviant scores across 2- to 6-year intervals (Koot, 1995). The presence of multiple problems increases the likelihood of stability. Age and gender of the child do not seem to be of major influence. Although most children show fluctuations over time in the level of deviant behavior, extreme changes are rare. There are indications that, at least from schoolage onwards, the stability of problem behavior is specific. Higher stabilities over time are reported within than across problem areas. Using the Child Behavior Checklist (CBCL) (Achenbach, 1991a,d), Externalizing scores were more predictive of later Externalizing scores than of Internalizing scores, and vice versa (Verhulst & Van der Ende, 1993a). When using rating scales, Internalizing Problems generally are almost as stable as Externalizing Problems. However, when clinical diagnoses are made, emotional disorders seem to show better prognosis than conduct or hyperactivity disorders. That is, children who persist in their deviant behavior tend to show oppositional, aggressive or antisocial behaviors, whereas the majority of children who improve initially showed fearful, inhibited, or depressive behaviors (Esser *et al.*, 1990; Verhulst *et al.*, 1993b).

Given the stability of problem behaviors, the next question is what the etiology of this stability is. Problem behaviors of children generally involve quantitative variations in behavior that most children display to some degree. These continuous variations in behavioral problems are hypothesized to be caused by multiple genes and environmental influences. The effects of genes and environment on variation in behavior can be studied with genetically informative subjects such as twins or adoptees. Likewise, the contributions of genetic and environmental factors to the covariation of behavior across time can be assessed with genetically informative subjects who are measured repeatedly across time. We have studied the etiology of problem behaviors during adolescence over a 3 year interval in a sample of internationally adopted children. In this sample of biologically related and unrelated adopted siblings and singletons, the stability and change of genetic and environmental influences on different problem behaviors were assessed, using the Child

Behavior Checklist (CBCL/4-18, Achenbach, 1991a) to obtain parental ratings of behavioral problems.

Longitudinal studies can resolve whether changes in heritability during adolescence are due to changes in genetic or environmental variances with age. More importantly, however, longitudinal studies can reveal how genes and environmental influences operate throughout development. For example, is an increase in heritability due to new, additional, genetic factors being expressed as children grow older, or is there an amplification of existing genetic influences? This second objective addresses the question to what extent phenotypic stability is due to the same genes being expressed at different ages and to what extent phenotypic stability is due to the same environmental influences being of importance. Contrary to popular points of view, genetically determined characters need not be stable, nor are longitudinally stable characters always influenced by heredity (Molenaar *et al.*, 1991).

Several studies have discussed the importance of genetic and environmental influences on children's problem behaviors (see Edelbrock *et al.*, 1995). However, we know of only one study that has prospectively assessed the stability and change of genetic and environmental influences on children's problem behaviors. Schmitz et al. (1995) collected CBCL data over a 5-year period for children who were almost 3 years old at the first assessment. In their relatively small longitudinal sample of 95 twin pairs, Schmitz et al. (1995) found that the same genes were operating at both the earlier and the later time point for the Aggressive Behavior scale. For the Somatic Complaints and Anxious/Depressed scales some genetic influences persisted, but newly expressed genetic variation during middle childhood had a greater impact. Shared environmental influences remained the same for all CBCL scales in early and middle childhood, although these influences only explained a significant proportion of the observed variances of the Internalizing scale and the Total Problem scale. As Schmitz et al. (1995) indicated, these interesting results should be replicated with a larger sample before definite conclusions can be drawn.

The present study comprises three groups: a group of 111 pairs of biologically related siblings, adopted into the same family; a group of 221 pairs of nonbiologically related siblings, also adopted into the same family; and a group of 1484 singly adopted adolescents. At the second assessment 75 pairs, 154 pairs and 1080 singletons, respectively, participated

again. Adoptees were aged 10 to 15 years at the first assessment; 95.9% of the sample was between 11 and 14 years of age. When they were assessed again three years later using the same instrument; 95.8% of the sample was between 14 and 17 years of age. A special feature of our study is that all groups are raised by adoptive parents. In most other studies adopted children are compared with controls who are raised by their biological parents. Of course, having the status of 'adopted child' or not, can have a profound influence on the measured variables. For some adopted children, this status might be difficult to accept, thereby possibly increasing the amount of problem behaviors shown. In this study, using solely adopted children, results can not be distorted by this interference. Also, biological children can show different estimates of genetic and environmental influences than adopted children do, because of possible interactions between the genotype and environment of parents and their children. Using only adopted children, we will be able to measure genetic and environmental estimates that are not distorted by this type of genotype-environment interaction.

Van den Oord et al. (1994) used the same adoption sample to determine the heritability of different problem behaviors at the first assessment. The authors did not use the scales as constructed by Achenbach (1991a,d), but developed their own scales that differed slightly from those by Achenbach. Van den Oord et al. (1994) found that the Internalizing scale showed almost no genetic influences. Nonshared environmental influences accounted for almost all of the variance. However, the Externalizing scale showed genetic effects that were larger than either nonshared or shared environmental influences. Van den Oord et al. (1994) found that variation in behavioral problems was neither influenced by the number of siblings, nor by the influence of siblings interacting with each other. Sex differences in heritability were found for most problem behaviors, showing larger genetic influences for boys (but the effect was small).

The goals of the current study were first, to estimate at two assessment points during adolescence the genetic and environmental influences on different problem behaviors. Second, to examine the continuity and change of these influences over the 3-year interval, addressing the question to what extent the genetic and environmental factors, expressed at the first assessment, remain important over time and to what extent new genetic and environmental factors become of importance.

Methods

Assessment instrument

The CBCL (Achenbach, 1991a,d) consists of 20 competence items and 120 problem items. Only the problem items were used in this study. They were scored by the 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. Using factor analyses, Achenbach (1991a) computed eight syndrome scales from these 120 problem items. The syndrome scales were named: Withdrawn, Somatic Complaints, Anxious/Depressed, Social Problems, Thought Problems, Attention Problems, Delinquent Behavior and Aggressive Behavior. The first three syndrome scales were summed to form a broad-band grouping, called Internalizing. The last two syndrome scales were summed to form a broad-band grouping called Externalizing. The Total Problem scale was computed by summing the scores given to the 120 problem items, with the exception of 2 problem items concerning allergy and asthma.

The good reliability and validity of the CBCL (Achenbach, 1991d) was confirmed for the Dutch version of the CBCL (Verhulst *et al.*, 1985; 1996). The test-retest reliability over a period of 2 weeks, measured in 89 children chosen at random form the Dutch population, was highest for the Total Problem scale (Pearson correlation of 0.91) and lowest for the Thought Problems scale (0.74), all correlations were significant ($p < 0.001$) (Verhulst *et al.*, 1996). De Groot et al. (1994) studied the cross-cultural generalizability of the Dutch version of the CBCL. Confirmatory factor analysis of the American syndromes in a sample of 2335 clinically referred Dutch children, aged 4- to 18 years, strongly supported the generalizability of the CBCL. In a sample consisting of 4- to 16-year-olds, drawn in 1983 from the Dutch province of Zuid-Holland (see Verhulst, *et al*, 1985), the stability over a four year interval was highest for the Aggressive Behavior scale (Pearson correlation of 0.65) and lowest for the Thought Problems scale (0.24). The Total Problem scale showed a four year stability of 0.64. Over a two year interval, the Pearson correlations for most scales were higher (Verhulst *et al.*, 1996).

The distribution of the summed scores on the different scales was skewed, because most adoptees showed either none or just a few behavior problems. Logarithmic transformations were applied to reduce skewness. After transformation, only the Somatic Problems and Thought Problems scales showed a skewness larger than 1.0 and only the Thought Problems scale showed a kurtosis larger than 1.3. These were the only scales deviating from normality, and they did so at both assessments.

Subjects

The prevalence of problem behaviors in adoptees was assessed twice, with a mean interval of 3.2 years (SD of 2.5 months). The original sample at the first assessment was selected from the central adoption register of the Dutch Ministry of Justice in 1986. It consisted of 3519 children, legally adopted by nonrelatives in the Netherlands and born outside the Netherlands between January 1, 1972 and December 31, 1975. Dutch adoption agency policies do not include selective placement. The adoptive parents were asked by letter to participate in the study. If they consented, a prepaid return envelope, a CBCL with instructions and a questionnaire about the history and health of the child were sent. If any help was needed, the parents were instructed to phone the investigators.

From the original sample, 162 adoptees had moved abroad, 39 were untraceable and 9 had died. Of the 3309 adoptees whose parents were sent the questionnaires, 2148 (64.9%) usable CBCLs were returned by mail; parents of 238 adoptees refused to participate and on 923 adoptees no response was received. For reasons of privacy, it was not permitted to contact the nonresponders or collect relevant data on them from the original adoption files. For this reason, responders, explicit refusers and nonresponders could only be compared on the adoptee's sex, actual age and age at placement in the adoptive home. The only difference found was a tendency of parents of adoptees that were placed in the adoption home at relatively later ages, to respond more than parents of adoptees that were placed in the adoption home at relatively earlier ages (Verhulst *et al.*, 1990). The respondents consisted of 45.4% mothers, 23% fathers, 28.5% mothers and fathers together filling out one questionnaire and 3.1% others (like the adoptee him/herself filling out, or assisting the parents with filling out the questionnaire). Parental occupation was measured on a 6-step

scale (van Westerlaak *et al.*, 1975). When both parents were employed, the highest level of one of them was used. The distribution of parental occupation was: 9.1% low (occupational levels 1 and 2); 25.8% middle (levels 3 and 4) and 65.1% high (levels 5 and 6). The majority of adoptive parents had a higher level of occupation (mean of 4.61, SD of 1.40). The distribution of adoptees across native countries was: Korea 32.0%, Colombia 14.6%, India 9.5%, Indonesia 7.9%, Bangladesh 6.7%, Lebanon 4.9%, Austria 5.0%, other European countries 4.2%, other non-European countries 15.2%. For the current study, the responders were divided into three groups: one group of 222 adolescents who were biologically related and adopted together into the same home, one group of 442 adolescents who were not biologically related but also adopted together into the same home and one group of 1484 adolescents who were adopted singly. There was never more than one pair of siblings in a family.

The responders of the first assessment were contacted again three years later. Of this group, 29 adoptees were untraceable, 8 had moved abroad, 3 had died and 37 were not approached because they were participating in another study. Parents of 2071 adoptees were sent the CBCL and a questionnaire about the general functioning of their adopted child(ren). A reminder was sent to the nonresponders and those who still did not respond were telephoned. Usable CBCLs were received from 1538 adoptees (74%). Adoptive parents that did not respond had adoptees that were slightly older and had slightly higher problem scores at the first assessment (Verhulst & Versluis-den Bieman, 1995). The respondents consisted of 61.3% mothers, 19.8% fathers and 18.9% mothers and fathers together filling out one questionnaire. The category others did not occur at the second assessment. Parental occupation and the distribution across native countries had not changed. For the current study, the responders were divided again into three groups: one group of 150 biologically related siblings, one group of 308 nonbiologically related siblings and one group of 1080 singly adopted adolescents.

Table 6.1 shows the relation between country of origin and the groups of biological siblings, nonbiological siblings and singletons. The χ^2 test statistic was significant at both assessments, indicating that there were differences among the three groups concerning their countries of origin. More biologically related siblings came from Korea and Columbia versus

other Asian countries and Europe. Within pairs, biologically related siblings and 78% of the nonbiologically related siblings came form the same country of origin. Within the group of nonbiological adoptees, siblings who came from different countries tended to be somewhat more physically neglected before their placement in the adoptive home than siblings who had the same country of origin. For all other measured characteristics no differences were found.

Table 6.1 *Countries of origin of adoptees in percentages.*

	Biological		Nonbiological		Singletons	
Country of origin	Time 1	Time 2	Time 1	Time 2	Time	Time 2
Korea	47.3	53.3	21.5	22.7	32.9	34.4
Colombia	26.6	22.0	13.3	14.0	13.2	13.3
India	2.7	2.7	10.0	11.7	10.3	10.5
Indonesia	9.9	8.7	6.6	6.8	8.0	7.8
Bangladesh	2.7	2.7	4.1	3.6	8.0	8.2
Lebanon	0.0	0.0	12.2	13.0	3.4	3.5
Austria	2.7	4.0	9.7	9.7	3.9	3.8
Other European	0.0	0.0	4.5	4.2	4.8	3.5
Other non-European	8.1	6.7	18.1	14.3	15.4	15.0
Number of children	222	150	442	308	1484	1080

Note. The χ^2 test statistic showed significant differences between the groups at both assessment points (Time 1: χ^2 test statistic = 202.08, df = 16, p = .000; Time 2: χ^2 test statistic = 140.59, df = 16, p = .000).

Table 6.2 shows the tests for differences between the groups of biological siblings, nonbiological siblings and singletons for different background characteristics at both assessments. The χ^2 test showed a significant difference between the groups at both assessment points in number of changes in the caretaking environment that the child experienced before it was adopted. Biological siblings had experienced more changes than singletons, who had experienced more changes than nonbiological siblings. No significant differences were found between the three groups in whether the child had been physically neglected or abused before placement in the adoptive home. Comparing the groups by age of placement in the adoptive home, the χ^2 test did show a significant difference at both assessment points. Biological siblings were placed in their adoptive homes later than singletons, who were placed later than nonbiological siblings. The child's physical health at the time of placement did not show a significant difference between the groups. ANOVA was

used as a test of group differences for the age of the adoptee at measurement. Although shown in the table in years, we used a measurement in months. Only at the second assessment did ANOVA show a difference between the groups in age. Post-hoc tests indicated that the biological siblings were significantly older than the singletons. Parental occupation, of which scale 1 and 2 of van Westerlaak et al. (1975) were taken together (constituting the category 'low' occupation) to get the right expected frequencies in the cells, did not show a difference between the groups.

Table 6.2 *The means and standard deviations per group, and the test of differences between the groups, for three conditions: before placement in the adoptive home, at placement in the adoptive home and at time of measurement, for assessment 1 and 2.*

	Biological	Nonbiological	Singletons	F / χ^2	df	p
Assessment 1:						
Conditions before placement						
changes in caretaking	1.86 (0.62)	1.60 (0.63)	1.70 (0.62)	31.41	4	.000 *
physical neglect	1.64 (0.76)	1.56 (0.71)	1.64 (0.75)	4.53	4	.339
physical abuse	1.20 (0.48)	1.14 (0.42)	1.17 (0.45)	3.09	4	.543
Conditions at placement						
age at placement	4.95 (1.84)	2.89 (1.92)	3.73 (2.21)	174.44	14	.000 *
physical health	1.40 (0.49)	1.41 (0.49)	1.44 (0.50)	2.72	2, 2145	.257
Conditions at measurement						
age of adoptee	12.5 (1.18)	12.4 (1.15)	12.3 (1.17)	2.52	2	.081
occupation of parents	4.71 (1.39)	4.63 (1.42)	4.59 (1.39)	11.28	8	.186
Assessment 2:						
Conditions before placement						
changes in caretaking	1.84 (0.58)	1.60 (0.61)	1.69 (0.59)	19.27	4	.001 *
physical neglect	1.59 (0.76)	1.57 (0.72)	1.64 (0.75)	3.59	4	.464
physical abuse	1.25 (0.52)	1.13 (0.40)	1.17 (0.46)	7.37	4	.118
Conditions at placement						
age at placement	4.97 (1.79)	2.86 (1.82)	3.69 (2.20)	136.05	14	.000 *
physical health	1.37 (0.49)	1.44 (0.50)	1.45 (0.50)	2.97	2	.227
Conditions at measurement						
age of adoptee	15.8 (1.17)	15.6 (1.20)	15.4 (1.16)	6.53	2, 1535	.002 *
occupation of parents	4.77 (1.30)	4.67 (1.42)	4.63 (1.39)	8.21	8	.413

Note. The variable " age of adoptee", given in years, used a measurement in months.
* = F or χ^2 test statistic showed a significant difference between the groups.

Missing data and different kinds of raters

At the second assessment a response bias was found. Parents who cooperated again, had indicated less problems for their adopted children at the first assessment, than parents who did not cooperate again. For the nonbiologically related and the singly adopted adolescents, this response bias was found only for the Delinquent Behavior scale (means of 2.54 versus 3.26 and 2.98 versus 3.49, respectively). However, for the biologically related siblings, ANOVA showed the same significant difference for 6 of the 11 CBCL syndrome scales. The mean reported problems at the first assessment of second time responders versus dropouts were accordingly, Anxious/Depressed: 3.77 versus 4.80, Social Problems: 2.31 versus 3.30, Delinquent Behavior: 2.45 versus 3.66, Aggressive Behavior: 5.47 versus 7.24, Externalizing: 6.29 versus 8.06, Total Problem: 10.83 versus 12.54.

This missing-data pattern at the second assessment is related to variables that have been measured (the CBCL scales at assessment 1) and thus the pattern is included in the analysis (Graham *et al.*, 1997). Although the data is not "missing completely at random", the missing-data pattern is consistent with "missing at random" (Little & Rubin, 1989; Graham *et al.*, 1996). Whether the data are missing on the later assessments is, at least in part, predicted by variables that are not missing. An appropriate statistical technique to handle such data is based on the maximization of the likelihood of the observed data. The likelihood gives an indication of how good the theoretical model, with its estimated parameters, represents the observed data. Even when the data are not strictly missing at random, maximum likelihood often reduces nonresponse biases (Little & Rubin, 1989; Muthén *et al.*, 1987). We used Mx, a structural equation modeling program that allows estimation of the raw maximum likelihood function at the level of the individual (Graham *et al.*, 1997; Neale, 1997b; Wothke & Arbuckle, 1995). This fitting function corrects for the nonresponse bias at the second assessment by calculating the appropriate mean vector and covariance matrix for each observation separately, using per observation all information available. By using raw maximum likelihood, the likelihood of the theoretical model was calculated separately for each pedigree and subsequently maximized over the different pedigrees (Neale, 1997b). Although the singletons' data did not give any information about the genetic or environmental

influences, their data did provide information on the variances at the first and second assessment and on the covariance between the assessments.

Different raters might vary in their tendency of reporting problem behaviors, for instance, mothers might report more problems than fathers. In order to be able to correct for this rater bias, while having only one questionnaire (one kind of rater) per child, we allowed different kinds of raters to have different means for reported problem behaviors. This can be done in Mx by a feature called definition variables, allowing 'multilevel' statistical analyses. Mx extracts the definition variable, in this case 'kind of rater', from the data and restricts modeling, separately for each kind of rater, to the other variables (the CBCL scales). The usual raw data log-likelihood function is computed for the theoretical model, while using the appropriate mean matrix for each 'kind of rater'.

Model

A genetic model was fitted to the variances and covariances between siblings. Nonbiologically related siblings, who only resemble each other because of similar shared environmental influences, were compared with biologically related siblings, who can also resemble each other because they share on average half of their genes. By comparing the similarity between the biologically related adoptees with the similarity between the nonbiologically related adoptees, identification of the model to estimate the contributions of genotype (A), shared environment (C) and nonshared environment (E) is achieved. If the biologically related adoptees resemble each other to the same degree as the nonbiologically related adoptees, only environmental factors can be of importance in explaining sibling resemblance. However, when the biologically related adoptees resemble each other more than the nonbiologically related adoptees, genetic factors are supposed to be of importance, since the only difference between the two groups is in genetic relatedness.

To estimate the longitudinal genetic and environmental factors on the different CBCL scales, a bivariate Cholesky decomposition (Neale & Cardon, 1992) was fitted to the log-10 transformed, raw data. This model, shown in Figure 6.1, decomposes the observed variance of the parental ratings into three latent factors that have, sequentially over time, an influence at both assessment points, i.e. genetic (A_1), shared environmental (C_1) and nonshared

environmental (E_1) factors, as well as three latent factors that only have an influence at the second assessment point, i.e. genetic (A_2), shared environmental (C_2) and nonshared environmental (E_2) factors. The relative influences of the latent genetic and environmental factors on the different CBCL scales are indicated by the paths (i.e. a, c, e). To estimate the total amount of genetic (or environmental) influences that are active at the second assessment, the squared path of the first genetic (or environmental) factor has to be summed with the squared path of the second genetic (or environmental) factor and divided by the summed squared paths of the total amount of genetic and environmental influences at the second assessment. The genetic (or environmental) influences that are expressed only at the second assessment can be estimated by dividing the squared path from the second genetic (or environmental) factor by the total variance at the second assessment.

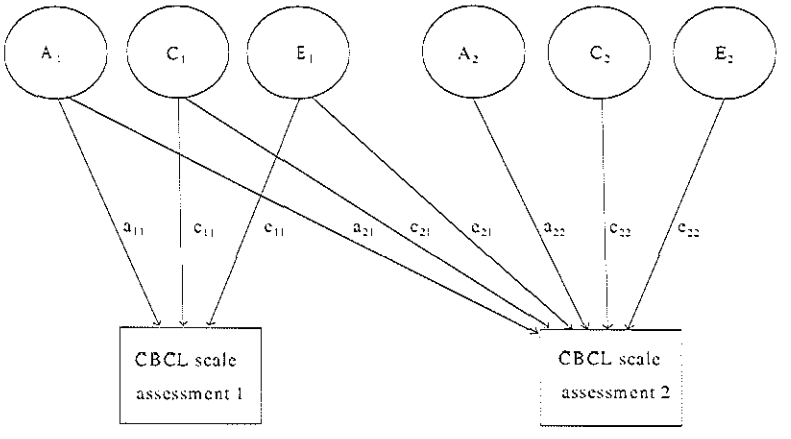

Figure 6.1 *Path diagram depicting the bivariate longitudinal ACE model.*
Latent variables A_1, C_1 and E_1 refer to the genetic, shared environmental and nonshared environmental factors that have an influence on the observed variance of the parental ratings at both assessment points. A_2, C_2, E_2 and correspond to the genetic, shared environmental and nonshared environmental factors that only have an influence at the second assessment point. The strength of the relative influences of the latent factors on the parental ratings are indicated by the path coefficients a_{11}, c_{11} and e_{11} for ratings at the first assessment and by a_{22}, c_{22} and e_{22} for ratings at the second assessment. The path coefficients a_{21}, c_{21} and e_{21} refer to the strength of the relative influences of the latent factors that retain their influences over time. The covariance between the two assessment points, for instance the genetic covariance, can be estimated by multiplying $a_{11}a_{21}$. The total covariance equals $a_{11}a_{21} + c_{11}c_{21} + e_{11}e_{21}$.

Using this bivariate Cholesky decomposition, it is possible to partition the covariance between the two assessment points into genetic, shared and nonshared environmental covariance. This indicates to which extent the stability of problem behaviors is caused by genes, shared, or nonshared environment. The percentage of covariance can be estimated by multiplying the path of the first latent factor, leading towards the scales measured at the first assessment, with the path leading from the first latent factor towards the scales measured at the second assessment and dividing this with the total covariance between the two assessment points.

Model fitting

An indication of how well a particular model fits the data is given by the likelihood. A good model is one that represents the observed results with a high likelihood. To be able to test the goodness of fit of the theoretical ACE model, the model's log-likelihood (LL) is subtracted from the LL of a less constrained model. By multiplying the result by 2, a χ^2 test statistic is obtained. This χ^2 test statistic indicates whether the theoretical ACE model describes the observed data adequately. The degrees of freedom for this test statistic are the number of parameters in the theoretical ACE model, subtracted from the number of parameters in the less constrained model.

First we tested whether the bivariate Cholesky model fitted the observed data significantly worse than a saturated model, which is a model without any constraints. The saturated model estimates the means and the variance-covariance matrices separately for each rater and for each group of adoptees. Second, when the bivariate Cholesky model did not show a significantly worse fit to the observed data, we tested whether the means between the three groups (biologically related adoptees, nonbiologically related adoptees and singletons) and between siblings (within the same family) could be constrained to be equal. Third we tested whether the means of the different kinds of raters and of the first and second assessment could be constrained to be equal. For each CBCL problem scale, the most simplified model for means was retained to analyze the causes of variation in the observed data and to test whether this best fitting ACE model could further be simplified by removing the genetic, shared and nonshared environmental factors. Finally, to get more detailed

information about the precision of the genetic, shared environmental and nonshared environmental estimates. 95% likelihood-based confidence intervals were estimated. These confidence intervals are estimated by finding the maximum and minimum values of the path estimate that - with all other paths of the model still free to vary - cause a loss of fit equal to a chi-squared of 3.84. (Neale & Miller, 1997a).

Results

Description of the data

Table 6.3 shows the means and standard deviations for singletons, oldest (first line) and youngest (second line) siblings and the correlations between the siblings for each group, at both assessments for all CBCL scales. The longitudinal correlations between the measurements are given in the last three columns. For all CBCL scales, the adoption sample showed higher means and higher standard deviations than the Dutch normative sample (Verhulst *et al.*, 1996). Within the adoption sample, the means and standard deviations were generally comparable among the three groups. Over time, the means of most CBCL scales increased, while on average the standard deviations remained the same. This indicates that more problem behaviors were reported for adoptees in their later adolescent years.

The longitudinal correlations between the two assessment points show the extent to which the scores of the adoptees keep their relative positions across time, irrespective of possible changes in mean scores. For all adoptees these correlations were mostly around .60, pointing to a considerable stability of the problem behaviors over time. Only the Somatic Complaints and Thought Problems scales showed lower correlations. However, their longitudinal correlations, ranging from .32 to .64, could still be considered moderate.

The correlations between the siblings at the first assessment showed, with the exception of the Internalizing scale, that the biologically related siblings were more similar than the nonbiologically related siblings. The lower correlations for the nonbiologically related siblings suggest that genetic factors could play a role in the etiology of these behaviors. At the second assessment the correlations between the siblings, especially between the biologically related siblings, tended to be lower compared with the first assessment. For the

Table 6.3 *Means and standard deviations (between parentheses) for oldest (first line) and youngest (second line) siblings and singletons, the correlations between siblings per group at assessment 1 and 2, and the longitudinal correlations between assessments 1 and 2 per group, for Achenbach's 1991 CBCL/4-18 profiles *. The number of adoptees per group is given in the last row.*

	Assessment 1			Assessment 2			Longitudinal correlations		
CBCL scales	biological	nonbiological	singletons	biological	nonbiological	singletons	bio.	nonbio.	single.
Broad-band groupings:									
total problem score	11.28 (4.29)	11.79 (4.33)	11.89 (4.31)	12.56 (3.87)	12.13 (4.24)	12.38 (4.20)	.65	.66	.71
	11.49 (4.39) .57	11.56 (4.23) .39		12.26 (4.26) .45	12.03 (4.39) .31		.54	.66	
Internalizing Problems	7.08 (3.78)	7.04 (3.80)	6.95 (3.78)	8.39 (3.78)	7.52 (3.89)	7.78 (3.86)	.69	.59	.63
	6.17 (3.96) .31	6.43 (3.77) .34		7.41 (3.73) .17	7.28 (3.92) .40		.53	.51	
Externalizing Problems	6.30 (4.49)	7.03 (4.80)	7.28 (4.58)	7.29 (4.41)	7.57 (4.85)	7.71 (4.56)	.72	.71	.70
	7.43 (4.54) .47	6.92 (4.68) .19		8.00 (4.80) .40	7.26 (4.94) .18		.52	.67	
Syndrome scales:									
withdrawn	5.03 (3.22)	4.54 (3.23)	4.51 (3.25)	5.92 (3.30)	4.99 (3.35)	5.30 (3.29)	.60	.59	.61
	3.54 (3.34) .20	3.97 (3.06) .16		4.84 (3.43) .03	4.75 (3.33) .21		.46	.51	
somatic complaints	1.20 (2.21)	1.55 (2.35)	1.53 (2.30)	1.82 (2.65)	1.76 (2.55)	2.11 (2.66)	.51	.49	.38
	1.47 (2.30) .27	1.45 (2.29) .18		1.98 (2.35) .18	1.71 (2.42) .26		.37	.37	
anxious / depressed	4.24 (3.54)	4.39 (3.60)	4.26 (3.53)	5.30 (3.88)	4.80 (3.72)	4.74 (3.73)	.70	.48	.59
	3.96 (3.41) .31	3.95 (3.46) .26		4.62 (3.44) .26	4.56 (3.70) .29		.57	.51	
social problems	2.74 (2.93)	2.97 (3.15)	3.09 (3.23)	3.34 (2.93)	2.79 (3.02)	2.99 (3.13)	.57	.56	.59
	2.52 (3.06) .37	3.13 (3.29) .18		2.58 (2.95) .24	3.14 (3.34) .16		.68	.70	
thought problems	1.17 (2.06)	1.16 (2.13)	1.10 (2.03)	1.63 (2.45)	1.14 (1.98)	1.30 (2.22)	.64	.45	.38
	0.95 (2.02) .24	0.89 (1.93) .15		1.26 (2.27) .03	1.14 (2.14) .11		.41	.32	
attention problems	5.07 (3.87)	5.52 (3.70)	5.57 (3.67)	5.99 (3.19)	5.51 (3.77)	5.96 (3.60)	.65	.63	.65
	5.28 (3.73) .33	5.24 (3.92) .08		5.78 (3.47) .25	6.04 (3.77) .10		.71	.70	
delinquent behavior	2.71 (3.25)	2.85 (3.33)	3.12 (3.35)	3.69 (3.29)	3.85 (3.79)	3.84 (3.69)	.60	.63	.61
	2.97 (3.52) .43	2.67 (3.20) .24		3.92 (4.16) .33	3.34 (3.83) .17		.44	.62	
aggressive behavior	5.46 (4.08)	6.31 (4.55)	6.44 (4.33)	6.17 (4.04)	6.50 (4.53)	6.64 (4.22)	.67	.70	.69
	6.62 (4.37) .42	6.23 (4.45) .13		6.90 (4.41) .36	6.34 (4.62) .14		.51	.70	
Number of pairs / singletons	111	221	1484	76	155	1080	76	155	1080

* Note. Data has been logtransformed (log 10) and multiplied by 10.

Total Problem, Externalizing, Aggressive Behavior, Delinquent Behavior, Attention Problems and Social Problems scales the biologically related siblings still had higher correlations than the nonbiologically related siblings. This suggests that genetic factors were, also at this second assessment point, of importance. However, for all other scales the correlations of the biologically related siblings were equal to or even lower than the correlations of the nonbiologically related siblings, indicating the importance of environmental influences.

Table 6.4 *χ^2 test statistics obtained from fitting the bivariate Cholesky ACE model, and its nested models.*

CBCL scales	saturated vs ACE model all means unequal df = 14	most simplified ACE model means equal, if not leading to a significantly worse fit	ACE vs AE model df = 3	ACE vs CE model df = 3	ACE vs E model df = 6
Broad-band groupings:					
total problem score	12.634	3.672 (df = 1)	43.426 *	9.901 *	106.275 *
internalizing problems	16.43	3.315 (df = 1)	39.738 *	6.372	58.831 *
externalizing problems	16.782	0.303 (df = 1)	11.304 *	10.937 *	49.501 *
Syndrome scales:					
withdrawn	11.584	5.653 (df = 2)	11.259 *	1.573	15.461 *
somatic complaints	8.921	5.329 (df = 7)	15.917 *	0.953	25.787 *
anxious / depressed	12.586	0.386 (df = 1)	25.782 *	7.993 *	46.338 *
social problems	12.931	0.001 (df = 1)	8.667 *	5.872	27.967 *
thought problems	19.692	0.333 (df = 1)	7.173	1.287	13.535 *
attention problems	16.575	1.976 (df = 2)	1.689	6.869	17.463 *
delinquent behavior	22.82	0.082 (df = 1)	15.027 *	4.236	40.916 *
aggressive behavior	16.63	4.683 (df = 2)	5.644	10.008 *	33.182 *

Note. * = χ^2 test of the model is significant: the model fits the observed data worse than a less constrained model. The critical χ^2 value (α = .05) with 14 df is 23.68, with 7 df is 14.06, with 6 df is 12.59, with 3 df is 7.81, with 2 df is 5.99 and with 1 df is 3.84.

Test of ACE model and of means

Table 6.4 shows the χ^2 test statistics obtained from fitting the bivariate Cholesky (ACE) model and its nested models. The first column shows the comparison between a saturated model and the full ACE model. For none of the scales did the theoretical model, specifying genetic, shared environmental and nonshared environmental factors, describe the observed data any worse than a saturated model.

In the second column, the χ^2 test statistics are given of the final ACE model. In this final ACE model, those means were constrained to be equal that did not lead to a significantly worse fit of the model. The means between the two sibling groups and the singleton group could be constrained to be equal for all CBCL syndrome scales. Between the oldest and youngest siblings the means could be constrained to be equal for all scales, with the exception of the Withdrawn scale. The oldest sibling obtained a higher score than the youngest sibling. Mean ratings of mothers and fathers at the first assessment could also be constrained to be equal for all scales, with the exception of the Somatic Complaints scale. Mothers reported more problems for this scale than fathers. At the second assessment mean ratings of mothers could not be constrained to be equal to father ratings for the Total Problem, Internalizing, Externalizing, Withdrawn, Somatic Complaints and Anxious/Depressed scales. Again, mothers reported more problems for these scales than fathers. For most scales, the means of mothers and fathers filling out one questionnaire together could be constrained to be equal to the means of other kinds of raters. Only the Somatic Complaints scale gave a significantly worse fit. Mothers and fathers filling out one questionnaire together indicated fewer problems on this scale than other raters. When still possible, the means between all four kinds of raters were constrained to be equal. For the Internalizing, Externalizing, Anxious/Depressed, Thought Problems and Delinquent Behavior scales this gave a significantly worse fit. Mothers and fathers indicated less problems for these scales than mothers and fathers filling out one questionnaire together or other kinds of raters. Finally, the means between the first and second assessment could only be constrained to be equal for the Social Problems scale. For all other scales the adoptees obtained significantly higher problem scores at the second assessment versus the first assessment.

The last three columns of Table 6.4 show the χ^2 test statistics obtained from fitting the nested models of the final ACE model. To test whether the ACE model could be simplified, the loadings of the shared environmental factors were constrained at zero (ACE versus AE model). Except for the Aggressive Behavior, Attention Problems and Thought Problems scales, this model fitted the observed data significantly worse. Thus, for most scales, the shared environmental factors had to be included in the model. Second, the genetic factors were removed from the model (ACE versus CE model). Only the Total Problem,

Externalizing, Aggressive Behavior and Anxious/Depressed scales showed a significantly worse fit when the CE model was compared to the full ACE model. For all other scales, the genetic factors were not statistically significant. However, one should be cautious with the interpretation of this result because this non-significantly worse fit for a model without genetic factors could have been caused by the lack of power to find genetic effects. Having almost twice as many nonbiologically related siblings as biologically related siblings, the power of this study to estimate genetic effects for the Internalizing, Withdrawn, Somatic Complaints and Thought Problems scales was low. Their power at $\alpha = .05$, assuming the estimated genetic influences at the first assessment to be true effects, was calculated to be about 25%. On the other hand, the power to detect shared environmental effects for these CBCL scales at $\alpha = .05$, assuming the estimated common environmental influences to be true effects, was calculated to be much higher than the power to detect genetic effects, around 89%.

As a final test of familial influences, both the shared environmental and the genetic factors were removed from the model, comparing this model with the full ACE model. For all scales this led to a significant decrease in fit, indicating that for all scales either genetic factors or shared environmental factors or both were necessary to explain the observed data.

Table 6.5 *Percentage of variance explained by the genetic, shared environmental and nonshared environmental factors of the bivariate Cholesky ACE model and their 95% confidence intervals between brackets.*

	Assessment 1	Assessment 2	Assessment 1	Assessment 2	Assessment 1	Assessment 2
CBCL scales	a^2	a^2	c^2	c^2	e^2	e^2
Broad-band groupings:						
total problem score	36 (5-66)	17 + 25 = 42 (1-79)	40 (28-49)	21 + 8 = 29 (15-41)	24 (2-50)	10 + 19 = 29 (0-63)
internalizing problems	16 (1-41)	8 + 0 = 8 (0-29)	30 (19-39)	29 + 4 = 33 (21-43)	54 (33-70)	34 + 25 = 59 (40-74)
externalizing problems	55 (17-90)	26 + 22 = 48 (3-88)	19 (6-30)	11 + 6 = 17 (2-29)	26 (0-58)	12 + 23 = 35 (3-74)
Syndrome scales:						
withdrawn	9 (0-41)	1 + 0 = 1 (0-29)	17 (5-27)	18 + 0 = 18 (6-28)	74 (46-90)	29 + 52 = 81 (56-93)
somatic complaints	20 (19-59)	0 + 0 = 0 (0-38)	18 (5-29)	15 + 9 = 24 (9-36)	62 (29-87)	9 + 67 = 76 (44-89)
anxious / depressed	25 (2-54)	8 + 0 = 8 (0-38)	26 (14-35)	28 + 0 = 28 (15-39)	49 (24-71)	41 + 23 = 64 (37-80)
social problems	52 (10-89)	17 + 0 = 17 (0-60)	17 (4-29)	7 + 6 = 13 (0-25)	31 (3-68)	12 + 58 = 70 (34-92)
thought problems	20 (0-22)	1 + 0 = 1 (0-33)	15 (2-25)	8 + 2 = 10 (0-23)	65 (32-90)	17 + 72 = 89 (80-99)
attention problems	53 (12-87)	19 + 9 = 28 (0-78)	7 (0-19)	5 + 2 = 7 (0-20)	40 (9-74)	20 + 45 = 65 (21-97)
delinquent behavior	34 (0-70)	34 + 3 = 37 (0-80)	25 (11-36)	8 + 7 = 15 (0-29)	41 (13-71)	4 + 44 = 48 (13-82)
aggressive behavior	61 (20-96)	37 + 15 = 52 (5-93)	13 (0-24)	7 + 5 = 12 (0-25)	26 (0-60)	5 + 31 = 36 (3-76)

Note I. Assessment 1: a^2, c^2, e^2 = percentage variance explained by first genetic, shared environmental and nonshared environmental factors at the first assessment. Assessment 2: a^2, c^2, e^2 = percentage variance explained by first + second = total genetic, shared environmental and nonshared environmental factors at the second assessment.

Note II. Some confidence intervals could not be estimated precisely because the tail of the distribution on the right side was too long.

Table 6.6 *Percentage of covariance between assessment 1 and 2, explained by the genetic, shared environmental and nonshared environmental factors of the bivariate Cholesky ACE model and their 95% confidence intervals between brackets.*

	Assessment 1 - 2	Assessment 1 - 2	Assessment 1 - 2
CBCL scales	a^2	c^2	e^2
Broad-band groupings:			
total problem score	36 (-8 - 77)	42 (26 - 55)	22 (-8 - 59)
internalizing problems	-18 (-31 - 4)	48 (34 - 61)	70 (48 - 87)
externalizing problems	55 (3 - 101)	20 (3 - 35)	25 (-11 - 69)
Syndrome scales:			
withdrawn	-7 (-20 - 30)	29 (13 - 43)	78 (45 - 98)
somatic complaints	1 (-7 - 75)	41 (14 - 64)	58 (-4 - 104)
anxious / depressed	-24 (-40 - 15)	46 (30 - 59)	78 (43 - 100)
social problems	50 (-4 - 104)	18 (3 - 34)	32 (-13 - 80)
thought problems	-11 (-53 - 58)	28 (1 - 48)	83 (24 - 99)
attention problems	48 (-7 - 100)	9 (-4 - 25)	43 (-3 - 93)
delinquent behavior	56 (-1 - 107)	23 (4 - 40)	21 (-19 - 70)
aggressive behavior	69 (15 - 116)	14 (-2 - 29)	17 (-19 - 63)

Note. Some confidence intervals could not be estimated precisely because the tail of the distribution on the right side was too long.

The estimates of the bivariate Cholesky ACE model

In Table 6.5 the percentage of variance explained by the genetic, shared environmental and nonshared environmental factors of the ACE model and their 95% confidence intervals are given. Estimates at the second assessment point have been divided into persistent factors that maintained their influence over time and new factors that only had an influence at the second assessment. Table 6.6 shows the percentage of covariance between the first and second assessment, indicating what kinds of influences are responsible for the longitudinal stability of the problem behaviors. As shown by Table 6.5, large genetic effects were found at both assessment points for the Aggressive Behavior and Externalizing scales. At the first assessment, genetic factors accounted for 61% of the variance of the Aggressive Behavior scale and 55% of the variance of the Externalizing scale. At the second assessment, genetic factors still had large effects, explaining 52% of the variance of the Aggressive Behavior scale and 48% of the Externalizing scale. Most of the genetic influences at the second assessment were caused by the continuing influences of genetic factors that had also exerted their influence at the first assessment. These persistent genetic factors maintained their importance over time, explaining at the second assessment 37% of the genetic variance of the

Aggressive Behavior scale and 26% of the genetic variance of the Externalizing scale. For this last scale, new genetic factors also had a large influence at the second assessment, explaining 22% of the genetic variance. The covariance between the two assessments (Table 6.6) was for both scales mostly explained by genetic factors, suggesting that the stability of these scales was mostly influenced by genes, which persisted in exerting their influence over time. Shared environmental effects were modest, explaining between 12% and 19% of the variance. At the second assessment, persistent and new shared environmental factors were almost of equal importance. Nonshared environmental factors explained between 26% and 36% of the variance. At the second assessment, new nonshared environmental factors accounted for more of the variance than the persistent factors, showing that the kinds of nonshared environmental influences that the adoptees experience probably change over time.

The Delinquent Behavior scale showed smaller genetic effects. At the first and second assessment, genetic factors explained 34% and 37% of the variance, respectively. Persistent genetic factors accounted for almost all of the genetic variance at the second assessment. The covariance was mostly explained by genetic influences indicating that also the stability of Delinquent Behavior was caused mostly by genes which maintained their influence over time. A large amount of the variance of the Delinquent Behavior scale at both assessments was also explained by nonshared environmental factors, 41% and 48% respectively. At the second assessment, these influences were mostly caused by new nonshared environmental factors, suggesting that the kinds of nonshared environmental influences on the Delinquent Behavior scale changed over time.

The Social Problems and Attention Problems scales showed large genetic effects at the first assessment, explaining 52% and 53% of the variance, respectively. However, at the second assessment the genetic factors had only moderate influences, explaining 17% and 28% of the variance, respectively. Still, almost all of the genetic influences at this second assessment were caused by persistent genetic factors. The covariance between the two assessments was for both factors mostly accounted for by genetic influences, suggesting that also the stability in having Social Problems or Attention Problems was caused mostly by genes which persisted in exerting their influence over time. Shared environmental factors were very modest for both scales, showing an almost equal influence of persistent and new

factors. Nonshared environmental influences increased over the three year interval, with almost all of the variance at the second assessment accounted for by new nonshared environmental factors. This shows that also for these scales the nonshared environmental influences had changed over time.

A different pattern of results was found for the Internalizing scale, its subscales Withdrawn, Somatic Complaints and Anxious/Depressed and for the Thought Problems scale. Although these scales showed modest genetic influences at the first assessment, almost no genetic influences were found for any of the scales at the second assessment. The nonshared environmental factors accounted for most of the variances at both assessments. At the second assessment, new nonshared environmental factors accounted for most of the variance of the Withdrawn, Somatic Complaints and Thought Problems scales. For Internalizing and the Anxious/Depressed scale, persistent nonshared environmental influences also maintained a large influence at the second assessment. The covariance between the two assessments was for all scales mostly explained by the nonshared environmental influences, suggesting that idiosyncratic experiences were largely responsible for the stability of these scales over a 3 year interval.

The only scale having the largest percentage of covariance explained by the shared environmental factors was the Total Problem scale. The genetic, shared environmental and nonshared environmental factors accounted for 36%, 40% and 24% of the variance, respectively, at the first assessment and for 42%, 29% and 29% of the variance, respectively, at the second assessment. Almost all of the shared environmental influences at the second assessment were caused by persistent shared environmental factors. This suggests that the stability of the Total Problem scale was caused mostly by continuing influences of the same shared environmental factors.

Discussion

In the present study of biologically related and unrelated adopted siblings and singletons, genetic factors are responsible for explaining a large part of the variance in the Externalizing scale at both assessment points. Persistent genetic factors, which are also expressed during

the young adolescent years, maintain their importance over time, explaining 26% of the genetic variance at the second assessment. New genetic factors explained 22% of the genetic variance. The estimated covariances between the first and second assessment indicate that the genetic factors are also mostly responsible for the stability of the Externalizing scale over time. The effects of shared environmental factors are modest, showing an almost equal influence of persistent and new factors at the second assessment.

For the Internalizing scale, nonshared environmental factors account for most of the variance at both assessments. Persistent and new nonshared environmental factors account for about the same part of the variance during the later adolescent years. The covariance between the two assessments is mostly explained by the nonshared environmental influences, suggesting that idiosyncratic experiences are largely responsible for the stability of these scales over a three year interval. The effects of shared environmental factors are modest. At the second assessment, the persistent factors account for most of the shared environmental variance, suggesting that the familial influences for this scale do not change over time.

The longitudinal correlations, which are mostly around .60, point to a considerable stability of the problem behaviors during the three year interval. Over time, the adopted adolescents show an increase in their problem scores for all CBCL scales. This increase in problem behaviors is, according to Verhulst and Versluis-den Bieman (1995), not significantly related to either their ethnicity or to preadoption influences, like neglect, abuse, age of the child at placement in the adoptive family or medical conditions at the time of placement. Nonadopted adolescents, however, show a slight decrease in their CBCL problem scores over time. Our results indicate that the causes for stability differ for different problem behaviors. While the genetic factors are mostly responsible for the stability of the Externalizing scale, nonshared environmental factors have the largest influence on the stability of the Internalizing scale. This suggests that idiosyncratic influences, like cognitive evaluations including those related to the self-esteem during adolescence, may cause the adoptees to retain high scores on the Internalizing scale. As was already concluded by Versluis-den Bieman and Verhulst (1995), adolescence, a period characterized by increasing cognitive skills, striving towards greater independence, sexual maturation and concerns over identity, may add to the problems experienced by these adopted adolescents.

Finding a low heritability for the Internalizing scale is in contrast with results obtained by twin studies (Edelbrock *et al.*,1995; Hewitt *et al.*, 1992; Schmitz *et al.*,1995; Van den Oord *et al.*, 1996; Van der Valk *et al.*, 1998b), which show modest to large genetic effects. This difference may be caused by the lack of power this study had to find genetic effects for the Internalizing scale and its subscales. We compared adopted biological and nonbiological siblings and singletons who were all raised by their adoptive parents and who were of similar ages. This design contains more information about the shared environmental influences than about the genetic influences (Heath *et al.*, 1985). The lack of power to detect genetic effects can be seen for example in the size of the confidence intervals of the estimates for genetic parameters. Estimates of genetic parameters have much larger confidence intervals than estimates of shared environmental influences, for which the power to detect effects was much larger. Another possible reason for the lack of finding genetic influences for the Internalizing scale might be that parents are less able to report on Internalizing Problems of adolescents. Especially with increasing age, parents are known to report less problems than their adolescent children do, probably because many of the Internalizing Problems the adolescents experience, such as anxiety and depression, remain unnoticed by their parents (Verhulst & van der Ende, 1992a).

The results obtained for the Externalizing scale and its subscales are in accordance with results obtained from twin studies. The Aggressive Behavior and Externalizing scales show large genetic effects at both assessment points. Edelbrock et al. (1995), using the CBCL in 99 pairs of monozygotic twins and 82 pairs of dizygotic same-sex twins, ages 7-15, found that genetic factors account for 60% of the variance of the Aggressive Behavior scale and 51% of the variance of the Externalizing scale. Schmitz et al. (1995), also using the CBCL, found in their sample of 66 pairs of monozygotic twins and 137 pairs of dizygotic twins, mean age 8, that genetic factors explain 55% of the variance of the Aggressive Behavior scale and 57% of the Externalizing scale. Our results show that genetic factors at the first assessment, mean age 12.4 (SD of 1.2), account for 61% of the variance of the Aggressive Behavior scale and 55% of the variance of the Externalizing scale. At the second assessment, mean age 15.5 (SD of 1.2), genetic factors still have large effects, explaining 52% of the variance of the Aggressive Behavior scale and 48% of the Externalizing scale. Consistent with the other two twin studies

mentioned above, shared environmental effects are modest, explaining between 12% and 19% of the variance. The genetic influences found for the Delinquent Behavior scale, the other subscale of the broad-band grouping Externalizing, are also quite similar to those obtained by Edelbrock et al. (1995). Their results indicate that 35% of the variance is accounted for by genetic effects, which is very close to the 34% that we have found at the first assessment. Schmitz et al.. (1995) however, have found a much larger effect of genetic factors on the Delinquent Behavior scale, explaining 79% of the variance.

The Social Problems and Attention Problems scales both show large genetic effects at the first assessment, explaining 52% and 53% of the variance, respectively. Again these results are very similar to the results found in twin studies. In the study of Edelbrock et al. (1995), genetic factors account for 61% and 66% of the variance, respectively, while Schmitz et al. (1995) show influences of genetic factors of 56% and 65%, respectively. At the second assessment however, genetic influences decrease to explaining 17% and 28% of the variance, respectively. Although this could be either a typical result of studying adopted adolescents or a normal developmental effect, it might also be that, just as with Internalizing Problems, parents are not well able to report on these kinds of problems for adolescents. Boomsma and Koopmans (1994) collected data on 1700 twin pairs, which were older than the twin pairs used in the studies mentioned so far (12-24 years). Using the Young Adult Self Report questionnaire (YASR; Achenbach, 1997), they found an estimated heritability of 45% for Social Problems and 42% for Attention Problems.

Only for the Total Problem scale did the shared environmental factors explain the largest percentage of the covariance between the two assessments. This is a striking result when considering that for all other scales either the genetic or the nonshared environmental factors accounted for most of the covariance. Schmitz et al. (1995) obtained similar results in their study, in which the Total Problem scale was one of the few scales for which the shared environmental factors explained a significant part of the variance. Van den Oord et al. (1996) noted that CBCL studies consistently find that shared environmental influences are larger for the Total Problem scale compared to the other scales. They hypothesized that this could be due to the fact that shared environmental influences are not expressed in a single scale but in multiple scales simultaneously.

At the second assessment, the persistent influences of the shared environmental factor explained for all problem scales the largest percentage of the variance. Apart from the continuing influence of the familial environment, this large persistent influence could also been caused by the fact that in 62% of the sample the same kind of rater filled out the questionnaire at both assessments. Although we did allow the means of different kinds of raters and at both assessment points to differ, we could not completely correct for rater bias because we had only one completed questionnaire per child. If rater bias continued to exist in the sample, this could have enlarged the estimates of the shared environmental factor.

The CBCLs were either filled out by the mother, the father, the mother and father together or by other kinds of raters. For the Internalizing, Externalizing, Anxious/Depressed, Thought Problems and Delinquent Behavior scales, mothers or fathers filling out the questionnaire alone reported significantly less problem behaviors for their children than mothers and fathers together or others as raters. Although this could be a rater effect, for instance, mothers and fathers reporting more problems when they fill out a questionnaire together, it is also possible that these differences are real. Maybe parents are more concerned with the behavior of their child when the child shows more problems. Being more concerned, they probably are more likely to both take some time to answer the questionnaire. When other raters had filled out the questionnaire, most of the time the adoptee him/herself had either filled out or had assisted with filling out the questionnaire. As noted above, adolescents are known to report more problems than their parents do, especially with increasing age.

In the sample of adoptees used, 95.9% of the children were between 11 and 14 years of age at the first assessment and 95.8% of the sample was between 14 and 17 years of age at the second assessment. This does give an overlap at the age of 14. However, the overlap is small since only 18% of the sample at the first assessment and 24% of the sample at the second assessment actually constituted the group of 14-year-olds.

Because of the special sample used in this study, not all results are easily comparable with previous twin studies. In order to get sufficient power to estimate possible genetic effects on the Internalizing scale or replicate the obtained longitudinal genetic and environmental influences on the different problem behaviors, this study should be replicated with a larger, longitudinal sample of genetically informative subjects. Also, possible sex

differences should be further investigated. In the adoption sample used, the group of biologically related adoptees consisted of 27% boy pairs, 31.5% girl pairs and 41.5% opposite sex pairs. The group of nonbiologically related adoptees showed a similar composition, having 20% boy pairs, 22% girl pairs and 58% opposite sex pairs. Van den Oord et al. (1994), using this sample at the first assessment, found small sex differences in heritability for most problem behaviors. Due to the small sample of biological siblings at the second assessment, we have not tested for sex differences in this study. However, these possible sex differences should be further examined with a larger longitudinal sample.

We estimated the likelihood based confidence intervals for all genetic, shared environmental and nonshared environmental estimates. These confidence intervals show that most genetic, shared environmental and nonshared environmental point-estimates have a rather large area in which they, depending on the precise sample and model used, can fall. Keeping this in mind, it is quite amazing that the point-estimates found in this adoption study, with the exception of the estimates of the Internalizing scale and its subscales, show so much similarity with the point-estimates found in twin studies. Both samples of genetically informative subjects have their own limitations. In twin samples for instance, congenital anomalies are more common and parental expectations might cause the monozygotic twins to behave more alike. In adoption samples, preadoption influences and the status of "being adopted" when they grow up might cause the sample to differ from the general population. Also, in the sample of adopted children used, some background characteristics differed between the three groups. For instance, the biologically related siblings experienced more changes in their caretaking environment than the singletons, who experienced more changes again than the nonbiologically related siblings. Significant differences between the three groups were also found for age of placement in the adoptive home. Biologically related siblings were placed at an older age than singletons, who were placed again at an older age than nonbiologically related siblings. However, because the point-estimates we found show so much similarity with the point-estimates found by twin studies that do not share the same limitations as this adoption study, these results are very encouraging.

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7

Summary and Conclusions

Summary and conclusions

The primary aim of this thesis was to study the genetic and environmental contributions to children's problem behaviors at ages 3 and 7. Also the determinants of continuity and change of problem behaviors were examined longitudinally from ages 3 to 7. To match most demands of statistical power required for the genetic analysis of kinship data we used all twin pairs of birth cohorts 1987 - 1991 of the population-based Netherlands Twin Registry (Boomsma *et al.*, 1992; Boomsma, 1998a). Questionnaires filled out by the parents, separately for oldest and youngest twin, were collected for 4016 3-year-old twin pairs (3873 pairs rated by mothers; 2087 pairs rated by fathers (for only half of the sample had fathers been asked to complete a CBCL)) and for 1940 7-year-old twin pairs (1924 pairs rated by mothers; 1545 pairs rated by fathers). Of all 3-year-old twin pairs for whom we had collected data, 54% had reached the age of 7 at the second assessment. Longitudinal data was obtained for 1638 twin pairs rated by mothers and 913 twin pairs rated by fathers.

We focussed on two broad groupings of problem behaviors, reflecting a distinction between anxious, inhibited behavior (Internalizing Problems) on the one hand, and aggressive, antisocial behavior (Externalizing Problems) on the other. In order to measure these problem behaviors parents were asked to fill out the Child Behavior Checklist (CBCL), a questionnaire developed to rate the behavioral and emotional problems of children. The CBCL for 2- and 3-year-old children (CBCL/2-3; Achenbach 1992) was used to rate the 3-year-old twins, while the CBCL for 4- to 18-year-old children (CBCL/4-18; Achenbach, 1991a) was completed for the 7-year-old twins. At each age the Internalizing and Externalizing broad-band scales were computed using the best fitting factor solutions for Dutch populations at that particular age. An advantage of using these broad-band scales as level of analyses, is that they are relatively unsensitive to population and/or age specific questionnaire differences because they are composed of a large number of similar items. Furthermore, several studies have found support for the validity of the internalizing - externalizing distinction (Achenbach, 1991a; Achenbach, 1992; De Groot, 1994; Koot *et al.*, 1997; Verhulst *et al.*, 1996), including the study of Hartman et al. (1999) testing the validity of the CBCL on a general population.

Genetic factors explained most of the variance for both problem behaviors at age 3 (see chapter 2 and 3). For mother's ratings of Internalizing Problems genetic factors explained 69% and for father's ratings genetic factors accounted for 59% of the variance, while for Externalizing Problems this was 52% and 56%, respectively. Four years later (see chapter 4), genetic influences for Externalizing Problems had not changed, suggesting a large continuing genetic influence for Externalizing Problems during childhood. For Internalizing Problems, however, estimates of genetic factors had decreased to explaining 38% of the variance for mother's ratings and 35% of the variance for father's ratings. Possibly this remarkable result was caused by developmental differences between older and younger children. Internalizing Problems of preschool children may predominantly be influenced by the child's genotype, while for schoolage children environmental influences shared between siblings (like style of parenting, socioeconomic level, or religion) may become relatively more important.

For 3-year-old twins, environmental influences shared between twins only had an influence on Externalizing Problems, explaining for mother's ratings 27% and for father's ratings 19% of the variance. Because often it is not family adversity as such but its persistence that predicts chronic problems (Campbell, 1995) finding shared environmental influences for children as young as 3-years of age seemed to be a remarkable finding. To examine whether this shared environmental effect was spuriously caused by siblings influencing each other, we tested for sibling interactions in chapter 2. Especially for behaviors which are easily observable for the other sibling, like aggressive behaviors, one can expect siblings to influence each other. Indeed, for Externalizing Problems, cooperative sibling interactions were found, indicating that twins reinforced each other's behaviors. However, no change in estimates occurred, showing that sibling interactions did not inflate the estimates of the shared environmental factors. Hudziak et al. (2000) proposed that the interaction effects we found could be synonymous with rater effects, meaning that parents compare the children with each other and thereby "distort" the behavioral ratings. Rater biases, i.e. tendencies of an individual rater to overestimate or underestimate scores consistently, may inflate the estimates of the shared environmental factors. To explore whether rater bias possibly inflated the estimates of the shared environmental factors we fitted Rater Bias and Psychometric models to the observed data. Results (see chapter 3)

showed that rater bias as measured in these models only had small effects, accounting for 8% of the variance. Again, the estimates of the shared environmental factors remained almost unchanged. It thus seems that for children as young as 3-years of age, pure shared environmental factors (unbiased by sibling interactions or rater biases) influence the occurrence of Externalizing Problems.

For 7-year-old twin pairs estimates of the shared environmental factors, both for mother and father ratings and both of Internalizing and Externalizing Problems, had increased to explaining 32% of the variance. Fitting Rater Bias and Psychometric models to the data (see chapter 4) showed that also for these older twin pairs possible rater biases were small, accounting at most for 14% of the variance. Thus also for these older children pure shared environmental factors influence both Internalizing and Externalizing Problems. Possibly, however, these shared environmental influences do not only refer to the environment children share within the family, but may also refer to the environment they share in the wider community. This point has also been stressed by Harris (1995) who argues that we should think about environmental effects on development in terms of group processes where peers play an important role. That is, phenomena such as within-group assimilation and between-group contrast that increase the homogeneity of behaviors within groups and widen differences between social groups could show as shared environment in a behavior genetic analysis. Thus, the possible larger shared environmental effects in schoolage versus preschool children could also reflect a developmental shift due to socialization experiences outside the home which become increasingly important as children grow older.

Environmental influences not shared between twins, i.e. idiosyncratic experiences like personal friends or diseases and trauma's, explained 31% of the variance of Internalizing Problems, both for mother and father ratings at ages 3 and 7. For Externalizing Problems these influences decreased a little over time, accounting for mother and father ratings at age 3 for 21% and 25% of the variance, respectively, and at age 7 for 16% and 14% of the variance, respectively. Measurement errors are incorporated in the estimates of the nonshared environment. Thus the assessment of problem behaviors of 7-year-old children with the CBCL/4-18 seems to have been just as well as the assessment of problem behaviors of 3-year-old children with the CBCL/2-3.

Although sex differences did exist for Externalizing Problems at both ages, genetic and environmental estimates for boys and girls were quite alike. For Internalizing Problems no sex differences emerged in genetic and environmental estimates, even though girls tended to get higher scores than boys. Fitting a Psychometric model to the data showed that behaviors similarly rated by both parents were more important to explain the etiology of problem behaviors than behaviors uniquely rated by one parent. No differences were found between the genetic and environmental estimates of mother and father ratings, neither for Internalizing Problems at age 3, nor for Externalizing Problems at ages 3 and 7. Only for Internalizing Problems at age 7 did the genetic and environmental estimates of mother and father ratings differ, although the estimates found were still quite comparable.

Genetic, shared environmental, and nonshared environmental contributions to continuity and change of problem behaviors at ages 3 and 7 were estimated using a two wave behavior genetic model (see chapter 5). The central findings of this study were that genetic influences underlie the stability of problem behaviors over a 4-year period. For Internalizing Problems the phenotypic stability ($r = .38$) was accounted for 66% by genetic factors, while for Externalizing Problems the phenotypic stability ($r = .54$) was explained for 55% by genetic factors. Some inborn vulnerability thus appears to exist for problem behaviors during childhood and even though children experience developmental changes, it seems that these genetic influences persist during development. Shared environmental influences also influenced the stability, accounting for 23% of the covariance for Internalizing Problems and 37% of the covariance of Externalizing Problems. This result is in accordance to results of epidemiological studies showing that, even though factors like family discord and disruption, lack of affection and poor supervision all predispose to problem behaviors (Rutter, 1985), it is often the persistence of these factors that predict chronic problems (Campbell, 1995).

Just as important as the finding of genetic continuity was the finding of genetic change for both problem behaviors during this 4-year period. That is, significant genetic effects were obtained for both problem behaviors at both ages that were independent of the continuing genetic influences. Indeed, about half of the genetic variance for both problem scales at both ages was independent of the continuing genetic variance, and thus influenced change. In other words, if genes are eventually found that account for genetic influences on Internalizing

and/or Externalizing Problems during childhood, these results suggest that different genes may contribute to variation in the problem behaviors from preschool to schoolage. The many developmental transitions, i.e. on physic, cognitive, social, and emotional levels, that children experience between ages 3 and 7 could be a possible explanation for this change in etiology. Schoolage children, in comparison with preschool children, experience many new environmental demands. These new environmental influences, together with the accompanying different interactions between these new environmental influences and the biological make-up of the child, may change the etiology of children's problem behaviors during this period.

Nonshared environmental factors largely had age specific effects, explaining 18% and 30% of Externalizing and Internalizing Problems, respectively. At both ages 3 and 7 these effects remained relatively the same. Although these results do not imply that nonshared environmental experiences, like illnesses or a possible trauma, are unimportant to children, they do suggest that these factors might be of a transient nature and that children appear to "recover" from them.

In order to study the determinants of continuity and change of problem behaviors during adolescence, data from a longitudinal adoption sample was used (see chapter 6). Apart from enabling us to study development in a genetically informative sample at an older age, this also allowed us to compare the results obtained by two different genetic designs. As discussed in chapter 1, each genetic design has its own limitations and finding similar results with different designs strengthens the representativeness of the findings. Parents of 111 pairs of adopted biological siblings, 221 pairs of adopted nonbiological siblings and 1484 adopted singletons completed the CBCL/4-18. At initial assessment all siblings were between 10 and 15 years of age. Three years later, parents completed the CBCL/4-18 for 75 biological pairs, 154 nonbiological pairs, and 1080 singletons, respectively. Remarkably, results of this longitudinal adoption sample were quite similar to the results of the twin sample. For Externalizing Problems genetic influences were most important, explaining 50% of the variance at both assessments. At the second assessment continuing genetic influences were as important as age specific genetic influences. Just as in the twin sample, this implied that apart from the continuing genetic influences, also different genes contributed to the variation in

Externalizing Problems during development. For Internalizing Problems at both assessments small genetic influences (explaining 16% and 8% of the variance, respectively) and larger shared environmental influences (explaining 30% and 33% of the variance, respectively) were found. Obtaining such similar results in both the twin and adoption samples gives a strong suggestion that for Internalizing Problems genetic influences decrease, while shared environmental influences increase over time. Of the shared environmental factor, continuing influences explained most of the variance at the second assessment point. It thus seems that also for this adoption sample the persistence of factors like, family discord and disruption, lack of affection and poor supervision, predict chronic problems (Campbell, 1995). Or possibly socialization experiences outside the home become increasingly important as children grow older (Harris, 1995).

Limitations and methodological issues

Although this study found large genetic influences for both problem behaviors at both ages these results should not lead to a sense of fatalism or genetic determinism for parents or for clinicians. As pointed out by Pike and Plomin (1996), even if genetic differences completely explain differences in problem behaviors - and this is not the case - does this by no means rule out the possibility of effective treatment, because environmental factors not widely represented at present in the population could have a major impact on these problem behaviors.

Quantitative genetic analyses done in this thesis assume an underlying continuous liability for behaviors, meaning that active genes which are not pathological in themselves are still associated with an increased (or decreased) risk for showing these behaviors. In this thesis, individuals showing extreme problem behaviors were thus not assumed to be qualitatively different, but to be variations of this particular behavior on a quantitative continuum. An underlying continuous liability for problem behaviors was found by Van den Oord & Rowe (1997) for a non-clinical population. Whether this assumption holds for clinical populations needs to be examined by further studies. For instance, if clinical depressions are affected by other genes or other environmental factors than "mood" differences between children in the general population, genetic and environmental etiologies

may be quite different for clinical and non-clinical populations.

Zygosity of the twin pairs was determined by blood/DNA tests either administered by the NTR, or (if the NTR had no zygosity data available) by their parents. In each chapter of this thesis we used all data available. For this reason, older chapters based the discriminant function for zygosity determination on fewer twin pairs for whom zygosity by blood/DNA was known than more recent chapters. The discriminant function, depending on the data available, obtained a 93% to 94% correct classification, suggesting that at most 3% to 4% of the twins' zygosity was wrongly classified. Misclassifying monozygotic twins (MZ) as dizygotic twins (DZ) will overestimate the DZ twin similarity, and misclassifying DZ twins as MZ twins will underestimate the MZ twin similarity. Therefore misclassifications always diminish the difference between MZ and DZ twin correlations, thereby underestimating genetic influences and overestimating shared environmental influences. In the appendix, an article is given describing the accuracy of zygosity determination by questionnaire items. In this article, a small preference is found for parents towards labeling a twin as dizygotic. Because 3% to 4% of the twins' zygosity might have been wrongly classified, estimates of shared environmental influences reported in this thesis could have been slightly overestimated. However, the effects of this misclassification will probably be small because most twins' zygosity (at least 96%) was correctly classified.

Future directions

Both at ages 3 and 7 (chapter 3 and 4, respectively), a Psychometric model fitted the data of Internalizing and Externalizing Problems significantly better than a Rater Bias model. This implied that rater differences did not merely reflect biases and/or measurement errors, but were also the result of parents assessing different aspects of the child's behavior. Thus at both ages, each parent provided unique information from his or her own perspective, apart from the behavioral views both parents shared. These results underscore the observation made by Achenbach (1992) "because any reports by any informants may be affected by characteristics of the informants, as well as by their own particular knowledge of the child's behavior, no single informant's reports can provide a complete picture". For future research it thus seems important to ask both parents to respond when collecting information about children's

behaviors, because no single rater may be able to provide a complete picture of the child's behavior.

In this thesis we conducted a prospective, longitudinal study to clarify the mechanisms involved in the etiology of Internalizing and Externalizing Problems. Knowing the relative genetic and environmental influences is important for future gene finding studies. Also, knowing how the etiological influences develop over time can help tremendously for finding genes at different ages. Results showed a major contribution of genetic influences to these childhood problems, especially in 3-year-olds. The most important determinants of stability of problem behaviors were genetic influences, unconfounded by possible sibling interactions, rater biases, and/or measurement errors. At each age also age specific genetic factors were expressed. This implied that if genes are eventually found that account for genetic influences on Internalizing and/or Externalizing Problems during childhood, different genes may contribute to variation in one or both of the problem behaviors from preschool to schoolage.

Further research is needed conducting similar analyses on the lower-order subscales at different ages and over time. Also the comorbidity between subscales, the fact that some subscales tend to occur together, needs to be better understood. Psychometric models should be applied to longitudinal data, studying the genetic and environmental contributions to continuity and change of problem behaviors while correcting for possible rater differences. Most importantly, the sample of twin pairs used in this thesis should be followed during their development. This shall enable future research to examine the genetic and environmental contributions to problem behaviors during development from child to young adult. Knowing the etiology of the problem behaviors will help researchers to locate genes underlying childhood disorders. Now that the human genome sequence is available and new methods of very precise genotyping have been developed, chances are much higher that genes will be located with linkage or association studies. However, because most problem behaviors are the result of a complex interplay of multiple genetic and environmental factors, finding genes and understanding their effects will not be an easy task. More research is needed to explore the ways in which genes interact with each other and with the environmental factors to influence an individual's susceptibility to showing problem behaviors. Essential for this kind of research is that the genetic risk can be measured directly, so molecular genetic findings

with strong effects will help tremendously (Plomin & Rutter, 1998). Further, discriminating measures of the environmental risk factors must be made, appropriate samples must be used, and statistical techniques must be employed that are well adapted to detect and test the postulated variety of genetic sensitivity (Kendler & Eaves, 1986). A more thorough description of the interplay between genes and environment is necessary to target appropriate intervention strategies which may improve or even prevent problem behaviors from occurring.

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Appendices

Appendix I

Zygosity Diagnosis in Young Twins by Parental Report

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Abstract

This study reports on zygosity determination in twins of childhood age. Parents responded to questionnaire items dealing with twin similarity in physical characteristics and frequency of mistaking one twin for another by parents, relatives, and strangers. The accuracy of zygosity diagnosis was evaluated across twins' ages 6, 8, and 10 and across parents. In addition, it was examined whether the use of multiple raters and the use of longitudinal data lead to an improvement of zygosity assignment. Complete data on zygosity questions and on genetic markers or blood profiles were available for 618 twin pairs at the age of 6 years. The method used was predictive discriminant analyses. Agreement between zygosity assigned by the replies to the questions and zygosity determined by DNA markers / blood typing was around 93%. The accuracy of assignment remained constant across age and across parents. Analyses of data provided by both parents and collected over multiple ages did not result in better prediction of zygosity. Details on the discriminant function are provided.

Keywords

twin zygosity; childhood; questionnaire; review; discriminant analysis.

Introduction

In 1927, Siemens [1] suggested that the diagnosis of zygosity in twins can take place by evaluating the degree of resemblance on genetically determined traits. Development of this method resulted in the frequent use of questionnaires, often including those criteria originally proposed by Siemens, for example.[2] Several studies have shown that the establishment of zygosity based on mailed questionnaires is of considerable accuracy, with around 95% correctly classified compared with blood or DNA typing. A summary of studies on the diagnosis of zygosity by mailed questionnaires are given as a supplement[3-23] at the end of this article.

The purpose of this paper is twofold. First, the validity of zygosity classification across childhood is examined in a large sample. One might expect the physical dissimilarity between dizygotic twins to become more obvious as they grow up. If so, the accuracy of classification is likely to improve with increasing age of the participants. A few studies have reported on this issue by evaluating the precision of zygosity diagnosis between samples varying in age,[8, 19, 23] and by test-retest estimation.[9] With the exception of the study of Cohen et al.[9] the findings are suggestive of an increased precision in zygosity prediction for older participants. However, findings may have suffered from a lack of statistical power due to a relatively small number of cooperating twins and parents.

To our knowledge there are no studies investigating this issue in a longitudinal sample. Since the availability of longitudinal data of various birth cohorts is increasing for several twin registers,[24] the establishment of zygosity incorporating longitudinal data deserves our attention. The Netherlands Twin Register collects questionnaire data on zygosity items at multiple ages in the same children by parental report. By making use of this longitudinal dataset it is possible to examine whether analyzing all available data collected at different ages increases the precision of classification or whether it is sufficient or possibly advisable to rely on information obtained at a specific age only. We are especially interested to determine if reliable classification of zygosity can take place as early as age 6.

The second objective is to investigate how to make optimal use of information provided by multiple caregivers. The majority of participating families registered with the Netherlands

Twin Register returns two completed questionnaires, usually filled out by the mother and father of the twin pair. In other twin studies of young children, typically the mother is used as primary informant.[17] It is of interest to find out whether the precision of the establishment of zygosity can further improve if information provided by a second informant is included in the analyses.

The Netherlands Twin Register has access to complete data on bloodgroup typing or DNA polymorphism and zygosity questionnaires collected in a sample of 618 twin pairs at age 6. This large number of participants provides sufficient statistical power to investigate above-mentioned issues.

Materials and methods

Subjects

The Netherlands Twin Register (NTR) is a population-based register, which contains 40% - 50% of all multiple births after 1986.[25] As part of an ongoing longitudinal study on the development of behavior problems, two questionnaires are sent to the registered parents or primary caregivers at multiple points in time with an average interval of 2 years. The present study used information by parental report on twin similarity and twin confusion at three ages in childhood, for cohorts born between 1986 and 1991. At the first occasion of data collection, around the 6th birthday of the twins (mean = 6.36 years, SD = .95), information on zygosity by report of the father was not requested. At the second and third assessment, age 8 (mean = 7.90 years, SD = .50) and age 10 (mean = 10.27 years, SD = .40) respectively, both parents provided information on zygosity items. For this study, only pairs of same sex with DNA/blood zygosity data were included in the analyses (N = 691 pairs). Twin pairs with missing items on the parental zygosity questions were excluded. Table I reports on the numbers of same sex twin pairs with complete data on the zygosity items and DNA/blood typing at each age.

Complete longitudinal data were available from 253 mothers (age 6, 8, and 10), and from 224 fathers (age 8 and 10). Data from both raters were collected in 316 twin pairs at age 8,

and in 257 twin pairs at age 10. The sample participating in this study was predominantly of Caucasian origin, with around 2% classified into other ethnic groups.

Table I *Number of twin pairs participating in the present study.*

	Age 6 Mother	Age 8 Mother	Age 8 Father	Age 10 Mother	Age 10 Father
Questionnaire & DNA/blood data	618	394	335	324	279
MZ	388	243	210	200	163
DZ	230	151	125	124	116

Zygosity questionnaire

The questionnaire used in the present study asked for information regarding similarity of the children and experiences of mistaking one for another (Table II). When the twins were aged 6, parents provided information on 8 items. In addition, a question concerning knowledge of zygosity classification based on DNA/blood testing was included. This item was used to identify those families with knowledge of zygosity prior to completing the questions. Two more items were added to the zygosity questionnaire at the second and third measurement occasion.

Table II *Translation of zygosity questionnaire, send to parents when twins reach the age of 6*

How much are the twins alike with respect to:			
1. Facial appearance	not	somewhat	exactly
2. Hair color	not	somewhat	exactly
3. Face color	not	somewhat	exactly
4. Eye color	not	somewhat	exactly
5. Are they alike as two peas in a pod?		no	yes
6. Does the mother or father mistake one for another?		no	yes
7. Do other family members mistake one for another?		no	yes
8. Do strangers have difficulty telling them apart?		no	yes
At age 8 and 10 of the twins, two more questions are added:			
9. Do you have difficulty to correctly identify each twin on new photographs?		no	yes
10. Do the twins have the same hair structures?	not	somewhat	exactly

Genotyping and blood polyphormism

A total of 691 same sex twin pairs participated in DNA/blood testing; 62% donated blood samples for analyses of blood grouping profiles and 38% provided a mouth swab sample for DNA isolation. Zygosity determination was performed using 8 highly polymorphic di-, tri- and tetranucleotide genetic markers. Based on heterozygosities of these marker loci, the chance that a DZ twin had an identical genotype for all loci (and thus was falsely typed as MZ) was 0.0078%. The zygosity testing included a multiplex PCR of markers D2S125, D8S1130, D1S1609, D5S816 and a second multiplex reaction of markers 15ActC, D21S1437, D7S2846, and D10S1423. These two multiplex PCR reactions were performed essentially by the protocol provided in the website from the Marshfield Institute (http://www.marshmed.org/genetics/). For the purpose of zygosity determination based on blood grouping profiles, red cells were typed with test sera for the following red cell blood group antigens: AB, CcDEe, MNSs, P_1, Kk, Kp^aKp^b, Fy^aFy^b, Jk^aJk^b, Lu^aLu^b. More details on the collection and treatment of these blood samples are given by Van Dijk et al.[26]

Statistical procedures

All parents of twins with DNA/blood data were informed about the zygosity results. Since the employment of DNA/blood testing varied across age, two groups of families could be distinguished. One group of parents with knowledge of the DNA/blood test results before completion of the questionnaire, and one group of parents whose twin pair had not yet participated in the DNA/blood testing. Since prior knowledge of the test results may affect one's responses to the zygosity questions, it was established first whether the two groups of parents differed in their item response pattern. If so, generalization of the application of the statistical function to samples for which no information on biological indices is available is seriously hampered. The tests were performed on each item separately by employment of χ^2 tests.

Predictive discriminant analysis was used for classifying subjects into MZ and DZ groups.[27-28] In the present study, the discriminant analysis generated a linear function of the weighted sum of the questionnaire items with the weightings chosen such that the distinction between MZ and DZ twins was optimal. The estimated success of classification or hit rate is

the proportion of correctly classified observations in the sample. It is sometimes argued that this hit rate is optimistically biased since the classification rule is derived from and applied to the same sample. This bias can be avoided in two ways, either through use of large samples or through application of an external classification analysis. In this study, both routes are taken. As a criterion for sample size, it is proposed that the minimum of observations in the smallest group should be at least five times the number questionnaire items. As can be seen in Table I, this requirement was easily met by each individual dataset. The leave-one-out procedure was chosen as the preferred external analysis. This method omits an observation, recalculates the classification rule from the remaining observations, classifies the deleted observation, and repeats these steps for each observation in the sample. The number of deleted observations correctly classified are counted and reported as cross-validated hit rates. Considering the proportion of same-sex MZ and DZ twins in the population, equal prior probabilities of group membership were used. To define the underlying construct that the discriminant function represents, inspection of the correlations between the discriminant function and each of the questionnaire variables was performed. The discriminant function and descriptive statistics were calculated using Statistical Package for Social Sciences / Windows 9.0.

Results

At age 6, out of 618 pairs with DNA/blood data, 411 mothers knew the result of zygosity testing and 199 mothers had not yet received a request for DNA/blood testing for their twins. Eight mothers had not answered the question. The ratio MZ and DZ was equal in both groups and data were pooled across zygosities to examine mothers' responses between groups. A difference in response pattern was observed for 1 item only, 'do strangers have difficulty telling them apart?' (χ^2 test statistic = 5.17 (1), $P = .02$). A positive answer was given by 65% of those mothers who were ignorant of zygosity, compared to 75% among mothers with knowledge of the DNA/blood test result. Overall, the two groups did not seem to differ allowing the discriminant function to be applied to both groups simultaneously.

Table III *Classification results by use of discriminant function analyses.*

		Age 6 Mother	Age 8 Mother	Age 8 Father	Age 10 Mother	Age 10 Father
Correctly classified	MZ	96.6%	95.1%	97.1%	97.5%	96.9%
	DZ	90.0%	86.8%	85.6%	88.7%	89.7%
Cross-validated	Total	94.2%	91.6%	91.9%	92.6%	93.9%

A summary of the results of the first series of discriminant analyses is given in Table III. Each analysis indicated a very accurate hit rate. Between 91.6% to 94.2% of all twin pairs were assigned the correct zygosity by the discriminant function. The precision of classification was not equally distributed across zygosities. Irrespective of age, correct classification for MZ twins was estimated around 97%, whereas around 88% of DZ twins were identified correctly.

Next, twin pairs with longitudinal questionnaire data were considered. The analysis of data collected at age 6, 8, and 10 by report of the mother resulted in a hit rate of 93.7%. Analysis of fathers' reports collected at age 8 and age 10 of the twins yielded a correct classification of 94.2%. Finally, data of mother and father were analyzed jointly. At age 8, 93.4% of all twin pairs were classified correctly. A hit rate of 93.8% was obtained at age 10.

Table IV *Unstandardized canonical discriminant function coefficients, constants and classification score to construct the classification rule.*

Item	Age 6 mother	Age 8 Mother	Age 8 father	Age 10 mother	Age 10 father
Facial appearance	0.618128	0.424786	0.546325	0.166356	0.522894
Hair color	0.431205	0.562038	0.385539	0.465518	0.176443
Face color	0.521933	0.059957	0.156256	0.170350	0.218696
Eye color	0.252118	0.242795	0.271036	0.192224	0.119514
Two peas	0.349174	0.329923	0.190973	0.086300	0.165164
Mother / Father	0.025022	0.086795	-0.10002	0.061590	-0.00264
Family members	1.098133	0.343303	0.638154	0.825344	0.452154
Strangers	0.358312	0.432926	0.568857	1.054857	1.688902
Photograph		-0.10844	-0.03261	-0.07711	-0.26824
Hair structure		0.778413	0.601257	0.611719	0.459194
Constant	-7.30262	-6.58742	-6.76956	-6.92407	-6.68708

Items are rated 1, 2, or 3 on three-point scale. Dichotomous items are rated 0 or 1. By multiplying each coefficient with the item score and summing these products with the constant, a zygosity score is obtained for each individual pair. This zygosity score is compared with the classification score that is generated by the discriminant function analysis. In this study, the classification score is – 0.4 for each individual dataset. Pairs whose zygosity score is greater than – 0.4 are assigned the label monozygotic, pairs with scores below this classification score are considered dizygotic

The above listed cross-validated hit rates indicated a minimal difference in the precision of assignment across the use of various datasets. The use of multiple raters and longitudinal data did not lead to an increased precision of zygosity prediction. Because the majority of twin studies are performed within cross-sectional designs, we believe it is of much practical use to report upon the discriminant function coefficients resulting from the first series of analyses. These parameter values together with the associated classification scores are given in Table IV. For interpreting the discriminant function, we have listed the correlations between each function and each questionnaire item in Table V.

Table V *Correlations between discriminant function and individual questionnaire items.*

Item	Age 6 mother	*rank*	Age 8 mother	*rank*	Age 8 father	*rank*	Age 10 mother	*rank*	Age 10 father	*rank*
Facial appearance	.72	*1*	.67	*3*	.72	*2*	.62	*6*	.66	*3*
Hair color	.67	*3*	.70	*2*	.67	*4*	.71	*2*	.58	*6*
Face color	.66	*4*	.63	*6*	.65	*6*	.68	*5*	.63	*5*
Eye color	.52	*6*	.53	*7*	.50	*7*	.51	*7*	.52	*7*
Two peas	.47	*7*	.46	*8*	.43	*8*	.39	*8*	.40	*8*
Mother/father	.32	*8*	.27	*9*	.28	*9*	.24	*9*	.28	*9*
Family members	.68	*2*	.64	*4*	.66	*5*	.70	*3*	.63	*4*
Strangers	.62	*5*	.64	*5*	.71	*3*	.75	*1*	.82	*1*
Photograph			.15	*10*	.15	*10*	.12	*10*	.23	*10*
Hair structure			.76	*1*	.75	*1*	.70	*4*	.68	*2*

Across age and parent, the majority of the correlations ranged from .50 to .80. Identification of those questionnaire items that show the largest overlap with the function helps to determine the underlying construct that the discriminant function represents. The zygosity questionnaire was developed along two dimensions, similarity of physical characteristics and confusion of identity. At either age and for either parent, the most informative correlations were not clustered in a sense that the function could easily be defined along one of these dimensions. Closer inspection revealed a few interesting details. With the exception of item 1 (facial appearance) and item 2 (hair color), a relative large degree of overlap was observed between mothers and fathers within age 8 and age 10 of the twins. Looking at the ranking of the items, parents evaluated the questions in the same general manner. When the percentage of correctly classified twins was taken into

consideration, this indicated that parents are interchangeable in assessing identity and fraternity in their children. Another interesting finding was the very small correlation found for item 5 (peas in pod). In contrast to numerous other studies, for example Magnus et al,[16] this item was of minor importance in defining the discriminant function. Even smaller correlations were observed for item 6 (confusion by mother or father) and item 9 (tell twins apart in photograph). The association among these three items seems obvious given that these questions rely on parental impression of global similarity and parental confusion of twins' identities. Apparently, parents themselves did not have difficulties in telling who is who.

Discussion

The primary focus of this study was to evaluate the accuracy of zygosity determination in young children. As young as age 6, the precision in zygosity prediction was high with 94% agreement between zygosity assigned by the parental replies to the questionnaire items and zygosity determined by blood typing or analyses of genetic markers. It was found that the accuracy of classification remained stable across childhood. The suggestion that determination improves with increasing age due to more obvious dissimilarities in dizygotic twin pairs was not confirmed. It was also found that mothers and fathers were equally effective in diagnosing their children.

Although the questionnaire items allow an accurate determination of zygosity, the accuracy resulting from the discriminant analyses was not equally distributed in monozygotic and dizygotic pairs. At each age and for both parents, a bias towards classification as monozygotic twins took place. This may have resulted either from a tendency by parents to overestimate similarities in their twin children or from a lack of sensitivity of these questions to detect fraternity. The former case seems less plausible, considering assessment of parental replies to a question that deals with their personal opinion of the twins' zygosity. This item is included in a questionnaire sent to parents shortly after registration with the NTR (before the twins' first birthday). Correct in 80% of the cases, parents misclassified true MZ twins more than 4 times as often than true DZ. This result may either reflect the fact that parents are misinformed by physicians or the parents' wish for fraternity or a combination of both. A

preference towards labeling a twin as dizygotic is commonly found both by use of parental report, as in Cohen et al[9] and self report.[29]

The sample used in the analyses was mainly Caucasian. This may imply that the use of the zygosity questionnaire and the application of the discriminant functions do not generalize to groups of non-Caucasian ethnic origin.

Concluding, the use of the zygosity questions and the employment of discriminant analysis as multivariate tool for classification seem of value in determining zygosity in young twins.

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Supplement: Summary of studies on zygosity determination by written questionnaire.

Study	Subjects	Mailed questionnaire	Method of Classification[1]	Results
Cederlöf, Friberg, Jonsson & Kaij 1961	200 pairs age 35 – 75	1 similarity item[2] & 1 multivariate[3] confusion item; completed by both twins.	- decision rules	- 98% of MZ correct, 92% of DZ correct, 10% of total sample left unclassified
Nichols & Bilbro 1966	123 pairs high school juniors	5 similarity items and 1 multivariate confusion item; completed by both twins.	- decision rules - intuitive decision was made in case the previous method left cases unclassified (7%)	- 93% of total sample correct
Jablon, Neel, Gershowitz & Atkinson 1967	232 pairs age 30 - 45	A short description of "identical" and "non-identical" was given by the investigators, followed by one single item that dealt with twins' own opinion; completed by both twins (complete agreement within pair) or individual twins.	Evaluation of zygosity diagnosis was performed on one item only: The joint opinion of a pair, and the opinion of the individual twin.	No difference in accuracy between individual twins and pairs. - 89% of MZ correct, 97% of DZ correct.
Hauge, Harvald, Fischer, Gotlieb-Jensen, Juel-Nielsen, Raebild, Shapiro & Videbech 1968	335 pairs, adults	Not clearly specified: multiple similarity items as well as 1 multivariate confusion item; completed by one twin or both twins, or by relatives.	- decision rules	- 97% of total sample correct
Schoenfeldt 1969	124 pairs, sample is identical to Nichols & Bilbro (1966)	Identical to Nichols & Bilbro (1966).	- decision rules based on one single score calculated from scores of both twins - discriminant analyses on same single score	- decision rules: 92% of total sample correct (cross-validated 79%) - discriminant: 88% of total sample correct (cross-validated 88%)

Cohen, Dibble, Grawe & Pollin 1973	Two samples: 120 pairs mean age 9.4 35 pairs mean age 4.2	7 similarity items and 1 multivariate confusion item; completed by the mother. Samples differed in age and in knowledge of zygosity by the mother.	- discriminant analyses - cutting point on summed raw scores	No difference in response pattern between groups varying in age and informed mothers. Groups were pooled. - discriminant: 98% of total sample correct - cutting point: 93% of MZ correct and 73% of DZ correct, with the remaining left unclassified
Cohen, Dibble, Grawe & Pollin 1975	275 pairs age 1 – 6	Identical to Cohen et al. (1973); completed by the mother.	- discriminant analyses - cutting point on summed raw score - principal component factor analysis	- hit rate is estimated at 90%
Martin & Martin 1975	47 pairs age 15	A description of "identical" and "non-identical" was given by the investigator, followed by one single item that dealt with the twins' own opinion; their joint answer had to be confirmed by the parents.	Since parents & twins all had to agree on the zygosity of the pair, evaluation of zygosity diagnosis was performed on one item only.	- 100% of total sample correct
Kasriel & Eaves 1976	178 pairs adults	1 similarity item and 1 univariate[3] confusion item; completed by both twins.	- decision rules	- 96% of total sample correct
Sarna, Kaprio, Sistonen & Koskenvuo 1978	104 pairs age 20 – 69	1 similarity item and 1 univariate confusion item; completed by both twins.	- deterministic decision tree	- 93% of total sample correct with 7% unclassified
Torgersen 1979	215 pairs age 18 – 67	1 similarity item and 1 multivariate confusion item; completed by both twins.	- cutting point on single summed raw score composed of scores of both twins - discriminant analyses on same summed raw score - decision tree	- cutting point: 95% of total sample correct - discriminant: 94% of MZ correct, 96% of DZ correct - decision tree: 96% of total sample correct

King, Friedman, Lattanzio, Rodgers, Lewis, Dupuy, Williams 1980	173 pairs, adults	1 similarity item that dealt with twins' own opinion; completed by both twins.	Evaluation of zygosity diagnosis was performed on one item only.	- 83% of MZ correct, 97% of DZ correct
Sarna & Kaprio 1980 This study is a follow-up of Sarna et al., 1978.	Two samples: 52 pairs previously left unclassified (2) 104 pairs	Identical to Sarna et al. (1978); completed by both twins.	- logistic regression, with (1) .50 and (2) .70 limit for a posteriori probability - discriminant analyses	- logistic regression: (1) all cases classified with 75% correct of total sample, cross-validated, (2) 100% correct of total sample with 53% left unclassified, cross-validated - discriminant: identical results
Magnus, Berg & Nance 1983	207 pairs age 33 –61	Originally[4] composed of 13 similarity items, 1 multivariate confusion item, and 1 item reflecting twins' own opinion; completed by one twin or both twins.	- discriminant analyses applied to 2 groups: (1) data from one twin only, (2) data from both twins. Intrapair mean of scores was used in case both twins responded.	- (1) 96% of total sample correct, cross-validated, (2) 98% of total sample correct, cross-validated
Bønnelykke, Hauge, Holm, Kristoffersen & Gurtler 1989	125 pairs age 0.5 – 6.5	4 similarity items and 1 univariate confusion item; completed by the mother.	- decision rules	- 91% of total sample correct, 4% misclassified, and 5% left unclassified
Eisen, Neuman, Goldberg, Rice & True 1989	4774 male pairs with insufficient blood typing data, adults	Identical to Magnus (1983); completed by both twins.	- discriminant analyses as employed by Magnus (1983) - 3 types of logistic regression including race-specific analysis	By combining the various methods, 9% of MZ twins were classified incorrectly. Variation in discriminating questions was observed for race.

Ooki, Yamada, Asaka & Hayakawa 1990	Two samples: 189 pairs age 12 – 16 93 pairs age 52 – 77	Identical to Torgersen (1979); completed by both twins.	- cutting point on single summed raw score composed of scores of both twins - discriminant analyses on same summed raw score	- cutting point: (1) 92% of MZ correct, 88% of DZ correct, (2) 100% of MZ correct, 77% of DZ correct - discriminant: (1) 92% of total sample correct, cross-validated in older sample resulted in 95% correct, (2) 94% of total sample correct, cross-validated in younger sample resulted in 67% correct
Ooki, Yamada & Asaka 1993	74 pairs highschool age	Identical to Torgersen (1979); completed by both twins and by the mother.	- cutting point on single summed raw score composed of (1) scores of both twins, and of (2) scores by mother	- (1) 98% of MZ correct, 77% of DZ correct, (2) 93% of MZ correct, 92% of DZ correct
Spitz, Moutier, Reed, Busnel, Marchaland, Roubertoux & Carlier 1996	79 pairs age 8 – 12.5	Adapted from Goldsmith (1991), originally composed of 18 items; completed by one parent.	- cutting point on mean score obtained by summing raw scores and dividing by number of items answered - logistic regression	- cutting point: 97% of total sample correct - logistic regression: 92% of total sample correct
Charlemaine, Duyme, Aubin, Guis, Marquiset, De Pirieux, Strub, Brossard, Jarry, Le Groupe Romulus, Frydman & Pons 1997	76 pairs age < 1	Adapted from Bønnelyke (1989), originally composed of 26 items; completed by one parent or both parents together.	- decision rules, various approaches - cutting point on summed raw score	- decision rules: ranging from 87% to 99% of total sample correct - cutting point: 96% of total sample correct

Chen, Chang, Wu, Lin, Chang, Chiu & Soong 1999	Two samples: 105 pairs age 12 – 16 47 pairs age 2 – 12	Adapted from Cohen et al. (1975), Goldsmith (1991), and culture-specific items. Originally composed of 20 (parental report) and 27 (self report) items; completed by (1) both parents and both twins, (2) one parent.	- logistic regression - cutting point on 3-item profiles for (1) only	- logistic regression: (1) 97% of total sample correct by parental report, 96% of total sample correct by self report, (2) 93% of total sample correct - cutting point: (1) identical to logistic regression

[1] Each study compares the assignment of zygosity based on questionnaire to the classification obtained through blood polymorphism or DNA markers, or a combination of both. [2] The question "are twins alike as two peas in pod?" is considered a similarity item. [3] Univariate versus multivariate: this reflects the number of sub-questions that deal with confusion of twin identity. Univariate: the occurrence of twin confusion is limited to one type of person, for instance "strangers". Multivariate: the occurrence of twin confusion by multiple types of persons, like "parents", "family members", "teachers", etc. [4] 'Originally' implies that the final analyses were performed on a reduced number of items.

Appendix II

Accompanying Letter of CBCL/2-3

Nederlands Tweelingenregister (NTR)

Datum
datum postmerk
Ons kenmerk
NTR/lijst 3

Uw brief van
Uw kenmerk

Telefax
020-44 48832
Telefoon
020-44 48787
woensdag t/m vrijdag

Bijlage(n)
vragenlijst 3
achtergrondinformatie
retour-enveloppe

Postadres: De Boelelaan 1111, 1081 HV Amsterdam

vrije Universiteit amsterdam

Geachte mevrouw/mijnheer,

Uw tweeling is inmiddels drie jaar oud en daarom krijgt u van ons de gedragsvragenlijst voor 2- en 3-jarigen. Deze vragenlijst gaat over gedragsproblemen die kunnen voorkomen in de eerste levensjaren. Over het ontstaan van gedragsproblemen is nog erg weinig bekend, vooral als het over een zo unieke groep als tweelingen gaat. In de bijlage vindt u meer informatie over de achtergronden van het onderzoek.

Jonge kinderen gedragen zich bij de ene ouder vaak anders dan bij de andere ouder. Bovendien is het zo dat iedere persoon het gedrag van een kind anders beoordeelt. Daarom vragen wij u of zowel vader als moeder de vragenlijsten wil invullen.

U vindt bij deze brief dan ook twee vragenlijsten voor de oudste van de tweeling (de groene vragenlijsten) en twee vragenlijsten voor de jongste (de oranje vragenlijsten). Het is de bedoeling dat de ouders ieder **hun eigen mening** geven over het gedrag van de kinderen, zoals het **nu** is of in de **afgelopen twee maanden** is geweest.

Mocht het niet mogelijk zijn dat beide ouders de vragenlijsten invullen, wilt u dan toch alle formulieren (ook de niet ingevulde) terugsturen?

Wilt u er op letten dat u de vragen bovenaan de vragenlijsten voor **beide** kinderen zo nauwkeurig mogelijk beantwoordt en dat u ook de vragen op de achterkant van de formulieren invult. (Zie ook de bijlage).

U kunt de vragenlijsten naar ons terugsturen in bijgaande portvrije enveloppe.
Bij voorbaat hartelijk dank voor uw medewerking!

Met vriendelijke groet en hoogachting,

dr. D.I. Boomsma
prof. dr J.F. Orlebeke

P.S. De volgende vragenlijst ontvangt u na de vijfde verjaardag van uw tweeling. In de tussenliggende tijd blijven wij u uiteraard de TWINFO toesturen. Wilt u zo vriendelijk zijn ons op de hoogte te houden van eventuele adreswijzigingen?

Vakgroep Psychonomie

Bezoekadres: De Boelelaan 1115
Provisorium I

Appendix III

Information for Parents: Reasons to Study Behavior Problems of 3-Year-Old Children

GEDRAGSPROBLEMEN BIJ TWEELINGEN VAN 3 JAAR

Opvoeden van kinderen is niet altijd makkelijk. Peuters kunnen veel aandacht en energie van hun ouders vergen, zeker als er twee ondernemende en onderzoekende kinderen van dezelfde leeftijd in het gezin zijn. Daarbij kent de ontwikkeling van elk kind op zijn tijd wel eens moeilijkheden. Gedragsproblemen kunnen te maken hebben met zindelijkheid, slapen, ongehoorzaamheid, agressief gedrag, problemen in de contacten met andere kinderen, angsten, enzovoorts. Bijna alle ouders kunnen aangeven dat er van dergelijke problemen wel eens sprake is geweest in een bepaalde periode.

De Sophia Stichting voor Wetenschappelijk Onderzoek ondersteunt al enige jaren onderzoek naar probleemgedrag. Met behulp van de 'gedragsvragenlijst voor kinderen van 2-3 jaar' proberen wij een antwoord te krijgen op drie belangrijke vragen:

1. Speelt erfelijke aanleg een rol bij het ontstaan van probleemgedrag?
2. Komen bij tweelingen meer gedragsproblemen voor dan bij eenlingen?
3. Hoe ontwikkelt probleemgedrag zich als kinderen ouder worden?

Dit onderzoek kan alleen uitgevoerd worden met tweelingen en dus alleen met uw medewerking. Vandaar dat u, wanneer uw tweeling 3 jaar oud is, een vragenlijst ontvangt over een aantal gedragsproblemen die bij 3-jarigen voor kunnen komen. Veel van deze gedragingen (bijvoorbeeld 'kan niet stilzitten, is onrustig') horen bij jonge kinderen. Er is dan ook niet meteen sprake van een probleem als u vindt dat sommige vragen van toepassing zijn op uw kind.

Iedere ouder heeft een eigen kijk op zijn of haar kinderen en bovendien gedragen kinderen zich ook vaak verschillend bij hun vader en moeder. Daarom vragen wij zowel de vader als de moeder de gedragsvragenlijst in te vullen. Is dit niet mogelijk, wilt u dan de formulieren toch terugsturen, ook al heeft slechts één van beide ouders de vragenlijsten ingevuld?

Wilt u voor **beide** kinderen **alle** vragen beantwoorden, dus ook de invuldatum en het soort dagopvang (vergeet a.u.b. niet de achterkant). Als uw kinderen geen dagopvang buitenshuis en geen oppas hebben, vult u bij beide kinderen 'geen' in. Als er een oppas binnenshuis is, vult u bij beide kinderen 'thuis met oppas' in. Voor de vergelijkbaarheid met ander onderzoek zijn gegevens over uw werk en opleiding van belang. Let u alstublieft op dat u deze vragen niet vergeet in te vullen. Alle gegevens worden anoniem bewaard en voor het onderzoek wordt alleen gewerkt met groepsgegevens en nooit met individuele familie-gegevens.

Heeft u nog vragen naar aanleiding van dit onderzoek, dan kunt u iedere woensdag voor meer informatie terecht bij drs. Jolande van der Valk, telefoonnummer 020-44.48827 (vanaf 10.30 uur). U kunt haar ook bellen als uw vragenlijst zoek geraakt of gescheurd is.

Alvast heel hartelijk bedankt voor uw medewerking. Wij houden u op de hoogte van het onderzoek, onder meer in de jaarlijkse TWINFO.

Appendix IV

CBCL/2-3 (same questionnaire was used for mother and father)

GEDRAGSVRAGENLIJST VOOR KINDEREN VAN 2 - 3 JAAR

NAAM VAN HET KIND | JONGSTE

GESLACHT ☐ Jongen ☐ Meisje | LEEFTIJD | Nationaliteit: Land van herkomst

DATUM VAN INVULLEN: Dag ..... Maand ..... Jaar .....

GEBOORTEDATUM KIND: Dag ..... Maand ..... Jaar .....

Soort dagopvang buitenshuis.

Aantal uren per week.

SOORT WERK VAN DE OUDERS, ook al werkt U op dit moment niet.
(s.v.p. zo duidelijk mogelijk - bijvoorbeeld: automonteur, onderwijzer, metaalarbeider, schoenverkoper enz., ook al woont het kind niet bij de ouder)

SOORT WERK VAN VADER: .....
Oefent beroep uit ☐ ja ☐ nee (WW, WAO, etc.), vanwege:
Sedert: .....

SOORT WERK VAN MOEDER: .....
Oefent beroep uit ☐ ja ☐ nee (WW, WAO, etc.), vanwege:
Sedert: .....

Laatst afgemaakte hoofdopleiding Vader: .....

Laatst afgemaakte hoofdopleiding Moeder: .....

Dit formulier werd ingevuld door:
☐ Moeder ☐ Vader ☐ Ander (geef aan): .....

Hier volgt een lijst met vragen die bepaalde gedrag ogen en eigenschappen van kinderen beschrijven. Bij iedere vraag die betrekking heeft op Uw kind zoals hij zij nu is of **in de afgelopen twee maanden** is geweest, wordt U verzocht een cirkeltje te zetten om de ② als de beschrijving **duidelijk of vaak van toepassing** is op Uw kind. Een cirkeltje om de ① als de beschrijving **een beetje of soms overeenkomt** met Uw kind. Wanneer de beschrijving **helemaal niet overeenkomt** met Uw kind, zet dan een cirkeltje om de ⓪.
Beantwoord s.v.p. de vragen zo goed mogelijk, ook als sommige niet van toepassing lijken te zijn op Uw kind.

0 = helemaal niet van toepassing (voor zover U weet) **1 = een beetje of soms van toepassing** **2 = duidelijk of vaak van toepassing**

0	1	2	1.	Pijnklachten zonder duidelijke medische oorzaak
0	1	2	2.	Gedraagt zich te jong voor zijn/ haar leeftijd.
0	1	2	3.	Is bang om iets nieuws te proberen.
0	1	2	4.	Kijkt andere mensen niet aan; vermijdt oogcontakt.
0	1	2	5.	Kan zich niet concentreren, kan niet lang de aandacht bij iets houden
0	1	2	6.	Kan niet stilzitten, is onrustig.
0	1	2	7.	Kan niet goed verdragen wanneer dingen anders staan of verplaatst zijn
0	1	2	8.	Kan geen uitstel verdragen; wil alles nu hebben, alles moet onmiddellijk gebeuren.
0	1	2	9.	Kauwt op dingen die niet eetbaar zijn
0	1	2	10.	Klampt zich vast aan volwassenen of is te afhankelijk
0	1	2	11.	Wil voortdurend geholpen worden
0	1	2	12.	Obstipatie; houdt ontlasting op
0	1	2	13.	Huilt veel
0	1	2	14.	Vreest voor dieren
0	1	2	15.	Uitdagend.
0	1	2	16.	Wil in alles direct zijn/ haar zin hebben.
0	1	2	17.	Vernielt eigen spullen.
0	1	2	18.	Vernielt spullen van andere gezinsleden of van andere kinderen.
0	1	2	19.	Diarree of dunne ontlasting zonder dat hij zij ziek is
0	1	2	20.	Ongehoorzaam.
0	1	2	21.	Is uit zijn/ haar evenwicht wanneer iets anders gaat dan hij zij gewoon is.
0	1	2	22.	Wil niet alleen slapen
0	1	2	23.	Geeft geen antwoord wanneer anderen tegen hem naar praten.
0	1	2	24.	Eet niet goed (geef aan): .....
0	1	2	25.	Kan niet goed opschieten met andere kinderen
0	1	2	26.	Kan geen pret maken; gedraagt zich als een kleine volwassene.
0	1	2	27.	Lijkt zich **niet** schuldig te voelen na zich misdragen te hebben.
0	1	2	28.	Wil het huis niet uit.
0	1	2	29.	Snel van streek als iets tegenzit.
0	1	2	30.	Snel jaloers.
0	1	2	31.	Eet of drinkt dingen die eigenlijk niet eetbaar of drinkbaar zijn (geen snoep) (geef aan): .....
0	1	2	32.	Is bang voor bepaalde dieren, situaties of plaatsen (geef aan): .....
0	1	2	33.	Verlit zich snel; beledigd of gekwetst
0	1	2	34.	Krijgt vaak ongelukken en/ of bezeert zich vaak.
0	1	2	35.	Vecht veel.
0	1	2	36.	Bemoeit zich met alles
0	1	2	37.	Raakt lovers overstuur wanneer hij zij gescheiden wordt van zijn/ haar ouders
0	1	2	38.	Heeft moeite met inslapen
0	1	2	39.	Hooipijnen (zonder medische oorzaak).
0	1	2	40.	Slaat anderen
0	1	2	41.	Houdt zijn/ haar adem in (geef aan): .....
0	1	2	42.	Doet dieren of mensen pijn zonder opzet.
0	1	2	43.	Maakt een ongelukkige indruk zonder duidelijke reden.
0	1	2	44.	Boze of kwade buien.
0	1	2	45.	Misselijk (zonder medische oorzaak).
0	1	2	46.	Zenuwachtige bewegingen of trekkingen (geef aan): .....
0	1	2	47.	Zenuwachtig, gespannen.
0	1	2	48.	Nachtmerries.
0	1	2	49.	Eet te veel.
0	1	2	50.	Oververmoeid.
0	1	2	51.	Te dik.
0	1	2	52.	Pijnlijke ontlasting
0	1	2	53.	Valt anderen aan
0	1	2	54.	Neuspeuteren, pulkt of trekt veel aan huid of andere lichaamsdelen (geef aan): .....
0	1	2	55.	Speelt teveel met eigen geslachtsdelen
0	1	2	56.	Onhandig, slechte coördinatie.
0	1	2	57.	Moeilijkheden met zien zonder duidelijke medische oorzaak (geef aan): .....
0	1	2	58.	Stotteren verandert zijn/ haar gedrag niet
0	1	2	59.	Gaat snel over van de ene bezigheid naar de andere.
0	1	2	60.	Huiduitslag of andere huidaandoeningen (zonder medische oorzaak).
0	1	2	61.	Weigert om te eten.
0	1	2	62.	Weigert om zelf aktief spelletjes te spelen.
0	1	2	63.	Herhaaldelijk hoofdbonzen of zelf met het hele lichaam wiegen.
0	1	2	64.	Is 's avonds niet naar bed te krijgen
0	1	2	65.	Wil niet zindelijk worden (geef aan): .....
0	1	2	66.	Schreeuwt of gilt veel.

S.V.P. aankruisen wat van toepassing is.

z.o.z.

versie 1.89

0 = helemaal niet van toepassing (voor zover U weet) **1 = een beetje of soms van toepassing** **2 = duidelijk of vaak van toepassing**

0	1	2	57.	Lijkt niet gevoelig voor liefdevolle aandacht of genegenheid van anderen.
0	1	2	68.	Schaamt of geneert zich snel.
0	1	2	69.	Egoïstisch, wil niet delen.
0	1	2	70.	Toont weinig liefdevolle aandacht of genegenheid voor anderen.
0	1	2	71.	Toont weinig belangstelling voor dingen om zich heen.
0	1	2	72.	Toont te weinig angst om zich te bezoren.
0	1	2	73.	Verlegen, schuchter
0	1	2	74.	Slaapt minder dan de meeste kinderen overdag en/of 's nachts (geef aan): _____
0	1	2	75.	Smeert of speelt met ontlasting.
0	1	2	76.	Spraakproblemen (geef aan welke): _____
0	1	2	77.	Staart zomaar voor zich uit of lijkt zich steeds met één ding bezig te houden
0	1	2	78.	Moeilijkheden of klachten (zonder medische oorzaak).
0	1	2	79.	Verzamelt dingen die hij/zij niet nodig heeft (geef aan): _____
0	1	2	80.	Vreemd gedrag (geef aan): _____
0	1	2	81.	Koppig, stuurs of prikkelbaar.
0	1	2	82.	Verandert plotseling van stemming/humeur
0	1	2	83.	Maakt veel ruzie.
0	1	2	84.	Praat of schreeuwt in slaap
0	1	2	85.	Driftbuier, snel kwaad.
0	1	2	86.	Overdreven netjes of te schoon.
0	1	2	87.	Te angstig of te bang.
0	1	2	88.	Wordt niet mee.
0	1	2	89.	Traag, te langzaam, te weinig "energie".
0	1	2	90.	Ongelukkig, verdrietig, gedeprimeerd.
0	1	2	91.	Is overdreven luidruchtig.
0	1	2	92.	Is snel van streek door onbekende mensen of situaties.
0	1	2	93.	Bniken (zonder medische oorzaak).
0	1	2	94.	Wordt 's nachts vaak wakker.
0	1	2	95.	Loopt zomaar weg van huis.
0	1	2	96.	Wil veel aandacht
0	1	2	97.	Dreinerig, jengelig.
0	1	2	98.	Teruggetrokken, komt niet tot contakt met anderen.
0	1	2	99.	Maakt zich zorgen.
			100.	Geef hier s.v.p. verder nog aan ieder ander probleem dat hierboven nog niet aan de orde is geweest.
0	1	2		_____
0	1	2		_____
0	1	2		_____
0	1	2		_____

N.B. Wilt U s.v.p. controleren of U bij **iedere** vraag **een** cijfer hebt omcirkeld?

Heeft Uw kind een lichamelijke ziekte, of lichamelijke of geestelijke handicap? ☐ nee ☐ ja (geef aan): _____

Is het kind na de 18e maand ooit ziek geweest? ☐ nee ☐ ja (geef aan): _____

Is het kind na de 18e maand door een arts behandeld? ☐ nee ☐ ja (geef aan): _____

Heeft het kind na de 18e maand in het ziekenhuis gelegen? ☐ nee ☐ ja (geef aan): _____

Is het kind na de 18e maand onder narcose geweest? ☐ nee ☐ ja (geef aan): _____

Heeft het kind na de 18e maand geneesmiddelen gebruikt? ☐ nee ☐ ja (geef aan): _____

Lichaamslengte en gewicht zoals gemeten op het consultatie buro (vanaf 18 maanden)

datum	lengte	gewicht	datum	lengte	gewicht
_____	_____ cm	_____ gram	_____	_____ cm	_____ gram
_____	_____ cm	_____ gram	_____	_____ cm	_____ gram
_____	_____ cm	_____ gram	_____	_____ cm	_____ gram

Appendix V

Reminder, Sent to Nonresponders of CBCL/2-3

Nederlands Tweelingenregister (NTR)

Datum	Uw brief van	Telefax	Bijlage(n)
datum postmerk		020-44.48832	vragenlijst 3
Ons kenmerk	Uw kenmerk	Telefoon	achtergrondinformatie
NTR/reminder 3		020-44.48787	retour-enveloppe
		woensdag t/m vrijdag	

Postadres: De Boelelaan 1111, 1081 HV Amsterdam

vrije Universiteit *amsterdam*

Geachte mevrouw/mijnheer,

Alweer geruime tijd geleden zonden wij u de gedragsvragenlijst voor 2- en 3-jarigen. Volgens onze gegevens hebben wij deze vragenlijst nog niet van u teruggekregen. Omdat u er misschien niet aan toe bent gekomen of omdat er bij de postbezorging of registratie iets mis is gegaan, zenden wij u de lijst nogmaals.

De vragenlijst gaat over gedragsproblemen die kunnen voorkomen in de eerste levensjaren. In de bijlage vindt u meer informatie over de achtergronden van het onderzoek.

Jonge kinderen gedragen zich bij de ene ouder vaak anders dan bij de andere ouder. Bovendien is het zo dat iedere persoon het gedrag van een kind anders beoordeelt. Daarom vragen wij u of zowel vader als moeder de vragenlijsten wil invullen.
U vindt bij deze brief dan ook twee groene vragenlijsten voor de oudste (de eerstgeborene) van de tweeling en twee oranje lijsten voor de jongste (de laatstgeborene). Het is de bedoeling dat de ouders ieder **hun eigen mening** geven over het gedrag van de kinderen, zoals het **nu** is of in **de afgelopen twee maanden** is geweest.
Mocht het niet mogelijk zijn dat beide ouders de vragenlijsten invullen, wilt u dan toch alle formulieren (ook de niet ingevulde) terugsturen?

Wilt u erop letten dat u de vragen bovenaan de vragenlijsten voor **beide** kinderen zo nauwkeurig mogelijk beantwoordt en dat u ook de vragen op de achterkant van het formulier invult (zie ook de bijlage).

Wij stellen het zeer op prijs wanneer u de vragenlijsten ingevuld aan ons retourneert in bijgaande portvrije enveloppe. Bij voorbaat hartelijk dank voor uw medewerking.

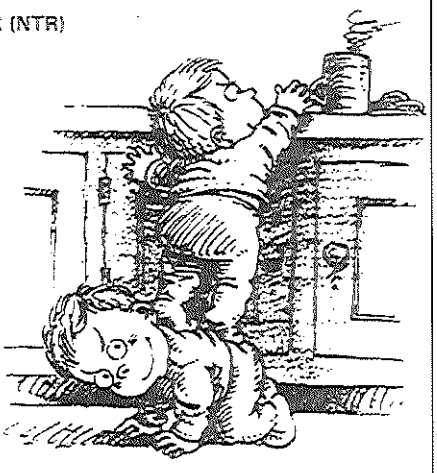
Met vriendelijke groet en hoogachting,

mevr.dr D.I. Boomsma
mevr.drs J.C. van der Valk

Appendix VI

Accompanying Letter to Collect Missing Information

NEDERLANDS TWEELINGENREGISTER (NTR)
Vrije Universiteit Amsterdam
De Boelelaan 1111
1081 HV Amsterdam
020-4448787



Geachte mevrouw / mijnheer,

Hartelijk bedankt voor het terugsturen van de "gedragsvragenlijst voor kinderen van 2-3 jaar". Door uw medewerking zullen wij een antwoord krijgen op een aantal belangrijke vragen over het ontstaan van probleemgedrag.

Helaas bent U een of meerdere vragen vergeten in te vullen. Voor de vergelijkbaarheid met ander onderzoek is het nodig dat wij ook op deze vragen een antwoord krijgen.

De op het bijgesloten blad aangekruiste vragen zijn door U nog niet ingevuld. Wilt U deze vragen a.u.b. alsnog beantwoorden en in bijgaande portvrije enveloppe aan ons retourneren.

Alle gegevens worden anoniem bewaard en voor het onderzoek wordt alleen gewerkt met groepsgegevens en nooit met individuele familie-gegevens. Heeft U nog vragen naar aanleiding van dit onderzoek, dan kunt U iedere woensdag voor meer informatie terecht bij Jolande van der Valk, telefoonnummer 020-4448827 (vanaf 10.30 uur).

Bij voorbaat hartelijk dank voor uw medewerking.

Met vriendelijke groet en hoogachting,

Dr. D.I. Boomsma
Drs. J.C. van der Valk

Appendix VII

Questionnaire to Collect Missing Information

Registratienummer NTR : _____

A.U.B. AANGEKRUISTE VRAAG / VRAGEN INVULLEN :

☐ Datum waarop de tweeling geboren werd : _____ (dag) _____ (maand) 19_____

☐ Geslacht oudste van de tweeling : (meisje of jongen) _____

☐ Geslacht jongste van de tweeling : (meisje of jongen) _____

☐ Soort oppas of opvang van de oudste van de tweeling (b.v. thuis met oppas, bij oma, peuterspeelzaal, etc.) :
(Als het kind geen oppas of opvang heeft, vult U dan a.u.b. het woord "geen" in.)

_____

☐ Totaal aantal uren oppas of opvang van de oudste van de tweeling per week : _____ uren

☐ Soort oppas of opvang van de jongste van de tweeling (b.v. thuis met oppas, bij oma, peuterspeelzaal, etc.) :
(Als het kind geen oppas of opvang heeft, vult U dan a.u.b. het woord "geen" in.)

_____

☐ Totaal aantal uren oppas of opvang van de jongste van de tweeling per week : _____ uren

☐ Soort beroep / werk wat de vader doet of gedaan heeft (b.v. operator van een vlakglasmachine) :
(Geen "huisman" invullen. Indien er nooit een beroep is uitgeoefend a.u.b. het woord "geen" invullen.)

_____

☐ Oefent vader beroep uit : (ja of nee) _____

☐ Soort beroep / werk wat de moeder doet of gedaan heeft (b.v. ambtenaar van burgerzaken bij de gemeente) :
(Geen "huisvrouw" invullen. Indien er nooit een beroep is uitgeoefend a.u.b. het woord "geen" invullen.)

_____

☐ Oefent moeder beroep uit : (ja of nee) _____

☐ Laatst afgemaakte soort hoofdopleiding van vader : (b.v. MAVO of verpleegkundige A opleiding)

_____

☐ Laatst afgemaakte soort hoofdopleiding van moeder : (b.v. INAS of gezondheidszorg kaderopleiding)

_____

☐ Vader is vergeten op de achterkant van de gedragsvragenlijst(en) de vragen 67 tot en met 100 in te vullen.
A.u.b. door vader alleen op de achterzijde van bijgevoegde gedragsvragenlijst(en) de vragen 67 tot en met 100 beantwoorden. Op de voorzijde alleen de vraag "datum van invullen" en de vraag "dit formulier werd ingevuld door" beantwoorden.

☐ Moeder is vergeten op de achterkant van de gedragsvragenlijst(en) de vragen 67 tot en met 100 in te vullen.
A.u.b. door moeder alleen op de achterzijde van bijgevoegde gedragsvragenlijst(en) de vragen 67 tot en met 100 beantwoorden. Op de voorzijde alleen de vraag "datum van invullen" en de vraag "dit formulier werd ingevuld door" beantwoorden.

☐ Vader is vergeten de achterkant van de gedragsvragenlijst(en) in te vullen.
A.u.b. door vader alleen op de achterzijde van bijgevoegde gedragsvragenlijst(en) alle vragen beantwoorden.
Op de voorzijde alleen de vraag "datum van invullen" en de vraag "dit formulier werd ingevuld door" beantwoorden.

☐ Moeder is vergeten de achterkant van de gedragsvragenlijst(en) in te vullen.
A.u.b. door moeder alleen op de achterzijde van bijgevoegde gedragsvragenlijst(en) alle vragen beantwoorden.
Op de voorzijde alleen de vraag "datum van invullen" en de vraag "dit formulier werd ingevuld door" beantwoorden.

Appendix VIII

Zygosity Questionnaire for 5-Year-Old Twins

Nederlands Tweelingenregister (NTR)

Datum	Uw brief van	Telefax	Bijlage(n)
datum postmerk 1997		020-44.48832	retourenveloppe
Ons kenmerk	Uw kenmerk	Telefoon	
NTR/JvdV/zyg.ist		020-44.48827/48787	

Postadres: De Boelelaan 1111, 1081 Hv Amsterdam

vrije Universiteit amsterdam

Geachte mevrouw/mijnheer,

Momenteel zijn wij bezig met een onderzoek naar de invloeden van erfelijkheid en omgeving op de ontwikkeling van gedrag. Hiervoor gebruiken wij ook de vragenlijsten die u destijds heeft ingevuld voor uw kinderen.

Voor dit onderzoek is het noodzakelijk dat de zygositeit van de tweelingen, of zij eeneiig of twee-eiig zijn, zo goed mogelijk ingeschat kan worden. Helaas is het voor ons op dit moment onmogelijk om uw tweeling goed te classificeren, omdat de gegevens die wij daarvoor nodig hebben ontbreken.

Omdat het voor dit onderzoek zeer belangrijk is dat wij de verzamelde gegevens van alle tweelingen gebruiken, willen wij u vragen of u zo vriendelijk wilt zijn om **de vragen op de achterzijde van deze brief te beantwoorden**. Alleen met behulp van deze gegevens is het namelijk voor ons op dit moment mogelijk om de zygositeit van uw tweeling in te schatten. U kunt de ingevulde brief retourneren in de bijgevoegde retourenveloppe, een postzegel is niet nodig.

Bij voorbaat heel hartelijk dank!

Met vriendelijke groet,

drs. Jolande van der Valk

Vakgroep Psychonomie

Bezoekadres: De Boelelaan 1115
Provincie 1-1-1

Nummer NTR: _____

Onderstaande vragen a.u.b. beantwoorden door het rondje van het juiste antwoord aan te kruisen

1. Wat is de geboortedatum van uw tweeling? _____

2.a. Is door DNA- of bloedonderzoek vastgesteld of de tweeling een-eiig of twee-eiig is?

O nee O ja

b. Zo ja, wat was de uitslag?

O een-eiig O twee-eiig

3. Hoeveel lijkt de tweeling op elkaar wat betreft:

	niet	enigszins	precies
a. gezicht	O	O	O
b. haarkleur	O	O	O
c. gelaatskleur	O	O	O
d. oogkleur	O	O	O

	nee	ja
4. Lijken ze als twee druppels water op elkaar?	O	O
5. Verwart vader of moeder ze soms wel eens met elkaar?	O	O
6. Verwarren andere familieleden ze wel eens?	O	O
7. Kunnen vreemden ze moeilijk uit elkaar houden?	O	O
8. Heeft U moeite om de tweeling op een recente foto te onderscheiden?	O	O

9. Is de structuur van de haren van de tweeling hetzelfde (fijn of dik haar; recht of krullend haar)?

O niet hetzelfde O enigszins hetzelfde O precies hetzelfde

HARTELIJK BEDANKT VOOR UW MEDEWERKING!

Appendix IX

Accompanying Letter for CBCL/4-18

Nederlands Tweelingenregister (NTR)

Datum	Uw brief van	Telefax	Bijlagen:
datum postmerk		020-44.48832	vragenlijst 7
Ons kenmerk	Uw kenmerk	Telefoon	achtergrondinformatie
NTR/lijst7		020-44.48787	retour-enveloppe
		woensdag t/m vrijdag	

Postadres: De Boelelaan 1111, 1081 HV Amsterdam

vrije Universiteit *amsterdam*

Geachte mevrouw/mijnheer,

Hierbij sturen wij u de gedragsvragenlijst voor kinderen van 4 tot 18 jaar met het verzoek deze in te vullen en aan ons terug te sturen. Deze vragenlijst maakt deel uit van een uniek onderzoek naar de ontwikkeling van gedrag bij jonge kinderen. In de bijlage vindt u meer informatie over de achtergronden van het onderzoek.

Bijgaand treft u twee vragenlijsten aan: één voor de moeder van de tweeling en een kortere vragenlijst voor de vader. In de linkerbovenhoek van de vragenlijst staat voor wie de lijst is bestemd. Het is de bedoeling dat de ouders ieder **hun eigen mening** geven over het gedrag van de kinderen, zoals het **nu** is of **in de afgelopen zes maanden** is geweest. Daarbij is het **belangrijk dat de kinderen niet met elkaar worden vergeleken.** Beantwoordt u de vragen voor de oudste van de tweeling a.u.b. onafhankelijk van de vragen voor de jongste van de tweeling. Wij hopen dat u beiden de tijd kunt vinden om de vragen te beantwoorden.

Wilt u bij het invullen op de volgende punten letten:

- *Zet bij iedere vraag* **met potlood** *een streepje in het vakje van het juiste antwoord.*
  Dus zo: ▬ *, en niet zo:* ⊄ *of* ⋕
- *Probeer fouten te vermijden door eerst de vraag goed te lezen;*
- *Als u een antwoord wilt veranderen, gumt u dan het onjuiste antwoord zorgvuldig uit en streep het juiste antwoord aan;*
- *Beantwoord alle vragen voor beide kinderen en ook voor beide ouders waar dat gevraagd wordt;*
- *Omdat de vragenlijst zowel geschikt is voor kinderen van 4 jaar als voor 18-jarigen, kunnen sommige vragen vreemd overkomen voor kinderen in de leeftijd van uw tweeling. Beantwoordt u deze vragen a.u.b. door het meest geschikte antwoord aan te strepen;*
- *Beantwoord de vragen zoals ze gesteld zijn; schrijf er niets bij als dat niet gevraagd wordt. Als u toch iets speciaals wilt opmerken doe dat dan op een apart papier;*
- *A.u.b. niet de bladzijden losscheuren of dubbelvouwen.*

Mocht het niet mogelijk zijn dat beide ouders de vragenlijst invullen, dan stellen wij het ook op prijs één vragenlijst terug te krijgen.

Bij voorbaat hartelijk dank voor uw medewerking.

mevr.dr D.I. Boomsma
prof.dr J.F. Orlebeke

Vakgroep Psychonomie

Bezoekadres: De Boelelaan 1115
Provisorium I

Appendix X

Information for Parents: Reasons to Study Behavior Problems of 7-Year-Old Children

VERVOLGONDERZOEK NAAR GEDRAG BIJ TWEELINGEN

Opvoeden van kinderen is niet altijd makkelijk. Bijna elk kind vertoont in een bepaalde periode van de ontwikkeling wel eens problemen. Deze problemen kunnen te maken hebben met slapen, ongehoorzaamheid, schoolproblemen, agressief gedrag, problemen in de contacten met andere kinderen, angsten, enzovoorts.

De Sophia Stichting voor Wetenschappelijk Onderzoek ondersteunt al enige jaren onderzoek naar probleemgedrag. Toen uw tweeling 3 jaar oud was heeft u waarschijnlijk de 'Gedragsvragenlijst voor kinderen van 2-3 jaar' ingevuld. Uit dit onderzoek bleek dat vooral erfelijke invloeden bepaalden of, en in welke mate, een peuter probleemgedrag vertoonde. Omgevingsinvloeden (b.v. het aantal broertjes en zusjes die in een gezin voorkwamen) bleken bijna geen invloed uit te oefenen!

Nu is uw tweeling ouder en hebben ze al veel meer hun eigen wereld. Naast hun ouders en broertjes/zusjes, hebben ze nu ook contacten met leeftijdgenoten en andere volwassenen zoals leerkrachten. Ook kunnen ze hun ideeën, wensen en eisen steeds beter uiten. Het is goed mogelijk dat met het ouder worden invloeden vanuit de omgeving (zoals vriendjes, school en clubs) een grotere invloed op het ontstaan van probleemgedrag zullen vertonen dan erfelijke factoren.

Met behulp van de 'Gedragsvragenlijst voor kinderen van 4-18 jaar' proberen wij nu de ontwikkeling van de kinderen te volgen en antwoord te krijgen op drie belangrijke vragen:

1. Hoe ontwikkelen kinderen zich die aanvankelijk problemen in het gedrag hadden: blijven de gedragsproblemen bestaan of verdwijnen deze naarmate het kind ouder wordt?

2. Neemt het aantal kinderen dat gedragsproblemen vertoont toe bij het ouder worden?

3. In welke mate spelen erfelijke en omgevingsinvloeden een rol bij het vertonen van probleemgedrag op schoolgaande leeftijd?

Dit onderzoek kan alleen uitgevoerd worden met tweelingen en dus alleen met uw medewerking. Vandaar dat wij u met klem willen vragen de vragenlijst in te vullen en op te sturen. Veel van de gedragingen waarnaar gevraagd wordt (bijvoorbeeld 'kan niet stilzitten, is onrustig') horen bij opgroeiende kinderen. Er hoeft dan ook niet altijd sprake te zijn van een probleem als u vindt dat sommige vragen van toepassing zijn op uw kind.

Iedere ouder heeft een eigen kijk op zijn of haar kinderen en bovendien gedragen kinderen zich ook vaak verschillend bij hun vader en moeder. Daarom vragen wij zowel de vader als de moeder de gedragsvragenlijst in te vullen. Is dit niet mogelijk, wilt u dan de formulieren toch terugsturen, ook al heeft slechts één van beide ouders de vragenlijsten ingevuld?

Voor de vergelijkbaarheid met ander onderzoek zijn gegevens over uw werk en opleiding van belang. Alle gegevens worden anoniem bewaard en voor het onderzoek wordt alleen gewerkt met groepsgegevens en nooit met individuele familiegegevens.

Heeft u nog vragen naar aanleiding van dit onderzoek, dan kunt u voor meer informatie terecht bij mevr. Stroet, telefoonnummer 020-4448827 (of het secretariaat 020-4448787). U kunt ook bellen als uw vragenlijst zoek is geraakt of is gescheurd.

Alvast heel hartelijk bedankt voor uw medewerking. Wij houden u op de hoogte van het onderzoek in de jaarlijkse TWINFO.

Appendix XI

CBCL/4-18 for Mother

MOEDER GEDRAGSVRAGENLIJST VOOR KINDEREN VAN 4 - 18 JAAR / NTR

Dit formulier werd ingevuld door:
☐ moeder ☐ ander (geef aan): .....

Datum van invullen: ..... - ..... - .....

Geboortedatum tweeling: ..... - ..... - .....

Geslacht oudste (de eerst geborene) van de tweeling:
☐ jongen ☐ meisje

Geslacht jongste (de laatst geborene) van de tweeling:
☐ jongen ☐ meisje

NIET INVULLEN!

Dit is een lijst met beschrijvingen van bepaalde gedragingen en eigenschappen van kinderen. Bij iedere beschrijving die van toepassing is op Uw kind zoals hij/zij nu is of **ook binnen de afgelopen zes maanden** is geweest, wordt U verzocht een potloodstreepje te zetten in het vakje van de 2 als de beschrijving **duidelijk of vaak van toepassing** is op Uw kind. Een streepje te zetten in het vakje van de 1 als de beschrijving **een beetje of soms van toepassing** is op Uw kind. Als de beschrijving **helemaal niet van toepassing** is op Uw kind, zet dan een potloodstreepje in het vakje van de 0. Beantwoord a.u.b. alle vragen zo goed mogelijk, ook al lijken sommige vragen niet op Uw kind betrekking te hebben.

Voornaam OUDSTE van de tweeling: _____ **Voornaam JONGSTE van de tweeling:** _____

0 = helemaal niet van toepassing (voor zover U weet) **1 = een beetje of soms van toepassing** **2 = duidelijk of vaak van toepassing**

OUDSTE niet	beetje soms	duidelijk vaak		JONGSTE niet	beetje soms	duidelijk vaak
☐	☐	☐	1. Gedraagt zich te jong voor zijn/haar leeftijd.	☐	☐	☐
			2. Allergie (geef aan):			
☐	☐	☐	oudste: _____			
			jongste: _____	☐	☐	☐
☐	☐	☐	3. Spreekt veel tegen of maakt veel ruzie.	☐	☐	☐
☐	☐	☐	4. Astma.	☐	☐	☐
☐	☐	☐	5. Gedraagt zich als iemand van het andere geslacht.	☐	☐	☐
☐	☐	☐	6. Doet ontlasting (poept) buiten de w.c. of in de broek.	☐	☐	☐
☐	☐	☐	7. Opscheppen, stoer doen.	☐	☐	☐
☐	☐	☐	8. Kan zich niet concentreren, kan niet lang de aandacht bij iets houden.	☐	☐	☐
			9. Kan bepaalde gedachten niet uit zijn/haar hoofd zetten; obsessies (geef aan):			
☐	☐	☐	oudste: _____			
			jongste: _____	☐	☐	☐
☐	☐	☐	10. Kan niet stil zitten, onrustig, of over-actief.	☐	☐	☐
☐	☐	☐	11. Klampt zich vast aan volwassenen of is te afhankelijk.	☐	☐	☐
☐	☐	☐	12. Klaagt over zich eenzaam voelen.	☐	☐	☐
☐	☐	☐	13. Is de war of wazig denken.	☐	☐	☐
☐	☐	☐	14. Huilt veel.	☐	☐	☐
☐	☐	☐	15. Wreed voor dieren.	☐	☐	☐
☐	☐	☐	16. Wreed, pesterig of gemeen voor anderen.	☐	☐	☐
☐	☐	☐	17. Dagdromen of gaat op in zijn/haar gedachten.	☐	☐	☐
☐	☐	☐	18. Verwondt zichzelf opzettelijk of doet zelfmoordpogingen.	☐	☐	☐
☐	☐	☐	19. Let veel aandacht op.	☐	☐	☐
☐	☐	☐	20. Vernielt eigen spullen.	☐	☐	☐
☐	☐	☐	21. Vernielt spullen van andere gezinsleden of van anderen.	☐	☐	☐
☐	☐	☐	22. Is thuis ongehoorzaam.	☐	☐	☐
☐	☐	☐	23. Is ongehoorzaam op school.	☐	☐	☐
☐	☐	☐	24. Eet niet goed.	☐	☐	☐
☐	☐	☐	25. Kan niet goed opschieten met andere jongens/meisjes.	☐	☐	☐
☐	☐	☐	26. Lijkt zich **niet** schuldig te voelen na zich misdragen te hebben.	☐	☐	☐
☐	☐	☐	27. Snel jaloers.	☐	☐	☐
			28. Eet of drinkt dingen die eigenlijk niet eet- of drinkbaar zijn, ***geen snoep*** (geef aan):			
☐	☐	☐	oudste: _____			
			jongste: _____	☐	☐	☐

 reg. nr. NTR _____

0 = helemaal niet van toepassing (voor zover U weet) 1 = een beetje of soms van toepassing 2 = duidelijk of vaak van toepassing

OUDSTE niet	een beetje soms	duidelijk vaak		JONGSTE niet	een beetje soms	duidelijk vaak
			29. Is bang voor bepaalde dieren, situaties, of plaatsen, uitgezonderd de school (geef aan):			
			oudste:			
			jongste:			
			30. Is bang om naar school te gaan.			
			31. Is bang dat hij/zij iets ondeugends of slechts zou kunnen doen of denken.			
			32. Vindt dat hij/zij perfect moet zijn.			
			33. Klaagt erover of heeft het gevoel dat niemand van hem/haar houdt.			
			34. Heeft het gevoel dat anderen het op hem/haar gemunt hebben.			
			35. Voelt zich waardeloos of minderwaardig.			
			36. Krijgt vaak ongelukken en/of verwondingen.			
			37. Vecht veel.			
			38. Wordt veel gepikt/gepest.			
			39. Gaat om met jongens/meisjes die in moeilijkheden verzeild raken.			
			40. Hoort geluiden of stemmen die er niet zijn (geef aan):			
			oudste:			
			jongste:			
			41. Impulsief of handelt zonder na te denken.			
			42. Is liever alleen dan met anderen.			
			43. Liegen of bedriegen.			
			44. Nagelbijten.			
			45. Zenuwachtig of gespannen.			
			46. Zenuwachtige bewegingen of trekkingen (geef aan):			
			oudste:			
			jongste:			
			47. Nachtmerries.			
			48. Anders jongens/meisjes mogen hem/haar niet.			
			49. Obstipatie, houdt ontlasting op, last van verstopping.			
			50. Is te angstig of te bang.			
			51. Last van duizeligheid			
			52. Te veel last van schuldgevoel.			
			53. Eet te veel.			
			54. Oververmoeid.			
			55. Te dik.			
			56. Lichamelijke problemen zonder bekende medische oorzaak:			
			a. pijnen (**geen hoofdpijn**)			
			b. hoofdpijn			
			c. misselijkheid			
			d. oogproblemen (geef aan):			
			oudste:			
			jongste:			
			e. huiduitslag of andere huidaandoeningen			
			f. maagpijn, buikpijn of buikkrampen			
			g. overgeven			
			h. andere problemen (geef aan):			
			oudste:			
			jongste:			
			57. Valt anderen lichamelijk aan.			

proj.nr. NTR

0 = helemaal niet van toepassing (voor zover U weet) 1 = een beetje of soms van toepassing 2 = duidelijk of vaak van toepassing

OUDSTE niet	OUDSTE beetje soms	OUDSTE duidelijk vaak		JONGSTE niet	JONGSTE beetje soms	JONGSTE duidelijk vaak
			58. Neuspeuteren, pulkt of trekt veel aan huid of aan andere lichaamsdelen (geef aan):			
			oudste: _____			
			jongste: _____			
			59. Speelt met eigen geslachtsdelen in het openbaar.			
			60. Speelt te veel met eigen geslachtsdelen.			
			61. Slechte schoolresultaten.			
			62. Onhandig of slechte coördinatie.			
			63. Is liever samen met oudere jongens/meisjes.			
			64. Is liever samen met jongere jongens/meisjes.			
			65. Weigert om te praten.			
			66. Herhaalt alsmaar bepaalde handelingen, dwanghandelingen (geef aan):			
			oudste: _____			
			jongste: _____			
			67. Loopt weg van huis.			
			68. Schreeuwt of gilt veel.			
			69. Gesloten, anderen weten niet goed wat er in hem/haar omgaat.			
			70. Ziet dingen die er niet zijn (geef aan):			
			oudste: _____			
			jongste: _____			
			71. Schaamt of geneert zich gauw.			
			72. Brandstichter.			
			73. Sexuele problemen (geef aan welke):			
			oudste: _____			
			jongste: _____			
			74. Raar of 'gek' doen om de aandacht te trekken.			
			75. Verlegen of schuchter.			
			76. Slaapt minder dan de meeste leeftijdgenoten.			
			77. Slaapt meer dan de meeste leeftijdgenoten overdag en/of 's nachts (geef aan):			
			oudste: _____			
			jongste: _____			
			78. Smeert of speelt met de ontlasting			
			79. Spraakproblemen (geef aan):			
			oudste: _____			
			jongste: _____			
			80. Kijkt met een lege of "wezenloze" blik.			
			81. Stoelt van huis.			
			82. Steelt buitenshuis.			
			83. Opsparen van dingen die hij/zij niet nodig heeft (geef aan welke):			
			oudste: _____			
			jongste: _____			

0 = helemaal niet van toepassing (voor zover U weet) 1 = een beetje of soms van toepassing 2 = duidelijk of vaak van toepassing

OUDSTE niet	OUDSTE beetje soms	OUDSTE duidelijk vaak		JONGSTE niet	JONGSTE beetje soms	JONGSTE duidelijk vaak
			84. Vreemd of raar gedrag (geef aan):			
			oudste:			
			jongste:			
			85. Vreemde of rare gedachten (geef aan):			
			oudste:			
			jongste:			
			86. Koppig, stuurs of prikkelbaar.			
			87. Verandert plotseling van stemming.			
			88. Mokken, pruilen.			
			89. Achterdochtig.			
			90. Vloeken, schuttingtaal.			
			91. Praat erover dat hij/zij zichzelf zou willen doden.			
			92. Slaapwandelen of hardop praten in de slaap (geef aan):			
			oudste:			
			jongste:			
			93. Praat te veel.			
			94. Plaagt veel.			
			95. Driftbuien of snel driftig.			
			96. Denkt te veel aan sex.			
			97. Bedreigt andere mensen.			
			98. Duimzuigen of zuigen op vingers.			
			99. Is teveel bezig met netjes of schoon zijn.			
			100. Slaapproblemen (geef aan):			
			oudste:			
			jongste:			
			101. Spijbelen, schoolverzuim.			
			102. Te weinig actief, beweegt zich langzaam, of gebrek aan energie.			
			103. Ongelukkig, verdrietig, gedeprimeerd.			
			104. Is erg luidruchtig.			
			105. Gebruikt alcohol of drugs (geef aan):			
			oudste:			
			jongste:			
			106. Vandalisme, vernielen.			
			107. Broekpinksen overdag.			
			108. Bedplassen.			
			109. Dromerig, lanqdiq.			
			110. Wil graag van het andere geslacht zijn.			
			111. Teruggetrokken, komt niet tot contact met anderen.			
			112. Maakt zich zorgen.			
			113. Geeft U a.u.b. verder nog aan ieder ander probleem dat hierboven nog niet aan de orde is geweest.			
			oudste:			
			jongste:			
			oudste:			
			jongste:			

Wilt U a.u.b. controleren of U in de linker en in de rechter kolom, bij **iedere** vraag een potloodstreepje in **een** vakje hebt gezet?

Gezondheid: Wilt U alle vragen voor het oudste en het jongste kind beantwoorden met ja of nee door het zetten van een potloodstreepje.
(De vragen moeten beantwoord worden zoals ze hier gesteld zijn. **U mag de vragen niet veranderen!**

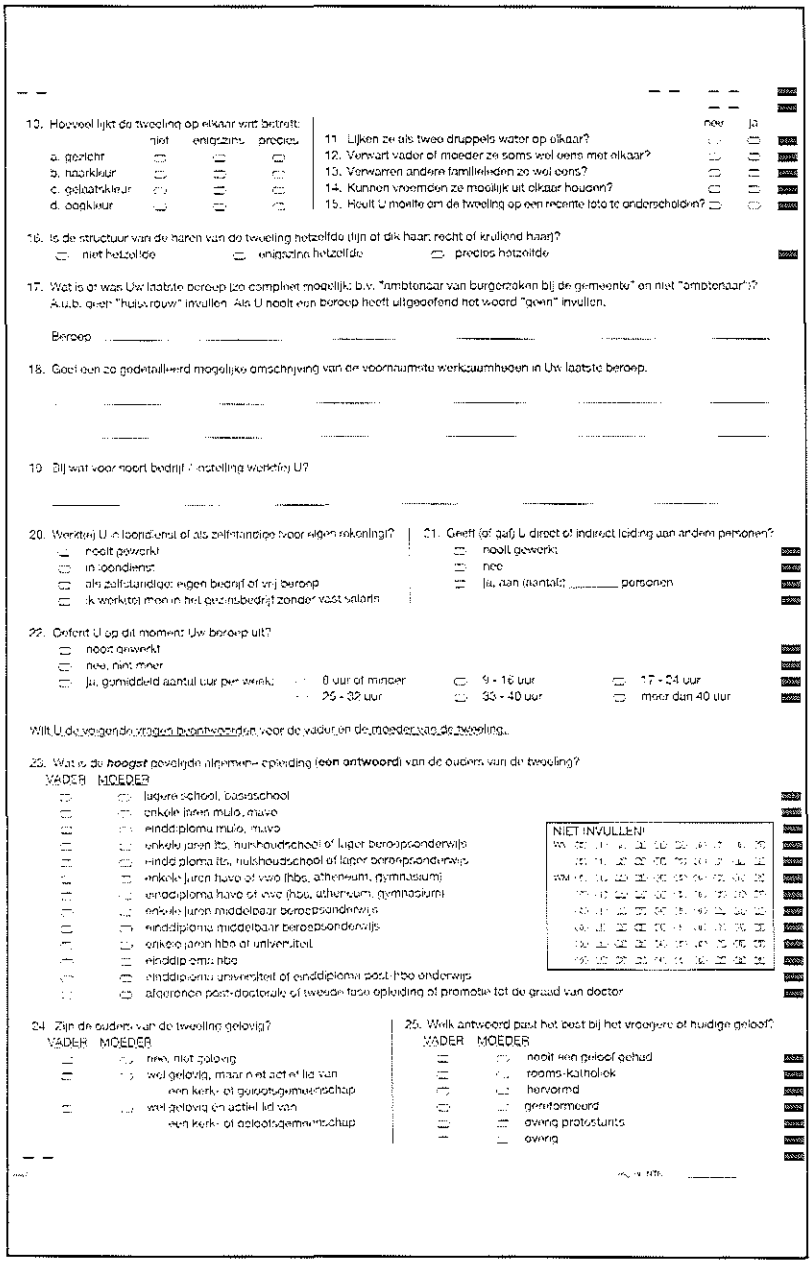
OUDSTE nee	OUDSTE ja		JONGSTE nee	JONGSTE ja
☐	☐	1. Heeft het kind een chronische lichamelijke aandoening of een lichamelijke handicap?	☐	☐
☐	☐	2. Heeft het kind een geestelijke handicap?	☐	☐
☐	☐	3. Heeft het kind een aandoening of handicap die het dagelijks functioneren in ernstige mate beïnvloedt, ondanks het eventuele gebruik van hulpmiddelen of medicijnen?	☐	☐
		4. Wilt U bij elk van de volgende aandoeningen aangeven of deze wel of niet van toepassing is.		
☐	☐	a. Astma, chronische bronchitis of CARA	☐	☐
☐	☐	b. Ontsteking van neusbijholte, voorhoofdsholte of kaakholte	☐	☐
☐	☐	c. Ernstige huidziekte of eczeem	☐	☐
☐	☐	d. Ernstige darmstoornissen, langer dan 3 maanden	☐	☐
☐	☐	e. Chronische blaasontsteking	☐	☐
☐	☐	f. Rugaandoening van hardnekkige aard, langer dan 3 maanden	☐	☐
☐	☐	g. Epilepsie	☐	☐
☐	☐	h. Ernstige hartafwijking	☐	☐
☐	☐	i. Suikerziekte	☐	☐
☐	☐	j. Kwaadaardige aandoening of kanker	☐	☐
☐	☐	k. Leverziekte of leverontsteking	☐	☐
☐	☐	l. Ernstige nierziekte	☐	☐
☐	☐	m. Gewrichtsontsteking of chronische reuma, langer dan 3 maanden	☐	☐
☐	☐	n. Doof of zeer slechthorend	☐	☐
☐	☐	o. Blind of zeer slechtziend	☐	☐
☐	☐	p. Spasticiteit	☐	☐
☐	☐	q. Aandoening van het bewegingsapparaat (orthopaedische aandoening)	☐	☐
☐	☐	r. Stofwisselingsziekte	☐	☐
☐	☐	s. Andere ernstige aangeboren of ernstige langdurige aandoeningen (geef aan):		
☐	☐	oudste: _____		
		jongste: _____	☐	☐
☐	☐	5. Wordt het kind voor een van de onder vraag 4 genoemde aandoeningen behandeld, of komt het kind hiervoor minimaal viermaal per jaar voor controle bij een specialist?	☐	☐
☐	☐	6. Heeft het kind na het 5e jaar in het ziekenhuis gelegen?	☐	☐
☐	☐	7. Is het kind na het 5e jaar onder narcose geweest of heeft het een "roesje" gehad?	☐	☐

8. Wat is op dit moment de lengte en het gewicht van het kind?

	lengte		gewicht		meetdatum
OUDSTE:	____	centimeter	_____	kilo	- -
JONGSTE:	____	centimeter	_____	kilo	- -

Algemene vragen: Wilt U bij de volgende vragen aankruisen wat van toepassing is.

9. a. Is door DNA- of bloedonderzoek vastgesteld of de tweeling één-eiig of twee-eiig is? ☐ nee ☐ ja
   b. Zo ja, wat was de uitslag? ☐ één-eiig ☐ twee-eiig



10. Hoeveel lijkt de tweeling op elkaar wat betreft:

	niet	enigszins	precies
a. gezicht			
b. haarkleur			
c. oogkleur			
d. oogkleur			

	nee	ja
11. Lijken ze als twee druppels water op elkaar?		
12. Verwart vader of moeder ze soms wel eens met elkaar?		
13. Verwarren andere familieleden ze wel eens?		
14. Kunnen vreemden ze moeilijk uit elkaar houden?		
15. Heeft U moeite om de tweeling op een recente foto te onderscheiden?		

16. Is de structuur van de haren van de tweeling hetzelfde (rijn of dik haar; recht of krullend haar)?
niet hetzelfde enigszins hetzelfde precies hetzelfde

17. Wat is of was Uw laatste beroep (zo compleet mogelijk; b.v. "ambtenaar van burgerzaken bij de gemeente" en niet "ambtenaar")?
A.u.b. geen "huisvrouw" invullen. Als U nooit een beroep heeft uitgeoefend het woord "geen" invullen.

Beroep _____

18. Geef dan zo gedetailleerd mogelijke omschrijving van de voornaamste werkzaamheden in Uw laatste beroep.

_____

19. Bij wat voor soort bedrijf / instelling werk(te) U?

_____

20. Werk(te) U in loondienst of als zelfstandige voor eigen rekening?
- nooit gewerkt
- in loondienst
- als zelfstandige: eigen bedrijf of vrij beroep
- ik werk(te) mee in het gezinsbedrijf zonder vast salaris

21. Geeft (of gaf) U direct of indirect leiding aan anderen personen?
- nooit gewerkt
- nee
- ja, aan (aantal): _____ personen

22. Oefent U op dit moment Uw beroep uit?
- nooit gewerkt
- nee, niet meer
- ja, gemiddeld aantal uur per week: 0 uur of minder / 9 - 16 uur / 17 - 24 uur / 25 - 32 uur / 33 - 40 uur / meer dan 40 uur

Wilt U de volgende vragen beantwoorden voor de vader en de moeder van de tweeling.

23. Wat is de ***hoogst*** gevolgde algemene opleiding (**een antwoord**) van de ouders van de tweeling?

VADER	MOEDER	
		lagere school, basisschool
		enkele jaren mulo, mavo
		einddiploma mulo, mavo
		enkele jaren lts, huishoudschool of lager beroepsonderwijs
		eindd.ploma lts, huishoudschool of lager beroepsonderwijs
		enkele jaren havo of vwo (hbs, atheneum, gymnasium)
		eindd.ploma havo of vwo (hbs, atheneum, gymnasium)
		enkele jaren middelbaar beroepsonderwijs
		eindd.ploma middelbaar beroepsonderwijs
		enkele jaren hbo of universiteit
		eindd.p.oma hbo
		eindd.p.oma universiteit of eindd.ploma post-hbo onderwijs
		afgeronden post-doctorale of tweede fase opleiding of promotie tot de graad van doctor

NIET INVULLEN!

24. Zijn de ouders van de tweeling gelovig?

VADER	MOEDER	
		nee, niet gelovig
		wel gelovig, maar niet actief lid van een kerk- of geloofsgemeenschap
		wel gelovig en actief lid van een kerk- of geloofsgemeenschap

25. Welk antwoord past het best bij het vroegere of huidige geloof?

VADER	MOEDER	
		nooit een geloof gehad
		rooms-katholiek
		hervormd
		gereformeerd
		overig protestants
		overig

Wilt U bij de volgende vragen aanstrepen wat van toepassing is.

26. Naar welk soort school gaat het kind?

OUDSTE		JONGSTE
☐	Basisschool / Montessori-onderwijs / Vrije school, etc.	☐
☐	MLK school (moeilijk lerende kinderen)	☐
☐	ZMLK school (zeer moeilijk lerende kinderen)	☐
☐	LOM school (leer- en opvoedingsmoeilijkheden)	☐
☐	ZMOK school (zeer moeilijk opvoedbare kinderen)	☐
☐	School voor doven en slechthorenden	☐
☐	MYTYL (school voor lichamelijk gehandicapten)	☐
☐	TYTYL (school voor meervoudig gehandicapten)	☐
☐	Pedologisch instituut	☐
☐	School voor langdurig zieke kinderen	☐
☐	School voor kinderen die zijn opgenomen in ziekenhuizen	☐
☐	School voor ernstig spraakgebrekkigen	☐
☐	School voor blinden en slechtzienden	☐

27. Huidige schoolresultaten:

OUDSTE	onvoldoende	zwak	voldoende	goed	zeer goed
Taal	☐	☐	☐	☐	☐
Rekenen	☐	☐	☐	☐	☐

JONGSTE	onvoldoende	zwak	voldoende	goed	zeer goed
Taal	☐	☐	☐	☐	☐
Rekenen	☐	☐	☐	☐	☐

28. Heeft het kind op school wel eens leerproblemen gehad?

OUDSTE: ☐ nee ☐ ja
JONGSTE: ☐ nee ☐ ja

29. Heeft het kind op school wel eens andere problemen (dan leerproblemen) gehad?

OUDSTE: ☐ nee ☐ ja
JONGSTE: ☐ nee ☐ ja

Als de vader van de tweeling zijn vragenlijst niet kan invullen,
wilt U dan zo vriendelijk zijn de onderstaande vragen te beantwoorden?

1. Wat is of was vader's laatste beroep (zo compleet mogelijk: b.v. "ambtenaar van burgerzaken bij de gemeente" en niet "ambtenaar")? A.u.b. geen "huisman" invullen. Als vader nooit een beroep heeft uitgeoefend het woord "geen" invullen.

   Beroep _____

2. Geef een zo gedetailleerd mogelijke omschrijving van de voornaamste werkzaamheden in vader's laatste beroep.

   _____

   _____

3. Bij wat voor soort bedrijf / instelling werk(te) vader?

   _____

4. Werk(te) vader in loondienst of als zelfstandige (voor eigen rekening)?
   - ☐ nooit gewerkt
   - ☐ in loondienst
   - ☐ als zelfstandige: eigen bedrijf of vrij beroep
   - ☐ hij werk(te) mee in het gezinsbedrijf zonder vast salaris

5. Geeft (of gaf) vader direct of indirect leiding aan andere personen?
   - ☐ nooit gewerkt
   - ☐ nee
   - ☐ ja, aan (aantal:) _____ personen

6. Oefent vader op dit moment zijn beroep uit?
   - ☐ nooit gewerkt
   - ☐ nee, niet meer
   - ☐ ja, gemiddeld aantal uur per week: ☐ 8 uur of minder ☐ 9 - 16 uur ☐ 17 - 24 uur ☐ 25 - 32 uur ☐ 33 - 40 uur ☐ meer dan 40 uur

HARTELIJK BEDANKT VOOR UW MEDEWERKING !

Appendix XII

CBCL/4-18 for Father

VADER GEDRAGSVRAGENLIJST VOOR KINDEREN VAN 4 - 18 JAAR / NTR

Dit formulier werd ingevuld door:
☐ vader ☐ ander (geef aan):

Datum van invullen: ... - ... - ...

Geboortedatum tweeling: ... - ... - ...

Geslacht oudste (de eerst geborene) van de tweeling:
☐ jongen ☐ meisje

Geslacht jongste (de laatst geborene) van de tweeling:
☐ jongen ☐ meisje

NIET INVULLEN!

Dit is een lijst met beschrijvingen van bepaalde gedragingen en eigenschappen van kinderen. Bij iedere beschrijving die van toepassing is op Uw kind zoals hij/zij **nu** is of ook **binnen de afgelopen zes maanden** is geweest, wordt U verzocht een potloodstreepje te zetten in het vakje van de 2 als de beschrijving **duidelijk of vaak van toepassing** is op Uw kind. Een streepje te zetten in het vakje van de 1 als de beschrijving **een beetje of soms van toepassing** is op Uw kind. Als de beschrijving **helemaal niet van toepassing** is op Uw kind, zet dan een potloodstreepje in het vakje van de 0. Beantwoord a.u.b. alle vragen zo goed mogelijk, ook al lijken sommige vragen niet op Uw kind betrekking te hebben.

Voornaam OUDSTE van de tweeling: ... **Voornaam JONGSTE van de tweeling:** ...

0 = helemaal niet van toepassing (voor zover U weet) **1 = een beetje of soms van toepassing** **2 = duidelijk of vaak van toepassing**

OUDSTE niet	een beetje soms	duidelijk vaak		JONGSTE niet	een beetje soms	duidelijk vaak
0	1	2	1. Gedraagt zich te jong voor zijn/haar leeftijd.	0	1	2
			2. Allergie (geef aan):			
0	1	2	oudste: ...			
			jongste: ...	0	1	2
0	1	2	3. Spreekt veel tegen of maakt veel ruzie.	0	1	2
0	1	2	4. Astma.	0	1	2
0	1	2	5. Gedraagt zich als iemand van het andere geslacht.	0	1	2
0	1	2	6. Doet ontlasting (poept) buiten de w.c. of in de broek.	0	1	2
0	1	2	7. Opschepper, stoer doen.	0	1	2
0	1	2	8. Kan zich niet concentreren, kan niet lang de aandacht bij iets houden.	0	1	2
			9. Kan bepaalde gedachten niet uit zijn/haar hoofd zetten; obsessies (geef aan):			
0	1	2	oudste: ...			
			jongste: ...	0	1	2
0	1	2	10. Kan niet stil zitten, onrustig, of over-actief.	0	1	2
0	1	2	11. Klampt zich vast aan volwassenen of is te afhankelijk.	0	1	2
0	1	2	12. Klaagt over zich eenzaam voelen.	0	1	2
0	1	2	13. In de war of warrig denken.	0	1	2
0	1	2	14. Huilt veel.	0	1	2
0	1	2	15. Wreed voor dieren.	0	1	2
0	1	2	16. Wreed, pesterig of gemeen voor anderen.	0	1	2
0	1	2	17. Dagdromen of gaat op in zijn/haar gedachten.	0	1	2
0	1	2	18. Verwondt zichzelf opzettelijk of doet zelfmoordpogingen.	0	1	2
0	1	2	19. Eist veel aandacht op.	0	1	2
0	1	2	20. Vernielt eigen spullen.	0	1	2
0	1	2	21. Vernielt spullen van andere gezinsleden of van anderen.	0	1	2
0	1	2	22. Is thuis ongehoorzaam.	0	1	2
0	1	2	23. Is ongehoorzaam op school.	0	1	2
0	1	2	24. Eet niet goed.	0	1	2
0	1	2	25. Kan niet goed opschieten met andere jongens/meisjes.	0	1	2
0	1	2	26. Lijkt zich **niet** schuldig te voelen na zich misdragen te hebben.	0	1	2
0	1	2	27. Snel jaloers.	0	1	2
			28. Eet of drinkt dingen die eigenlijk niet eet- of drinkbaar zijn, ***geen snoep*** (geef aan):			
0	1	2	oudste: ...			
			jongste: ...	0	1	2

 Leg. nr. NTR ...

0 = helemaal niet van toepassing (voor zover U weet) 1 = een beetje of soms van toepassing 2 = duidelijk of vaak van toepassing

OUDSTE niet	OUDSTE beetje soms	OUDSTE duidelijk vaak		JONGSTE niet	JONGSTE beetje soms	JONGSTE duidelijk vaak
			29. Is bang voor bepaalde dieren, situaties, of plaatsen, uitgezonderd de school (geef aan):			
0	1	2	oudste: _____			
			jongste: _____	0	1	2
0	1	2	30. Is bang om naar school te gaan.	0	1	2
0	1	2	31. Is bang dat hij/zij iets ondeugends of slechts zou kunnen doen of denken.	0	1	2
0	1	2	32. Vindt dat hij/zij perfect moet zijn.	0	1	2
0	1	2	33. Klaagt erover of heeft het gevoel dat niemand van hem/haar houdt.	0	1	2
0	1	2	34. Heeft het gevoel dat anderen het op hem/haar gemunt hebben.	0	1	2
0	1	2	35. Voelt zich waardeloos of minderwaardig.	0	1	2
0	1	2	36. Krijgt vaak ongelukken en/of verwondingen.	0	1	2
0	1	2	37. Vecht veel.	0	1	2
0	1	2	38. Wordt veel geplaagd.	0	1	2
0	1	2	39. Gaat om met jongens/meisjes die in moeilijkheden verzeild raken.	0	1	2
			40. Hoort geluiden of stemmen die er niet zijn (geef aan):			
0	1	2	oudste: _____			
			jongste: _____	0	1	2
0	1	2	41. Impulsief of handelt zonder na te denken.	0	1	2
0	1	2	42. Is liever alleen dan met anderen.	0	1	2
0	1	2	43. Liegen of bedriegen.	0	1	2
0	1	2	44. Nagelbijten.	0	1	2
0	1	2	45. Zenuwachtig of gespannen.	0	1	2
			46. Zenuwachtige bewegingen of trekkinger (geef aan):			
0	1	2	oudste: _____			
			jongste: _____	0	1	2
0	1	2	47. Nachtmerries.	0	1	2
0	1	2	48. Andere jongens/meisjes mogen hem/haar niet.	0	1	2
0	1	2	49. Obstipatie, houdt ontlasting op, last van verstopping.	0	1	2
0	1	2	50. Is te angstig of te bang.	0	1	2
0	1	2	51. Last van duizeligheid.	0	1	2
0	1	2	52. Te veel last van schuldgevoel.	0	1	2
0	1	2	53. Eet te veel.	0	1	2
0	1	2	54. Oververmoeid.	0	1	2
0	1	2	55. Te dik.	0	1	2
			56. Lichamelijke problemen zonder bekende medische oorzaak: .			
0	1	2	a. pijnen (geen hoofdpijn)	0	1	2
0	1	2	b. hoofdpijn	0	1	2
0	1	2	c. misselijkheid	0	1	2
			d. oogproblemen (geef aan):			
0	1	2	oudste: _____			
			jongste: _____	0	1	2
0	1	2	e. huiduitslag of andere huidaandoeningen	0	1	2
0	1	2	f. maagpijn, buikpijn of buikkrampen	0	1	2
0	1	2	g. overgeven	0	1	2
			h. andere problemen (geef aan):			
0	1	2	oudste: _____			
			jongste: _____	0	1	2
0	1	2	57. Valt anderen lichamelijk aan.	0	1	2

0 = helemaal niet van toepassing (voor zover U weet) 1 = een beetje of soms van toepassing 2 = duidelijk of vaak van toepassing

OUDSTE niet	OUDSTE beetje soms	OUDSTE duidelijk vaak		JONGSTE niet	JONGSTE beetje soms	JONGSTE duidelijk vaak
			58. Neuspeuteren, pulkt of trekt veel aan huid of aan andere lichaamdelen (geef aan):			
			oudste:			
			jongste:			
			59. Speelt met eigen geslachtsdelen in het openbaar.			
			60. Speelt te veel met eigen geslachtsdelen.			
			61. Slechte schoolresultaten.			
			62. Onhandig of slechte coördinatie.			
			63. Is liever samen met oudere jongens/meisjes.			
			64. Is liever samen met jongere jongens/meisjes.			
			65. Weigert om te praten.			
			66. Herhaalt alsmaar bepaalde handelingen, dwanghandelingen (geef aan):			
			oudste:			
			jongste:			
			67. Loopt weg van huis.			
			68. Schreeuwt of gilt veel.			
			69. Gesloten, anderen weten niet goed wat er in hem/haar omgaat.			
			70. Ziet dingen die er niet zijn (geef aan):			
			oudste:			
			jongste:			
			71. Schaamt of geneert zich gauw.			
			72. Brandstichten.			
			73. Sexuele problemen (geef aan welke):			
			oudste:			
			jongste:			
			74. Raar of 'gek' doen om de aandacht te trekken.			
			75. Verlegen of schuchter.			
			76. Slaapt minder dan de meeste leeftijdgenoten.			
			77. Slaapt meer dan de meeste leeftijdgenoten overdag en/of 's nachts (geef aan):			
			oudste:			
			jongste:			
			78. Smeert of speelt met de ontlasting.			
			79. Spraakproblemen (geef aan):			
			oudste:			
			jongste:			
			80. Kijkt met een lege of 'wezenloze' blik.			
			81. Steelt van huis.			
			82. Steelt buitenshuis.			
			83. Opsparen van dingen die hij/zij niet nodig heeft (geef aan welke):			
			oudste:			
			jongste:			

reg. nr. NTR

0 = helemaal niet van toepassing (voor zover U weet) 1 = een beetje of soms van toepassing 2 = duidelijk of vaak van toepassing

OUDSTE niet	OUDSTE beetje soms	OUDSTE duidelijk vaak		JONGSTE niet	JONGSTE beetje soms	JONGSTE duidelijk vaak
			84. Vreemd of raar gedrag (geef aan):			
			oudste:			
			jongste:			
			85. Vreemde of rare gedachten (geef aan):			
			oudste:			
			jongste:			
			86. Koppig, stuurs of prikkelbaar.			
			87. Verandert plotseling van stemming.			
			88. Mokken, pruilen.			
			89. Achterdochtig.			
			90. Vloeken, schuttingtaal.			
			91. Praat erover dat hij/zij zichzelf zou willen doden.			
			92. Slaapwandelen of hardop praten in de slaap (geef aan):			
			oudste:			
			jongste:			
			93. Praat te veel.			
			94. Plaagt veel.			
			95. Driftbuien of snel driftig.			
			96. Denkt te veel aan sex.			
			97. Bedreigt andere mensen.			
			98. Duimzuigen of zuigen op vingers.			
			99. Is teveel bezig met netjes of schoon zijn.			
			100. Slaapproblemen (geef aan):			
			oudste:			
			jongste:			
			101. Spijbelen, schoolverzuim.			
			102. Te weinig actief, beweegt zich langzaam, of gebrek aan energie.			
			103. Ongelukkig, verdrietig, gedeprimeerd.			
			104. Is erg luidruchtig.			
			105. Gebruikt alcohol of drugs (geef aan):			
			oudste:			
			jongste:			
			106. Vandalisme, vernielen.			
			107. Broekplassen overdag.			
			108. Bedplassen.			
			109. Dreinerig, jengelig.			
			110. Wil graag van het andere geslacht zijn.			
			111. Teruggetrokken, komt niet tot contact met anderen.			
			112. Maakt zich zorgen.			
			113. Geeft U a.u.b. verder nog aan ieder ander probleem dat hierboven nog niet aan de orde is geweest.			
			oudste:			
			jongste:			
			oudste:			
			jongste:			

Wilt U a.u.b. controleren of U in de linker en in de rechter kolom, bij **iedere** vraag een potloodstreepje in **één** vakje hebt gezet?

4+?

reg. nr. NTR

Algemene vragen: Wilt u bij de volgende vragen aankruisen wat van toepassing is.

1. Hoeveel lijkt de tweeling op elkaar wat betreft:

	niet	enigszins	precies
a. gezicht	☐	☐	☐
b. haarkleur	☐	☐	☐
c. gelaatskleur	☐	☐	☐
d. oogkleur	☐	☐	☐

	nee	ja
2. Lijken ze als twee druppels water op elkaar?	☐	☐
3. Verwart vader of moeder ze soms wel eens met elkaar?	☐	☐
4. Verwarren andere familieleden ze wel eens?	☐	☐
5. Kunnen vreemden ze moeilijk uit elkaar houden?	☐	☐
6. Heeft U moeite om de tweeling op een recente foto te onderscheiden?	☐	☐

7. Is de structuur van de haren van de tweeling hetzelfde (fijn of dik haar; recht of krullend haar)?
   ☐ niet hetzelfde ☐ enigszins hetzelfde ☐ precies hetzelfde

8. Wat is of was Uw laatste beroep (zo compleet mogelijk: b.v. "ambtenaar van burgerzaken bij de gemeente" en niet "ambtenaar")? A.u.b. geen "huisman" invullen. Als U nooit een beroep heeft uitgeoefend het woord "geen" invullen.

   Beroep _____

9. Geef een zo gedetailleerd mogelijke omschrijving van de voornaamste werkzaamheden in Uw laatste beroep.

10. Bij wat voor soort bedrijf / instelling werkt(e) U?

11. Werkt(e) U in loondienst of als zelfstandige (voor eigen rekening)?
   ☐ nooit gewerkt
   ☐ in loondienst
   ☐ als zelfstandige: eigen bedrijf of vrij beroep
   ☐ ik werk(te) mee in het gezinsbedrijf zonder vast salaris

12. Geeft (of gaf) U direct of indirect leiding aan andere personen?
   ☐ nooit gewerkt
   ☐ nee
   ☐ ja, aan (aantal): _____ personen

13. Oefent U op dit moment Uw beroep uit?
   ☐ nooit gewerkt
   ☐ nee, niet meer
   ☐ ja, gemiddeld aantal uur per week: ☐ 8 uur of minder ☐ 9 - 16 uur ☐ 17 - 24 uur ☐ 25 - 32 uur ☐ 33 - 40 uur ☐ meer dan 40 uur

Wilt U de volgende vragen beantwoorden voor de vader en de moeder van de tweeling.

14. Wat is de ***hoogst*** gevolgde algemene opleiding (**één antwoord**) van de ouders van de tweeling?

VADER	MOEDER	
☐	☐	lagere school, basisschool
☐	☐	enkele jaren mulo, mavo
☐	☐	einddiploma mulo, mavo
☐	☐	enkele jaren lts, huishoudschool of lager beroepsonderwijs
☐	☐	einddiploma lts, huishoudschool of lager beroepsonderwijs
☐	☐	enkele jaren havo of vwo (hbs, atheneum, gymnasium)
☐	☐	einddiploma havo of vwo (hbs, atheneum, gymnasium)
☐	☐	enkele jaren middelbaar beroepsonderwijs
☐	☐	eindiploma middelbaar beroepsonderwijs
☐	☐	enkele jaren hbo of universiteit
☐	☐	eindiploma hbo
☐	☐	eindiploma universiteit of eindiploma post-hbo onderwijs
☐	☐	afgeronde post-doctorale of tweede fase opleiding of promotie tot de graad van doctor

NIET INVULLEN:
VW 00 01 02 03 04 05 06 07 08 09
10 11 12 13 14 15 16 17 18 19
VM 00 01 02 03 04 05 06 07 08 09
10 11 12 13 14 15 16 17 18 19
20 21 22 23 24 25 26 27 28 29
30 31 32 33 34 35 36 37 38 39
40 41 42 43 44 45 46 47 48 49
50 51 52 53 54 55 56 57 58 59
60 61 62 63 64 65 66 67 68 69

15. Zijn de ouders van de tweeling gelovig?

VADER	MOEDER	
☐	☐	nee, niet gelovig
☐	☐	wel gelovig, maar niet actief lid van een kerk- of geloofsgemeenschap
☐	☐	wel gelovig en actief lid van een kerk- of geloofsgemeenschap

16. Welk antwoord past het best bij het vroegere of huidige geloof?

VADER	MOEDER	
☐	☐	nooit een geloof gehad
☐	☐	rooms-katholiek
☐	☐	hervormd
☐	☐	gereformeerd
☐	☐	overig protestants
☐	☐	overig

HARTELIJK BEDANKT VOOR UW MEDEWERKING !

Appendix XIII

Reminder, Sent to Nonresponders of CBCL/4-18

Nederlands Tweelingenregister (NTR)

Datum datum postmerk	Uw brief van	Telefax 020-44.48832	Bijlage(n) achtergrondinformatie
Ons kenmerk NTR/reminder 7	Uw kenmerk	Telefoon 020-44 48787 woensdag t/m vrijdag	

Postadres: De Boelelaan 1111, 1081 HV Amsterdam

vrije Universiteit *amsterdam*

Geachte mevrouw/mijnheer,

Enige tijd geleden ontving u van ons "De gedragsvragenlijst voor kinderen van 4 - 18 jaar". Volgens onze administratie hebben wij deze vragenlijst nog niet van u teruggekregen. Misschien heeft u nog geen tijd gehad om de lijst in te vullen of bent u het vergeten. Hierbij willen wij u nogmaals vriendelijk verzoeken de vragenlijst in te vullen.

Tevens willen wij u erop wijzen dat wanneer het niet mogelijk is dat beide ouders een vragenlijst invullen, wij het ook zeer op prijs stellen één vragenlijst van u terug te krijgen.

Wanneer u niet meer in het bezit bent van de vragenlijsten dan kunt u bellen naar mevrouw Stroet (020-4448827) of het secretariaat (020-4448787) voor nieuwe exemplaren. Achtergrondinformatie over dit onderzoek en de vragenlijst voegen wij nogmaals bij deze brief.

Bij voorbaat hartelijk dank voor uw medewerking.

Met vriendelijke groet en hoogachting,

prof.dr J.F. Orlebeke
mevr.dr D.I. Boomsma

Vakgroep Psychonomie

Bezoekadres: De Boelelaan 1115
Provisorium I

Appendix XIV

Letter Asking the Local Government for the Correct Address of a Family.

Nederlands Tweelingenregister (NTR)

Datum datum postmerk	Uw brief van	Telefax 020-44.48832	Bijlage(n) Adresformulier(en)+retourenvelop
Ons kenmerk	Uw kenmerk	Telefoon 020-44.48827(gem!)	E-mail

Postadres: De Boelelaan 1111, 1081 HV Amsterdam

Aan de Afdeling Burgerzaken/Bevolkingsregister

van de Gemeente .....

vrije Universiteit *amsterdam*

Geachte mevrouw, heer,

In 1987 is aan de Vrije Universiteit te Amsterdam het Nederlands Tweelingen Register opgezet, een adressenbestand van gezinnen met een meerling die bereid zijn **op vrijwillige basis** mee te doen aan **wetenschappelijk onderzoek**. Het betreft hier voor het overgrote deel meerlingen die vrij kort na hun geboorte worden aangemeld en door ons in hun ontwikkeling worden gevolgd door middel van vragenlijsten.

Veel van de bij ons geregistreerde jonge gezinnen verhuizen. Hoewel het merendeel van deze gezinnen ons een verhuisbericht stuurt, zijn er ook die dat vergeten. Op bijgaand adresformulier(en) vindt u de naam en het oude adres van een gezin met een meerling dat in uw gemeente heeft gewoond en is verhuisd. Wij zouden het zeer op prijs stellen wanneer u ons kunt inlichten over het nieuwe adres van dit gezin. Indien de ouders inmiddels gescheiden zijn, zouden wij graag het adres ontvangen van de ouder bij wie de meerling thans woonachtig is. Voor alle duidelijkheid: wij zoeken slechts één adres en om de kosten voor ons zo laag mogelijk te houden, verzoeken wij u vriendelijk ons **niet** meerdere uittreksels uit het bevolkingsregister te sturen.
U kunt bijgaand adresformulier(en) in meegestuurde portvrije enveloppe aan ons retourneren. Wilt u bij eventuele facturering/correspondentie verwijzen naar ons kenmerk? U vindt dit kenmerk op ieder adresformulier in de rechterbovenhoek van de adressticker en bovenaan deze brief.

Wij danken u bij voorbaat voor uw medewerking.

Hoogachtend,

mevr.drs. Th.M. Stroet

Bijlage(n): ____ adresformulier(en)

Vakgroep Psychonomie

Bezoekadres: De Boelelaan 1115
Provisorium I

Vrije Universiteit
Nederlands Tweelingenregister
De Boelelaan 1111
1081 HV Amsterdam

Adresformulier t.b.v. Nederlands Tweelingenregister

Oud adres gezin:

Roepnamen meerling: _____

_____

_____

Geboortedatum meerling: _____

Aanvullende informatie: _____

_____

_____

Nieuw adres gezin: (Indien de ouders inmiddels gescheiden zijn, ontvangen wij graag het adres van de ouder bij wie de meerling thans woonachtig is)

Straat + huisnummer: _____

Postcode: _____

Woonplaats: _____

Telefoon: _____

Samenvatting

Samenvatting

In dit proefschrift worden de genetische en omgevingsinvloeden op probleemgedrag bij kinderen van 3 en 7 jaar beschreven. Tevens zijn de determinanten van stabiliteit en verandering van probleemgedrag over de tijd heen onderzocht van 3- naar 7-jarige leeftijd.

Probleemgedragingen komen bij kinderen relatief veel voor (ongeveer 13% van alle kinderen vertonen probleemgedragingen). Tijdens de ontwikkeling blijken de meeste kinderen niet over het probleemgedrag heen te groeien. Alhoewel kinderen wel variaties vertonen in de mate waarin ze probleemgedragingen vertonen, blijken grote veranderingen in gedrag zeldzaam te zijn. Om de oorzaken van individuele verschillen in probleemgedrag van jonge kinderen te onderzoeken is een gedragsgenetisch onderzoek uitgevoerd. Hiertoe hebben zowel moeders als vaders van 4016 Nederlandse 3-jarige tweelingparen en 1940 Nederlandse 7-jarige tweelingparen een gedragsvragenlijst (de Child Behavior Checklist) ingevuld, voor zowel het oudste als het jongste kind.

Twee brede groepen van probleemgedrag, die een onderscheid reflecteren tussen agressief/overactief gedrag (Externaliserende Problemen) en bang/teruggetrokken gedrag (Internaliserende Problemen) zijn onderzocht. Genetische invloeden bleken zowel op 3- als op 7-jarige leeftijd een grote invloed te hebben op het vertonen van probleemgedrag. Voor Externaliserende Problemen verklaarden de genetische factoren 52 % van de variantie in de gerapporteerde problemen, zowel op 3- als op 7-jarige leeftijd. Voor Internaliserende Problemen nam de genetische invloed over de tijd heen wat af. Op 3-jarige leeftijd werd 59% van de variantie in gerapporteerde problemen door genetische factoren verklaard, terwijl dit op 7-jarige leeftijd nog 40% van de variantie was. Zowel peuters als schoolgaande kinderen blijken dus een biologische gevoeligheid te kunnen hebben voor het vertonen van Externaliserende en/of Internaliserende Problemen. Familiale omgevingsinvloeden, zoals de sociaal economische status, het geloof, of de opvoedingsstijl van de ouders, bleken voor Externaliserende gedragingen zowel op 3- als op 7-jarige leeftijd een invloed te hebben, terwijl deze familiale invloeden voor Internaliserende gedragingen enkel voor 7-jarige kinderen gevonden werden. Voor Internaliserende Problemen bleken de genetische invloeden kleiner en de familiale invloeden groter te worden tijdens de ontwikkeling.

De stabiliteit van het vertonen van probleemgedrag over een periode van 4 jaar bleek voor beide probleemgedragingen vooral door genetische invloeden bepaald te worden. De stabiliteit voor Externaliserende Problemen (r = .54) werd voor 55% door genetische factoren verklaard, en voor 37% door familiale omgevingsinvloeden, terwijl de stabiliteit van Internaliserende Problemen (r = .38) voor 66% door genetische factoren en voor 23% door familiale omgevingsinvloeden verklaard werd. Behalve een biologische gevoeligheid blijken familiale omgevingsfactoren, zoals bijvoorbeeld onenigheid in de familie, gebrek aan genegenheid en slecht toezicht op de kinderen, dus ook invloed te hebben op het voortduren van probleemgedragingen.

Voor beide probleemgedragingen en op beide leeftijden bleken genetische factoren behalve continue invloeden ook leeftijdsspecifieke invloeden te hebben. Deze leeftijdsspecifieke invloeden waren onafhankelijk van de continue effecten en beïnvloeden dus verandering in gedrag. In ander woorden, het vinden van leeftijdsspecifieke invloeden duidde erop dat waarschijnlijk verschillende genen een bijdrage leveren aan de variatie van probleemgedrag van kleuterleeftijd tot schoolgaande leeftijd.

Idiosyncratische omgevingsinvloeden, zoals bijvoorbeeld ziekten of trauma's, bleken vooral leeftijdsspecifieke invloeden te hebben. Deze factoren verklaarden respectievelijk 18% en 30% van de variantie in gerapporteerde Externaliserende en Internaliserende Problemen. De invloeden bleven voor beide gedragsproblemen op beide leeftijden gelijk. Alhoewel deze resultaten niet impliceren dat idiosyncratische omgevingsinvloeden onbelangrijk zijn voor kinderen, suggereren zij wel dat deze invloeden van een voorbijgaande aard zijn waar kinderen van 'herstellen'.

Uit de resultaten blijkt dat de stabiliteit van probleemgedrag vooral bepaald wordt door genetische invloeden en in mindere mate ook door familiale omgevingsinvloeden. Als jonge kinderen probleemgedrag vertonen is het dus niet aan te raden om een afwachtende houding aan te nemen. De kans is namelijk groot dat kinderen, die een biologische gevoeligheid hebben om probleemgedrag te vertonen en ongunstige omgevingsinvloeden blijven ervaren, het probleemgedrag tijdens hun verdere ontwikkeling blijven vertonen.

Dankwoord

Dankwoord

Zeer veel mensen hebben aan dit onderzoek een bijdrage geleverd. Enkele daarvan wil ik hier bedanken. Allereerst alle ouders van tweelingen die geheel belangeloos aan dit onderzoek hebben meegewerkt. Dankzij hun inzet heeft dit onderzoek kunnen plaatsvinden!

Grote dank ben ik verschuldigd aan Prof.dr. D.I. Boomsma. Waar ook ter wereld zij was, één e-mail en binnen enkele uren had ik een antwoord. Behalve dat zij een zeer kundig gedragsgeneticus is, straalt zij ook een enorm enthousiasme uit in haar werk. In moeilijke tijden was één remedie altijd effectief: een half uurtje in Dorret's kamer en alle (oude) problemen verdwenen als sneeuw voor de zon! Dorret, bedankt, zowel voor je kundige begeleiding die geresulteerd heeft in dit proefschrift, alsook omdat ik door jou het vak gedragsgenetica met zijn "BGA faculty" heb leren kennen. Een enthousiastere groep wetenschappers zal ik waarschijnlijk nooit meer tegenkomen! Eveneens ben ik veel dank verschuldigd aan Prof.dr. F.C. Verhulst. Door zijn gedrevenheid in de Kinder- en Jeugdpsychiatrie heb ik geleerd hoe belangrijk het is om goed kwalitatief onderzoek uit te voeren en daar op een wetenschappelijke manier over te rapporteren. Ondanks zijn drukke werkzaamheden heeft hij toch altijd de tijd kunnen vinden om mijn manuscripten door te lezen en mij te wijzen op mogelijk interessante artikelen. Frank, bedankt voor je professionele begeleiding en voor je vertrouwen! Het zal niet vaak voorkomen dat je een AIO moet begeleiden die 's middags en 's avonds komt werken omdat zij 's ochtends haar paard gaat trainen. Heel blij ben ik dat Dr. E.J.C.G. van den Oord als copromotor heeft willen fungeren. Zijn deskundige hulp bij het analyseren en schrijven van de laatste drie tweeling-artikelen had ik niet willen missen. Edwin, bedankt voor je enthousiasme en het delen van je kennis, zowel over de gedragsgenetica als over de ontwikkelingspsychologie! Voor mij staat vast dat jij over niet al te lange tijd een onmisbaar lid van de BGA faculty zult zijn!

Het verzamelen van zoveel vragenlijsten was niet mogelijk geweest zonder de deskundige hulp van Drs. T.M. Stroet. Duizenden vragenlijsten worden elk jaar verstuurd en ontvangen. Eén typefout en de waardevolle gegevens van een hele familie raken zoek. Maar onder Thérèse's toeziend oog hoeven we daar niet bang voor te zijn. Zelden heb ik iemand zo precies zien werken. Thérèse, heel erg bedankt voor al je hulp! The analyses reported in this

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Verder wil ik de studenten van de Vrije Universiteit bedanken die hebben willen meehelpen met het versturen en ontvangen van de vragenlijsten: Willie van Weele, Babette Bijlsma en Ilja Bongers. Ook ben ik dank verschuldigd aan alle studenten en werknemers op het Sophia Kinderziekenhuis die mij geholpen hebben met het coderen van de vragenlijsten, met name Carolien van Geer, Christel Rolefes, en Carina van Westen. Allemaal heel erg bedankt voor het vele werk dat jullie voor mij verricht hebben!

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