Summary

This thesis describes the outcome of two longitudinal studies. Two important phenotypes are considered in a large longitudinal sample of Dutch twins: cognitive abilities and childhood psychopathology. Cognitive abilities were studied in a longitudinal sample of 400 children. Measures of intelligence were collected at 5, 7, 10, and 12 years of age. Additional information on cognitive abilities at age 12 was collected by means of the CITO score for 1495 children. Behavioral and emotional problems were assessed longitudinally, by parental report, in over 10,000 children at ages 3 and 7, in 6000 children at age 10 and in 3000 children at age 12. Finally, salivary cortisol samples were collected at two consecutive days in 180 twelve-year-old twin pairs, who participated in the longitudinal study on cognitive abilities.

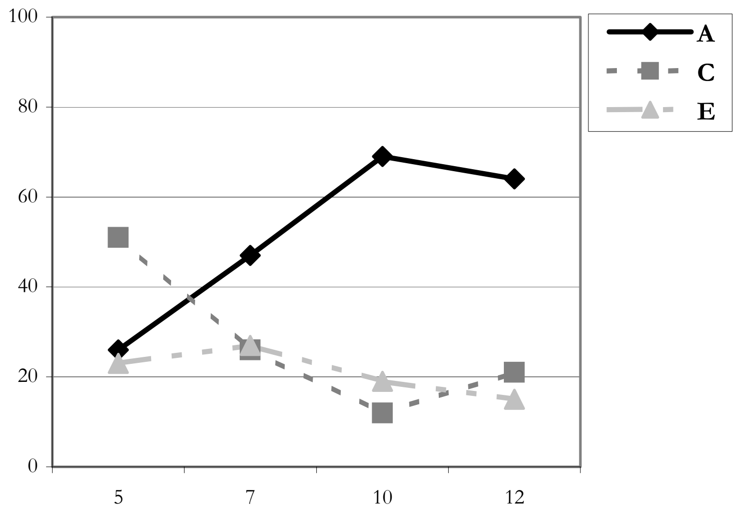
The longitudinal study on cognitive abilities

It can be concluded that the development of general cognitive abilities is a continuous process, represented by high correlations over time ($r_{(5\text{-}7)}$= .65; $r_{(5\text{-}10)}$= .65; $r_{(5\text{-}12)}$=.64; $r_{(7\text{-}10)}$=.72; $r_{(7\text{-}12)}$=.69 and $r_{(10\text{-}12)}$=.78). Stability in cognitive ability throughout development is mainly accounted for by genetic factors. Seventy-two percent of the between age covariance, representing stability in cognitive abilities over time, was accounted for by additive genetic factors. The remaining 28% could be explained by environmental influences shared by both members of a twin pair. The developmental pattern of additive genetic influences (A) on cognition is best described by a common factor structure. Thus, an underlying set of genes influences cognition from the beginning onwards. However, the importance of these genes increases greatly during childhood (see Figure I). Environmental influences shared by both members of a twin pair, the so-called shared environmental influences (C), are less important over time. The developmental pattern is also best captured by a common factor structure. Besides this common factor structure, significant age specific influences of shared environment in cognitive abilities are found. Nonshared environmental influences, environmental influences unique for each person (E), show no continuity, thus mainly account for change in cognitive functioning over the years.

As depicted in figure I, an increase in heritability of IQ over the years was found. At age 5, 26% of the total variance was accounted for by genetic influences, while at age 10, 69% of the total variance was explained by genetic factors. A complementary decrease in shared environmental influences is observed.

The correlation between scholastic achievement, assessed with the CITO score at age 12, and cognitive abilities at ages 5, 7, 10 and 12 years (.41, .50, .60, and .63 resp.) is explained by genetic and shared environmental factors. Individual differences in CITO score are mainly accounted for by additive genetic influences, explaining 60% of the total variance. Small but significant influences of shared environment are found, explaining about 25% of the total variance. The remaining 15% is accounted for by nonshared environmental influences.

Figure I.
Graphical representation of the variance decomposition in additive genetic (A), shared environmental (C), and nonshared environmental (E) factors for cognitive abilities at age 5, 7, 10, and 12 years.

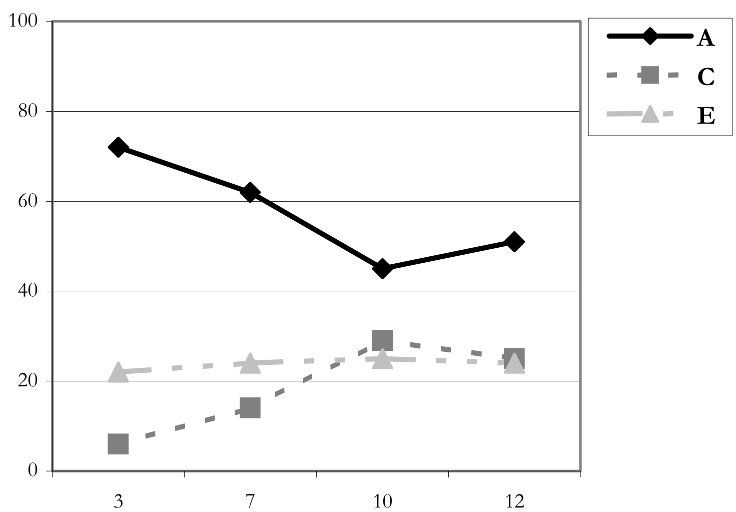


The longitudinal study on behavioral and emotional problems
Behavioral and emotional problems are highly prevalent in Dutch children aged 3 to 12 years. Twenty-five to 30% of the children in the sample showed some kind of behavioral problem. The prevalence of behavioral problems, though, varies depending on the kind of behavior, the rater, and the age and gender of the child. Internalizing problems (anxious/depressed behavior, withdrawn behavior) are more prevalent in girls than boys and Externalizing problems (aggressive behavior, rule breaking behavior) are more prevalent in boys than girls. Overall, mothers report more problem behaviors than fathers and prevalence of problem behavior, as rated by the parents, decreases over age.

As for cognitive abilities, it can be concluded that the development of Internalizing and Externalizing problem behavior is a continuous process, represented by moderate to high correlations over time. The observed stability coefficients for the four- seven-, and nine-year time intervals were, respectively, .37, .33, .30 for Internalizing behavior and .55, .49, and .48 for Externalizing behavior. Stability in problem behaviors can be explained by genetic and environmental influences on the covariances over time. For Internalizing behavior in boys stability is for 65%, 26%, and 9% explained by additive genetic, shared environmental and nonshared environmental influences, respectively. Forty-seven percent of the stability in girls is accounted for by additive genetic factors. Stability in Internalizing behavior in girls is accounted for 43% by shared environmental factors. The remaining 10% can be explained by nonshared environmental factors. Genetic influences are the main factor for stability in Externalizing behavior in boy, explaining 76% of the covariance over time. Nineteen percent is accounted for by shared environmental influences. Only 5 % of the stability in Externalizing behavior in boys is accounted for by nonshared environmental factors. For Externalizing behavior in girls, both genetic and shared environmental factors are important for stability over the years, explaining 62% and 31% respectively. The remaining 7% is accounted for by nonshared environmental factors. For both Internalizing and Externalizing behavioral problems the developmental pattern of genetic, shared and nonshared environmental influences is best described by a simplex pattern. So, influences are transmitted from age to age and new influences come into play at each age.

Figure II.

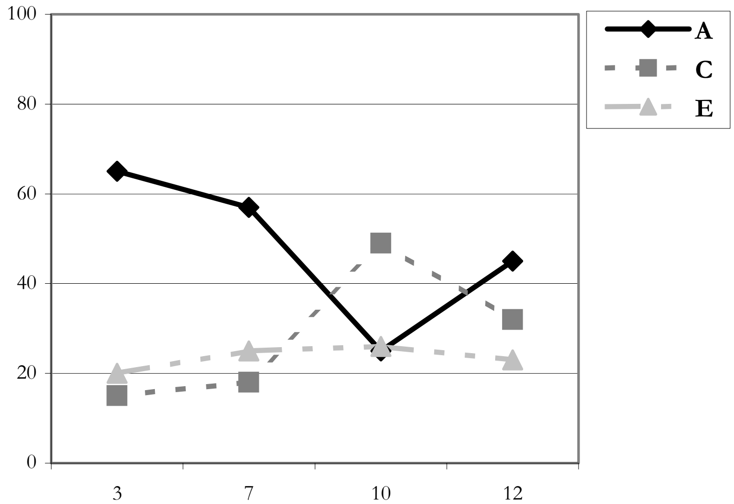
Graphical representation of the variance decomposition in additive genetic (A), shared environmental (C), and nonshared environmental (E) factors for Internalizing behavior in boys, similar assessed by both parents, at age 3, 7, 10, and 12 years.



For Internalizing behavior (See Figure II) in both boys and girls a decrease in genetic influences and a complementary increase of shared environmental influences is observed.

Relative stability in the strength of genetic and environmental influences in boys is reached from age 10 onwards.

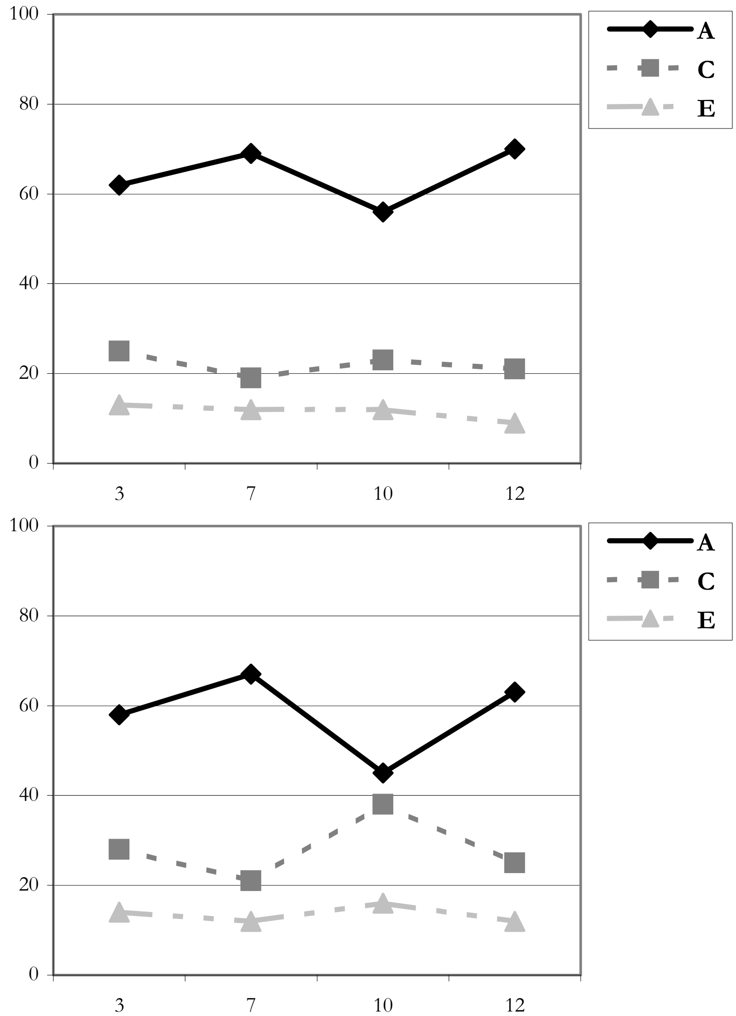
Figure II-cont.
Graphical representation of the variance decomposition in additive genetic (A), shared environmental (C), and nonshared environmental (E) factors for Internalizing behavior in girls, similar assessed by both parents, at age 3, 7, 10, and 12 years.



For Externalizing problem behavior less change in the strength of genetic and environmental influences is observed (see Figure III). Stability in Externalizing problem behaviors throughout development in boys and girls is mainly accounted for by additive genetic influences. For both Internalizing and Externalizing behavior it can be seen that the influences of nonshared environmental influences, representing pure idiosyncratic experiences, remains stable throughout development.

It can be concluded from this study that the developmental processes of genetic and environmental influences on the different phenotypes (cognition, Internalizing behavior, and Externalizing behavior) show distinct patterns. While a common set of genes influences cognition during childhood, a transmission process including new genetic influences at distinct ages best describes genetic influences on behavioral problems during childhood. Further, the strength of genetic and environmental influences changes during childhood, with an increase of genetic influences on cognition, a decrease of genetic influences on Internalizing behavior and relatively stable genetic influences on Externalizing behavior.

Figure III.
Graphical representation of the additive genetic (A), shared environmental (C), and nonshared environmental (E) influences on Externalizing problem behavior, similar assessed by both parents, for boys (upper diagram) and girls (lower diagram) throughout development.



The use of multiple raters in studying the development of both problem behaviors is recommended. Agreement between parents for each assessment (age 3, 7, 10 and

12) was about .6, which indicates that part of the behavior is similar assessed by mothers and fathers. It is further found that disagreement between the parents, indicated by the less than perfect agreement, is not merely the result of unreliability and/or rater bias, but each parent also provides unique information from his/her own perspective on the child's behavior. These parental unique views show almost no continuity over the years, so this parent specific view is important for behavioral assessment at a certain age but is not significant for understanding the development of problem behavior during childhood. However, about 20% of the stability in Internalizing and Externalizing problem behavior over the years is accounted for by so-called rater bias. In other words, a part of the observed stability in problem behavior is accounted for by characteristics of the rater instead of factors of 'real' behavior. This finding emphasizes the importance of the use of multiple raters in studying the development of problem behavior.

Cortisol is mainly known for its pivotal role in generating an adequate response to physical and emotional stressors. However, it may also exert strong behavioral effects that are already apparent during childhood. In general biological, neurophysiological, electrophysiological, and behavioral indices of the pathways that connect genes and the trait under investigation, such as cortisol, are called endophenotypes. Before cortisol can be considered as an endophenotype in studying individual differences in the development of cognitive abilities and psychopathology, it is clearly essential to demonstrate that this measure of cortisol levels is strongly related to psychopathology or cognition, that both phenotypes are influenced genetically, and that genes that influence cortisol also are likely to be involved in the etiology of behavioral problems or cognitive abilities. Previous studies report an association between cortisol and cognitive abilities or childhood psychopathology. Further, the significance of genetic influences on childhood psychopathology and cognitive abilities are well established. However, more insight into the etiology of individual differences in cortisol levels, especially in children, still need to be gained.

For the determination of cortisol levels in children four saliva samples were collected at two consecutive days in a subsample (N=180 twin pairs) of the sample that participated in the longitudinal study of cognitive abilties. Results of the analyses showed a significant genetic contribution to the variation of basal cortisol levels in the morning and afternoon samples. Heritability did not differ for boys and girls and was highest (60%) for cortisol levels during the sample taken about 45 minutes after awakening. This cortisol awakening response provides a useful endophenotype in the search for genes that may affect hypothalamic-pituitary adrenocortical functioning in children.

Low correlations were found between cortisol levels at different points in time during the day. It was hypothesized that the heritability of cortisol levels varies inversely with the strength of the negative feedback signal exerted by cortisol at the glucocorticoid receptors (GR) and mineralocorticoid receptors (MR). Changes in the strength of this feedback signal are reflected in changes in the absolute cortisol level, although time lagged, because the effects of cortisol on the GR and MR receptors are largely genomic.

Preliminary results show no significant correlation between cortisol levels assessed at age 12 and Internalizing or Externalizing behavior at ages 3, 7, 10, and 12. Further, no significant association is observed between cognitive abilities at ages 5, 7, 10, and 12 and cortisol levels at age 12. Future studies are necessary to gain more insight into the presence or absence of these associations and the possible value of cortisol levels as an endophenotype in studying individual differences is the development of cognition and childhood psychopathology.

Based on the results of this thesis it can be concluded that genetic influences are pervasive during childhood. Genes affect two major phenotypes, behavioral problems and cognitive abilities, as well as a possible endophenotype, basal cortisol levels. Genes also affect various aspects of development and are very important for continuity and change throughout development. It can be stated that genetic studies are not only important for estimating size of genetic and environmental effects, but can shed light on fundamental questions in child development. For this reason, genetic studies supply phenotypic studies and are an essential addendum for research in developmental psychology.