GENERAL COGNITIVE ABILITY AND THE INTERPLAY BETWEEN GENES AND ENVIRONMENT

Annabelle Vinkhuyzen

Classical twin studies have shown that individual differences in general cognitive ability in adults are largely due to differences at a genetic level. These studies, however, rely on several assumptions that may not hold for general cognitive ability. Based on an extended twin family study, we show that genetic factors underlying individual differences in general cognitive ability in adults are not only due to additive genetic factors, but also to genetic dominance and genetic variation due to positive assortative mating and that the relative contribution of genetic and environmental factors is not equal across the entire population, but varies as a function of exposure to environmental conditions. This implies that the well recognized high influence of additive genetic factors partly reflects more complex processes such as genetic dominance, positive phenotypic assortment, gene-environment correlation and gene-environment interaction.

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A M S T E R D A M

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Chapter 1

General introduction

GENERAL INTRODUCTION

General cognitive ability, or *intelligence,* has fascinated scientists for more than a century. Its definition, however, differs widely across disciplines, time and places. In 1904, Spearman introduced the term *g* to explain the concept of intelligence. The general factor *g* is based on the observation that individuals who score high on one test of cognitive ability, also tend to score high on other tests of cognitive ability. According to Spearman, *g* explains a large part of the variance in performance on diverse tests of cognitive ability. The concept of *g* is however highly debated in the 20th century; scientists focused more on a multifactorial concept rather than a unitary concept of cognitive ability. For example, Thurstone (1938) focused on several primary mental abilities, such as verbal comprehension, memory and number facility, rather than a general factor of intelligence. In 1986, Sternberg and Detterman (1986) summarized the views of 52 scientists, collected on a symposium on intelligence (Gottfredson, 1997):

> *"Intelligence is a very general mental capability that, among other things, involves the ability to reason, plan, solve problems, think abstractly, comprehend complex ideas, learn quickly and learn from experience. It is not merely book learning, a narrow academic skill, or test-taking smarts. Rather, it reflects a broader and deeper capability for comprehending our surroundings-, 'catching on,' 'making sense' of things, or 'figuring out' what to do."*

For pragmatic reasons, the term *general cognitive ability* will be used throughout this thesis, to refer to intelligence such as it is measured with a psychometric intelligence test ("Intelligence as the tests test it"; Boring, 1923).

General cognitive ability is commonly assessed using psychometric tests that cover cognitive domains such as verbal comprehension, perceptual organization, processing speed, and working memory. Psychometric tests of intelligence show high reliability and validity. Outcomes of such tests are often transformed into standardized IQ scores such that the mean is 100 and the standard deviation is 15. IQ scores follow a normal distribution within a population (see Figure 1.1). About 68% of the population has IQ scores between 85 and 115 (i.e., one standard deviation from the mean), ~95% of a population has IQ scores between 70 and 130 (i.e., two standard deviations from the mean), and ~99% has IQ scores between 55 and 145 (i.e., three standard deviations from the mean).

Figure 1.1 Theoretical normal distribution for general cognitive ability within a general population.
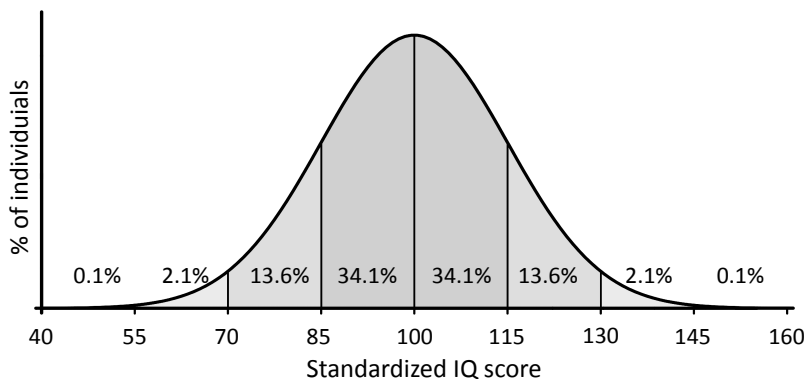
Causes of Individual Differences in General Cognitive Ability

As general cognitive ability is strongly related to e.g. educational performance, occupational status, socio-economic status, social competences, and mortality risk (Gottfredson, 1997; Huisman et al., 2005; Johnson et al., 2006; Batty et al., 2007), causes of individual differences in general cognitive ability are considered of great practical and social importance. The question *why* individuals differ has been subject of research and philosophical reasoning for many centuries. Galton (1822-1911) attributed causes of individual differences in general cognitive ability to 'heritable factors' as well as 'environmental factors'. In his book *Hereditary Genius (1869)*, Galton declared that the closer the familial relatedness of two individuals, the more these people are thought to resemble each other for general cognitive ability. Based on this assumption, genetically informative designs, such as adoption studies, twin studies, and family studies have been used to estimate the relative influence of genetic and environmental factors on total trait variation. The most widely used design is the classical twin design (See Appendix I for an extensive description).

In the second half of the 20th century, a wealth of classical twin studies showed considerable evidence that individual differences observed in general cognitive ability were to a large extent due to individual differences at a genetic level (Bouchard, Jr. & McGue, 1981; Plomin, 1999). In addition, it has been reported that the relative contribution of genetic factors increases from childhood (41%) to adolescence (55%), to young adulthood (66%), and to middle and late adulthood (85%) (Posthuma et al., 2001a; Haworth et al., 2009).

Genetics of general cognitive ability, knowns and unknowns

Most of the reported heritability estimates for general cognitive ability are based on classical twin studies. Although such studies have provided a wealth of information on causes of individual differences in general cognitve ability, they are also known to rely on several assumptions, some of these assumptions do not necessarily hold for general cognitive ability.

First, in the classical twin design it is assumed that genes and environment act in an additive manner. It is however conceivable that more complex processes are operating. For example, individuals who have a genetic predisposition for e.g. attaining high cognitive ability, may select (passively, reactively, or actively) environmental conditions in which their genetic disposition can prosper and become manifest (Plomin et al., 1977). The environment is then selected based on a genetic propensity. In this situation, genetic and environmental factors do not act in an additive manner anymore, but are correlated (i.e., gene-environment correlation: $r_{(GE)}$).

Second, environmental factors (e.g., education, parental rearing style) may have different impact in individuals with a different genetic makeup, or vice versa, expression of genes may be dependent on an individual's exposure to a particular environment. In this situation, genetic and environmental factors interact such that genes control an individual's sensitivity to environmental factors, or environmental factors control the expression of the genes (i.e., gene-environment interaction: GEI).

A third assumption of the classical twin design is that the phenotypes of the parents of the twins are uncorrelated. It has however been reported that mates select

each other on the basis of similar levels of general cognitive ability, also known as positive assortment (Jencks et al., 1972; Loehlin, 1978; Mascie-Taylor, 1989).

Fourth, in classical twin models, trait related environmental factors that are transmitted form parents to offspring (i.e., cultural transmission) cannot be distinguished from genetic transmission from parents to offspring.

Fifth, genetic influences due to dominance deviation (i.e., genetic non-additivity) and environmental factors that are shared between twins cannot be estimated simultaneously within the classical twin design. Consequently, either dominance deviation, or the contribution of shared environmental factors is assumed to be absent in the classical twin design, such that true effects of these factors can be underestimated.

When any of these assumptions is violated, estimates of the relative importance of genetic and environmental influences will be biased in classical twin studies (Jinks & Fulker, 1970; Eaves et al., 1977; Plomin et al., 1977; Purcell, 2002).

The classical twin design is the predominant design in heritability studies, however, little is known about the effects of the processes discussed above with respect to individual differences in many traits, including general cognitive ability. At the start of this PhD project only few studies, mainly in children and adolescents, considered $r_{(GE)}$, GEI, assortative mating, cultural transmission, and simultaneously modeling of genetic dominance deviation and shared environmental factors. More research on these topics, particularly in adults, is essential for a better understanding of genetic and environmental influences on individual differences in general cognitive ability.

Aims and outline of this thesis

The main aim of this thesis is to study the interplay between genetic and environmental factors (i.e., $r_{(GE)}$ and GEI) as well as assortative mating and cultural transmission in the context of general cognitive ability in adults. The hypothesis is that the high heritability estimates that have frequently been reported for cognitive ability in adults partly reflect these complex processes and that considering these processes will help us to understand the etiology of the individual differences that are observed in general cognitive ability. A clear understanding of the sources of individual differences in general cognitive ability may eventually facilitate gene finding studies, which have so far been less successful than expected (as discussed in Plomin & Davis, 2009; Posthuma et al., 2009; Deary et al., 2010). To this end, we extended the classical twin design to an extended twin family design and besides measuring cognitive ability, we measured a set of carefully selected environmental moderators.

In Chapter 2, characteristics and implications of $r_{(GE)}$, GEI, assortative mating, and cultural transmission are discussed in more detail. In addition, this chapter contains a description of the sample on which most of the studies reported on in this thesis are based, as well as a description of the measures of cognitive ability and environmental indices on which the studies in Chapters 3 to 8 are based. In Chapter 3, genetic and environmental influences on individual differences in cognitive ability are studied in an extended twin-family design, taking into account the effects of assortative mating, cultural transmission, and $r_{(GE)}$. In Chapter 4, the contribution of genetic influences to presumed 'environmental' factors such as childhood environment, social environment and behavior, leisure time

activities, and life events is examined. A study on sex differences in academic and general achievement motivation is described in Chapter 5. In Chapter 6, moderation effects of achievement motivation and general cognitive ability on the variance decomposition of educational attainment are studied. Moderation effects of influential life events and experience seeking behavior on the variance decomposition of general cognitive ability are described in Chapters 7 and 8, respectively. The heritability of aptitude and exceptional talent across different domains is the topic of Chapter 9. Finally, the results of these studies are summarized and discussed in Chapter 10, together with a view on future studies on elucidating the role of genes and environment in general cognitive ability.

Chapter2

Theoretical background, sample characteristics, and data collection

OUTLINE OF THIS CHAPTER

In the first part of this chapter, a theoretical background is provided of twin-family modeling, together with a description of complex processes such as gene-environment interaction and correlation, assortative mating, and cultural transmission that may underlie individual differences in general cognitive ability. We will describe how these mechanisms may affect the estimates of genetic and environmental influences such as obtained in classical twin studies, in which those effects cannot be modeled. In addition we will describe how these processes can be modeled within an extended twin family design.

In the second part of this chapter, a description of the sample, on which most of the studies in this thesis are based, and data collection on which studies in chapters three to eight are based, is given. The actual measures of cognitive ability and environmental indices that were reported in this PhD thesis are described in the third part of this chapter.

THEORETICAL BACKGROUND

The extended twin family design

In classical twin studies, data from monozygotic (MZ) and dizygotic (DZ) twins are used to decompose the total variance of a trait, also called the 'phenotypic or observed variance', into two main sources of variation: genetic variation and environmental variation. Based on the observed MZ and DZ twin correlations, as well as their known genetic and environmental relatedness, the relative proportions of genetic and environmental factors to the overall variation in a trait can be estimated (Falconer & Mackay, 1989).

To deal with the limitations of the classical twin design as discussed in Chapter 1, we extended the classical twin design by including siblings of twins, spouses of twins and of their siblings, and either the parents or the offspring of the twins and siblings (depending on age). Figure 2.1 shows two pedigrees for the extended twin family design as used in this PhD project.

Figure 2.1 Pedigrees for the two extended twin family designs as applied in this thesis
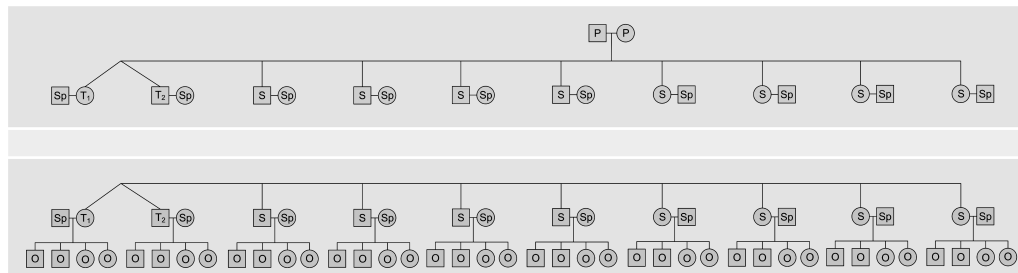
Notes: P = parent; T = twin; S = non-twin sibling, Sp = spouse; O = offspring of twins and their siblings; squares denote men; circles denote women. Please note that this figure illustrates the idealized pedigree: the maximum number of parents observed in one sample is two, the maximum number of twins is two, the maximum number of siblings is eight and the maximum number of offspring of twins or siblings is four.

Whereas in the classical twin design, only two crucial relationships are distinguished (i.e., MZ and DZ twin pairs), the extended twin family design, as used in this thesis, holds fifteen familially different relationships that can be increased to 22 if relationships involving DZ

twins are distinguished from relationships involving siblings. Moreover, a total number of 102 relationships can be distinguished if the gender of the relatives is taken into account (See Appendix II for an overview of all possible relationships within the extended twin family design). When assuming the absence of sex differences and DZ-sibling differences, this large number of familial relationships can be reduced to six unique relations that provide information to the estimates of genetic and environmental factors. In Table 2.1, coefficients of the additive genetic covariance, genetic dominance covariance, and shared and non-shared environmental covariance are provided for all six distinctive pairs of relatives within the present study.

Table 2.1 Coefficients for the additive genetic and genetic dominance components and shared and non-shared environmental components of the covariance between relatives for an equilibrium population under random mating (extended from Lynch and Walsh, 1998, Table 7.3, page 148).

Relationship	$\hat{\sigma}_A^2$	$\hat{\sigma}_D^2$	$\hat{\sigma}_C^2$	$\hat{\sigma}_E^2$
MZ	1	1	1	0
DZ/sibs	½	¼	1	0
PO / AVMZ	½	0	0	0
AVDZ / COMZ	¼	0	0	0
CODZ	⅛	0	0	0
IN-LAWS	0	0	0	0

Notes: Notation follows Lynch and Walsh (1998): $\hat{\sigma}_A^2$ = standardized additive genetic variance; $\hat{\sigma}_D^2$ = standardized genetic dominance variance; $\hat{\sigma}_C^2$ = standardized shared environmental variance, $\hat{\sigma}_E^2$ = standardized non-shared environmental variance. Assortative mating is assumed to be absent. Correlations are assumed equal across twins and regular siblings and across sex; MZ=twin-twin MZ; DZ/ sibs=twin-twin DZ/sibling; PO=parent-offspring; AVMZ=cousins avuncular through MZ; AVDZ=cousins avuncular through DZ/sibling; COMZ=nieces/nephews through MZ; CODZ=niece/nephews through DZ/ sibling; IN-LAWS represent sister/brother in law through MZ, sister/brother in law through DZ/sibling, spouse-spouse through MZ, spouse-spouse through DZ/sibling, aunt/uncle-cousin in law through MZ, aunt/uncle-cousin in law through DZ/sibling, and parent-offspring in law.

Including parental information in the twin family design allows the assessment of additive genetic influences, genetic dominance deviation, effects of assortative mating, shared- and non-shared environmental influences, parental influences (i.e., cultural transmission), and $r_{(GE)}$ that is induced by the co-occurrence of additive genetic influences and cultural transmission. Additionally, including information on the spouses of the twins allows the resolution of the mechanism underlying assortative mating (e.g., phenotypic assortment and social homogamy) and the test whether the extent and type of assortative mating is equal over generations. Including information on the children of the twins allows one to test whether effects of cultural transmission remain equal over generations. Siblings of the twins, as well as the spouses and children of the siblings, provide information on whether twins and siblings differ with respect to (individual differences in) general cognitive ability, and these additional data increase statistical power to detect shared environmental and genetic influences (Posthuma & Boomsma, 2000).

COMPLEX GENE-ENVIRONMENT MECHANISMS

Gene environment correlation: r(GE)

$r_{(GE)}$ refers to a situation where genes control an individuals' exposure to environmental factors, or a situation in which gene frequencies differ in different environments. In this state, environmental factors that influence an individuals' phenotype are not a random sample of the entire range of possible environments, but are correlated with, or a function of, the genotype of an individual. Usually, three different types of gene-environment correlation are distinguished (Plomin et al., 1977): passive, evocative and active $r_{(GE)}$. Passive $r_{(GE)}$ occurs when parents transmit both their genotypes and for the trait relevant environmental factors. For example, intellectual gifted parents may transmit genetic variants that are related to high cognitive ability and also provide their children with 'intelligence boosting' experiences. Evocative $r_{(GE)}$ occurs when people's behavior towards an individual is a reaction to the genetic predisposition of the individual. For example, different genetic makeup may induce different treatment by teachers in the classroom. Active $r_{(GE)}$ occurs when individuals actively shape or seek out their own environment, based on their genetic predisposition. That is, individuals will select environments that fit their genetic predisposition and construct an environment in which they can thrive.

When any of these forms of $r_{(GE)}$ occur, the effects of genes can no longer be considered independent of the effects caused by environmental factors. Ignoring the $r_{(GE)}$ in statistical genetic models may lead to biased estimates of the relative importance of both genetic and environmental factors (Purcell, 2002; Eaves et al., 1977). If $r_{(GE)}$ concerns the correlation between genes and *non*-shared environmental factors, ignoring it's presence will result in overestimation of the effects of the genetic factors, while ignoring $r_{(GE)}$, if it concerns the correlation between genes and *shared* environmental factors, will result in overestimation of the effects of the shared environmental factors (Purcell, 2002). Given the high estimates of genetic factors and absence of shared environmental factors for general cognitive ability, potential $r_{(GE)}$ is expected to concern the correlation between genes and non-shared environmental factors.

Gene environment interaction (GEI)

GEI refers to a situation where genes control an individual's sensitivity to environmental factors, or a situation in which the environment controls the (level of) expression of genes. For example, individual differences in genetic makeup related to general cognitive ability may become more pronounced and visible when educational quality is low, compared to when educational quality is high.

In the presence of GEI, the relative contribution of genetic and environmental factors to individual differences in a particular phenotype fluctuates across different environmental and genetic conditions. Consequently, point estimates of genetic and environmental effects may not accurately reflect the total range of heritabilities across all levels of an environmental factor.

When GEI concerns interaction between genes and *non*-shared environmental factors, ignoring the influences of GEI in statistical models will result in overestimation of the effects of the non-shared environmental factors. If GEI interaction concerns the

interaction between genes and *shared* environmental influences, ignoring its presence will result in overestimation of the effect of genetic factors (Jinks & Fulker, 1970; Eaves et al., 1977; Purcell, 2002). As estimates of genetic factors for general cognitive ability are generally high, interaction between genes and shared environmental factors rather than interaction between genes and non-shared environmental factors is expected. Explicit modeling of GEI effects is thus important if one wishes to distinguish and understand the factors that cause individual differences in general cognitive ability.

Assortative mating

Behavior geneticists speak of 'assortative mating' when mates show higher or lower resemblance than expected by chance. Positive assortative mating may increase while negative assortative mating may decrease the genetic and environmental correlations between mates. This, in turn, will respectively increase or decrease the genetic resemblance between e.g. DZ twin pairs, relative to MZ twin pairs. Three main processes of assortative mating can be distinguished: social homogamy, phenotypic assortment and social (or marital) interaction; these processes can occur simultaneously. Social homogamy refers to the situation in which individuals who grow up in a similar social background are more likely to mate with individuals from that same background. That is, under social homogamy, assortment takes place within groups that are differentiated environmentally (Falconer & Mackay, 1989). Phenotypic assortment refers to the situation in which mates select each other on the basis of similarities (positive phenotypic assortment) or dissimilarities (negative phenotypic assortment) in observable characteristics, such as general cognitive ability. That is, given positive phenotypic assortment, individuals with high levels of cognitive ability tend to mate individuals with high levels of cognitive ability, while individuals with lower levels of cognitive ability tend to mate individuals with lower levels of cognitive ability. Social interaction refers to the situation in which mates resemble each other more and more as a consequence of living together and influencing each others' behavior, such that the longer mates interact, the greater their resemblance. Since the data in the present thesis are not sufficient to model social interaction, only social homogamy and phenotypic assortment are considered in this thesis.

Social homogamy and phenotypic assortment can be studied by comparing spousal resemblance, as expressed with a phenotypic correlation, of different spouse combinations (e.g., *direct spouses*: a twin and his/her spouse and parental spouse pairs; *cross-sibling-spouse pairs*: a twin and the spouse of his/her co-twin; *spouse-spouse pairs*: the spouse of a twin and the spouse of the twins' co-twin) within a sample. Assortative mating due to social homogamy reflects a shared social environment and therefore the effect of sharing an environment on the mating process is similar for all relatives. No difference is expected between different spouse pairings. In the situation of pure social homogamy, the correlation between direct spouses is therefore expected to be similar to the correlation between cross-sibling-spouse pairs and spouse-spouse pairs.

In the situation of phenotypic assortment, however, mate selection is purely based on the observed phenotype, which may be influenced by both genetic and environmental factors. Under positive phenotypic assortment on a heritable trait, observed phenotypic correlations between spouses are expected to decline with the genetic distance of the

relationship between family members; correlations of spouse-spouse pairs and cross-sibling-spouse pairs are expected to be lower than the correlation of direct spouse pairs. Since MZ twins have more genes in common compared to DZ twins, cross-sibling-spouse correlations and spouse-spouse correlations are expected to be different for MZ and DZ twin pairs, depending on the extent to which the phenotype under study reflects the genotype. Consequently, in the situation of positive phenotypic assortment on a heritable trait, such as cognitive ability, cross-sibling-spouse and spouse-spouse correlations are expected to be higher for MZ twins.

Possible consequences for the estimates of genetic and environmental factors in case assortative mating is not considered, depend on the process underlying the mate selection, i.e., social homogamy or phenotypic assortment. In the situation of pure social homogamy, spousal correlations resulting from pure social homogamy are purely environmental. Consequently, no genetic correlation between mates exists, and the contribution of genetic factors is not affected (Falconer & Mackay, 1989).

If positive phenotypic assortment is the underlying process for mate selection, additive genetic factors and dominance genetic factors will be correlated in spouse pairs (Fisher, 1918; Rice et al., 1978; Heath & Eaves, 1985). If increased genetic resemblance between relatives is not considered in a twin-family model, estimates of genetic and environmental parameters will be biased.

Cultural transmission

Parents may transmit not only their genetic material, but also their environment to their children. Cultural transmission refers to the transmission of environmental factors that are related to a trait (e.g., general cognitive ability) from the parental phenotype to the offspring's environment. Since children who are raised in the same home grow up within a common environment as created by the parents, cultural transmission is by definition part of the shared environment in the offspring generation.

When cultural transmission exists in the presence of genetic transmission, environmental influences become correlated with genetic influences ($r_{(GE)}$). Consequently, when cultural transmission and the resulting $r_{(GE)}$ are not modeled, parent-offspring correlations, but also twin/sibling correlations, will exceed correlations that are expected under genetic transmission alone, leading to inflated estimates of shared environmental factors.

SAMPLE CHARACTERISTICS AND DATA COLLECTION

This thesis reports on the results from a large ongoing project on the genetics of cognition (Posthuma et al., 2001a). The study was initiated in 1997 with the collection of anatomical, electrophysiological and behavioral indices of cognitive ability. Data on behavioral indices of cognitive ability from 788 twins and their non-twin siblings were collected between 1997 and 2001 (first wave of data collection), see Posthuma (2002) for an extensive description of sample characteristics and data collection.

To be able to model complex processes that may underlie individual differences in cognitive ability, the existing sample was extended with partners and either the parents or the children of the twins and siblings, as well as twins and siblings that were not measured in the first wave of data collection. All relatives were subjected to an extensive test protocol to

measure general cognitive ability between 2007 and 2009 (second wave of data collection). In addition, questionnaire data on environmental indices were collected between 2007 and 2009 in all participants (i.e., twins, siblings, their spouses and either their parents or their children) using the Life Experiences List (LEL, developed within this project). Saliva samples were also collected as part of a companion PhD project (T. Sampaio Rizzi).

Within the first wave of data collection, data on cognitive ability were collected at the laboratory of the VU University Amsterdam. Within the second wave of data collection, data were collected either at the laboratory of the VU University Amsterdam or at the participants' home, depending on preference of the participants. The majority of the participants preferred testing at home (60%). Both waves of data collection were performed with understanding and written consent of each participant. The study was approved by the Central Committee on Research Involving Human Subjects in the Netherlands.

Twins and siblings that were part of the first wave of data collection were registered at the Netherlands Twin Register (NTR; Boomsma et al., 2006). To recruit participants for the second wave of data collection, non-registered family members of the twins and their non-twin siblings were contacted after permission from their registered family members. All participants were registered in the NTR at the time of measurement.

In total, data were available for 1419 participants. Data on cognitive ability were available for 1350 participants (317 families, 45.9% men), and questionnaire data were available for 1072 participants (260 families, 44.3% men). 69 participants did supply questionnaire data but data on cognitive ability were absent. 337 participants did have data on cognitive ability, but questionnaire data were missing. On average 4.46 (SD = 2.57) subjects per family participated (range 1-22, median = 4). In Table 2.2 the composition of the sample is summarized, together with frequencies of relatives with data on cognitive ability and on environmental indices. The relatively large number of 337 participants that did not have questionnaire data is partly due to the fact that 17.4% of the participants from the first wave of data collection were no longer registered in the NTR (137 participants) at the time of the second wave of data collection. The overall response rate for the LEL was 76%.

Table 2.2 Sample sizes (individuals) by type of relative for cognitive ability and environmental indices

	Cognitive ability	Environmental indices (LEL)
Twins	603 (including 3 triplets)	388 (including 1 triplet)
Siblings of twins	263	172
Parents of twins/sibs	152	167
Spouses of twins	139	138
Spouses of sibs	18	18
Children of twins	140	149
Children of sibs	34	39
Spouse of child of twin	1	1
Total	1350	1072

Notes: relatives are expressed in relation to the twins; LEL = Life Experiences List.

Figure 2.2 Age distribution of the total sample
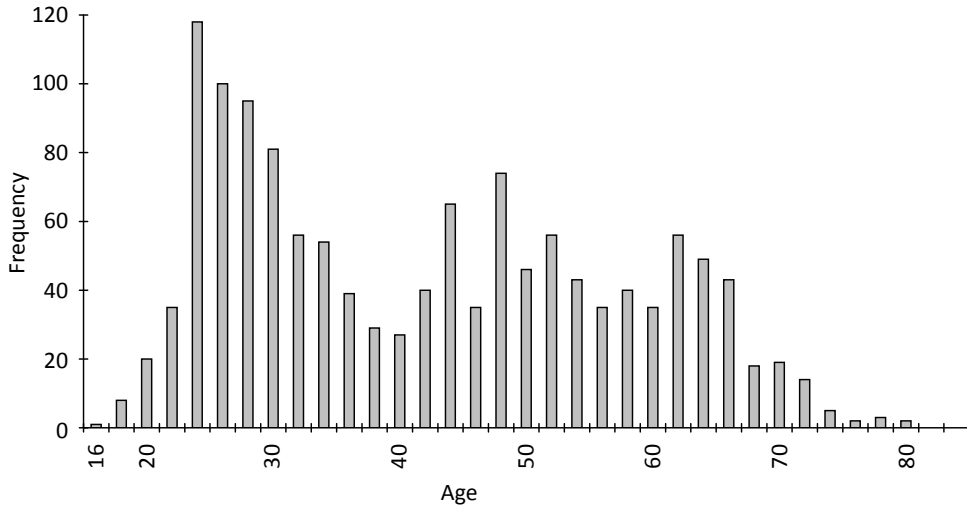
Notes: the age displayed in the above figure is the age of the participants at the time of the cognitive assessment

The age distribution of the sample is depicted in Figure 2.2. Average age of the participants was 41.11 years (SD = 15.06; range: 15.71 – 79.87) at the time they completed the cognitive assessment.

Zygosity

Zygosity of same-sex twins was based on DNA polymorphisms (114 pairs, 83%) or, if information on DNA markers was not available, on questions about physical similarity and confusion of the twins by family members and strangers. Agreement between zygosity diagnoses from survey and DNA was 97% (Willemsen et al., 2005). All five zygosity groups were well represented: monozygotic males (MZM: 20.6%), monozygotic females (MZF: 25.4%), dizygotic males (DZM: 12.4%), dizygotic females (DZF: 22.4%) and dizygotic opposite sex (DOS: 19.2%).

Cognitive ability

The cognitive test protocol of the second wave of data collection lasted two and a half up to three hours, including break and formal precedures. The order of the tests is shown in Table 2.3. The Verbal Learning & Memory Task exists of two parts with an interval of twenty minutes between the end of the first part and the start of the second part. To avoid any verbal interference, no verbal or linguistic tests were administered within this interval. During the entire assessment, verbal conversation was restricted to a minimum.

Table 2.3 Cognitive test protocol as assessed within the second wave of data collection

Phenotype	Test
Psychometric IQ	WAIS-IIIR (Wechsler, 1997)
Verbal learning and memory	Verbal Learning & Memory Task (part 1) (Mulder et al., 1996)
Time perception	Time Perception Application (Barkley, 1998)
Visuo-spatial memory	Corsi Block Tapping Task (Corsi, 1972)
Executive functioning	Trail Making Test (Reitan, 1955)
Verbal learning and memory	Verbal Learning & Memory Task (part 2)
Inspection Time	Inspection Time Task (Luciano et al., 2001)
Linguistic ability	Non Words Test (reading/repeating)
Linguistic ability	Word Stress Task (Schiller, 2006)
Behavior during test and characteristics of test setting and participant.	Task Observation Form

During the assessment, a Task Observation Form was filled out by the test administrator. Characteristics of the test setting (i.e., test location, time of the day and particularities that may influence the assessment) and the participants (i.e., physical and mental conditions that may influence the assessment) were recorded. Participants were paid €25,- if they completed the cognitive test protocol. In case participants were tested at the laboratory of the VU University Amsterdam, traveling-expenses were refunded.

DESCRIPTION OF MEASURES OF COGNITIVE ABILITY AND ENVIRONMENTAL INDICES
In the last part of this chapter, the measures are described on which the studies reported in Chapters 3 to 8 are based. The cognitive measures that were collected during this PhD project but that were not reported on in this thesis, are described in appendix III. Statistical descriptives and phenotypic correlations between all measures of cognitive ability that were collected within this project are provided in appendix IV and appendix V, respectively.

General cognitive ability
General cognitive ability (or psychometric IQ) was assessed with the Dutch version of the WAIS-IIIR. Participants whose IQ was assessed in the first wave of data collection (785 participants: twins and siblings) completed eleven subtests of the WAIS-IIIR: Block design, Letter-number sequencing, Information, Matrix reasoning, Similarities, Picture completion, Arithmetic, Vocabulary, Digit symbol-coding, Digit-symbol pairing and Digit symbol-free recall. Participants whose IQ was assessed in the second wave of data collection (617 participants: twins, siblings, parents, offspring of twins and siblings and spouses of twins and siblings) completed seven subtests of the WAIS-IIIR: Block design, Letter-number sequencing, Information, Matrix reasoning, Arithmetic, Vocabulary and Digit symbol-coding. Correlation between full scale IQ assessed with eleven subtests and full scale IQ assessed with seven subtests was substantial (Pearson's r = .97, N = 785, p<.001). To measure test-retest reliability, 59 participants participated in both the first and the second wave of data collection. Test-retest reliability for full scale IQ was substantial (Pearson's r = .85, N = 59, p<.001), full scale IQ was based on seven subtests at both time points for computation of the test-retest reliability. For those 59 subjects whose IQ was assessed twice, data from the first wave data collection were used in the analyses. In total, sex and age corrected IQ scores were available for 1343 participants.

Environmental Indices

Environmental indices were measured with the Life Experiences List (LEL). The LEL was developed to measure environmental indices and individual traits and qualities that were expected to be related to cognitive ability and/or individual differences in cognitive ability. The LEL consisted of a combination of acknowledged questionnaires as well as questions that were specifically developed for this project. An overview of the subjects covered by the LEL is shown in Table 2.4. The combination of cognitive and environmental data allows us to investigate the complex interplay between genes and environment in the context of general cognitive ability.

Table 2.4 Indices of the Life Experiences List (LEL)

Demographics
Response date, first name, gender, birth date, and zip code

Family composition
Childhood living situation, partner selection, and current family size

Sport
Frequency of participation in specific sports: current and past (between ages 6-18 years).
Way of travelling to work/school (e.g., walk, bike, scooter, car, train or bus), and average daily travel time

Music and other leisure time activity
Frequency of participation in specific music and other leisure time activities: current and past (between ages 6-18 years)

Leisure time activity
A list of leisure time activities used to quantify time spend on certain activities: current and past (between ages 6-18 years)

Parental rearing style and general childhood
Subjective assessment of parental rearing style
Subjective assessment of parental attitude towards educational attainment
Questions on reading behavior during childhood
Information on breastfeeding
Information on body composition compared to peers at elementary school and high school
Information on teasing by peers at elementary school and high school

Life events
Information on influential Life events (past five years and over lifetime).

Family functioning
General Functioning subscale of the Family Assessment Device (Epstein et al., 1983)
Conflict subscale of the Family Environment Scale (Moos & Moos, 1976)

Own rearing style and leisure activities with offspring
Subjective assessment of own rearing style
Subjective assessment of own attitude towards educational attainment offspring
Questions on reading behavior

Education and profession
Received education and current work status

Education and profession of parents, partner and close friend
Received education and current work status

Social support and social behavior

Social Support Questionnaire-6 (Sarason et al., 1987; Sarason et al., 1990). Two aspects of perceived social support: (i) number of people available in six specified problem situations (ii) degree of satisfaction with the perceived support

Decomposed Game Measure (Van Lange et al., 1997). Someone's general tendencies toward others.

Achievement motivation

Achievement Motivation Test (short version) (Hermans, 1970). This questionnaire assesses general and school related achievement motivation

Experience seeking

Experience Seeking scale of the Sensation Seeking List (Zuckerman, 1996). Degree of unconformable life style and desire to expand one's experience through the mind and senses.

Autistic traits

Autism Quotient (short version) (Baron-Cohen et al., 2001). This questionnaire quantifies autistic traits in the normal population

Self report

Young Adult Self Report (short version) (Achenbach, 1990; Achenbach, 1997; Achenbach, 1991). Only items related to the attention subscale were included
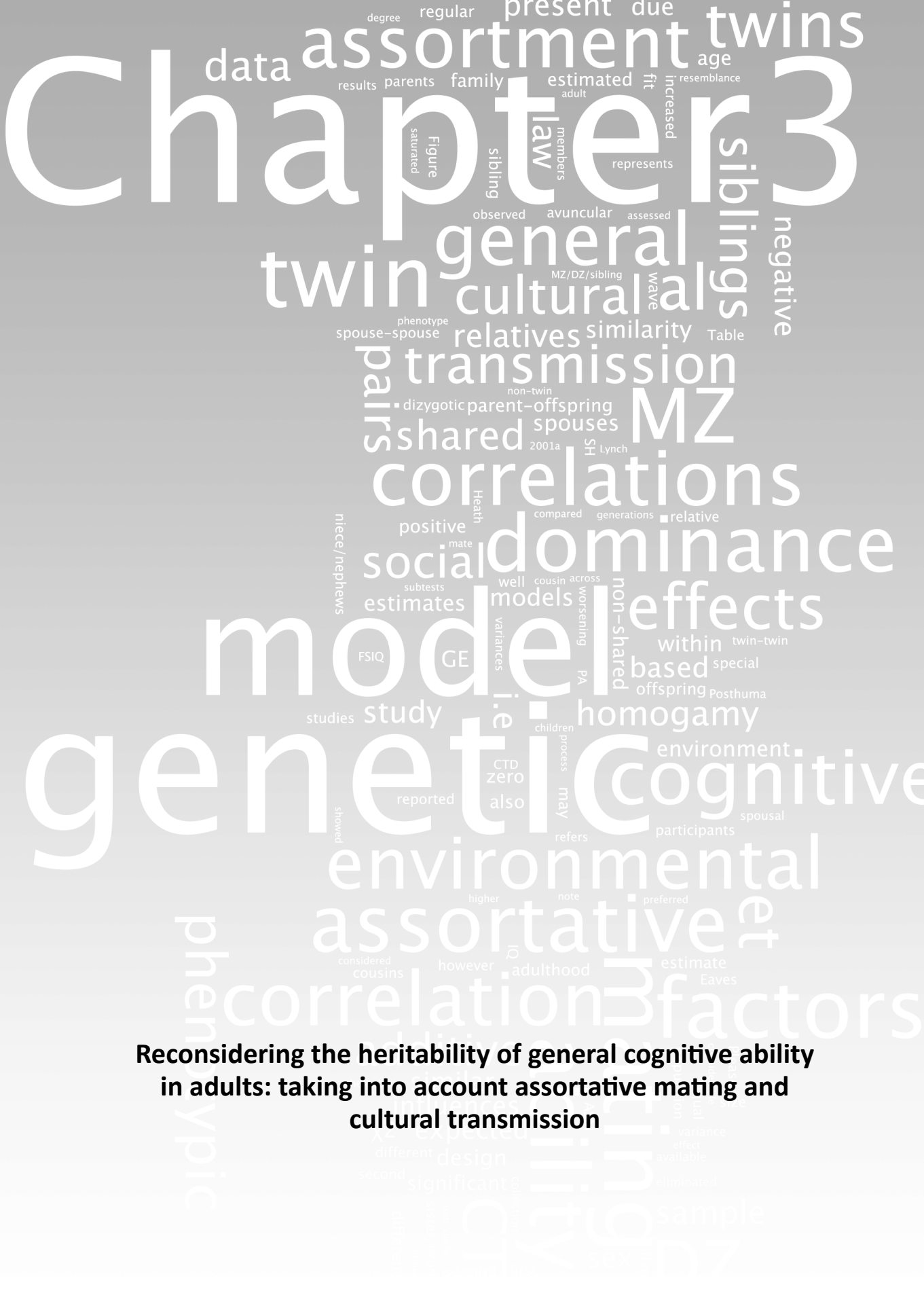
Chapter 3

Reconsidering the heritability of general cognitive ability in adults: taking into account assortative mating and cultural transmission

ABSTRACT

Heritability estimates of general cognitive ability in adulthood generally range from 75% to 85%, with all heritability due to additive genetic influences, while genetic dominance and shared environmental factors are absent or too small to be detected. These estimates are derived from studies based on the classical twin design (CTD) and are based on the assumption of random mating among others. Yet, considerable positive assortative mating has been reported for general cognitive ability.

Unmodelled assortative mating increases the DZ twin correlation and thereby inflates the estimates of shared environmental factors and deflates estimates of genetic dominance in a CTD. The reported absence of both these effects for general cognitive ability in adulthood may be due to the presence of assortative mating that is not accounted for.

In the present study, an extended twin family design was used to allow modeling of effects of assortative mating, additive genetic factors, genetic dominance and shared and non-shared environmental factors. Psychometric IQ data were available for adult monozygotic and dizygotic twins, their siblings, the partners of the twins and siblings, and either the parents or the adult offspring of the twins and siblings (N=1314).

Results showed that variation of general cognitive ability in adulthood is not only due to additive genetic factors (44%) and non-shared environmental factors (18%), but also to genetic dominance (27%) and positive assortative mating (11%). Considering non-additive effects in future gene finding studies might enhance their success for general cognitive ability.

INTRODUCTION

Considerable evidence from classical twin studies shows that individual differences in general cognitive ability in adults are largely explained by genetic factors. Heritability estimates range from 75% to 85% (Plomin, 1999; Bouchard, Jr. & McGue, 1981; Ando et al., 2001; Luciano et al., 2001; Posthuma et al., 2001a). These estimates are based on the classical twin design (CTD) in which the phenotypic resemblances of monozygotic (MZ) and dizygotic (DZ) twins are compared (Plomin et al., 2001a). MZ twin correlations of ~.80 and DZ twin correlations of ~.40 are typically reported and suggest absence of both shared environmental influences and genetic dominance.

At the same time there is evidence for strong assortative mating on general cognitive ability, i.e., non-random mating of spouse pairs. Spousal correlations for general cognitive ability range from .20 to .50 (Jencks et al., 1972; Loehlin, 1978; Mascie-Taylor, 1989; Reynolds et al., 2000; van Leeuwen et al., 2008). Assortative mating for a heritable trait leads to a non-random distribution of genetic variants important for that trait as spouses will be more similar genetically than expected by chance. Unmodelled assortative mating will consequently increase the correlation of DZ twin pairs, while the MZ twin correlation remains unaffected. As shared environmental factors are expected if the DZ twin correlation is more than half the MZ twin correlation whereas genetic dominance is expected if DZ twin correlation is less than half the MZ twin correlation, increased DZ twin correlations will deflate estimates of genetic dominance due to unmodelled assortative mating in a CTD (Keller et al., 2009).

A second mechanism that also tends to inflate DZ twin correlations is cultural transmission (Fulker, 1982). Since cultural transmission is part of the offspring's shared environment, unmodelled cultural transmission leads to increased DZ twin correlations relative to the MZ twin correlations. Consequently, cultural transmission inflates estimates of shared environmental effects, which may go undetected in the CTD, in the presence of genetic dominance.

We set out to investigate the influences of assortative mating, cultural transmission, additive genetic factors, genetic dominance, and shared- and non-shared environmental influences on general cognitive ability in an adult population using an extended twin-family design. Two mechanisms underlying assortative mating were considered: social homogamy and phenotypic assortment. Social homogamy refers to the situation in which individuals are likely to mate partners from the same social background. Under social homogamy, assortment takes place within groups that are differentiated environmentally (Falconer & Mackay, 1989). Positive phenotypic assortment refers to the situation in which mates select each other on the basis of similar phenotypes, such as similar level of general cognitive ability. (A third form of assortative mating is social interaction, in which mates resemble each other more as a function of the time they have been together. Since the data in the present study are not sufficient to model social interaction, social interaction was not considered here.)

Different mechanisms of mate selection result in different expectations for familial resemblance (Fisher, 1918; Rice et al., 1978; Heath & Eaves, 1985; Falconer & Mackay, 1989). Basically, under social homogamy, resemblance between relatives is a function of shared environment (social resemblance), whereas under phenotypic assortment, trait

resemblance is a function of genetic resemblance between relatives, such that phenotypic correlations between individuals decrease with increasing genetic distance.

To determine whether the effects of assortative mating, cultural transmission, genetic dominance, additive genetic factors, and shared and non-shared environmental factors are important for general cognitive ability in adulthood, we collected psychometric IQ data in 1314 individuals from 317 families. Families consisted of twins and their non-twin siblings, the spouses of the twins and siblings, and either the parents of the twins and siblings, or the children of the twins and siblings.

METHOD

Sample

This study was part of a large ongoing project on the genetics of cognition. In a first wave of data collection (Posthuma et al., 2001a; Posthuma et al., 2001b), data on psychometric IQ from twins and their non-twin siblings were collected between 1997 and 2001. To be able to model complex processes such as assortative mating and cultural transmission, the data set has been extended with psychometric IQ data from relatives from multiple generations (parents, children and spouses of the twins and their non-twin siblings) between 2007 and 2009 in a second wave of data collection. All participants were registered in the Netherlands Twin Register (NTR) (Boomsma et al., 2006). In the present study, data were available for 1314 participants (317 families, 45.7% men). On average 4.1 subjects per family participated.

Zygosity of same-sex twins was based on DNA polymorphisms (114 pairs, 83%) or, if information on DNA markers was not available, on questions about physical similarity and confusion of the twins by family members and strangers. Agreement between zygosity diagnoses from survey and DNA was 97% (Willemsen et al., 2005). All five zygosity groups were well represented: monozygotic males (MZM: 20.6%), monozygotic females (MZF: 25.4%), dizygotic males (DZM: 12.4%), dizygotic females (DZF: 22.4%) and dizygotic opposite sex (DOS: 19.2%). Average age of the participants was 41.11 years (SD = 15.06; range: 15.71 – 79.87). Table 3.1 shows frequencies of all relatives that are included in the sample, grouped by zygosity of the twins.

Table 3.1 Number of subjects indicated by zygosity of the twin in the family.

	MZ	DZ/DOS
MZ twins	276	-
DZ/DOS twins	-	323
Siblings of twins	102	140
Parents of twins/siblings	67	84
Spouses of twins	78	58
Children of twins	73	67
Spouses of siblings	10	6
Children of siblings	17	13
Total (1314)	623	691

Notes: MZ=monozygotic; DZ=dizygotic same sex; DOS=dizygotic opposite sex.

Tasks and instruments

General cognitive ability, operationalized as scores on a psychometric intelligence test (Full Scale IQ, FSIQ), was assessed with the Dutch version of the WAIS-IIIR (Wechsler, 1997). Participants assessed in the first wave of data collection (770 participants: twins and siblings) completed eleven subtests of the WAIS-IIIR: Block design, Letter-number sequencing, Information, Matrix reasoning, Similarities, Picture completion, Arithmetic, Vocabulary, Digit symbol-coding, Digit-symbol pairing and Digit symbol-free recall. Participants assessed in the second wave of data collection (544 participants: twins, siblings, parents, offspring of twins and siblings and spouses of twins and siblings) completed seven subtests of the WAIS-IIIR: Block design, Letter-number sequencing, Information, Matrix reasoning, Arithmetic, Vocabulary and Digit symbol-coding. Correlation between FSIQ assessed with eleven subtests, and FSIQ assessed with seven subtests, was very high (Pearson's r = .97, N = 770, p<.001). 59 participants participated in both the first and the second wave of data collection, test-retest reliability over 7-10 years was substantial (Pearson's r = .85, N = 59, p<.001, based on 7 subtests). The present sample was representative of the Dutch population with respect to educational level (Posthuma et al., 2001a). As effects of age and sex on FSIQ scores were still observed after standardization, and the present sample size exceeds the WAIS-IIIR standardization sample, the residual effects of sex and age were partialled out. In total, sex and age corrected FSIQ scores were available for 1314 participants (see Table 3.1).

To eliminate possible discrepancies between FSIQ data collected in the first and in the second wave of data collection, Z-transformed scores were used in the analyses. FSIQ-scores were Z-transformed in both groups separately (wave 1 and wave 2) such that the scores had equal means and variances in both waves. For convenience, these z-scores were transformed such that the overall mean was 100, and the SD was 15, as is standard in IQ research.

Power

Power simulations have shown that large sample sizes are required to resolve contributions of phenotypic assortment and social homogamy to mate selection (Heath & Eaves, 1985). According to Heath and Eaves (1985), data on DZ and sibling pairs and their spouses are more informative to resolve the nature of the process of mate selection than data on MZ pairs and their spouses. The high phenotypic correlation between MZ twin pairs complicates distinguishing phenotypic assortment and social homogamy. Both MZ and DZ twin pairs are however required to disentangle genetic and environmental influences on individual differences in general cognitive ability. A mixed homogamy model, in which both social homogamy and positive phenotypic assortment act simultaneously, requires a larger sample size than the one currently available (Heath & Eaves, 1985). The size and composition of the present sample should however allow distinction between pure social homogamy and pure positive phenotypic assortment (Heath & Eaves, 1985), but is too small to examine possible sex and age effects on the genetic and environmental parameters.

Analyses

This study consists of three parts. First, a saturated model was fitted to the data to estimate model free correlations between pairs of different genetic and social relatedness and to test whether correlations between DZ twins differed from correlations between regular siblings. In the saturated model there are no assumptions on mating behavior; we however assumed sex and age effects on the variances to be absent. A total number of 102 different correlations between relatives can be estimated when all correlations are subdivided by sex of the twin pairs. Even more correlations can be estimated when birth cohort is taken into account (i.e., correlations subdivided by birth cohort of the relatives). Due to a relatively small sample size, the precision of the correlations is low, especially for more distant relatives (Keller et al., 2010). It was therefore decided to disregard possible sex and age effects on the variances and covariances. Previous analyses in a partly overlapping sample showed no significant sex effects on variances and covariances of sub dimensions of general cognitive ability, while effects of age were significant with direction depending on the dimension (Posthuma et al., 2001b). To test whether the DZ twin correlation differed from the regular sibling correlation, significance of the difference of these correlations was tested by constraining correlations through DZ twins to be equal to correlations through regular siblings (e.g., DZ twin correlation = sibling correlation, nieces/nephews through DZ twins = nieces/nephews through siblings, etcetera). A significant worsening of the model fit is indicative of a special twin environment. A model without special twin environment and without sex and age effects on the variances and covariances, would leave us with 15 different relations: twin-twin MZ, twin-twin DZ/sibling, parent-offspring, cousins avuncular through MZ, cousins avuncular through DZ/sibling, niece/nephews through MZ, niece/nephews through DZ/sibling, spouse-pairs, sister/brother in law through MZ, sister/brother in law through DZ/sibling, spouse-spouse through MZ, spouse-spouse through DZ/ sibling, parent-offspring in law, aunt/uncle cousin in law through MZ, and aunt/uncle cousin in law through DZ/ sibling. Please note that the grandparent-grandchild correlation is omitted since none of the families in our sample comprised three generations.

Second, within a genetic model, two competing assortment models (i.e., *social homogamy* versus *phenotypic assortment*) were fitted to the data, to investigate whether social homogamy or positive phenotypic assortment is the most likely underlying process of assortative mating for general cognitive ability. Both models were compared to the saturated model. Under the social homogamy model, assortative mating is due to a similar environment that renders individuals with similar social backgrounds more alike. Mate selection is purely based on environmental similarities. Consequently, correlations are expected to be similar for any combination of sibling-spouse pairs[1] ($r_{spouses} = r_{co\text{-}twin\text{-}spouse} = r_{spouse1\text{-}spouse2}$). Under the positive phenotypic assortment model, mate selection is purely based on the phenotype of the spouses (i.e., similar general cognitive ability). Consequently, correlations between sibling-spouse pairs are expected to decline with the distance of the genetic relationship ($r_{spouse} > r_{co\text{-}twin\text{-}spouse} > r_{spouse1\text{-}spouse2}$), and cross-sibling-spouse correlations are expected to be higher for MZ twins compared to DZ twins, depending on the extent

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1   All relations are expressed in relation to the twin. Twin-spouse relations do also incorporate spousal relations between the parents of the twins and between the sibling with its spouse.

to which the phenotype under study reflects the genotype. Preference of the assortment model was based on maximum likelihood estimation. The preferred assortment process was modeled in subsequent analyses of the relative contribution of genetic and environmental factors. Both assortment models are depicted in Figure 3.1.

Third, individual differences in general cognitive ability were modeled as a function of genetic and environmental effects, taking into account the preferred underlying process of assortative mating (ASM; i.e., phenotypic assortment or social homogamy) as well as cultural transmission (CT), additive genetic factors (A), genetic dominance (D), special twin environmental factors (T), shared (C) and non-shared (E) environmental factors (Eaves et al., 1999). 'A' represents additive effects of alleles summed over all loci. 'D' represents the extent to which the effects of alleles at a locus are not additive, but interact with each other (genetic dominance). 'ASM' represents genetic influences due to assortative mating. 'C' represents common environmental influences that render offspring of the same family more alike. CT represents shared environmental factors due to cultural transmission. Presence of both cultural transmission and genetic transmission will result in a correlation between A and CT (i.e., $r_{(GE)}$). 'E' represents all environmental influences that result in differences between members of a family. E also includes measurement error.

Because of the limited size of the sample, we needed to assume that assortative mating, genetic inheritance, shared environmental influences, and cultural transmission remain constant from generation to generation. This implies that phenotypic variances and correlations between relatives are equal over generations as a state of equilibrium has been reached (Falconer & Mackay, 1989).

Analyses were carried out using the raw data option in Mx (Neale, 1994; Maes et al., 2009).

Figure 3.1 Assortment models for a DZ twin pair with parents, spouses and offspring: *social homogamy* (upper panel) and *positive phenotypic assortment* (lower panel).
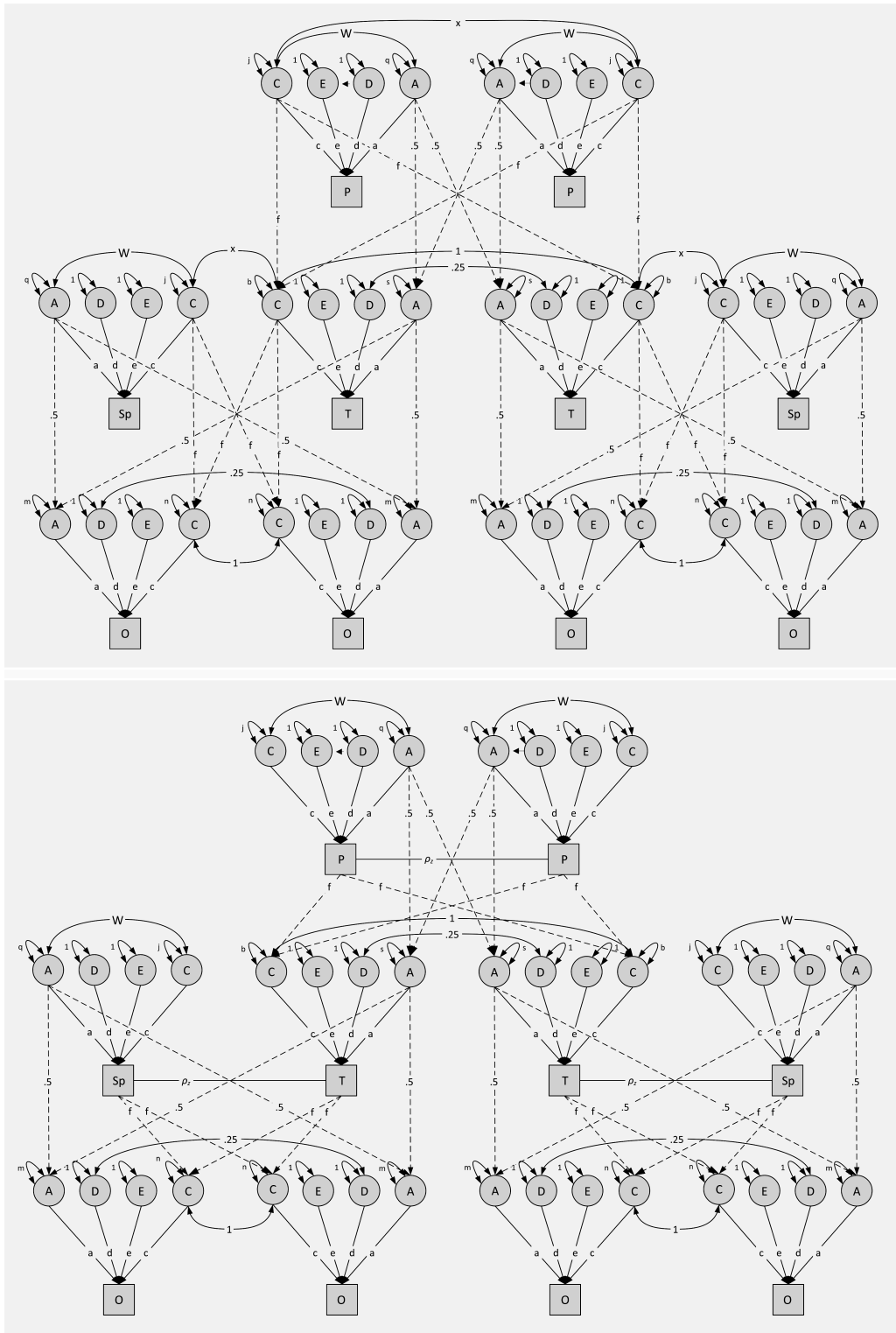
Notes: A = additive genetic effects, D = genetic dominance, E = non-shared environmental effects, C = shared environmental effects, f = cultural transmission path, w = gene-environment correlation, q = variance additive genetic effects, j = variance shared environmental effects, σ_z = assortative mating co-path, P = parent, T = DZ twin, Sp = spouse, O = offspring. Please note that additional siblings (and their spouses and offspring) are not included in the figure for reasons of convenience.

RESULTS

Within the saturated model, correlations via DZ twin pairs and regular sibling pairs could be constrained to be equal without a significant worsening of the model fit (model 2: $\chi^2(6)=6.08$, *ns*), implying that there is no special twin environment that renders members of a twin pair more similar for general cognitive ability than regular siblings. This is in line with Posthuma et al. (2001a). As the special twin environment was insignificant and elimination of special twin environmental effects does not directly influence estimates of other variance components, it was decided to specify a genetic model without special twin environment in order to increase the stability of the solutions.

Figure 3.2 shows observed correlations (and 95% confidence intervals) and expected genetic correlations between relatives grouped by degree of additive genetic similarity (A) and degree of similar contribution of genetic dominance (D). Please note that the degree of additive genetic similarity increases within a population undergoing assortative mating for all pairs of relatives except MZ twin pairs. Similarly, dominance genetic similarity is increased by assortative mating for cousins avuncular through MZ/DZ/sibling, niece/nephews through MZ/DZ/sibling, sister/brother in law through MZ/DZ/sibling, spouse-spouse through MZ/DZ/sibling and aunt/uncle cousin in law through MZ/DZ/sibling within a population undergoing assortative mating, where under random assortment there would be no dominance genetic similarity (Fisher, 1918; Nagylaki, 1978; Lynch & Walsh, 1998). Please see the Supplementary Information for coefficients for A and D.

Figure 3.2 shows a higher correlation (r=.82) for family members that share 100% of their genetic material (i.e., MZ twin pairs), compared to family members that share 50% of A and 25% of D (r=.37) (i.e., DZ twin pairs). The figure illustrates that correlations do not steadily decrease for relatives that share less genetic material. Moreover, correlations vary around the same level for relatives that (under the assumption of absence of assortment) do not share genetic material (i.e., spouse pairs). This pattern of correlations suggests strong influence of genetic factors as well as a considerable contribution of assortative mating.

Figure 3.2 Mean correlation (95% CI) of general cognitive ability between relatives grouped by degree of theoretical additive genetic similarity and dominance genetic similarity.
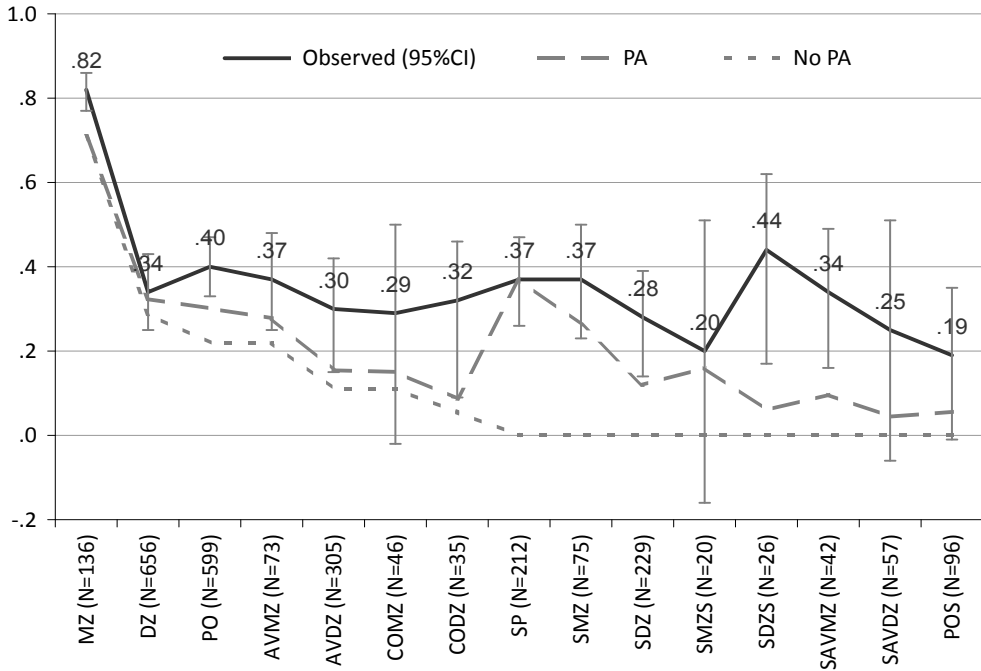
Notes: Observed=observed correlation; PA=expected genetic similarity (A+D) under phenotypic assortment; No PA, expected genetic similarity (A+D) assuming no phenotypic assortment; 95% CI= 95% confidence interval; correlations are constrained to be equal across twins and regular siblings and across sex; MZ=twin-twin MZ; DZ=twin-twin DZ/sibling; PO=parent-offspring; AVMZ=cousins avuncular through MZ; AVDZ=cousins avuncular through DZ/sibling; COMZ=niece/nephews through MZ; CODZ=niece/ nephews through DZ/sibling; SP=spouse-pairs; SMZ=sister/brother in law through MZ; SDZ=sister/ brother in law through DZ/sibling; SMZS=spouse-spouse through MZ; SDZS=spouse-spouse through DZ/ sibling; SAVMZ=aunt/uncle cousin in law through MZ; SAVDZ=aunt/uncle cousin in law through DZ/sibling; POS=parent-offspring in law. Please note that the degree of additive genetic similarity increases within a population undergoing assortative mating for all pairs of relatives except MZ twin pairs. Similar, dominance genetic similarity is induced by phenotypic assortative mating for AVMZ, AVDZ, COMZ, CODZ, SMZ, SDZ, SMZS, SDZS, SAVMZ and SAVDZ within a population undergoing assortative mating, where under random assortment there would be no dominance genetic similarity (Fisher, 1918; Nagylaki, 1978; Lynch & Walsh, 1998). For the expected correlations we assumed $h^2 = .44$, $d^2 = .27$, (as estimated under the reduced model, i.e., Model 6 in Table 3.2) and $\sigma_z = .37$ (i.e. the observed spousal correlation); Please see the Supplementary Information for coefficients for σ_A^2 and σ_D^2.

Table 3.2 Model fitting results for general cognitive ability within an extended twin-family design.

	Model	against	-2LL	df	par	cs	χ^2	Δdf	p
1	saturated model		10462.12	1293	24	5			
2	equal DZ/sib corr.	1	10468.20	1299	18	5	6.08	6	.414
3	full SH-model	2	10532.64	1305	11	4	64.44	6	.000
4	full PA-model	2	10489.78	1305	11	4	21.58	6	.001
5	no C	4	10489.78	1306	10	4	.00	1	1
6	**no C-CT/r$_{(GE)}$***	**5**	**10491.39**	**1308**	**8**	**4**	**1.61**	**2**	**.446**
7	no C/CT/r$_{(GE)}$/-A/D	6	10792.15	1310	6	4	300.76	2	.000
8	no C/CT/r$_{(GE)}$-D	6	10519.42	1309	7	4	28.03	1	.000
9	no C/CT/r$_{(GE)}$-ASM	6	10532.68	1309	7	4	41.28	1	.000
10	**no C/D**	**5**	**10489.78**	**1307**	**9**	**4**	**.00**	**1**	**1**
11	no C/D-CT/r$_{(GE)}$	10	10519.42	1309	7	4	29.64	2	.000
12	no C/D-A/r$_{(GE)}$**	10	10605.78	1309	7	4	116.00	2	.000
13	no C/D-ASM	10	10533.60	1308	8	4	43.82	1	.000

Notes: -2LL=minus 2 log likelihood; par=number of estimated parameters; cs=number of constraints; χ^2=Chi square (difference in -2LL); p=p-value; preferred models are printed in bold font; rDZ=correlation DZ twin pair; rSIB=correlation regular sibling pair; * r$_{(GE)}$ refers to the correlation between A and CT, if CT is eliminated from the model, r$_{(GE)}$ has to be fixed to zero as well. ** if A is dropped from the model, D and r$_{(GE)}$ have to be fixed to zero as well. Models in which the effects of D are estimated but the effects of A are fixed to zero are biologically implausible (Falconer & Mackay, 1989). r$_{(GE)}$ refers to the correlation between A and CT, if A or CT are eliminated from the model, r$_{(GE)}$ has to be fixed to zero as well.

Table 3.2 shows the model fitting results of the social homogamy (SH) model (model 3: $\chi^2(6)=$ 64.44, p<.001), and the phenotypic assortment (PA) model (model 4: $\chi^2(6)=$ 21.58, p<.01) compared to the constrained saturated model (i.e., model 2 in which correlations for all relations trough DZ and sibling pairs were constrained to be equal). Although both models resulted in a significant decrease in model fit, the SH model fitted the data comparatively worse than the PA-model, and the PA model is therefore to be preferred. The worsening of the model fit in both SH and PA models was largely attributable to observed spousal correlations being higher than spousal correlations expected under both assortment models, with discrepancies being largest under the SH model. Moreover, under the SH model, correlations were expected to be similar for any combination of sibling-spouse pairs while in the present data, spousal correlations generally decreased with increasing distance between relatives. In the SH model, the only way to accommodate such a decrease in observed correlations, is by increasing the D component (which was indeed considerable in the SH model solution), which resulted in overall misfit.

Within the PA model, relative contributions of genetic and environmental factors were investigated. Effects of A (58%) and ASM (23%) were substantial, effects of CT (8%) and E (11%) were modest, and effects of C (0%) and D (0%) were estimated at zero in the full model. The model induced correlation between A and CT was estimated at -.36 (See Figure 3.3). The unstandardized parameter estimate of CT is negative, implying that CT induces a negative correlation between the parental phenotype and the offspring's environment.

Eliminating shared environmental factors C (model 5: $\chi^2(1)=$ .00, *ns*) or CT (model 6: $\chi^2(2)=$ 1.61, *ns*) from the model did not result in a significant worsening of the model fit. Subsequently eliminating genetic factors A (model 7: $\chi^2(2)=$ 300.76, p<.001) or D (model 8: $\chi^2(1)=$ 28.03, p<.001) from the model resulted in a significant worsening of the model fit, implying that individual differences in general cognitive ability are to a large extent

explained by genetic factors. If the genetic factors A and D are fixed to zero, the relative influence of ASM decreased from 11% to 0%, implying that phenotypic assortment is based on a phenotype that completely reflects the genotype.

Within model 6, the estimate of D, increased dramatically (from 0% to 27%) when CT was eliminated from the model. Subsequently, eliminating D from the model while CT was already fixed to zero led to a significant worsening of the model fit. From the above it is clear that although D was estimated at zero in the full model, its estimate increases when non-significant environmental factors are dropped from the model; D then becomes highly significant. To test the reverse, i.e., whether the estimate of CT changed when D was eliminated from the model first (i.e., CT is included in the model), we conducted a second series of nested models: eliminating D from the model including CT did not change the estimate of CT (models 9 and 10: CT = 8%) and did not result in a worse model fit (model 10: $\chi^2(1)$= .00, *ns*). Although D and CT were both insignificant when separately fixed to zero while the other effect was estimated freely, both effects could not be eliminated simultaneously (model 8: $\chi^2(1)$= 28.03, p<.001 and model 11: $\chi^2(2)$= 29.64, p<.001).

Estimates of D and negative CT are identified by a similar pattern of correlations. D is identified by a higher DZ correlation relative to the parent offspring correlation since dominance effects are correlated in DZ twin pairs (.25) but not in parent-offspring pairs. Negative CT is also identified by higher DZ correlation relative to the parent-offspring correlation: negative CT results from an inhibiting effect from parents on their offspring's general cognitive ability. However, like the effect of positive CT, the effect of negative CT is similar for both members of a DZ twin pair, resulting in an increased DZ twin correlation. Thus, both D and CT are expected to increase the DZ twin correlation relative to the parent-offspring correlation. Apparently, the current study design lacks information and power to reliably estimate both parameters simultaneously.

Summarizing the results for both reduced models: the first model (model 6) includes additive genetic factors (44%), genetic dominance (27%), phenotypic assortment (11%) and non-shared environmental factors (18%). The second model (model 10) includes additive genetic factors (58%), phenotypic assortment (23%), negative cultural transmission (8%) and non-shared environmental factors (11%); correlation between A and CT was -.36.

Parameter estimates of the full and both reduced models are presented in Figure 3.3.

Figure 3.3 Standardized variance components for general cognitive ability based on full (upper) and reduced (lower) PA-models.
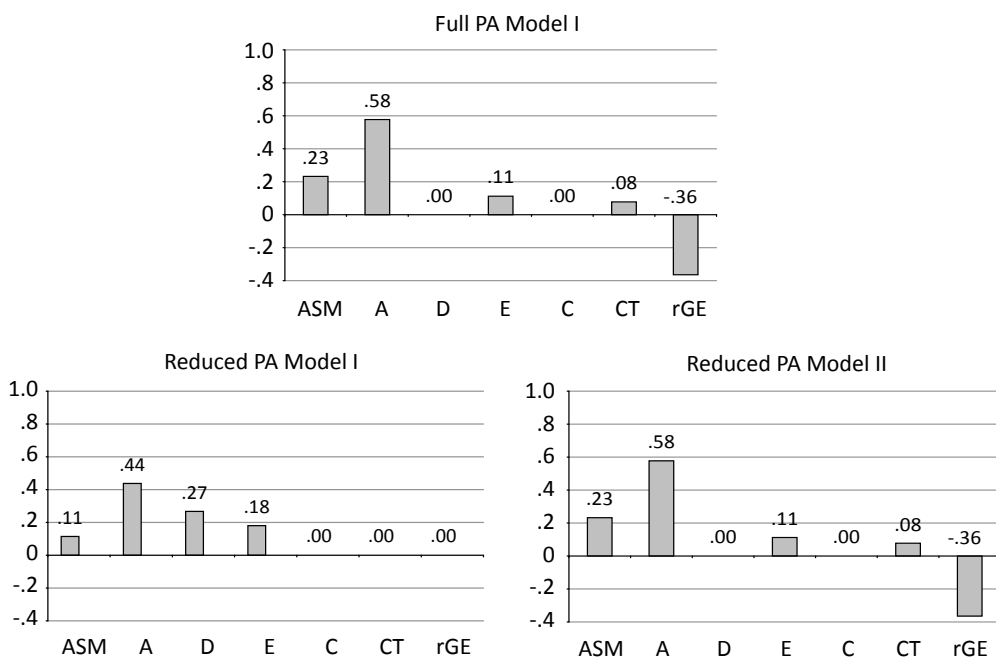
Notes: ASM = positive phenotypic assortment; A = additive genetic factors; D = genetic dominance; E = non-shared environmental factors; C = shared environmental factors; CT = cultural transmission; $r_{(GE)}$ = correlation between A and CT; $r_{(GE)}$ is negative since the unstandardized parameter estimate of CT is negative; Reduced PA Model I refers to model 6 in Table 3.2; Reduced PA Model II refers to model 10 in Table 3.2.

DISCUSSION

Simultaneous modeling of assortative mating, cultural transmission, genetic dominance, additive genetic factors, and shared and non-shared environmental factors showed that variation in general cognitive ability in adulthood is not only due to additive genetic factors and non-shared environmental factors, but also to phenotypic assortment, and genetic dominance *or* negative cultural transmission.

In the present study we could not readily distinguish between genetic dominance and negative cultural transmission. The two alternative models were PA-I, a model including genetic dominance but not negative cultural transmission, or PA-II, a model including negative cultural transmission but not genetic dominance. Within the context of general cognitive ability, significant negative cultural transmission may seem somewhat implausible. Negative cultural transmission has been reported in personality related traits, such as smoking behavior (Maes et al., 2006) and borderline personality disorder (Distel et al., 2009b) in which parental behavior is suggested to have inhibiting effects on their offsprings behavior. If PA-II is the preferred model, general cognitive ability in the parental generation would have inhibiting effects on offspring's general cognitive ability. PA-I seems more realistic and showed that estimates of genetic dominance increased from 0% to 27%

if negative cultural transmission was eliminated from the model. This would support our our hypothesis that in adults, genetic dominance might go undetected due to the presence of assortative mating when assortment is not adequately modeled.

In children, considerable influences of the shared environment on general cognitive ability are reported (van Leeuwen et al., 2008; Haworth et al., 2009), while dominance is usually said to be non-existent. This shift in genetic and environmental architecture of general cognitive ability from childhood to adulthood may be due to dominant genetic influences coming into play at a later age. It is also possible that dominance variance is present in children as well, but goes undetected due to larger shared environmental variance in childhood. Or, alternatively, the effects of the shared environment as seen in childhood (either real shared environmental effects or induced by cultural transmission or assortative mating), may only be temporary and the increase in heritability in adulthood is caused by active gene-environment correlation ($r_{(GE)}$). As children grow up, they increasingly select, modify and create their own experiences, partly based on their genetic predisposition (Haworth et al., 2009). Consequently, the high impact of genetic factors on individual differences in general cognitive ability will also reflect the influences of environmental factors that are correlated with genetic factors. Please note that the $r_{(GE)}$ (active correlation between genetic and unique environmental factors) discussed by Haworth et al. (2009) is different from the $r_{(GE)}$ (passive correlation between genetic factors and cultural transmission) reported in the present study.

Thus far, only a few studies suggested the presence of genetic dominance for general cognitive ability in adults (Jinks & Fulker, 1970; Fulker & Eysenck, 1979; Chipuer et al., 1990); results, however, were based on combined samples with different measures of cognitive ability. Reynolds et al. (2000) emphasized the importance of considering assortative mating in a twin-family study on educational attainment and fluid ability in adults. Effects of social homogamy and phenotypic assort were modeled simultaneously (i.e., mixed assortment) in a sample of 116 twin-spouse sets; effects of cultural transmission and genetic dominance were however not considered in this study. Both social homogamy and phenotypic assort contributed to the spousal similarities for educational attainment and fluid ability in a multivariate design. Considering both social homogamy and positive phenotypic assortment in the context of general cognitive ability would be very interesting, but requires larger sample sizes than we had currently available (Heath & Eaves, 1985).

The present study is unique in the sense that general cognitive ability is measured with the same standardized IQ test in a large adult sample including MZ and DZ twins, their non-twin siblings and the parents, spouses and adult offspring of the twins and non-twin siblings. Our results show that the well-known heritability of ~80% for general cognitive ability is not only attributable to additive genetic factors but also to genetic dominance, and that assortative mating is considerable.

Several limitations should however be considered. First, within the present study it is assumed that the phenotype on which assortment is based reflects the same genotype across generations. If this assumption is not met, cross-generational correlations may have been overestimated. Second, cohort differences in assortment were not considered within the present study. It is conceivable that the process underlying assortative mating differs for different birth cohorts. Mating in the first half of the 20th century may generally have

been based on similar social milieus of the spouses; urbanization and increasing equality of educational opportunities may have increased the influence of phenotypic assortment in latter generations. The present sample size was however too small to consider cohort differences in assortment. Third, the study design (i.e., twins and siblings with their spouses and their parents or offspring) together with the present sample size seemed insufficient to consistently model both negative cultural transmission and genetic dominance. Different relatives, such as half-sibs or adoptees should be included to disentangle those two processes.

General conclusion

Estimating effects of assortative mating, cultural transmission and genetic dominance within an extended twin family design showed the importance of genetic dominance and assortative mating, suggesting that in the CTD, which does not allow the accommodation of assortative mating, the effect of genetic dominance is masked by assortative mating. The conclusion that in adulthood, the genetic variation of general cognitive ability is not only due to additive genetic factors, but also to genetic dominance and assortative mating (i.e., phenotypic assortment) is important in the context of gene finding studies for general cognitive ability. Genome wide association studies generally assume allelic effects to add up (additive genetic variation), and not to interact (Plomin et al., 2001b; Seshadri et al., 2007; Butcher et al., 2008). Considering non-additive genetic effects within future gene finding studies for general cognitive ability might enhance their success (Manolio et al., 2009).

SUPPLEMENTARY INFORMATION

Coefficients for the additive genetic and genetic dominance components of the covariance between relatives for an equilibrium population under phenotypic assortative mating (extended from Lynch and Walsh, 1998, Table 7.4, p158).

Relationship	$\hat{\sigma}_A^2$	$\hat{\sigma}_D^2$
MZ*	1	1
DZ/sibs*	$\frac{1}{2}\left(1+\rho_z\hat{h}^2\right)$	¼
PO*	$\frac{1}{2}\left(1+\rho_z\right)$	0
AVMZ	$\frac{1}{2}\left(1+\rho_z\hat{h}^2\right)$	$\frac{1}{2}\rho_z\hat{h}^2$
AVDZ*	$\frac{1}{4}\left(1+\rho_z\hat{h}^2\right)^2$	$\frac{1}{8}\rho_z\hat{h}^2$
COMZ	$\frac{1}{4}\left(1+\rho_z\hat{h}^2\right)^2$	$\frac{1}{4}\left(\rho_z\hat{h}^2\right)^2$
CODZ*	$\frac{1}{8}\left(1+\rho_z\hat{h}^2\right)^3$	$\frac{1}{16}\left(\rho_z\hat{h}^2\right)^2$
SMZ	ρ_z	ρ_z
SDZ	$\frac{1}{2}\rho_z\left(1+\rho_z\hat{h}^2\right)$	$\frac{1}{4}\rho_z$
SMZS	ρ_z^2	ρ_z^2
SDZS	$\frac{1}{2}\rho_z^2\left(1+\rho_z\hat{h}^2\right)$	$\frac{1}{4}\rho_z^2$
SAVMZ	$\frac{1}{2}\rho_z\left(1+\rho_z\hat{h}^2\right)$	$\frac{1}{2}\left(\rho_z\hat{h}\right)^2$
SAVDZ	$\frac{1}{4}\rho_z\left(1+2\rho_z\hat{h}^2+\rho_z^2\hat{h}^4\right)$	$\frac{1}{8}\left(\rho_z\hat{h}\right)^2$
POS	$\frac{1}{2}\rho_z\left(1+\rho_z\right)$	0

*Notes: Notation follows Lynch and Walsh, 1998, i.e. the equilibrium heritability is $\hat{h}^2 = \hat{\sigma}_A^2 / \hat{\sigma}_z^2$, where $\hat{h}^2$ = the heritability, $\hat{\sigma}_A^2$ = standardized additive genetic variance, and $\hat{\sigma}_z^2$ = the standardized total variance. In the absence of assortative mating, $\rho_z = 0$, where ρ_z = the spousal correlation. * coefficients in these rows are as reported by Lynch and Walsh (1998). Correlations are assumed equal across twins and regular siblings and across sex; MZ=twin-twin MZ; DZ=twin-twin DZ/sibling; PO=parent-offspring; AVMZ=cousins avuncular through MZ; AVDZ=cousins avuncular through DZ/sibling; COMZ=niece/nephews through MZ; CODZ=niece/nephews through DZ/sibling; SMZ=sister/brother in law through MZ; SDZ=sister/brother in law through DZ/sibling; SMZS=spouse-spouse through MZ; SDZS=spouse-spouse through DZ/sibling; SAVMZ=aunt/uncle-cousin in law through MZ; SAVDZ=aunt/uncle-cousin in law through DZ/sibling; POS=parent-offspring in law. Shared environmental influences (C) are assumed to be absent.*

Genetic influences on "environmental" factors

ABSTRACT

Childhood environment, social environment and behavior, leisure time activities, and life events have been hypothesized to contribute to individual differences in cognitive abilities and physical and emotional well-being. These factors are often labeled 'environmental', suggesting they shape but do not reflect individual differences in behavior. The aim of this study is to test the hypothesis that these factors are not randomly distributed across the population but reflect heritable individual differences. Self-report data on *Childhood Environment*, *Social Environment and Behavior*, *Leisure Time Activities*, and *Life Events* were obtained from 560 adult twins and siblings (mean age 47.11 years). Results clearly demonstrate considerable genetic influences on these factors with mean broad heritability of .49 (.00-.87). This suggests that what we think of as measures of 'environment' are better described as *external factors* that might be partly under genetic control. Understanding causes of individual differences in external factors may aid in clarifying the intricate nature between genetic and environmental influences on complex traits.

INTRODUCTION

Complex traits, such as cognitive ability, physical well-being or psychiatric dysfunctioning, are known to be influenced by both genetic and environmental factors. Although current research mainly targets dissecting genetic influences on complex traits, charting environmental influences seems at least of equal importance to understanding individual differences in such traits. Few studies have reported on the influence of environmental factors (such as socio-economic status or life events), on for example cognitive ability (Turkheimer et al., 2003) and psychiatric dysfunctioning (Middeldorp et al., 2008). However, it has been reported that these proposed environmental factors are under genetic control themselves (Rowe, 1983; Plomin et al., 1988; Plomin et al., 1989; Plomin et al., 1994b; Kendler & Baker, 2007), suggesting that these factors are not randomly distributed across the population but reflect heritable individual differences. If true, this will introduce bias to models that treat environmental factors as purely environmental in origin and may therefore impede our understanding of individual differences in complex traits.

Such bias is perhaps most notable when environmental factors are used to investigate environmental moderation of genetic effects (gene-environment interaction; GEI). If the environmental moderator is itself under genetic control and part of the genes that influence the environmental moderator also have a direct effect on the trait under investigation (i.e. a genetic correlation; $r_{(GG)}$) ignoring genetic effects on the measured environmental factor leads to an overestimation of the moderating effect of the environmental factor (Purcell, 2002). Both $r_{(GE)}$ and GEI interaction have been reported in the context of cognitive ability, physical well-being and psychiatric dysfunctioning (Scarr & McCartney, 1983; Plomin et al., 1985; Plomin & Bergeman, 1991; Plomin & Daniels, 1987; Boomsma et al., 1999; Rowe et al., 1999; van der Sluis et al., 2008b). If environmental factors are partly under genetic control, some of these reports may have overestimated effects of the environmental moderators on the genetic influences of a trait.

Kendler and Baker (2007) recently reviewed the findings of 55 independent studies on the genetic influences on 'environmental factors' that are of etiological importance for psychiatric (dys)functioning. The overall weighted heritability estimate across all environmental factors was .27 (range .07-.47). An essential limitation of this study put forward by the authors themselves, is the possibility of publication bias with respect to the studies included in the review, i.e., studies demonstrating genetic control on external factors might be more likely to be accepted for publication than studies reporting on the absence of genetic influence. Since environmental factors are also involved in other domains, it is important to systematically study external factors that are relevant outside the psychiatric domain as well.

Measured factors in the domains of *Childhood Environment*, *Social Environment and Behavior*, *Leisure Time Activities*, and *Life Events,* all generally labeled as environmental, have been hypothesized to contribute to individual differences in various complex traits. The goal of the present study is to test the hypothesis that these factors are not randomly distributed across the population but reflect heritable individual differences.

METHODS

Sample

This study is part of a large ongoing project on the genetics of cognition (e.g., Posthuma et al., 2001a) from the Netherlands Twin Register (NTR; Boomsma et al., 2006). The study was approved by the Central Committee on Research Involving Human Subjects which oversees medical research involving human subjects in the Netherlands. Information on environmental factors was gathered using the Life Experiences List (LEL) which is described in more detail below. The study was undertaken with the understanding and written consent of each participant. Data were available for 560 twins and siblings (59% female) from 256 different families: 150 complete twin pairs (55% MZ), 87 incomplete twin pairs (32% MZ), and 173 siblings (number of participating siblings per family ranges from 0 to 5). From 19 families, only sibling data were available. The average age of the participants was 47.11 years (SD=12.40, range: 23.44–75.61) at the time they completed the LEL. Zygosity of same-sex twins was based on DNA polymorphisms (97 pairs, 74%) or, if information on DNA markers was not available, on questions about physical similarity and confusion of the twins by family members and strangers. Agreement between zygosity diagnoses from survey and DNA was 97% (Willemsen et al., 2005). All five zygosity groups were reasonably well represented: monozygotic males (MZM: 21%, 119 participants), monozygotic females (MZF: 27%, 150 participants), dizygotic males (DZM: 12%, 66 participants), dizygotic females (DZF: 23%, 131 participants) and dizygotic opposite sex (DOS: 17%, 94 participants). Non-twin sibling data were available for 81 (47%) brothers and 91 sisters. The non-twin siblings were included in the analyses to enhance the statistical power to detect genetic and environmental effects (Posthuma & Boomsma, 2000).

The sample of participating twins and siblings was representative of the general Dutch population with regard to educational level (See Posthuma et al., 2001a for details). Prevalences and means of sport participation, having a partner and average number of children per women among others, were also comparable to national large scale surveys (CBS, 2008) implying that the sample is representative of the Dutch population.

A small, independent sample of 52 participants (26 parent-offspring pairs, 75% women; age range 17-71, mean: 39.95, SD: 16.19) completed the survey twice in a period of two months. These data were used to calculate test-retest reliability.

Measures

A short description of the measures used in this study is presented below; see Table 4.1 for an ordered overview of all 34 measures reported on in this study.

Life Experiences List (LEL)

The Life Experience List (LEL) comprises a variety of separate short questionnaires, categorized into four domains of environmental factors: *Childhood Environment, Social Environment and Behavior, Leisure Time Activities,* and *Life Events.*

Childhood Environment

Fourteen environmental factors in the domain of C*hildhood Environment* were measured: *Rearing style* (1=*very strict* to 5=*very tolerant*); *Parental interest in school* (1=*not at all* to 5=*to a great extent*); *School achievements discussed by parents* (1=*never* to 5=*very often*); *To be read to* was (1=*never* to 4=*almost daily*); *Reading books ≤ 12 years/Reading books ≥ 13 years* (1=*no reading* to 6=*4 to 7 times a week*); *Relativel height and weight at primary/ secondary school,* i.e., height/weight compared to peers (1=*smaller* to 3=*bigger*). *Being bullied at primary/secondary school* (1=*rarely* to 4=*regularly*). *Family Conflict* was assessed with the Conflict Scale from the Family Environment Scale (FES; Moos, 1974), a 12-item scale measuring hostility, aggression and discord within the family. This scale has been translated/back translated into Dutch (Coole & Jansma, 1983). The Conflict Scale of the FES (Dutch version) shows internal consistency of .63 (Cronbach's alpha) and a test-retest reliability of .83. *Family Functioning* was assessed using the General Functioning (GF) subscale of the Family Assessment Device (FAD/GF; Epstein et al., 1983), a 12-item scale measuring the overall health/pathology of the family, with 6 items worded to describe healthy functioning and 6 items worded to describe unhealthy functioning. It has been translated/back translated into Dutch (Wenniger et al., 1993). The GF scale (Dutch version) has an alpha of .89, the FAD showed the same factor structure in the Dutch and U.S. samples, and good convergent and discriminative validity with other measures of family functioning and psychopathology.

Social Environment and Behavior

Nine environmental factors in the domain of *Social Environment and Behavior* were measured: *Age leaving parental home; Level of education partner/good friend* (1=*no education* to 11=*doctorate degree*); *Having children/partner* (1=*no*, 2=*yes*); *Number of children; Duration of relationship partner (*years and months). *Size of social support network* and *satisfaction with social support* were assessed with the short version of the Social Support Questionnaire (SSQ-6; Sarason et al., 1990). The SSQ-6 consists of six questions about number of significant others and satisfaction with received social support (the latter ranging from 1=*very dissatisfied* to 6=*very satisfied*). The internal consistency of the Number scale is .90 and of the Satisfaction scale is .87. The correlation between the two scales is r=.49, p<.001. The SSQ-6 correlates well (.95 for SSQ-Number and .96 for SSQ-Satisfaction) with the full questionnaire.

Leisure Time Activities

Five factors were measured in the domain of *Leisure Time Activities*, reflecting *exercise/ sports* and *music participation. Sports participation* was quantified in number of years and times per week in specific sports, both at a recreational and a competitive level, and both in the past (between ages 6-18 years) and current. Questions were developed for an ongoing study on life style in Dutch adult twins (Netherlands Organization for Scientific Research; NWO-MW 904-61-193). *Music participation* was assessed in a similar manner as *sports participation*.

Life Events

Six environmental factors in the domain of *Life Events* were measured: *Positive, Negative and Neutral influential Life Events* (between ages 0-18 years and 19 years-present) were assessed using the *List of Threatening Experiences* (Brugha & Cragg, 1990; adjusted). *Positive Life Events* was based on a sum score of items concerning: graduation, getting promotion, marriage, driving license, and birth of a child. *Negative Life Events* was based on a sum score of items concerning: severe illness, violent assault, divorce, falling-out/breaking up with friends/relatives, severe trouble with friends/relatives, death of friends/relatives, receiving mental health treatment, severe offence, robbery, sexual abuse, being dismissed, and unemployment. *Neutral Life Events* was based on a sum score of items concerning changing schools in childhood, moving house, and retirement.

The LEL was sent out to participants by mail with an overall response rate of 76%. Test-retest reliability of all reported items was investigated in the independent sample of 52 participants (see Sample description for details) who completed the LEL twice within a period of two months. Test-retest reliability of quantitative items was calculated in SPSS, test-retest reliability of ordinal and dichotomous items was calculated in PRELIS (Joreskog & Sorbom, 2006).

Analyses

Analyses were carried out using the raw data option in Mx (Neale, 1994; Posthuma & Boomsma, 2005). Age and sex were included as covariates in the model. Ordinal items were assumed to reflect an underlying normal distribution of liability (Falconer & Mackay, 1989). Since the liability is a theoretical construct, its scale is arbitrary. For straightforward interpretation, the liability was assumed to be standard normally distributed with zero mean and unit variance and the number of thresholds a function of the number of ordered categories minus 1.

First, twin and sibling correlations for all traits were estimated. Means or thresholds, and variances were constrained equal across twins and non-twin siblings and across all zygosity groups for all domains. Correlations for monozygotic (MZ) twins, dizygotic (DZ) twins, and siblings were allowed to differ. A difference between DZ and sibling correlations may represent a true twin environmental influence on a trait or may be induced when the environmental factor is something that happens at a fixed time-point and at the same time affects all family members (such as parental divorce).

Second, genetic models were specified in which individual differences (in liability, in case of ordinal data) were modeled as a function of genetic and environmental effects. Genetic factors A and D, and environmental factors T, C and E, were considered. 'A' represents additive effects of alleles summed over all genetic loci. 'D' represents non-additive or dominant genetic effects. 'T' represents a special twin environment that renders twins more alike than regular siblings. 'C' represents common environmental influences that render members of the same family more alike. 'E' represents all environmental influences that result in differences between members of a family, including measurement error. In a twin-sibling design, the effect of C and D are confounded and cannot be estimated simultaneously. In the present study, the variance (in liability, in case of ordinal data) was decomposed as due to A, C, T and E, or due to A, D, T and E. If sibling correlations were

significantly different from twin correlations, a special twin environment (T) was included in the genetic model. When DZ twin correlations are at least half the MZ twin correlations, additive genetic effects are implied and an ACE or ACTE model was fitted to the data. DZ twin correlations less than half the MZ twin correlations suggest the presence of genetic dominance, in which case an ADE or ADTE model is deemed more suitable. Significance of parameters was tested by comparing the fit of nested (increasingly more restricted) models to the fit of less restricted models. Goodness-of-fit of these sub-models was assessed by hierarchic likelihood-ratio-tests. The difference in log-likelihoods between two models (which follows a χ^2 distribution) was evaluated. If the χ^2-difference test is significant, the constraints imposed on the nested models are not tenable. If the χ^2-difference test is not significant, the nested, more parsimonious model is to be preferred. A criterion level α of .05 was adopted for all tests.

RESULTS

Table 4.1 lists frequencies of all ordinal measures and means and standard deviations of the continuous measures, as well as test-retest reliabilities and missingness. Means and thresholds could be constrained to be equal across all zygosity groups without significantly deteriorating the fit of the model.

Original categories from the LEL were maintained for the ordinal analyses, except for a few factors: Because the endorsement rate of the highest categories of the items concerning 'parental interest in school achievement' and 'being bullied at primary and secondary school' was very low, it was decided to merge the two highest categories. The ordinal items concerning 'being read to' and 'current musical and physical activity' were dichotomized because of low test-retest reliability of the higher order versions. The item concerning 'being read to' was categorized into 'yes' if being read to took place at least once a week, and 'no' for all other categories. Finally, items on the frequency of playing an instrument and participation in physical activity were dichotomized and should be interpreted as 'yes' versus 'no' items.

In general, the percentage missing (see Table 4.1) is reasonable except for factors concerning 'educational level of the participants' partner' and 'educational level participants' friend'. A relatively large proportion of participants did not know or left blank the level of education of their partner (22%) and good friend (50%). The high percentage of missingness with respect to 'educational level partner' was mainly attributable to the older participants of this study. 33% of the participants above 45 years of age did not report the educational level of their partner. Most likely, the missingness was dictated by educational changes over the last decades, with the categories presented in the questionnaire not exactly matching the former educational system.

Test-retest reliability (see Table 4.1) was above .80 for the majority of the items (24 out of 34 items). Test-retest reliability within the domain of *Childhood Environment* was exceptionally high. Within the domain of *Leisure Time Activities*, the item concerning 'number of years sport participation' showed relatively low test-retest reliability: .37. Two items within the domain of *Social Environment and Behavior* showed relatively low test-retest reliability as well (Social Support Numbers: r = .44, Social Support Satisfaction: r =.46).

Table 4.1 Number of participants (N-values), test-retest reliability, means and standard deviations, or prevalences, for all measured environmental factors

	N-values	Reliability	Mean (SD)	Prevalences				
				1	2	3	4	5
Childhood Environment								
Rearing style (O)	556	.83	-	3.75	30.36	44.46	18.57	2.68
Parental interest in school achievement (O)	554	.92	-	8.21	39.82	47.32	3.57	-
School achievements discussed by parents (O)	557	.86	-	5.71	75.18	13.93	4.64	-
To be read to (O)	560	.94	-	47.68	52.32	-	-	-
Reading books ≤ 12 years (O)	560	.70	-	30.00	22.14	23.21	24.64	-
Reading books ≥ 13 years (O)	560	.78	-	27.32	23.21	21.96	27.50	-
Being bullied at primary school (O)	557	.94	-	63.93	13.39	16.79	5.36	-
Being bullied at secondary school (O)	548	.89	-	70.00	13.93	9.82	4.11	-
Family conflict (C)	557	.88	3.70 (2.32)	-	-	-	-	-
Family functioning (C)	557	.91	11.34 (5.87)	-	-	-	-	-
Relative height at primary school (O)	552	1.00	-	22.50	56.07	20.00	-	-
Relative height at secondary school (O)	535	.98	-	19.11	61.96	16.25	-	-
Relative weight at primary school (O)	554	1.00	-	26.61	65.18	7.14	-	-
Relative weight at secondary school (O)	534	1.00	-	23.75	65.54	7.86	-	-
Social Environment and Behavior								
Age leaving parental home (C)	557	.99	21.65 (4.52)	-	-	-	-	-
Level of Education Partner (C)	369	.91	-	-	-	-	-	-
Level of Education Friend (C)	274	.86	-	-	-	-	-	-
Children yes/no (O)	558	1.00	-	31.43	68.21	-	-	-
Number of children (C)	557	1.00	1.61 (1.36)	-	-	-	-	-
Partner yes/no (O)	557	1.00	-	15.89	83.57	-	-	-
Duration of relationship partner (C)	517	1.00	21.99 (13.39)	-	-	-	-	-
Social Support – Numbers (C)	541	.44	23.63 (12.79)	-	-	-	-	-
Social Support – Satisfaction (C)	524	.46	8.48 (3.43)	-	-	-	-	-
Leisure Time Activities								
Number of years music lessons (C)	558	.92	1.88 (2.96)	-	-	-	-	-
Musical instrument / lesson current (O)	552	1.00	-	83.75	13.04	-	-	-
Number of years sport participation (C)	553	.37	.39 (1.35)	-	-	-	-	-
Number of years sport competition (C)	560	.61	6.42 (4.49)	-	-	-	-	-
Sport current (O)	512	1.00	-	62.55	-	-	-	-
Life Events								
Life Events positive (≤18ys) (C)	560	.57	1.38 (1.13)	-	-	-	-	-
Life Events negative (≤18ys) (C)	560	.88	.90 (1.67)	-	-	-	-	-
Life Events neutral (≤18ys) (C)	560	.94	1.17 (1.90)	-	-	-	-	-
Life Events positive (≥19ys) (C)	560	.72	5.67 (4.06)	-	-	-	-	-
Life Events negative (≥19ys) (C)	560	.68	5.09 (5.36)	-	-	-	-	-
Life Events neutral (≥19ys) (C)	560	.78	2.80 (2.33)	-	-	-	-	-

Notes: C = continuous data, O = ordinal data, SD = standard deviation. In the case of dichotomous data, the first category represents 'no' and the second category represents 'yes'. In case of ordinal data, lower categories represent lower endorsement. In case of continuous data, lower values represent a lower score.

Table 4.2 shows the MZ, DZ and sibling (including twin-sib) correlations for all environmental factors, with the type of correlation depending on the measurement level of the factors (tetrachoric (TC) for dichotomous items, polychoric (PC) for ordinal items, and Pearson (PE) for continuous items). Correlations for MZ, DZ and sibling pairs were based on a maximum of 83, 67 and 315 pairs respectively.

Sibling correlations did not differ from DZ correlations except for two items in the domain of Life Events (Positive and Neutral Life Events up to the age of 18) in which DZ correlations exceeded the sibling correlations. The factor Neutral Life Events mainly exist of events that happen within a family at a fixed time point. The difference in twin and sibling correlations is therefore most likely attributable to twins being of the same age when an event takes place, while regular siblings are not. For these two factors, special twin environment T was estimated in addition to environment shared by all twins and siblings (C).

In general, MZ twin correlations exceeded the DZ and sibling correlations suggesting the presence of genetic influences. The point estimate of the DZ twin correlation of the item 'Level of Education Friend' exceeds the point estimate of the MZ twin correlation. This is likely dictated by the relatively low number of complete DZ twin pairs, percentage missingness of this itm was 50%. DZ twin correlations, however, were not significantly different from sibling correlations for this factor resulting in a lower DZ/sib than MZ correlation.

For 23 out of the 34 factors the pattern of MZ, DZ/sib correlations suggested an ADE pattern, for 11 factors an ACE pattern was suggested for subsequent genetic modeling. For the two environmental factors for which the DZ correlation significantly exceeded the sibling correlation, the decision between and ACTE or ADTE model was based on the difference between the MZ and DZ twin correlation. For each environmental factor, the selected model is reported in tables 4.3-4.6 (* denotes ACE, ** denotes ADE, *** denotes ACTE). Tables 4.3-4.6 list the proportions of variance explained by genetic (additive and non-additive) and environmental (special twin, shared and non-shared) influences in full and reduced models for each domain.

For some measured environmental factors both an AE and a CE model described the observed data well. In that case, preference of an AE or CE model was based on Akaike's Information Criterium (AIC, computed as $\chi^2 - (2*df)$), were the preferred model was indicated by a lower AIC.

Within the domain of *Childhood Environment* (Table 4.3), genetic influences were significant for the majority of the measured factors. Based on the full models, the mean of the broad sense heritability (i.e., a^2+d^2) calculated across all fourteen measured childhood factors was .66 (range: .47-.87). Genetic influences were relatively low for the item 'school achievements discussed by parents' and were relatively high for factors concerning 'relative height at primary and secondary school', 'to be read to' and 'to be bullied at primary school'.

Within the domain of *Social Environment and Behavior* (Table 4.4), genetic influences were significant for the majority of the measured factors. Based on the full models,

Table 4.2 Twin correlations (95% confidence intervals) for all measured environmental factors

	rMZ (95% CI) range: 69-83 pairs	rDZ (95% CI) range: 57-67 pairs	rSIB (95% CI) range: 275-315 pairs
Childhood Environment			
Rearing style	.66 (.46-.78)	.60 (.36-.75)	.38 (.22-.50)
Parental interest in school achievement	.67 (.47-.80)	.30 (.01-.54)	.43 (.28-.56)
School achievements discussed by parents	.51 (.25-.69)	.01 (-.37-.39)	.04 (-.12-.23)
To be read to	.80 (.58-.92)	.33 (-.03-.65)	.45 (.25-.62)
Reading books ≤ 12 years	.72 (.56-.83)	.06 (-.24-.35)	.17 (.03-.31)
Reading books ≥ 13 years	.73 (.57-.83)	.11 (-.22-.41)	.15 (.02-.29)
Being bullied at primary school	.74 (.54-.86)	.41 (.06-.67)	.11 (-.06-.29)
Being bullied at secondary school	.52 (.22-.73)	.23 (-.15-.56)	.18 (.04-.39)
Family conflict	.69 (.58-.77)	.28 (.03-.45)	.35 (.21-.46)
Family functioning	.64 (.51-.73)	.17 (-.09-.28)	.13 (-.02-.28)
Relative height at primary school (O)	.87 (.74-.95)	.07 (-.23-.35)	.20 (.03-.37)
Relative height at secondary school (O)	.84 (.66-.93)	.40 (.11-.63)	.30 (.13-.45)
Relative weight at primary school (O)	.57 (.32-.74)	.34 (-.06-.65)	.23 (.05-.40)
Relative weight at secondary school (O)	.66 (.45-.81)	.20 (-.20-.54)	.21 (.04-.37)
Social Environment and Behavior			
Age leaving parental home	.67 (.56-.75)	.24 (.02-.46)	.11 (.00-.23)
Level of Education Partner*	.44 (.14-.63)	.09 (-.24-.41)	.35 (.17-.50)
Level of Education Friend**	.35 (.06-.58)	.55 (.24-.73)	.31 (.04-.52)
Children yes/no	.75 (.48-.91)	.46 (.02-.77)	.19 (-.05-.44)
Number of children	.49 (.29-.61)	.32 (.11-.48)	.17 (.05-.30)
Partner yes/no	.75 (.45-.92)	.13 (-.40-.61)	.10 (-.12-.35)
Duration relationship partner	.13 (-.05-.30)	.35 (.08-.55)	.15 (-.03-.32)
Social Support – Numbers	.30 (.09-.47)	.21 (.00-.39)	.04 (-.10-.19)
Social Support – Satisfaction	.10 (-.12-.31)	.15 (-.23-.39)	-.08 (-.06-.20)
Leisure time activities			
Number of years music lessons	.81 (.73-.87)	.62 (.46-.72)	.53 (.39-.63)
Musical instrument / lesson current	.86 (.57-.97)	.50 (-.13-.86)	.29 (-.05-.58)
Number of years sport participation	.45 (.04-.66)	-.05 (-.24-.14)	-.07 (-.18-.08)
Number of years sport competition	.67 (.53-.76)	.46 (.27-.61)	.36 (.23-.49)
Sport current	.59 (.26-.75)	.51 (.11-.72)	.17 (.02-.33)
Life Events			
Life Events positive (≤18ys)	.27 (.02-.49)	.14 (-.09-.34)	.12 (.01-.34)
Life Events negative (≤18ys)	.50 (.26-.65)	.44 (.30-.56)	.08 (-.13-.31)
Life Events neutral (≤18ys)	.77 (.68-.84)	.67 (.53-.77)	.41 (.29-.52)
Life Events positive (≥19ys)	.59 (.40-.71)	.30 (-.15-.56)	.07 (-.04-.20)
Life Events negative (≥19ys)	.15 (-.02-.30)	-.01 (-.21-.19)	.09 (-.04-.23)
Life Events neutral (≥19ys)	.44 (.24-.59)	.21 (.00-.40)	.22 (.09-.35)

Notes: rMZ = MZ twin correlation, rDZ = DZ twin correlation, rSIB = regular sibling correlation (includes twin-sibling correlation), CI = confidence interval. *Due to high percentage of missingness, number of complete MZ twin, DZ twin and sibling pairs is 39, 29, and 148, respectively. ** Due to high percentage of missingness, number of complete MZ twin, DZ twin and sibling pairs is 20, 21, and 138, respectively.

models, mean broad sense heritability across all nine items was .36 (range: .00 - .74). No significant genetic influences were observed for two items ('education good friend' and 'duration of relationship with partner') while relatively high heritability was observed for 'having children'. Absence of genetic influences for 'education good friend' might however be related to the relatively high percentage of missingness of this factor. Both AE and CE models described the data well for factors concerning 'education of partner', 'education of good friend' and 'duration of the relationship with partner'. Based on the AIC, an AE model was preferred for 'education partner' while CE models were preferred for 'education good friend' and 'duration of relationship with partner'.

Within the domain of *Leisure Time Activities* (Table 4.5), genetic influences were significant for all measured factors. Mean broad sense heritability was .52 (range: .31-.87). The lowest heritability was found for the 'number of years music lessons', while highest heritability was reported for the factor concerning 'current musical activity'. Both AE and CE models described the data well for 'number of years music lesson' and 'number of years sport participation', with AE the preferred model based on AIC.

Within the domain of *Life Events* (Table 4.6), genetic influences were significant for 'Positive Life Events' (< age 18 and ≥ age 19) and for 'Neutral Life Events ≥ age 19. Mean broad heritability was .29 (range: .12-.57). In general, higher heritability estimates were reported for life events occurring later in life (after age 19). Both an AE and a CE model described the data well for 'neutral life events ≥ age 19, with AE the preferred model based on AIC. Special twin environmental influences were significant for 'negative and neutral life events ≤ 18.

Table 4.3 Standardized estimates and confidence intervals of genetic, shared and non-shared environmental influences on measured environmental factors in the domain Childhood Environment

	Full model				Reduced (preferred) model				Full model χ^2 ($\Delta df = 1$) p-value	AE-model χ^2 ($\Delta df = 1$) p-value	CE-model χ^2 ($\Delta df = 1$) p-value	E-model χ^2 ($\Delta df = 2$) p-value
	a^2	d^2	c^2	e^2	a^2	d^2	c^2	e^2				
Childhood Environment												
Rearing style*	.48 (.07-.78)	-	.18 (.00-.45)	.34 (.22-.54)	.69	-	-	.31	3.25 p=.07	1.53 p=.21	5.04 p<.05	62.86 p<.001
Parental interest in school achievement*	.53 (.10-.80)	-	.14 (.00-.43)	.33 (.20-.53)	-	-	.46	.54	.89 p=.35	.84 p=.36	5.61 p<.05	59.73 p<.001
School achievements discussed by parents**	.00 (.00-.46)	.47 (.00-.67)	-	.53 (.33-.78)	.36	-	-	.64	.99 p=.32	3.15 p=.08	-	12.37 p<.001
To be read to*	.74 (.24-.92)	-	.06 (.00-.42)	.20 (.08-.42)	.81	-	-	.19	.40 p=.53	.09 p=.77	7.93 p<.001	5.41 p<.001
Reading books ≤ 12 years**	.00 (.00-.45)	.72 (.22-.82)	-	.28 (.18-.44)	.00	.72	-	.28	.62 p=.43	7.16 p<.05	-	45.04 p<.001
Reading books ≥ 13 years**	.00 (.00-.41)	.72 (.27-.82)	-	.28 (.18-.43)	.00	.72	-	.28	.36 p=.55	8.36 p<.001	-	48.61 p<.001
Being bullied at primary school**	.00 (.00-.20)	.74 (.64-.81)	-	.26 (.16-.36)	.00	.74	-	.26	2.68 p=.10	5.36 p<.05	-	33.13 p<.001
Being bullied at secondary school**	.26 (.00-.68)	.26 (.00-.73)	-	.48 (.27-.76)	.48	-	-	.52	.07 p=.79	.34 p=.56	-	14.32 p<.001
Family conflict**	.64 (.14-.77)	.04 (.00-.56)	-	.31 (.23-.42)	.69	-	-	.31	.38 p=.54	.03 p=.86	-	9.76 p<.001
Family functioning**	.00 (.00-.48)	.63 (.13-.73)	-	.37 (.27-.50)	.00	.63	-	.37	.14 p=.71	5.79 p<.05	-	53.80 p<.001
Relative height at primary school**	.00 (.00-.45)	.87 (.39-.94)	-	.13 (.06-.27)	.00	.87	-	.13	1.04 p=.31	1.36 p<.001	-	54.92 p<.001
Relative height at secondary school**	.44 (.00-.89)	.39 (.00-.92)	-	.16 (.07-.34)	.80	-	-	.20	.46 p=.50	1.48 p=.22	-	55.84 p<.001
Relative weight at primary school**	.41 (.00-.71)	.16 (.00-.73)	-	.43 (.26-.66)	.57	-	-	.43	.31 p=.58	.17 p=.68	-	24.36 p<.001
Relative weight at secondary school**	.05 (.00-.72)	.62 (.00-.81)	-	.33 (.19-.56)	.63	-	-	.37	.11 p=.74	1.83 p=.18	-	3.85 p<.001

*Notes: * = model with additive genetic, shared environmental and non-shared environmental parameters (ACE)); ** = model with additive genetic, genetic dominance and non-shared environmental parameters (ADE)); - = not estimated; χ² =chi square test statistic; Δ df, difference degrees of freedom. The full model was evaluated versus the saturated model to test whether the DZ twin correlation differs from the sibling correlation. A difference between DZ twin and sibling correlations may represent a true twin environmental influence on a trait or may be induced when the environmental factor is something that happens at a fixed time-point and at the same time affects all family members (such as parental divorce).*

Additional information

As relative height and weight are expected to be partly related to absolute height and weight and therefore partly expected to be under genetic control, we tested the correlation between the relative and absolute measures. For the majority of the sample (N≥465), data on actual height and weight in adulthood were available, besides data on relative height and weight compared to school peers. Correlations between the relative and actual measures of height and weight were modest (mean r =.51; ranging from .31 for 'relatively weight at primary school' in men to .74 for 'relatively height at secondary school' for women). This modest correlation could suggest that genetic influences on relative height and weight overlap only partly with genetic influences on actual height and weight.

Table 4.4 Standardized estimates and confidence intervals of genetic, shared and non-shared environmental influences on measured environmental factors in the domain Social Environment and Behavior

	Full model a²	Full model d²	Full model c²	Full model e²	Reduced model a²	Reduced model d²	Reduced model c²	Reduced model e²	Full model χ^2 (Δdf = 1) p-value	AE-model χ^2 (Δdf = 1) p-value	CE-model χ^2 (Δdf= 1) p-value	E-model χ^2 (Δdf = 2) p-value
Social Environment and Behavior												
Age leaving parental home**	.00 (.00-.32)	.66 (.32-.74)	-	.34 (.26-.45)	.00	.66	-	.34	1.38 p=.24	11.76 p<.001	-	76.17 p<.001
Level of Education Partner*	.29 (.00-.63)	-	.15 (.00-.45)	.56 (.37-.80)	.48	-	-	.52	1.97 p=.16	.50 p=.48	.81 p=.37	21.37 p<.001
Level of Education Friend*	.00 (.00-.56)	-	.36 (.00-.51)	.64 (.42-.82)	-	-	.36	.64	2.61 p=.11	2.08 p=.15	.00 p=1.00	14.67 p<.001
Children yes/no**	.25 (.00-.86)	.49 (.00-.90)	-	.25 (.10-.52)	.70	-	-	.30	1.33 p=.25	.98 p=.32	-	26.28 p<.001
Number of children (C)**	.37 (.00-.58)	.11 (.00-.58)	-	.53 (.40-.69)	.46	-	-	.54	1.60 p=.21	.16 p=.69	-	34.97 p<.001
Partner yes/no**	.00 (.00-.70)	.73 (.00-.91)	-	.27 (.09-.57)	.60	-	-	.40	.44 p=.51	3.35 p=.07	-	18.71 p<.001
Duration relationship partner*	.00 (.00-.29)	-	.17 (.00-.29)	.83 (.69-.95)	-	-	.17	.83	2.15 p=.14	2.17 p=.14	.00 p=1.00	8.65 p<.05
Social Support – Numbers**	.06 (.00-.40)	.23 (.00-.47)	-	.70 (.53-.90)	.25	-	-	.75	1.81 p=.18	.55 p=.46	-	9.64 p<.05
Social Support – Satisfaction**	.00 (.00-.21)	.07 (.00-.27)	-	.93 (.73-.00)	-	-	-	1.0	.64 p=.42	.29 p=.59	-	.42 p=.81

*Notes: * = model with additive genetic, shared environmental and non-shared environmental parameters (ACE); ** = model with additive genetic, genetic dominance and non-shared environmental parameters (ADE); - = not estimated; χ^2 =chi square test statistic; Δ df, difference degrees of freedom. The full model was evaluated versus the saturated model to test whether the DZ twin correlation differs from the sibling correlation. A difference between DZ twin and sibling correlations may represent a true twin environmental influence on a trait or may be induced when the environmental factor is something that happens at a fixed time-point and at the same time affects all family Members (such as parental divorce).*

Table 4.5 Standardized estimates and confidence intervals of genetic, shared and non-shared environmental influences on measured environmental factors in the domain Leisure Time Activities

	Full model				Reduced model				Full model χ²	AE-model χ²	CE-model χ²	E-model χ²
	a²	d²	c²	e²	a²	d²	c²	e²	(Δdf = 1) p-value	(Δdf = 1) p-value	(Δdf= 1) p-value	(Δdf = 2) p-value
Leisure Time Activities												
Number of years music lessons*	.31 (.00-.73)	-	.26 (.00-.60)	.43 (.26-.69)	.60	-	-	.40	.09 p=.76	1.01 p=.31	1.03 p=.31	22.55 p<.001
Musical instrument / lesson current**	.51 (.00-.63)	.36 (.00-.97)	-	.13 (.03-.40)	.85	-	-	.15	2.60 p=.11	.35 p=.56	-	26.64 p<.001
Number of years sport participation*	.35 (.00-.97)	-	.10 (.00-.40)	.55 (.37-.80)	.48	-	-	.52	.37 p=.54	.29 p=.59	1.45 p=.23	22.81 p<.001
Number of years sport competition**	.24 (.00-.69)	.35 (.00-.75)	-	.41 (.25-.71)	.51	-	-	.49	2.76 p=.10	.88 p=.35	-	15.99 p<.001
Sport current**	.00 (.00-.42)	.46 (.00-.72)	-	.54 (.28-.90)	.29	-	-	.71	1.73 p=.19	2.73 p=.10	-	6.41 p<.05

*Notes: * = model with additive genetic, shared environmental and non-shared environmental parameters (ACE); ** = model with additive genetic, genetic dominance and non-shared environmental parameters (ADE)); - = not estimated; χ² =chi square test statistic; Δ df, difference degrees of freedom. The full model was evaluated versus the saturated model to test whether the DZ twin correlation differs from the sibling correlation. A difference between DZ twin and sibling correlations may represent a true twin environmental influence on a trait or may be induced when the environmental factor is something that happens at a fixed time-point and at the same time affects all family members (such as parental divorce).*

Table 4.6 Standardized estimates and confidence intervals of genetic, shared and non-shared environmental influences on measured environmental factors in the domain Life Events

	Full model				Reduced model				Full model χ^2	AE-model χ^2	CE-model χ^2	E-model χ^2
	a^2	d^2	c^2	e^2	a^2	d^2	c^2	e^2	$(\Delta df = 1)$ p-value	$(\Delta df = 1)$ p-value	$(\Delta df = 1)$ p-value	$(\Delta df = 2)$ p-value
Life Events												
Life Events positive (≤18ys)**	.22 (.00-.42)	.06 (.00-.49)	-	.73 (.51-.91)	.26	-	-	.74	.02 p=.89	.03 p=.87	-	9.28 p<.05
Life Events positive (≥19ys)**	.00 (.00-.30)	.57 (.20-.69)	-	.43 (.31-.62)	.57	-	-	.43	2.04 p=.15	7.33 p<.05		23.07 p<.001
Life Events negative (≥19ys)**	.09 (.00-.27)	.06 (.00-.30)	-	.85 (.70-.99)	-	-	-	1.0	.64 p=.43	.04 p=.84		4.25 p=.12
Life Events neutral (≥19ys)*	.44 (.00-.58)	-	.00 (.00-.30)	.56 (.42-.76)	.44	-	-	.56	.01 p=.92	.00 p=1.00	3.77 p=.05	3.40 p<.001

	Full model					Reduced model				Full model χ^2	ACE-model χ^2	ATE-model χ^2	CTE-model χ^2	TE-model χ^2	E-model χ^2
	a^2	d^2	c^2	t^2	e^2	a^2	c^2	t^2	e^2	(par)	$(\Delta df = 1)$ p-value	$(\Delta df = 1)$ p-value	$(\Delta df = 1)$ p-value	$(\Delta df = 2)$ p-value	$(\Delta df = 3)$ p-value
Life Events negative (≤18ys) (C)***	.12 (.00-.45)	-	.03 (.00-.30)	.36 (.10-.55)	.50 (.36-.66)	-	-	.45	.55	2098.43 (7)	7.93 p<.001	.03 p=.87	.24 p=.62	.74 p=.69	.74 p<.001
Life Events neutral (≤18ys) (C)***	.20 (.00-.49)	-	.31 (.11-.48)	.26 (.11-.41)	.23 (.16-.32)	-	.41	.31	.27	2162.15 (7)	10.72 p<.001	8.44 p<.001	2.49 p=.11	41.62 p<.001	141.74 p<.001

Notes: * = model with additive genetic, shared environmental and non-shared environmental parameters (ACE)); ** = model with additive genetic, genetic dominance and non-shared environmental parameters (ADE)); - = not estimated; χ^2 =chi square test statistic; Δ df, difference degrees of freedom. The full model of the upper four items was evaluated versus the saturated model to test whether the DZ twin correlation differs from the sibling correlation. A difference between DZ twin and sibling correlations may represent a true twin environmental influence on a trait or may be induced when the environmental factor is something that happens at a fixed time-point and at the same time affects all family members (such as parental divorce). The full ACTE model of the lower two items cannot be compared with the saturated model since both models have the same number of degrees of freedom; consequently a chi-square difference test cannot be conducted. -2LL of both models was however identical.

DISCUSSION

In this study the hypothesis was tested that measured environmental factors from four general domains (*Childhood Environment*, *Social Environment and Behavior*, *Leisure Time Activities*, and *Life Events*) are not randomly distributed across the population but reflect heritable individual differences. Results of this study demonstrate considerable genetic influences on factors that are often labeled as 'environmental', in keeping with the idea of the environment as an 'extended phenotype' (Dawkins, 1982). Overall, mean broad sense heritability, h^2 ($a^2 + d^2$), was .49 (range .00 - .87) (without items 'relatively height and weight', mean broad sense heritability was .46). The largest estimates of the broad sense heritability were reported within the domain of *Childhood Environment* (mean h^2 = 66, without items 'relatively height and weight', mean h^2 = .62 (range .00 - .87)), followed by *Leisure Time Activities* (mean h^2 = .52) and *Social Environment and Behavior* (mean h^2 = .36), and the lowest heritability in the domain *Life Events* (mean h^2 = .29). Only two measured environmental factors, both in the domain *Social Environment and Behavior* were found to be purely environmental: 'the level of education of a good friend' and 'the duration of relationship with partner'. Our results suggest that what we think of as *environmental* factors are perhaps better described as *external* factors that might be partly under genetic control. Including such external factors in etiologic models of complex traits therefore necessitates a correct specification of both genetic and environmental influences on external factors. For example, external factors may be correlated with the genetic effects on complex traits ($r_{(GE)}$), and this $r_{(GE)}$ can appear as gene-environment interaction (GEI) if the $r_{(GE)}$ is not accommodated explicitly in the model (Purcell, 2002). The finding that environmental factors are partly under genetic control has therefore major implications on studies on interactions between genes and environmental influences.

Some of the measured external factors investigated here have been investigated previously. For example, within the domain of *Childhood Environment* current heritability estimates for 'family environment' exceeded estimates from previous studies; (Plomin et al., 1988; Jacobson & Rowe, 1999) while the heritability estimates for 'being bullied' were lower in the present study (Ball et al. (2008). No previous studies reported on etiology of one's intellectual environment (domain *Social Environment and Behavior*), i.e. the external factors 'educational level of partner' and 'educational level of good friend'. The finding that the level of education of an individual's partner is under genetic influence may be grounded in assortative mating for intelligence, i.e. non random mating of spouse pairs. As intelligence is a highly heritable trait, and intelligence has a strong phenotypic and genotypic correlation with educational level (Rowe et al., 1998), educational level of an individual's partner may be correlated with genes that are related with intelligence. The finding that external factors as 'having children', 'having partner' and 'duration of relationship with partner' are partly under genetic control may not be surprising since these factors are likely to be related to other qualities known to be influenced by genetic factors, including conscientiousness and conservatism (Bouchard, Jr. et al., 2003).

Previous studies on sport and musical participation show considerable evidence of genetic influences, comparable with the results of the *Leisure Time Activities* domain of the present study (Coon & Carey, 1989; Stubbe et al., 2006; Vinkhuyzen et al., 2009). Studies on the heritability of *Life Events* were reviewed by Kendler and Baker (2007)

in the context of psychiatric (dys)functioning. Life Events are related to psychiatric (dys) functioning (Middeldorp et al., 2008) but may also be related to other domains of interest in genetic epidemiology (Buckley et al., 2000; Brandes et al., 2002; Hart, Jr. et al., 2008). Kendler and Baker (2007) reported mean weighted heritability estimates of .34, .39 and .17 for positive, negative, and neutral life events, respectively. The results of the present study are partly in line herewith, with broad range heritability estimates of .26/.44 and .40/.41 for positive/neutral life events up to age 18 and from age 19, respectively. In contrast to the findings of the studies reviewed by Kendler and Baker, genetic influences on negative life events were not significant in the present study.

Limitations

First, all information on the external factors in this study was gathered through self-report. This induces the possibility of analyzing the heritability of *the selective recall and subjective perception of* the factor, rather than the actual factor itself. Kendler and Baker (2007) reported weighted heritability estimates for external factors by rating method; weighted heritability estimates based on self-report data (.29) were somewhat higher than estimates based on informant report data (.26), and substantially higher than direct rater or videotape observation data (.14). This suggest that genetic influences on external factors as reported in the present study might be somewhat inflated due to the use of self-report only. In future studies that aim to investigate genetic influences on environmental factors, it would be valuable to make use of external raters in addition to self report data to test for the possible selective recall or subjective perception of the participants.

Second, it should be noted that factors of which the variance is naturally attributable to shared environmental influences – such as parental divorce, or parental death - were not considered in this study.

Third, variances were assumed to be equal between MZ and DZ twins. For six items, however, the MZ variances were significantly different (p-values ranging from .00 to .02) than the DZ variances: 'Age leaving parental home', 'Number of years music lessons', 'Life Events positive (≥19ys)', Duration of relationship partner', and 'Positive and Negative Life Events (≤18ys)'. The observed pattern of MZ and DZ variances and covariances of the first three items was suggestive of competitive sibling interaction (i.e. the behavior of one child leads to opposite behavior in the other child), the observed pattern of MZ and DZ variances and covariances of the latter three items was suggestive of cooperative sibling interaction (i.e., the behavior of one child leads to similar behavior in the other child). We choose not to incorporate possible sibling interaction in the genetic models for two reasons. First, sibling interaction was beyond the scope of this study as our main aim was to establish whether external factors are under genetic pressure. Second, a much larger sample size is required to test both sibling interaction and genetic dominance. Consequently, as the statistical power to detect sibling interaction in the context of genetic dominance would have been very poor with the current sample size (see e.g., Rietveld et al., 2003) it is very likely that we would have ended up with the same results as presented now. Ignoring sibling interaction may lead to inflated estimates of genetic dominance and deflated estimates of additive genetic factors (Rietveld et al., 2003). It does however not change the broad sense heritability, which was the main focus of this study.

Fourth, in case of intermediate levels of heritability, the statistical power to resolve dominance genetic effects can be quite poor when only data from twins and siblings are available (Eaves, 1969; Martin et al., 1978), and sample sizes in the order of 2000 participants are often required. The use of ordinal data necessitates even larger sample sizes to detect genetic dominance, depending on the prevalences and number of thresholds (Neale et al., 1994). In addition, the (partly retrospective) self-report method used in the questionnaire may have rendered some of the measures less reliable, which also affects the power to detect genetic effects. We tried to deal with these limitations by focusing our discussion on the broad sense heritability h^2, rather than distinguishing between a^2 and d^2, and on the overall heritability of the four general domains, rather than the 34 individual external factors. For reasons of power, we also adopted a somewhat liberal pose by testing all effects against a criterion level α of .05, rather than using e.g., Bonferroni correction to correct for multiple testing. However, as can be seen in Tables 3-6, almost all genetic effects would have been considered statistically significant if a more stringent criterion level of .01 or even .001 would have been used.

General conclusion

To conclude, this study shows significant heritability of various aspects of *Childhood Environment, Social Environment and Behavior, Leisure Time Activities,* and *Life Events* that play a prominent role in the social sciences literature. This suggests that what we think of as measures of the 'environment' are better described as *external factors.* These results are a valuable addition to existing discussions on how environmental factors shape individual differences in behavior (Scarr & McCartney, 1983; Plomin et al., 1985; Plomin & Daniels, 1987; Kendler & Baker, 2007) and have crucial implications for understanding the complex nature between genetic and environmental influences on complex traits.

Chapter 5

Sex differences in adults' motivation to achieve

ABSTRACT

Achievement motivation is considered a prerequisite for success in academic as well as non-academic settings. We studied sex differences in academic and general achievement motivation in an adult sample of 338 men and 497 women (age 18 - 70 years). Multi-group covariance and means structure analysis (MG-CMSA) for ordered categorical data was used to establish the location of possible sex differences, i.e., on the level of the latent factors or on the level of the observed items (i.e., sex-related item bias). Five of the 28 achievement motivation items showed severe bias with respect to sex, exemplifying the usefulness of MG-CMSA in locating the source of sex differences. The Academic Achievement Motivation scale consisted of two latent factors: Dedication and Persistence. Sex differences were observed for the factor Dedication only, with women showing more dedication towards their academic work than men. The General Achievement Motivation scale consisted of five latent factors: Pressure, Accomplishment, Work Approach, Future Orientation, and Competition. Sex differences were significant for the factor Future Orientation, with women contemplating less about the future than men, and a trend towards significance (p=.06) was observed for the factor Competition, with women being less actuated by competitive motives than men. These results suggest that sex-related item bias merits attention in achievement motivation research, but that men and women still differ in aspects of achievement motivation when biased items are eliminated from the analyses.

INTRODUCTION

Achievement motivation is considered a prerequisite for success, not only in academic, but also in sports- and job-related situations. In academic settings, the interest in motivation is partly inspired by the notion that students' motivation, operationalized, e.g. as their competency beliefs and value beliefs, could be more malleable than their cognitive ability, and as such could prove to be a potential lead for the educational system for improving learning and achievement processes in students (e.g. Spinath et al., 2006).

Sex differences in achievement motivation have been studied widely (Meece et al., 2006). In the context of academic achievement, gender role stereotypes are confirmed when motivation is studied domain-specifically, with boys being more confident and interested in mathematics and science compared to girls, while girls prefer, and feel more confident about language-related domains compared to boys. Researchers have studied whether these sex differences in motivation can predict sex differences in academic achievement (e.g. Freudenthaler et al., 2008; Steinmayr & Spinath, 2008). In all these studies, motivation-related items and subscale scores are compared directly between boys and girls. It has, however, never been verified whether these items or subscales are actually directly comparable, i.e., are measurement invariant across sex (see below). Yet, if the factor structure of a motivational instrument is not equal in boys and girls, differences in item-, or sumscores should be interpreted with caution. That is, when the measurement model is not equivalent across sex, differences between boys and girls in test scores do not necessarily reflect differences in achievement motivation. The present study is concerned with sex differences in academic achievement motivation and general achievement motivation in an adult sample, and explicitly deals with the question of whether the motivational instrument is measurement invariant across sex.

In 2006, Meece and colleagues (Meece et al., 2006) published a comprehensive review of studies on sex differences in motivation. Studies on motivation have mainly focused on the school-going population, and report sex differences for motivation-related constructs such as expectations for success, causal attribution of failure/success, competency beliefs, value beliefs (i.e., perceived importance, usefulness, interest, and costs of academic activities), and self-efficacy judgements (i.e., one's confidence in learning, performing and succeeding academically). These sex differences mostly follow gender norms and stereotypes. Boys are more confident than girls with respect to math, science, and sports related abilities. In addition, boys value these abilities more highly, and attribute their success in these domains to ability while girls attribute their math or science related success mostly to effort and hard work. Contrarily, girls are more confident than boys in domains concerning verbal and language abilities, value these abilities more highly than boys do, and attribute their success in these domains to their own ability. Noteworthy, however, is that these findings are not consistent, and seem to depend not only on the achievement domain for which motivation is measured, but also on socioeconomic status, ethnicity, and actual ability level. In addition, all these studies focus on sex differences observed in adolescents, while sex differences in adults' work- or career-related achievement motivation have not received much attention.

In adolescents, studies focussed on academic achievement motivation, examining whether motivation predicts academic success independently of cognitive ability. Sex

differences in academic achievement have been observed in many countries (USA: Epstein et al., 1998; Grant & Rong, 1999; Japan: Wong et al., 2002; Belgium: Van Houtte, 2004; Netherlands: de Knecht-van Eekelen et al., 2007; CITO, 2009). The question logically following from this is whether these sex differences in achievement can be explained by sex differences in motivation.

In 17 year olds, Steinmayr and Spinath (2009) report that motivational aspects like hope for success, fear of failure, and need for achievement contributed to the prediction of academic achievement over and above general IQ and prior achievement. Although the additional effects of the motivational constructs to the prediction of academic success were smaller ($R^2 < 10$ %) than the effects of general intelligence ($R^2 \approx 12\%$) and of prior achievement ($R^2 \approx 24\text{-}52\%$), the authors emphasized the importance of motivation because of its possible susceptibility to intervention.

In another study in 17 year olds, Steinmayr and Spinath (2008) observed sex differences for almost all motivation-related predictors included in their study. On average, girls expressed less hope for success, less work avoiding behaviour, and less confidence in their math-related ability, while at the same time rating math as less interesting, important and useful than boys. Boys, on the other hand, showed less fear of failure, less interest in learning as a goal in itself, and they were less confident about their German-language related ability, but also valued language as less important and useful than girls. Sex differences were however not apparent for performance-avoidance (i.e., avoiding mistakes) and performance-approach (seeking other people's appreciation of one's own intellectual ability), and the relations of these motivational predictors to academic achievement were similar across sex.

Conversely, Freudenthaler et al. (2008) did report sex differences in prediction of academic achievement in 14 year olds. In boys, self-esteem, intrinsic motivation, performance avoidance, and school anxiety predicted academic achievement over and above IQ, while in girls, only work avoidance (i.e., doing no more than strictly required) and self-esteem did. In yet another study in 13-year old female students, Gagné and St Père (2002) observed no relation whatsoever between self-reported motivation on the one hand, and IQ and academic achievement on the other. In that study, only self-reported persistence was slightly related to academic achievement.

In sum, sex differences in motivational constructs, and sex differences in the relation between these motivational constructs on the one hand, and actual academic achievement on the other, have been found, but not consistently. Mediating effects of socioeconomic status, ethnicity, age, and actual ability level have been put forward as explanations for the inconsistencies. Another possible source of inconsistency, however, is that the tests and items used to measure motivation are not identical across studies, leaving open the possibility that the inconsistencies between studies are due to the use of different instruments. In addition, inconsistency may result when test- and item-scores are not directly comparable between boys and girls, i.e., when items do not measure exactly the same constructs in boys and girls, e.g., because the connotation of the item is sex dependent. Such item bias could result in different relationships between items in boys and girls (and thus different underlying factor structures), and the sex differences observed on such biased items may not be indicative of sex differences in actual achievement

motivation. If a test or items of a test are biased with respect to sex, then sex differences in the scores on this test are difficult to interpret.

One flexible framework for testing, and accommodating, group differences within the context of factor models is multi-group covariance and mean structure analysis (MG-CMSA, Sorbom, 1974; Little, 1997; Widaman & Reise, 1997). This method, which has been used in studies on group differences in intelligence (e.g., Dolan & Hamaker, 2001; Wicherts et al., 2004; Dolan et al., 2006; van der Sluis et al., 2006; van der Sluis et al., 2008a), provides a model-based means to investigate the main source(s) of group differences. MG-CMSA allows one to test whether sex-differences observed at the level of specific items are indeed a function of sex-differences on the level of the latent trait(s) underlying the response to these items. When differences in scores on individual motivation items are not indicative of differences in actual motivation, then this may indicate that the item differences reflect a situation- or ability-specific difference between boys and girls, rather than a difference in motivation per se. In the context of MG-CMSA, items are considered 'biased' when the mean differences observed on the level of the item can not be explained by mean differences on the level of the latent factor. The term 'bias' does not imply that the observed sex difference on the item is not real, but simply that the difference observed for the item is smaller or greater than the difference expected based on the means of the underlying factor, and can therefore not be taken as indicative of a sex difference in the latent trait. MG-CMSA can be used to locate such bias.

In addition, MG-CMSA allows one to evaluate and compare the fit of different models that reflect different hypotheses. In most research on motivation, researchers have used sum scores. The implicit assumption with respect to the sum score model is that the factor model underlying the test is 1-dimensional, and that all items are equally informative of the trait of interest. Whether such a highly-restricted model fits the data, i.e., describes the variance-covariance and means structure of the data adequately, is usually not tested. However, if that model does not describe the data adequately, then the sex differences are tested within the context of a poorly fitting model, which could result in incorrect conclusions with respect to the presence, and source, of sex differences.

The aim of the present paper is to investigate sex differences in academic achievement motivation and general achievement motivation in adults using MG-CMSA. Specifically, we investigate whether sex differences in achievement motivation test scores are really indicative of sex differences in the achievement motivation trait, or more likely of sex-related item bias. Below, we will first outline the MG-CMSA procedure for categorical data that we used to investigate the sources of sex differences in our motivational instruments. For convenience, results are presented separately for academic achievement motivation and general achievement motivation.

METHOD

Participants

All participants in this study were volunteer members of the Netherlands Twin Register (Boomsma et al., 2006) who participated in a larger ongoing study on the interplay between genes and environment on cognition. As part of this extended family study,

participants were asked to fill out a questionnaire, which included the 28 questions on achievement motivation, which are used in the present study. At the time of publication, data were available from 284 families, including data from twins, and their siblings, and the parents, children, and partners of these twins and sibling (note that not all relations were represented in all families). The sample comprised 835 subjects in total: 338 men and 497 women. The overrepresentation of women in our study sample may affect the generalizability of this study's results to other populations (see Discussion). It does not, however, detract from the illustrative value of using MG-CMSA in the context of motivation research.

Because of the nature of the data collection, the age range was considerable (from 18 to 70, M=45.37, SD=14.08), but age did not differ significantly between men and women (t(833)<1, ns). Age was included as a covariate in all confirmatory factor analyses.

Instrument

The items used in this study were part of a larger questionnaire on life experiences, which was administered as part of the study on the interplay between genes and environment on cognition. The entire questionnaire took about 50 minutes to complete. The 28 multiple-choice achievement motivation items were adopted from the Dutch 'Prestatie Motivatie Test' (Dutch Achievement Motivation Test, DAMT; Hermans, 2004)[2]. Ten of the 28 achievement motivation items focused on the academic achievement motivation subscale (AAM, e.g., "When I was in school, the demands that I made on myself concerning studying were very high / high / pretty high / low"; "Studying hard in school was something I did not like at all / did not like much / liked a lot"), while the other 18 focused on the general achievement motivation subscale (GAM, e.g., "The demands that I make on myself at work are very high / high / pretty high / not that high"; "The urge to surpass myself is very strong / pretty strong / not very strong")[3]. All items were categorical in nature with 2 to 4 ordered answer options (See Supplementary Information for more example items). Negative items were recoded such that for all 28 items, higher scores reflect higher achievement motivation. The reliability of the AAM and the GAM subscales was .83, and .75, respectively.

Like many motivation instruments, AAM and GAM are self-report measures. In addition, our adult participants were asked to retrospectively evaluate their academic and general achievement motivation. Both the retrospective character and the self-reporting nature of the scales formed a potential source of bias in the evaluation of a person's motivation to achieve (see Discussion). It does not, however, detract from the illustrative value of using MG-CMSA in the context of motivation research.

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2   The original DAMT consists of three more subscales, tapping into positive and negative fear of failure and social desirability, but these were not included in the larger questionnaire for reasons of efficiency.

3   The original general achievement motivation subtest consists of 20 rather than 18 items. Two items were, however, eliminated because they did not correlate with the other 18, which hindered the factor model fitting. As the content of these two items was also very different from the other 18 (one item asked whether one likes to organize things, the other asked the participant's opinion on the expression 'time is money'), we decided to discard these two items from all subsequent analyses.

STATISTICAL ANALYSES

Exploratory factor analysis

The factor structure of the two subscales of the DAMT has not been studied before. We therefore first conducted exploratory factor analyses for ordered-categorical items to investigate the number of factors required to describe the structure of the AAM and GAM subscales, and, if multiple factors were required, to establish the pattern of factor loadings. These exploratory analyses were conducted in *Mplus* version 5 (Muthen & Muthen, 2005), for men and women separately, and were followed by an oblique rotation (geomin).

Confirmatory factor analysis and testing for the presence of measurement invariance

To examine sex differences with respect to the latent factors of academic and general achievement motivation, one first needs to establish whether the AAM and GAM subscales are measurement invariant with respect to sex. Measurement invariance with respect to sex implies that the distribution of the observed scores of subjects i on an item j (y_{ij}), given a fixed level of the latent factor (η), depends on the score on the latent factor η only, and not on sex, i.e., $f(y_{ij}|η,sex) = f(y_{ij}|η)$ (Mellenbergh, 1989). That is, given equal latent factor scores η, men and women should score similarly on item j. In the case of continuous items, and given normally distributed data, measurement invariance can be defined in terms of the means and variances of y_{ij} given η. With ordered-categorical data the definition is however somewhat different.

In factor models for ordered-categorical data, the observed scores for item y_{ijk}, i.e., the jth ordered categorical measure for the ith person in the kth group (where sex defines the two groups in the present paper), are assumed to be determined by the unobserved scores on the latent response variate y^*_{ijk}. These latent response variates are continuous in scale, and the observed measures y_{ijk} can be considered a categorized versions of the latent variates y^*_{ijk}, where the scores on the categorized items y_{ijk} depend on the threshold parameters $v_{jk(0...c-1)}$, where c is the number of categories, of the jth item in the kth group (Millsap & Yun-Tein, 2004).

Given p items, the scores on the vector of latent response variates for the ith person in the kth group, y^*_{ik}, are within each subgroup assumed to be multivariate normally distributed (y^*_{ik} ~ MVN($μ^*_k, Σ^*_k$)), where $μ^*_k$ is a p x 1 vector of means of the latent response variates, and $Σ^*_k$ is a p x p covariance matrix for the latent response variates, each estimated separately in each subgroup k.

Given the latent response variate y^*_{ijk}, the factor model is specified as:

$$y^*_{ijk} = τ_{jk} + λ_{jk}η_{ik} + ε_{ijk}, \tag{1}$$

where $τ_{jk}$ is a latent intercept parameter, $λ_{jk}$ is a r x 1 vector of factor loadings of the jth variate on the r factors, $η_{ik}$ is the r x 1 vector of factor scores of the ith person in the kth group, and $ε_{ijk}$ denotes the jth unique factor score for that person. If $ε_{ik}$ is the 1 x p vector of unique factor scores, it is assumed that $η_{ik}$ ~ MVN($κ_k, Ψ_k$), where $κ_k$ is the r x 1 vector of factor means and $Ψ_k$ denotes the r x r factor covariance, and that $ε_{ik}$ ~ MVN($0, Θ_k$), where $Θ_k$ denotes the p x p (usually diagonal) matrix of residual (or unique) variances, i.e., the variance not explained by the latent factors η.

The model implied expected values for the vector of latent response variates $\mathbf{y^*}_{ik}$ are given as:

$$E(\mathbf{y^*}_{ik}) = \mathbf{\mu^*}_k = \mathbf{\tau}_k + \mathbf{\Lambda}_k\mathbf{\kappa}_k, \tag{2}$$

and the model implied covariance matrix is given as:

$$Cov(\mathbf{y^*}_{ik}) = \mathbf{\Sigma^*}_k = \mathbf{\Lambda}_k\mathbf{\Psi}_k\mathbf{\Lambda'}_k + \mathbf{\Theta}_k, \tag{3}$$

where $\mathbf{\Lambda}_k$ is the p x r matrix of factor loadings, with $\mathbf{\Lambda'}_k$ denoting the transpose of this matrix. Note that to begin with, all factor model parameters ($\mathbf{\tau}_k$, $\mathbf{\Lambda}_k$, $\mathbf{\kappa}_k$, $\mathbf{\Psi}_k$, $\mathbf{\Theta}_k$) are estimated separately in the different groups (as denoted by subscript k). However, not all parameters may be identified, especially when the observed items are ordered-categorical.

To establish measurement invariance with respect to sex in a factor model for ordered-categorical data, one needs to establish whether the relation between the observed item scores y_{ijk} (via the latent variates y^*_{ijk}) and the underlying latent factor(s) $\mathbf{\eta}$ is the same in men and women. Measurement invariance with respect to sex can be examined through a series of constraints on the model parameters (Meredith, 1993; Millsap & Yun-Tein, 2004), which are, to begin with, estimated separately in men and women.

To test whether the mean structure and the covariance structure of the AAM and GAM subscales were measurement invariant across sex, multi-group confirmatory factor analysis for ordered categorical data had to be carried out. Below we will give a short overview of the constraints required to identify the factor model, and to test for measurement invariance when data are categorical. We refer to Millsap & Yun-Tein (2004) for more details on and the rationale behind these constraints. All steps required to test for measurement invariance were previously described and discussed in detail by Horn & McArdle (1992) and Widaman & Reise (1997).

The first step (Model 1) in testing for measurement invariance concerned the test for 'configural invariance', i.e., the test of whether the pattern of factor loadings (and correlated residuals, if present) was the same in men and women, while the actual values of these parameters were allowed to differ across sex. Several constraints were required to identify this model. In all subsequent analyses, we chose the male group as a reference group. In this group, the latent intercepts $\mathbf{\tau}$ and the factorial means $\mathbf{\kappa}$ needed to be fixed to 0, and all thresholds $\mathbf{v}$ were estimated freely. In the women, however, we needed to constrain one threshold per item to be sex-invariant, i.e., to be equal to the threshold of the men. In addition, we needed to pick r reference items (i.e., one for each latent factor) for which the second threshold was constrained to be sex-invariant as well. All remaining thresholds were estimated freely in the women, just as the factorial means $\mathbf{\kappa}$, which were identified due to the constraints on the thresholds. The latent intercepts $\mathbf{\tau}$ were however fixed to 0 in women as well. As with continuous data, one needs to fix the arbitrary scale of the latent factor; we chose to fix the factorial variances to 1 in both groups. The categorical nature of the observed data requires one to also adopt a scale for the continuous latent variates underlying the categorical response data. To this end, the residual variances were fixed to 1 in the male reference group (i.e., the so-called theta parameterization in Mplus, see Muthen & Muthen, 2005), but these parameters could then be estimated freely in

the women (unless an item is dichotomous in nature, in which case its' residual variance needs to be fixed to 1 in the women as well). We refer to Millsap & Yun-Tein (2004) for an elaborate discussion of these constraints.

In the second step (Model 2), we tested for 'metric invariance'. Metric invariance implies that the relations between the observed items on the one hand and the latent factor on the other are the same across sex. The test for metric invariance thus involves constraining all factor loadings to be equal across sex. Note that metric invariance is a prerequisite for meaningful comparison of the latent factors across sex: only when the factor loadings are equal across sex, can we be sure that the latent factors themselves are identical, and thus comparable, between men and women. Metric invariance is said to be tenable when the equality constraints on the factor loadings do not result in a significant deterioration of the overall model fit. Note that as a result of these constraints on the factor loadings, fixation of the factorial variances in both groups became superfluous: the factorial variances remained fixed to 1 in the male reference group, but could now be estimated freely in the women.

In the third step (Model 3), we tested for 'strong factorial invariance'. Strong factorial invariance implies that the mean differences that are observed between men and women on the level of the observed items can all be accounted for by the latent factor, i.e., are indicative of mean differences on the latent trait of interest. The test for strong factorial invariance thus involves constraining all thresholds to be equal across sex. These constraints allowed free estimation of the factorial means of the female group, while the factorial means in the male reference group remained fixed to 0 for identification purposes. Modeled as such, the factorial mean of the women should be interpreted as deviation from the factorial means of the men (i.e., deviations from zero). Note that in this model, sex differences in observed scores y_{ijk} can only result from sex differences in factorial means, because, at this point in the model fitting sequence, these factorial means are the only parameters that differ across sex in the regression of the items on the latent factors. In other words, if the constraints implied by strong factorial invariance hold, i.e., do not lead to a significant deterioration of the model fit, then the assumption that the expected observed scores depend only on a subject's factor score and not on the subject's sex holds, i.e., $E(y_{ijk}|\eta,sex) = E(y_{ijk}|\eta)$. If these constraints do however result in a significant deterioration of the model fit, then the latent factors cannot account for the sex differences in observed scores, i.e., one or more of the differences in thresholds between men and women cannot be accounted for by the latent factors. Comparing men and women with respect to their latent factor means is only meaningful if strong measurement invariance holds. Those items, for which the sex differences observed on the level of the thresholds cannot be explained by sex differences on the level of the latent factor, are considered biased with respect to sex.

The fourth step (Model 4) tested for strict factorial invariance. Strict factorial invariance implies that the residual variances, i.e., the parts of the observed items that are not explained by, or related to, the latent factor, are also equal across sex. Strict factorial invariance thus involves constraining the residual variances to be also equal across sex. Note that because of the categorical nature of the items, the residual variances were fixed to 1 in the male reference group, and were estimated freely in the women. In the context of categorical data, the test for strict factorial invariance thus implies fixing the residual

variances in women to 1 as well. If these constraints were tenable, we concluded that all sex differences with respect to the observed scores on the items, and the relations between the items, could be accounted for by sex differences on the level of the latent factor. Note however that for the comparison of threshold or factor means between men and women, strict factorial invariance is not required (i.e., strong factorial invariance suffices).

Finally (Model 5), when at least strong factorial invariance holds (i.e., the constraints in Model 4 are tenable), we were ready to test whether the factorial means were the same in men and women. Note that for reasons of identification, the factorial means were fixed to 0 in the male reference group, and were freely estimated in the women. The test for equal factor means thus involves fixing the factorial means of the women to zero as well. If this constraint resulted in a significant deterioration of the model fit, then we concluded that men and women differed with respect to the latent trait of interest (i.e., achievement motivation in the present study).

General model fitting strategies

For reasons of convenience in reporting results and estimation of parameters, all analyses were conducted separately for the academic achievement motivation (AAM) subscale and the general achievement motivation (GAM) subscale. Note that in theory, the factor structure and the model fitting results could be different for subsets of items, compared to the results for the complete item set, e.g. because items of the AAM subscale can not load on the factors of the GAM subscales if they are analyzed separately. However, when the separate factor models of the AAM and the GAM were eventually combined in one overall model (the Total Model in the Results section), this model showed good fit, and no large modification indices (indices of local misfit in the model) or large residuals (i.e., parts not explained by the model). The choice to start with exploratory and confirmatory factor analyses in the two subscales separately turned therefore out to be justified.

All items were regressed on a standardized measure of age to correct for possible age effects.

Because the data were collected within families, the observations could not be considered independent. As treating within-family data as if they are independently distributed observations results in incorrect standard errors and incorrect χ^2 goodness of fit statistics, all analyses were performed in *Mplus* version 5 (Muthen & Muthen, 2005), which computes corrected standard errors and Satora-Bentler scaled χ^2-tests with adjusted number of degrees of freedom, taking into account the dependence of the observations. The fit of nested models can then be compared through a weighted χ^2-difference test (Satorra, 2000). More restricted (i.e., nested) models are accepted if their fit is not significantly worse than the fit of the less restricted model, i.e., if the weighted χ^2-difference test (henceforth χ^2_{diff}) is not significant. Below, we will not report the scaled χ^2-values for each model, as these are not informative, but rather report the weighted χ^2_{diff} tests for the comparisons of competing models.

The fit of ensuing models to the data were also evaluated using the Root Mean Square Error of Approximation (RMSEA) and the Comparative Fit Index (CFI Bentler, 1990; Bollen & Long, 1993; Joreskog, 1993; Schermelleh-Engel et al., 2003). The RMSEA is a measure of the discrepancy (i.e., error of approximation) between the covariance and

mean structure implied by the fitted model, and the covariance and mean structure in the population. Calculating the discrepancy per degree-of-freedom, this fit index favours more parsimonious models. Generally, as a rule of thumb, RMSEA values < .05 are taken as indicative of good fit (i.e., good approximation), RMSEA-values between .05 and .08 indicate acceptable fit, and values larger than .08 indicate poor fit (Brown et al., 1983; Schermelleh-Engel et al., 2003). The CFI is based on the comparison between the independence model, i.e., the model in which all variables are modelled as unrelated, and the user-specified model. The CFI, for which theoretically values range between 0 and 1.00, favours more parsimonious models, and takes on larger values when the difference between the independence model and the hypothesized model increases. Usually, values > .95 are taken to indicate good model fit, and values between .90 and .95 indicate acceptable fit (Hu & Bentler, 1999; Schermelleh-Engel et al., 2003).

The RMSEA and the CFI were used only as indication of the general fit of models, while the scaled χ^2-tests and weighted χ^2_{diff} tests were used specifically when testing the effects of the constraints required for measurement invariance. Modification indices, which express the expected drop in scaled χ^2 if constrained parameters are estimated freely, were used to detect local misfit in models.

Raw data maximum likelihood estimation was used to accommodate missingness (mean percentage of missingness across the entire 28-item DAMT was 1.47 % (SD=1.05) with a maximum of 4.4 % for one of the academic motivation items[4]).
For all analyses, α was set at .05.

RESULTS

Preliminary analyses

Table 5.1 shows the endorsement rated in valid percentages for the 10 items of the AAM subscale for men and women separately. Effect size r is calculated as the Z-score obtained from a Mann-Whitney test (i.e., the non-parametric test comparing two independent groups with respect to their ranks scores on a categorical measure: the Z-score is a measure of whether the smallest sum of ranks deviates from the expected sum of ranks), divided by the square root of the total number of observations, i.e., Z/√N (Rosenthal, 1991). Most effect sizes for the AAM items were small and positive, implying that women scored overall somewhat higher than men, i.e., were somewhat more motivated or more zealous. The largest effect size was observed for item AAM4 ("In school, people thought I was quite lazy/ not very diligent / diligent"), where women remembered themselves more often as being considered more zealous than men.

The polychoric correlations between the 10 AAM items are shown in Table 5.2 for men and women separately.

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4   Note that missingness on some of the academic achievement motivation items was significantly related to the age of the participants, with missingness being more frequent in older subjects. This could suggest that questions about academic achievement motivation are more difficult to answer when the school years are in the remote past, or that academic training was less often granted to the older participants, rendering questions about e.g. homework unsuitable.

Table 5.1 Endorsement rates of the 10 Academic Achievement Motivation (AAM) items for men and women separately

	Men				Women				Effect size r
	Cat 1	Cat 2	Cat 3	Cat 4	Cat 1	Cat 2	Cat 3	Cat 4	
AAM1	8.9	50.3	40.8	-	6.7	42.5	50.8	-	.10
AAM2	59.9	40.1	-	-	58.6	41.4	-	-	.01
AAM3	21.0	61.0	18.0	-	16.4	62.9	20.7	-	.06
AAM4	28.1	25.4	46.5	-	20.7	8.0	71.3	-	.21
AAM5	9.7	44.8	40.9	4.5	4.5	34.1	52.9	8.5	.17
AAM6	36.7	47.4	15.9	-	27.0	53.9	19.1	-	.10
AAM7	22.5	42.3	29.1	6.0	18.5	37.6	34.1	9.9	.09
AAM8	61.8	31.5	6.7	-	54.7	34.3	11.0	-	.08
AAM9	14.3	31.3	40.4	14.0	18.1	26.7	41.9	13.3	-.01
AAM10	10.5	38.4	51.1	-	7.7	37.9	54.4	-	.04

Notes: Number of ordered answer options varies across items (range: 2 – 4). Higher categories correspond to higher motivation. Effect size r is calculated as Z/√N, where Z is obtained in a Mann-Whitney test, and N is the effective sample size (men + women) for each individual item. Positive effect sizes denote higher academic achievement motivation for women.

Table 5.2 Polychoric correlations between the 10 Academic Achievement Motivation (AAM) items for men (below diagonal) and women (above diagonal) separately

	AAM 1	AAM 2	AAM 3	AAM 4	AAM 5	AAM 6	AAM 7	AAM 8	AAM 9	AAM 10
AAM1		.37	.44	.41	.57	.34	.55	.39	.54	.55
AAM2	.41		.33	.29	.40	.44	.33	.33	.27	.23
AAM3	.34	.35		.46	.35	.27	.54	.42	.50	.35
AAM4	.49	.27	.46		.47	.28	.55	.47	.57	.32
AAM5	.49	.47	.34	.43		.48	.47	.57	.50	.52
AAM6	.35	.44	.37	.31	.45		.30	.42	.29	.39
AAM7	.38	.27	.57	.58	.44	.36		.44	.57	.44
AAM8	.38	.41	.37	.37	.50	.45	.38		.44	.37
AAM9	.53	.22	.39	.48	.38	.32	.47	.33		.50
AAM10	.47	.27	.39	.39	.37	.39	.38	.35	.48	

The endorsement rates (in valid percentages) for the 18 GAM items are shown in Table 5.3. The effect sizes for the GAM items were mostly small but the more sizable ones were negative, implying that women scored somewhat lower than men. The largest effect size was observed for item GAM4 ("As the manager of a factory you are often very busy and overworked. I would certainly not want such a job / would not readily accept such a job / would really like such a job".)

Table 5.3 Endorsement rates of the 18 General Achievement Motivation (GAM) items for men and women separately

	Men				Women				
	Cat 1	Cat 2	Cat 3	Cat 4	Cat 1	Cat 2	Cat 3	Cat 4	Effect size r
GAM1	2.4	15.7	56.4	25.5	1.4	22.2	48.0	28.4	-.01
GAM2	1.2	14.5	54.7	29.6	.6	13.3	57.6	28.5	.00
GAM3	19.6	55.2	25.2	-	13.9	64.2	21.8	-	.01
GAM4	22.0	49.7	28.3	-	33.8	55.7	10.5	-	-.21
GAM5	6.5	74.7	18.8	-	6.4	82.8	10.9	-	-.09
GAM6	13.4	39.2	38.3	9.2	9.9	51.1	32.3	6.7	-.05
GAM7	35.7	34.5	25.9	3.9	42.6	35.3	18.7	3.4	-.09
GAM9	5.3	24.9	69.7	-	9.0	34.2	56.8	-	-.13
GAM10	47.6	36.5	15.9	-	46.2	39.5	14.4	-	.00
GAM11	15.5	37.8	29.2	17.6	15.1	34.0	33.0	17.9	.03
GAM12	27.5	46.2	26.3	-	20.6	50.7	28.7	-	.06
GAM13	14.9	38.2	36.4	10.4	10.6	39.7	40.7	9.0	.03
GAM14	14.9	15.8	69.3	-	12.7	18.2	69.1	-	.00
GAM15	13.9	40.6	45.5	-	11.6	47.0	41.4	-	-.02
GAM16	13.6	50.1	36.2	-	22.8	55.8	31.4	-	-.03
GAM17	6.6	42.9	46.8	3.6	3.3	39.8	50.6	6.3	.08
GAM19	49.1	22.5	23.1	5.4	59.7	22.0	15.7	2.6	-.12
GAM20	4.8	37.0	49.4	8.7	5.1	33.7	50.3	10.8	.03

Notes: Number of ordered answer options varies across items (range: 3 – 4). Higher categories correspond to higher motivation. Effect size r is calculated as Z/√N, where Z is obtained in a Mann-Whitney test, and N is the effective sample size (men + women) for each individual item. Positive effect sizes denote higher academic achievement motivation for women.

The polychoric correlations between the 18 GAM items are shown in Table 5.4 for men and women separately. Important to note is that, although some correlations were higher than .35, many correlations between these categorical items were lower than .20.

Whether the small differences observed between men and women on the categorical items, were indicative of differences on the latent level, was further examined using multi-group covariance and means structure analysis (MG-CMSA). First, however, the factor structure of the AAM and the GAM was established using exploratory factor analysis.

Exploratory factor analyses (EFA)
Because the factor structure of the subscales AAM and GAM has not been studied before, exploratory factor analyses were conducted in order to get a first impression of the pattern of factor loadings. As explained before, analyses were conducted separately for the AAM and the GAM.

Academic Achievement Motivation
With respect to the AAM, an exploratory factor solution with two correlated factors showed a good fit in both men (CFI=.98, RMSEA=.036) and women (CFI=.98, RMSEA=.046). Table 5.5 shows the geomin rotated factor loadings of the 10 AAM items on the two correlated factors for men and women separately.

Table 5.4 Polychoric correlations between the 18 General Achievement Motivation (GAM) items for men (below diagonal) and women (above diagonal) separately

	GAM 1	GAM 2	GAM 3	GAM 4	GAM 5	GAM 6	GAM 7	GAM 9	GAM 10	GAM 11	GAM 12	GAM 13	GAM 14	GAM 15	GAM 16	GAM 17	GAM 19	GAM 20
GAM1		.30	.06	.31	.18	.41	.22	.06	.52	.24	.28	.20	-.02	.08	.20	.23	.38	.39
GAM2	.31		.10	.21	.18	.16	.14	.10	.27	.10	.18	.16	.06	.02	.20	.44	.10	.43
GAM3	.16	.08		.13	.19	.15	-.04	.16	.10	.10	.05	.16	.50	.22	.04	-.02	.12	.15
GAM4	.29	.30	.12		.25	.15	.25	.14	.28	.16	.11	.11	.09	.26	.36	.08	.34	.16
GAM5	.25	.15	.16	.27		.11	.06	.14	.10	.04	.04	.06	.10	.28	.16	-.02	.21	.16
GAM6	.36	.12	.13	.04	.02		.12	.16	.38	.16	.15	.06	.10	.10	.07	.11	.21	.16
GAM7	.25	.17	.16	.28	.26	.09		-.11	.23	.15	.08	.21	-.07	.20	.64	.06	.25	.06
GAM9	.13	.15	.04	.15	.09	.13	.11		.06	.06	-.03	.03	.43	.07	.15	-.09	-.02	.20
GAM10	.49	.17	.12	.25	.18	.35	.36	.02		.26	.33	.20	.07	.23	.32	.21	.50	.30
GAM11	.23	.20	.09	.21	.17	.08	.12	.14	.21		.11	.16	.13	.12	.23	.02	.18	.33
GAM12	.07	.05	.08	-.02	.02	-.04	.17	-.15	.22	-.00		.17	.01	.13	.05	.10	.45	.20
GAM13	.16	.02	.24	.14	-.05	.14	.25	-.01	.17	.06	.18		.17	.26	.18	.13	.26	.16
GAM14	.18	.17	.52	.23	.12	.07	.27	.22	.02	.19	.03	.15		.34	.15	-.03	-.01	.19
GAM15	.19	.03	.32	.33	.16	-.04	.22	-.01	.11	.09	.28	.28	.31		.36	.01	.34	.12
GAM16	.17	.11	.23	.32	.24	.09	.66	-.01	.34	.16	.14	.19	.27	.45		.12	.27	.21
GAM17	.09	.41	.03	.19	-.09	.02	.18	.03	.12	-.03	.05	-.05	.17	.04	.16		.09	.21
GAM19	.43	.22	.05	.33	.27	.13	.27	.01	.58	.13	.28	.37	.10	.33	.39	.17		.15
GAM20	.41	.44	.13	.27	.31	.18	.20	.19	.26	.33	.06	.15	.22	.12	.17	.27	.26	

Table 5.5 Geomin rotated (oblique) exploratory factor solution for the 10 Academic Achievement Motivation (AAM) items for men and women separately

	Men (N=338)		Women (N=497)	
	Factor 1 Dedication	Factor 2 Persistence	Factor 1 Dedication	Factor 2 Persistence
AAM1	**.313**	.412	**.374**	.405
AAM2	-.231	**.829**	.038	**.514**
AAM3	**.634**	.013	**.695**	-.017
AAM4	**.613**	.088	**.723**	.085
AAM5	**.637**	.096	**.629**	.086
AAM6	.056	**.692**	.000	**.823**
AAM7	**.878**	-.128	**.812**	-.004
AAM8	.013	**.629**	-.146	**.734**
AAM9	.005	**.662**	.185	**.516**
AAM10	**.377**	.260	**.192**	.497

Notes: Factor loadings in bold print are estimated freely in the subsequent confirmatory multi-group covariance and means structure analyses.

The items loading on the first factor all represent Dedication (willingness to study and allocate time to homework), while the items loading on the second factor mostly refer to focus or Persistence (the ease with which one could start and continue doing school work in spite of distraction). Item 1 loaded on both factors, and item 10 loaded mainly on factor 1 in men, and on factor 2 in women. Based on the content of these items and the model fit statistics, however, we choose to let these items load on the Dedication factor only in all subsequent confirmatory factor analyses. In these analyses, the Persistence factor was thus indicated by 4 items (items 2, 6, 8, and 9), and the Dedication factor by 6 items (items 1, 3, 4, 5, 7, and 10). This configuration of factor loadings was used for the multi-group CFA analyses, with the bold factor loading of Table 5.5 estimated freely, and all other factor loadings fixed to zero.

General Achievement Motivation

Exploratory factor analyses on the 18 items of the GAM subscale showed that a factor solution with 5 factors described the data structure adequately in both men (CFI=.96, RMSEA=.029) and women (CFI=.96, RMSEA=.032). Table 5.6 shows the geomin rotated factor loadings of the 18 items on the 5 correlated factors for men and women separately.

Based on the content of the items, factor 1 represents the extent to which subjects experience time pressure as a result of their work (Pressure; items 2, 4, 17 and 20), factor 2 represents the intrinsic motivation to accomplish goals and to surpass oneself (Accomplishment; items 1, 5, 6, 10, 11, and 20), factor 3 gives an indication of work approach or avoidance, i.e., how much subjects are inclined to work in general (Work Approach; items 3, 9, 14 and 15), factor 4 gives an indication of how future-oriented subjects are (Future Orientation; items 4, 7 and 16), and factor 5 represents the extrinsic motivation of subjects to compete with others and to earn respect (Competition; items 10, 12, 13, 15 and 19). The pattern of factor loadings of items 4, 5 and 9 was somewhat different for men and women, but based on the content of these items, it was decided to start with a confirmatory factor model in which item 5 loaded on the Accomplishment factor, item 9 on the Work Approach factor, and item 4 on both factors Pressure and Future. This configuration of factor loadings was used for the multi-group CFA analyses, with the bold factor loading of Table 5.6 estimated freely, and all other factor loadings fixed to zero.

Table 5.6 Geomin rotated (oblique) exploratory factor solution for the 18 General Achievement Motivation (GAM) items for men and women separately

	Men (N=338)					Women (N=497)				
	Pressure	Accomplishment	Work Approach	Future Orientation	Competition	Pressure	Accomplishment	Work Approach	Future Orientation	Competition
GAM1	.081	**.563**	.074	-.017	.258	.037	**.732**	-.112	.005	.096
GAM2	**.787**	.015	-.025	-.078	.020	**.916**	-.010	.014	.016	-.004
GAM3	-.044	.070	**.664**	-.026	.029	.020	.023	**.559**	-.155	.141
GAM4	**.299**	.065	.087	**.221**	.113	.053	.151	.117	**.231**	.200
GAM5	.131	**.198**	-.046	.283	.015	.077	**.018**	.251	.044	.196
GAM6	-.128	**.456**	.058	-.026	.041	-.115	**.574**	.070	-.065	.001
GAM7	.042	.068	.005	**.691**	.017	-.008	.035	-.184	**.642**	.120
GAM9	.154	.254	**.031**	.077	-.205	-.006	.243	**.417**	.040	-.215
GAM10	.000	**.361**	-.189	.227	**.491**	.036	**.490**	-.021	.074	**.321**
GAM11	.104	**.284**	.091	.084	-.066	-.038	**.315**	.109	.117	.002
GAM12	.022	-.241	.112	-.026	**.493**	.142	.115	-.038	-.136	**.489**
GAM13	-.158	.022	.345	-.057	**.407**	.118	-.017	.175	.062	**.269**
GAM14	.192	.029	**.707**	.050	-.163	.026	.023	**.870**	-.045	-.026
GAM15	.011	-.243	**.474**	.140	**.361**	-.078	-.129	**.409**	.179	**.392**
GAM16	-.040	-.067	.065	**.914**	.011	.048	.012	.019	**.990**	-.024
GAM17	**.592**	-.208	-.011	.018	.006	**.483**	.027	-.135	-.008	.049
GAM19	.118	.059	-.024	.068	**.771**	-.022	.093	.003	.008	**.825**
GAM20	**.459**	**.300**	.071	-.003	.041	**.341**	**.353**	.149	.022	-.025

Notes: Factor loadings in bold print are estimated freely in the subsequent confirmatory multi-group covariance and means structure analyses.

Multi-Group Covariance and Means Structure Analysis (MG-CMSA)

Academic Achievement Motivation

The results and fit statistics of the multi-group CFA of the AAM items are presented in Table 5.7.

In Model 1, we tested for configural invariance, with 4 items loading on the Persistence factor, and 6 on the Dedication factor. No cross-loadings were modelled (i.e., congeneric structure), and all residual terms were modelled as uncorrelated. To correct for possible age effects, all 10 items were regressed on age in men and women separately. The CFI (.98) and the RMSEA (.06) indicated that Model 1 fitted the data well.

In Model 1a we tested whether the age regressions could be constrained to be equal in men and women, but this was not the case (Model 1a vs Model 1: χ^2_{diff}(6)=30.19, p<.001). In all subsequent models, age effects were therefore modelled separately in men and women. Note that this part of the model was saturated (i.e., all regressions on age were estimated) so that the age-correction could not contribute to model misfit.

To test for metric invariance, all factor loadings were constrained to be equal in men and women in Model 2, and the factor variances were estimated freely in the women (and fixed to 1 for reasons of identification in the male reference group). The model fit did not deteriorate significantly as a result of these constraints (Model 2 vs Model 1: χ^2_{diff}(7)=11.34, ns), implying that metric invariance across sex was tenable for the AAM subscale.

In Model 3, strong factorial invariance was tested by constraining all thresholds to be equal across sex, and estimating the factor means freely in women, while these remained fixed to 0 in the male reference group for reasons of identification. These constraints did however result in a significant deterioration of the model fit (Model 3 vs Model 2: χ^2_{diff}(9)=23.61, p<.01), implying that not all threshold differences observed between men and women could be accounted for by differences on the level of the factors. The modification indices indicated that the misfit was mainly due to item 4. Note that this is the diligence-item for which the largest effect size was observed in the item specific analyses (Table 5.1). In Model 3a, we constrained all thresholds equal across sex except the thresholds of item 4. This set of constraints did not result in a significant drop in model fit (Model 3a vs Model 2: χ^2_{diff}(8)=9.23, ns). For the AAM, strong factorial invariance was thus established for 9 out of 10 items, while the sex difference on item AAM4 was too large to be accounted for by the model, i.e., this item is biased in the context of this model. In the subsequent models, the thresholds for item 4 were therefore estimated freely in both groups. Note that free estimation of the thresholds for this item implies that this item no longer contributes to the estimation of the differences between men and women in the mean of the latent factor Dedication (Byrne et al., 1989). The mean of the Dedication factor was thus not biased, but directly comparable between men and women.

Strict factorial invariance was tested in Model 4 by restricting all residuals in the women to be equal to the residuals in the male reference group, i.e., equal to 1. The fit did not deteriorate significantly (Model 4 vs Model 3a: χ^2_{diff}(8)=9.14, ns), implying that strict factorial invariance was tenable. Table 5.8 shows the factorial correlations and factor means taken from Model 4 for men and women separately.

Given that the factor model was invariant across sex, we could subsequently

meaningfully test whether men and women differed with respect to the means of the two factors, Persistence and Dedication. In Model 4, the factor means were fixed to 0 in the male reference group for reasons of identification, while they were freely estimated in women, such that these estimates can be considered deviations from the factor means of the men. In Model 5, the mean of the Persistence factor was fixed to 0 in women, which did not result in a significant drop in model fit (Model 5 vs Model 4: $\chi^2_{diff}(1)=2.36$, ns), meaning that men and women did not differ significantly with respect to persistence. In Model 6, the mean of the Dedication factor was fixed to 0 in the women, resulting in a significant deterioration of the model fit (Model 6 vs Model 5: $\chi^2_{diff}(1)=9.52$, p<.01). The factor mean of the women was estimated at .33 (SD=1.05), implying that, on average, women remembered themselves to be more dedicated to their academic work than men.

The biased item (item 4) only loaded on the Dedication factor. If we would have calculated simple sum scores across the items of the Dedication factor (rather than subjecting the items to a factor model), and compared men and women with respect to these sum scores, as is common practice, then the presence of the biased item would have lead to an overestimation of the effect size of the sex difference in sum scores of .06 (effect size is .33 with, and .27 without the biased item).

Table 5.7 Results of the multi-group covariance and means structure analyses (MG-CMSA) for the Academic Achievement Motivation (AAM) subscale

		CFI	RMSEA	vs model	*df*	χ^2	*p*
Model 1	Configural invariance	.98	.058				
Model 1a	Age correction equal across sex	.97	.068	Model 1	6	30.19	<.001
Model 2	Metric invariance	.98	.055	Model 1	7	11.34	*ns*
Model 3	Strong factorial invariance	.97	.056	Model 2	9	23.61	.005
Model 3a	Strong factorial invariance, bar item 4	.98	.051	Model 2	8	9.23	*ns*
Model 4	Strict factorial invariance	.98	.047	Model 3a	8	9.14	*ns*
Model 5a	Mean Persistence factor equal across sex	.98	.048	Model 4	1	2.36	*ns*
Model 6	Mean Dedication factor equal across sex	.97	.061	Model 5	1	9.53	<.01

Notes: CFI = comparative fit index; RMSEA = root mean square error of approximation; vs = versus; df = degrees of freedom; χ^2 =chi square test statistic; p = p-value.

General Achievement Motivation

The results and fit statistics of the multi-group CFA of the GAM are presented in Table 5.9. In Model 1, we tested for configural invariance, with 4 items loading on Pressure, 6 on Accomplishment, 4 on Work Approach, 3 on Future Orientation, and 5 on Competition, and four cross-loadings (i.e., items 4, 10, 15 and 20 all loaded on two factors: non-congeneric structure). All residual terms were modelled as uncorrelated. In addition, all 18 items were regressed on age in men and women separately, in order to correct for possible age effects. The RMSEA (.059) indicated that Model 1 described the data adequately, while the CFI was rather low (.90).

Table 5.8 Correlations between the two latent Academic Achievement Motivation factors Persistence and Dedication for men (below diagonal) and women (above diagonal), and the means and SD for men and women on these factors

Correlations			
	Persistence	Dedication	
Persistence	1	.90	
Dedication	.79	1	
(Men below diagonal, women above diagonal)			

Means (SD)			
	Men (N=338)	Women (N=497)	Effect Size
Persistence	0 (1)	.14 (1.01)	.14
Dedication	0 (1)	.33 (1.05)	.32

Notes: The means of the women should be interpreted as deviations from the means of the men. The mean for the factor Dedication was significantly higher in women (see Model 6, Table 5.7).

It should be noted that because of the way the CFI is calculated (i.e., as the difference in fit between the independence model and the hypothesized model), this fit index can never take on high values if the intercorrelations between the modelled items are small to begin with. In that case, the fit of the independence model will not be very bad, and the difference with the hypothesized model can therefore not become large. Experience thus teaches that the CFI is never high when the intercorrelations between the modelled items are low overall, and in the present data, many intercorrelations were smaller than .20. As the RMSEA indicated adequate fit, and the residual terms (i.e., the part of the data not predicted by the model) were all small, Model 1 was accepted as baseline model for further testing for measurement invariance across sex.

In Model 1a, we tested whether the age effects could be constrained equal across sex, but as this was not the case (Model 1a vs Model 1: $\chi^2_{diff}(13)=28.44$, p<.01), we chose to leave this part of the model saturated. That is, all age-regressions are estimated separately in men and women in all following models, and this part of the model did therefore not contribute to any model misfit.

Metric invariance was tested in Model 2 by fixing all factor loadings to be equal across sex. Factorial variances were estimated freely in the women, but remained fixed to 1 in the male reference group for identification. This set of constraints proved tenable (Model 2 vs Model 1: $\chi^2_{diff}(14)=21.63$, ns), implying that metric invariance across sex was tenable for the GAM subscale.

To test for strong factorial invariance, all thresholds were constrained to be equal across sex in Model 3. This set of constraints, however, resulted in a significant deterioration of the model fit (Model 3 vs Model 2: $\chi^2_{diff}(18)=67.61$, p<.001). By systematically testing for strong factorial invariance for each of the 5 factors separately, it appeared that 4 of the 18 items (items 4, 5, 9, and 12) were biased with respect to sex. Note that in the item-specific analyses (Table 3), large effect sizes were observed for items GAM4 and GAM9. The effect sizes for items GAM5 and GAM12 were smaller, but the factor loadings for these items were not that large (although significant), meaning that these items were not strongly related to the latent factors. Constraining all thresholds, bar the thresholds of these 4 items, to be equal across sex, did just result in a significant drop of the model fit (Model 3a vs

Model 2: χ^2_{diff}(15)=25.61, p=.04), but as the overall fit of Model 3a was satisfactory, we accepted this model. For the GAM, strong factorial invariance was thus established for 14 out of 18 items, while sex-differences on 4 items were too large to be accounted for by the model. In the subsequent models, the thresholds of these 4 items were therefore estimated freely in both groups, and as such no longer contributed to the means of the underlying latent factors. The means of these factors were thus directly comparable between men and women.

In Model 4 we tested for strict factorial invariance, by constraining all residual variances in the women equal to those of the male reference group, i.e., equal to 1. These constraints were however not tenable (Model 4 vs Model 3a: χ^2_{diff}(15)=50.08, p<.001). In Model 4a, all residuals except the residual for item 12, were fixed to be equal in men and women, and this set of constraints was tenable (Model 4a vs Model 3a: χ^2_{diff}(15)=23.83, ns). This implies that the reliability of item 12 was not equal across sex: the residual variance was smaller in women, implying that the reliability of this item was higher in women. Table 5.10 shows the factor correlations and factor means taken from Model 4a for men and women separately.

Given that the greater part of the factor model was invariant across sex, while the parts that were not were freely estimated and thus no longer contributed to any sex differences, we could now meaningfully compare the five factor means across sex. In Model 4a, all factor means in the women's group were freely estimated while the factor means in the male reference groups were fixed to 0 for reasons of identification. In Model 5, we fixed all factor means to 0 in the women. This did not result in a significant drop in model fit (Model 5 vs Model 4a: χ^2_{diff}(4)=7.86, p=.10). However, this omnibus test disguised what was already apparent from the effect sizes shown in Table 5.10, namely the fact that the mean of the factor Future Orientation was actually significantly different between men and women (Future Orientation: χ^2_{diff}(1)=5.67, p<.05) while a trend was observed for the factor Competition (χ^2_{diff}(1)=3.22, p=.07). In the final model, Model 5a, we freely estimated these means in the women, and fixed the means of the other three factors to zero (Model 5a vs Model 4a: χ^2_{diff}(3)=.92, ns). The means of the factors Future Orientation and Competition were negative in women, implying that women were somewhat less future-oriented, and less driven by motives related to competition with others.

The four biased items (4, 5, 9, and 12) affected all factors of the GAM. If we would have calculated simple sum scores across the items of each of the five factors (rather than subjecting the items to a factor model), and compared men and women with respect to these sum scores, as is common practice, then the presence of the biased items would have lead to considerable over- or underestimation of the effect sizes of the sex difference for the factors Pressure (effect size with the biased item: .05, effect size without the biased item: -.13, difference: -.18), Accomplishment (with: .03, without: .00, difference: -.03), Work Approach (with: .08, without: -.01, difference: -.09), Future Orientation (with: .29, without:.14, difference: -.15), and Competition (with: .02, without: .08, difference: .06).

Finally, in order to estimate the correlations between the academic and the general achievement motivation factors, we combined the final models from the AAM (Model 5) and the GAM (Model 5a) into one overall model. The fit of this model, which we denoted the Total Model, was adequate (CFI=.92, RMSEA=.053), and the correlations between the

7 subscales are shown in Table 5.11. All correlations between the AAM factors and the GAM factors were positive and most of them were significant. Note that the modification indices of the Total Model were all small, as were the residuals (i.e., the part not explained by the model), which implies that the choice to analyze the AAM and the GAM subscales separately before combining them, was justified (i.e., there were no cross-loading between the AAM and the GAM factors, and no correlated errors, etc.).

Table 5.9 Results of the Multi-Group Covariance and Means Structure Analyses (MG-CMSA) for the General Achievement Motivation (GAM) subscale

		CFI	RMSEA	vs model	*df*	X^2	*p*
Model 1	Configural invariance	.90	.059				
Model 1a	Age correction equal across sex	.90	.058	Model 1	13	28.44	<.01
Model 2	Metric invariance	.91	.057	Model 1	14	21.63	*ns*
Model 3	Strong factorial invariance	.90	.059	Model 2	18	67.61	<.001
Model 3a	Strong factorial invariance, bar items 4, 5, 9, and 12	.91	.056	Model 2	15	25.61	.04
Model 4	Strict factorial invariance	.90	.057	Model 3a	15	50.08	<.001
Model 4a	Strict factorial invariance bar residuals items 6 and 12	.91	.055	Model 3a	15	23.83	*ns*
Model 5	Factorial means equal across sex	.91	.054	Model 4a	4	7.86	*ns*
Model 5a	Factorial means equal across sex bar for factors Future Orientation and Competition	.92	.053	Model 4a	3	.92	*ns*

Notes: CFI = comparative fit index; RMSEA = root mean square error of approximation; vs = versus; df = degrees of freedom; χ2 =chi square test statistic; p = p-value.

Table 5.10 Correlations between the five latent General Achievement Motivation factors Pressure, Accomplishment, Work Approach, Future Orientation and Competition for men (below diagonal) and women (above diagonal), and the means and SD for men and women on these factors

Correlations					
	Pressure	Accomplishment	Work Approach	Future Orientation	Competition
Pressure	1	.50	.13	.19	.29
Accomplishment	.44	1	.26	.41	.60
Work Approach	.25	.33	1	.14	.13
Future Orientation	.23	.44	.43	1	.50
Competition	.20	.50	.16	.57	1

Notes: men below diagonal, women above diagonal.

Means (SD)			
	Men (N=338)	Women (N=497)	Effect Size
Pressure	0 (1)	.08 (.84)	.09
Accomplishment	0 (1)	.02 (1.06)	.02
Work Approach	0 (1)	.05 (1.00)	.05
Future Orientation	0 (1)	-.22 (.85)	-.24
Competition	0 (1)	-.18 (.70)	-.22

Notes: The means of the women should be interpreted as deviations from the mean of the men. The mean for the factor Future Orientation is significantly lower in women, and a trend towards significance was observed for the factor Competition.

Table 5.11 Correlations between the two latent Academic Achievement Motivation factors and the five General Achievement motivation factors for men and women separately.

	Men		Women	
	Persistence	Dedication	Persistence	Dedication
Pressure	.06	.11	.07	.25**
Accomplishment	.39**	.33**	.46**	.58**
Work Approach	.37**	.20**	.42**	.32**
Future Orientation	.18*	.13[†]	.13[†]	.14*
Competition	.18*	.32**	.15*	.36**

*Notes: Signs denote the significance of the observed correlations: ** p<.01, * p<.05, [†] p<.08.*

DISCUSSION

In this study, sex differences in academic achievement motivation and general achievement motivation were examined in adult subjects using categorical multi-group covariance and mean structure analysis (MG-CMSA).

Academic achievement motivation was measured with 10 items. A two-factor solution, with factors Dedication and Persistence, described the relations between these items adequately. On the level of the latent factors, men and women differed significantly with respect to the mean of the factor Dedication, with women considering themselves to have been more dedicated to their academic work than men. No mean difference was observed for the factor Persistence, i.e., men and women did not differ in their retrospective evaluation of how well they had been able in their school years to allocate time to, and focus on, homework. The questionnaire, of which the DAMT was part, also included two retrospective questions on whether the parents of the participants had considered school important, and whether the participants' school results were discussed at home. The men and women in this study did not respond differently to these questions (Z=-1.74, *ns*, and Z=-.71, *ns*, respectively). This suggests that the differences in Dedication observed between men and women in this study were most likely not due to a difference in how they experienced their academic upbringing. One academic achievement motivation item proved biased with respect to sex, i.e., the sex difference on this item was too large to be explained by the underlying latent factor Dedication, and this item-specific sex difference was not indicative of a sex difference in Dedication. On this item, which concerned the question of whether others had thought the participant to be diligent in school, women scored much higher than men, i.e., women thought they were perceived as more diligent by others.

General achievement motivation was measured with 18 items. A five-factor solution, with factors Pressure, Accomplishment, Work approach, Future Orientation, and Competition, described the relations between those items adequately. On the level of the latent factors, sex differences were observed for the factors Future Orientation and a trend was observed for the factor Competition. On both factors, women scored lower than men. This means that women cogitated less about the future and made less future-related plans, compared to men, and achieving more than others was considered less important by women compared to men. Men and women did not differ with respect to the means of the factors Pressure, Accomplishment, and Work approach, i.e., men and women did not differ in their perception of how occupied they are by their work, in their assessment of the demands they put on themselves, and in their evaluation of how important work/employment is in their lives. Four of the 18 general achievement motivation items were biased with respect to sex, i.e., the sex difference observed on the items were not indicative of the sex difference on the underlying factors. On three of the four items, women scored lower then men: women aspired less after a busy management job at a factory (item 4), were less often of the opinion that other people could work harder (item 5), and perceived working on something for a long time as more tiring (item 9). At the same time, women were more concerned about other peoples' opinion about their achievements than men (item 12). It should be noted that in the exploratory factor analysis, the pattern of factor loadings for some of the biased items differed between men and women. In MG-CMSA, item bias is defined within the context of a specific factor model, i.e., an item is considered biased if the mean differences observed for this item cannot be explained by the specified model. This means that in theory, bias can originate from model misspecification in one of the groups. To verify whether this was the case, we ran alternative models in which the biased items were allowed to load on other factors as well. The bias however remained significant, implying that it was not the result of misspecifications in the factor structure.

In our analyses, we chose to leave items for which the bias was uniform (i.e., limited to the intercepts) in the model. This strategy is justified as uniformly biased items no longer contribute to the misfit of the model when their intercepts are freely estimated and thus allowed to vary across the groups. This strategy is, however, not recommended when the bias is *non*-uniform (implying significant differences in factor loadings between groups). In that case, one should remove the item from the model before testing for strong and strict measurement invariance.

Individual items which clearly showed differences in endorsement rates between the sexes were indeed flagged as biased in the MG-CMSA analyses. However, although the sample sizes in our study were considerable (N=338 and N=497, respectively), the statistical power to detect mean differences between groups on the level of the latent factors was not optimal. For example, even though the sex difference in the factor Competition was associated with an effect size of -.22, the effect was only marginally significant (p=.07).

These results show that items that measure motivation-related concepts can be biased with respect to sex. It is possible that the sex difference on these items was just too large to be accounted for by underlying latent factors (i.e., the sex difference is item specific), but it is also possible that the connotation of these items was different for men and women to such an extent that the responses of men and women on the biased items were actually incomparable. MG-CMSA can only point out the location of the bias, but

further research into the content and interpretation of these items would be required to uncover the exact nature of the bias. The present results are of course limited to these specific academic and general achievement motivation subscales of the DAMT. Yet, the study shows that researchers should be cautious in directly comparing motivation-related scores of men and women without first studying their comparability. Our calculations based on sum scores showed that the effect sizes of the sex differences in achievement motivation can be very much affected by the presence of a few biased items. As a result, sex differences in achievement motivation may be exaggerated or underestimated in one study, and may fail to replicate in subsequent studies, in which different instruments are used to measure achievement motivation.

One advantage of studying academic achievement motivation and general achievement motivation simultaneously is that one can calculate the correlation between these two types of motivation. In this study, the two academic achievement motivation factors and the five general achievement motivation factors correlated positively. Correlations were particularly strong between the 2 academic achievement motivation factors Persistence and Dedication on the one hand, and the 3 general achievement motivation factors Accomplishment, Work Approach and Competition on the other.

One disadvantage of studying academic achievement motivation in an adult population is that such a study is by definition retrospective. For some of the participants in our sample, which was particularly heterogeneous with respect to age, the schooldays were a distant past. Retrospective assessments of one's own academic achievement motivational levels may not always be reliable. The fact that we find clear factor structures, and significant correlations between academic and general measures of achievement motivation, suggests that the answers must at least have been consistent within subjects, but how reliably such retrospective assessments reflect the past reality, cannot be answered with the present data.

In this study, age effects were accounted for by partialling out the effects of age on the level of the items before fitting the factor models. Of the 28 DAMT items, 12 showed significant age effects in men, and 15 showed significant age effects in women. Moreover, especially for the academic achievement motivation items, age effects were markedly different for men and women, not only in size (e.g., AAM items 1, 7 and 9) but even in sign (e.g., AAM for items 2 and 5). The aim of this paper was not to study the effect of age on motivation. We therefore decided to keep the age-corrective part of the model saturated, which implies that the effects of age were fully controlled for in men and women separately, and not studied in more detail. Yet, the finding that age did affect the responses, and that it did so in a different manner for men and women, does suggest that inconsistencies between former studies in whether or not sex differences in motivation were observed, and whether motivation was related to actual achievement, could be due to differences between these studies in the age-range of their study-samples.

The heavy reliance on self-report measures in research on achievement motivation forms another potential source of bias since subjective and objective evaluations of a person's motivation, effort and dedication, may not always be in agreement, especially retrospectively. Especially with respect to the Academic Achievement Motivation scale, we emphasize that we measured our participants' personal recollection of how dedicated and persistent they were when they were in school. It is possible that sex bias, such as observed for the diligence item of the AAM scale, represented a difference between women and men

in how they perceived and recalled reactions from their environment, rather than objective differences in diligence with respect to academic work. Besides the problems related to self-report measures, the lack of standardized and validated measures of academic and general achievement motivation hampers the generalizability of results across studies. Still, the present study shows that MG-CMSA is useful in locating the exact source of sex differences in motivation, and that the study of item bias may be advantageous in the field of sex differences in achievement motivation.

The present sample consisted of family data, i.e., twins and their (in-law) family members, and one question of interest is whether twin-samples can be considered representative of the general population. In general, twins are born in all strata of society, and they are on average somewhat more willing to participate in research, as are their relatives (Martin et al., 1997). To date, no studies have been performed on whether twins differ from non-twins in motivation-related characteristics. At present, there is however no reason to believe that motivational differences between the sexes should be different for men and women born as twins or coming from twin families. Another question of interest is whether the sex differences observed in the present sample are representative of sex differences in the Dutch population. Generally, men and women differ in their willingness to participate in research (women being somewhat more willing). If this sex difference in willingness to participate in research is in turn related to, or dependent on, social status or success (i.e., men are more willing to participate if they are socially more successful, while women's willingness to participate is independent of their social status) then the sex differences observed in achievement motivation could be a function of the sex difference in the willingness to participate.

In principle, this could be tested by comparing the within-pair differences in motivation observed between opposite-sex twins or opposite sex siblings[5], to the sex differences observed in unrelated individuals. That is, if the sex differences in motivation such as observed *across* families are also observed *within* families (where brothers and sisters are matched with respect to social background and social economic status), then the possible distortion (due to sex differences in willingness to participate, or due to studying twins rather than non-twins) is probably minor. Our family data included 47 complete opposite-sex twin pairs and opposite sex sibling pairs. Wilcoxon non-parametric signed-rank tests showed that even within this limited number of opposite-sex pairs, brothers and sisters scored markedly differently on items AAM4, GAM4 and GAM12, which were all labelled as severely biased in this study. The fact that the sex effects as reported in the total sample were also observed within families, confirms our expectation that selection effects were absent or minor. Yet, the question of whether the development of motivation-related traits is influenced by the presence of a co-twin or sibling, does merit further study. Such studies could possibly even provide insight into the origin of sex-differences in motivation. Similarly, the question of whether the willingness to participate in research is itself related to achievement motivation is worth following-up.

5   Note that in principle, father-daughter and mother-son relations could also be included in the within-family comparisons, in addition to brother-sister relations. The advantage of brother-sister comparisons is, however, that these relatives are of approximately the same age, grew up at approximately the same juncture, and were nursed under approximately the same (social economic) circumstances, i.e., these relatives are matched with respect to background variables, while such matching is not as obvious across generations.

This study was the first to examine measurement invariance and sex differences in the context of motivational research using MG-CMSA in a large sample of adult participants. It was shown that five motivation items (1 academic, 4 general achievement motivation) were biased with respect to sex. Once these biased items were effectively removed from the means model, sex difference were still observed for Dedication (academic achievement motivation), and for Future-Orientation and Competition (general achievement motivation). Further studies into the nature of the sex-bias observed for some items are merited. In addition, it would be interesting to study how the sex differences observed in subjects' self-reported motivation, relate to more objective measures. For example, in the present study, sex differences were absent with respect to the factor Pressure, implying that men and women do not differ in their perception of the extent to which they are engaged by their work. It would be interesting to relate this subjective perception to an objective measure such as the number of hours of work per week. Such studies could be used for validation, but could also enhance our insight into the relation between achievement motivation related constructs on the one hand, and actual achievement on the other.

SUPPLEMENTARY INFORMATION
Example items of the Dutch Achievement Motivation Test (DAMT)

Academic Achievement Motivation (AAM)

Dedication:
AAM7: "When I was in school, the demands that I made on myself concerning studying were very high, high, pretty high, low" (R)

Persistence:
AAM8: "When I'm studying, my thoughts often wander / I'm not easily distracted / I work ceaselessly"

General Achievement Motivation (GAM)

Pressure:
GAM2: "Usually, I'm busy / quite busy / not very busy / not busy at all" (R)

Accomplishment (intrinsic motivation):
GAM10: "The urge to surpass myself is very strong / pretty strong / not very strong" (R)

Work approach:
GAM14: "For me, working is something which I would like to do only occasionally / which I like to do, but which generally takes me a lot of effort / which I always enjoy doing"

Future Orientation:
GAM7: "When thinking about my future, I usually plan very far ahead / plan far ahead / I plan ahead quite a bit / I do not usually plan ahead very far" (R)

Competition:
GAM19: "Achieving more than others, is very important for me / is important for me / is quite important for me / is not that important for me" (R)

Chapter6

**Environmental variation in educational attainment
is moderated by general cognitive ability
and by achievement motivation**

ABSTRACT

Educational attainment is a heritable trait (h^2 40-70%) that is known to be related to general cognitive ability and achievement motivation. The mechanisms underlying these relations are not completely understood. We used twin and sibling data (N=864) to investigate the direct causes of co-variation and to test whether causes of variation in educational attainment are moderated by general cognitive ability and/or achievement motivation.

Results confirmed a phenotypic correlation between educational attainment and general cognitive ability (r=.47, p<.001) and between educational attainment and achievement motivation (r=.31, p<.001). The association between educational attainment and general cognitive ability was found to be due to both genetic and environmental influences, whereas the association between educational attainment and achievement motivation was completely of genetic origin. Furthermore, general cognitive ability moderated the shared environmental variance component of educational attainment whereas achievement motivation moderated the non-shared environmental variance component of educational attainment. The relative contribution of environmental influences was increased in individuals with either low or high levels of general cognitive ability and in individuals with high levels of achievement motivation. Understanding the mechanisms underlying individual differences in educational attainment may be useful in social and political programs concerning education, but also for studies on gene finding.

INTRODUCTION

Educational attainment, i.e., the highest level of education an individual has completed, is a valuable predictor of social and economic success (von Stumm et al., 2009; von Stumm et al., 2010), and is positively related to physical health in later life (Johnson et al., 2010). Individual differences in educational attainment are, to a large extent, due to genetic factors with heritability estimates ranging from ~40% to ~70% (Vogler & Fulker, 1983; Heath et al., 1985; Tambs et al., 1989; Lichtenstein et al., 1992; Baker et al., 1996; Lichtenstein & Pedersen, 1997; Reynolds et al., 2000). The remaining variance is explained by shared (~20% to ~50%) and non-shared environmental factors (~10% to ~30%). Educational attainment is also known to be associated with general cognitive ability (Kaufman & Wang, 1992) and, although to a lesser extent, with the motivation or capacity to set high but obtainable personal goals, i.e., achievement motivation (Spinath et al., 2006). However, underlying mechanisms of these associations are not thoroughly understood. Phenotypic correlations may be due to shared genetic factors, such that genes affecting educational attainment also affect general cognitive ability (and/or achievement motivation). Phenotypic correlations may also be due to environmental factors, such as rearing style, that affect both educational attainment and general cognitive ability (and/or achievement motivation).

In addition, general cognitive ability and achievement motivation may *moderate* underlying mechanisms that control individual differences in educational attainment, such that the extent to which genetic and environmental effects cause individual differences in educational attainment depends on levels of general cognitive ability and achievement motivation. For example, high general cognitive ability/achievement motivation may trigger the expression of genes that cause individual differences in educational attainment. As such, general cognitive ability and achievement motivation may act as proximal processes, i.e., processes that enhance effective development and increase the contribution of genetic factors ('Bio-ecological model', Bronfenbrenner & Ceci, 1994). Alternatively, the 'Diasthesis-stress model' (Gottesman, 1991) hypothesizes increased contribution of genetic factors in less advantageous circumstances, such that individuals who are genetically at risk are more sensitive to environmental risk factors. Following this model, *low* general cognitive ability/achievement motivation may trigger the expression of genes that cause individual differences in educational attainment. Only one study reported moderation effects of general cognitive ability on genetic and environmental influences on educational attainment in a sample of adolescents and young adults (Johnson et al., 2009), whereas no studies reported on moderation effects of achievement motivation.

In this study, twin- and sibling data are used to study whether and how general cognitive ability and achievement motivation are related to educational attainment. We first investigate the phenotypic associations between educational attainment and general cognitive ability, and between educational attainment and achievement motivation. Next, we investigate (i) the extent to which these phenotypic associations are mediated by common genetic and/or common environmental factors, and (ii) the extent to which the underlying genetic and environmental mechanisms that account for individual differences in educational attainment depend on general cognitive ability and/or achievement motivation.

METHODS

Sample

This study is part of a large ongoing project on the genetics of cognition (Posthuma et al., 2001a) and was performed with understanding and written consent of each participant. The study was approved by the Central Committee on Research Involving Human Subjects in the Netherlands. Data were available for 864 twins and siblings (55.8% female) from 317 different families from the Netherlands Twin Registry (NTR, Boomsma et al., 2006). The sample consisted of 288 complete twin pairs (47.2% MZ), 23 incomplete twin pairs (8.7% MZ) and 265 siblings (number of participating siblings per family ranges from 0 to 5). From 6 families, only sibling data were available. The average age of the participants was 46.61 years (SD=12.40, range: 23.44–75.61) at the time they completed the Life Experience List (LEL, see Measures; Vinkhuyzen et al., 2010a). All five zygosity groups were reasonably well represented: monozygotic males (MZM: 20.7%, 179 participants), monozygotic females (MZF: 24.4%, 211 participants), dizygotic males (DZM: 12.6%, 109 participants), dizygotic females (DZF: 22.0%, 190 participants) and dizygotic opposite sex (DOS: 20.3%, 175 participants). Non-twin sibling data were available for 127 brothers (47.9%) and 138 sisters. Zygosity of same-sex twins was based on DNA polymorphisms (127 pairs, 88.2%) or, if information on DNA markers was not available, on questions about physical similarity and confusion of the twins by family members and strangers. Agreement between zygosity diagnoses from survey and DNA was 97% (Willemsen et al., 2005). The sample was previously shown to be representative of the general Dutch population with regard to educational attainment (see Posthuma et al., 2001a for details).

Measures

Educational attainment

Information on educational attainment was collected using an open-end question concerning educational attainment that was incorporated in the Life Experiences List (LEL) (Vinkhuyzen et al., 2010a). Participants were asked to list all types/levels of education that they had completed. All educational levels were then recoded into seven ordinal categories (1=nursery; 2=primary school; 3=first stage secondary school, 4=second stage secondary school, 5=higher education, bachelors degree; 6=higher education, masters degree; 7=doctorate degree), following the Dutch Standard Classification of Education (SCE, CBS 2006). Participants' highest completed level of education was used as a measure of educational attainment in the present study. Data on educational attainment were available for 547 participants.

Test-retest reliability of educational attainment was studied in an independent sample of 62 participants (31 parent-offspring pairs, 75.4% women; age range 17-71, mean: 39.95, SD: 16.19), who completed the LEL twice within a period of two months. Test-retest reliability was .76 (p<.001). 16 individuals reported different levels of education. Differences were mainly due to cases where in the first questionnaire subjects listed first and second stage secondary school, while in the second questionnaire subjects listed only first stage secondary school. Differences were also due to subjects giving a description of the educational level in the first questionnaire without a specific level (e.g., 'accountancy') and gave the explicit level in the second questionnaire (e.g., 'accountancy with university degree').

General cognitive ability

General cognitive ability was operationalized as Full Scale Intelligence Quotient (FSIQ) and assessed with the Dutch version of the WAIS-IIIR (Wechsler, 1997). Data collection took place at two time points. In the first wave of data collection (1997-2001), participants (N=785) completed eleven subtests of the WAIS-IIIR: Block design, Letter-number sequencing, Information, Matrix reasoning, Similarities, Picture completion, Arithmetic, Vocabulary, Digit symbol-coding, Digit-symbol pairing, and Digit symbol-free recall, and FSIQ was based on these 11 subtests. In the second wave of data collection (2007-2009), participants (N=74) completed seven subtests of the WAIS-IIIR: Block design, Letter-number sequencing, Information, Matrix reasoning, Arithmetic, Vocabulary, and Digit symbol-coding, and FSIQ was based on these seven subtests. Data on FSIQ were available for 859 participants. In a partly overlapping sample (N=785), the correlation between FSIQ assessed with eleven subtests and FSIQ assessed with seven subtests was very high (Pearson's *r* =.97, p<.001). To evaluate test-retest reliability of FSIQ, 59 participants completed the WAIS twice with an interval of ~10 years (first and second wave of data collection). Test-retest reliability was calculated from the FSIQ score based on seven subtests at both time points and was .85 (p<.001).

Achievement motivation

Information on achievement motivation was collected using 28 multiple-choice achievement motivation items that were adopted from the Dutch 'Prestatie Motivatie Test' (Dutch Achievement Motivation Test (DAMT), Hermans, 2004). The Academic Achievement motivation[6] (AAM) subscale that is used in the present study is originally based on ten items (e.g., "Studying during the weekend is hard for me / is not a problem for me" and "In school, people thought I was diligent / not very diligent / quite lazy"). In the present study, one item (item A4) was excluded from the analyses because that item showed severe bias with respect to sex (van der Sluis et al., 2010). As the number of answer-categories of the items of the AAM varies between 2 and 4, sum-scores were based on a weighted summation of the items, i.e., each items score (1 to 4) was divided by the maximum number of answer-categories of that particular item. If more than 3 out of nine items were missing, the AAM sum-score was considered unreliable and the AAM data were excluded from analysis. Consequently, sum-scores were based on a summation of 6 (minimum) to 9 (maximum) items, and all sum-scores were divided by the number of items that they were based on to assure comparability. All items were recoded such that high scores imply high AAM. Data on AAM were available for 534 participants. Test-retest reliability of AAM was studied within an independent sample of 62 participants (31 parent-offspring pairs, 75.4% women; age range 17-71, mean: 39.95, SD: 16.19), who completed the LEL twice within a period of two months. Test-retest reliability was .92 (p<.001).

All measures were corrected for age and sex effects before analysis.

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6 Please note that the original DAMT consists of five subscales: Positive and Negative Fear of Failure, Social Desirability, General Achievement motivation and Academic Achievement motivation. For reasons of efficiency, only the 28 items on general achievement motivation (GAM) and academic achievement motivation (AAM) were included in the LEL. Within the present study, only the AAM subscale is considered, as this subscale is most interesting in the context of educational attainment.

Response rate

A total number of 859 participants completed the IQ test and 559 participants completed the LEL. The LEL was sent out to participants who completed, or were scheduled for, the IQ test. The overall response rate of the LEL was 76%. Five participants did complete the LEL but did not complete the IQ test and 305 participants did complete the IQ test but did not complete the LEL. 17.4% of the participants that completed the IQ test between 1997 and 2002 dropped out from the study before the LEL was sent out.

Statistical analyses

Phenotypic analyses

A saturated model was fitted to the data to estimate model free MZ twin, DZ twin, and sibling correlations for educational attainment, general cognitive ability and achievement motivation. Within the saturated model, difference between zygosity groups in means and variances of educational attainment, general cognitive ability and achievement motivation were tested using likelihood ratio tests. In addition, differences between DZ twin correlations and regular sibling correlations were tested.

Subsequently, phenotypic correlations between educational attainment and general cognitive ability and between educational attainment and achievement motivation were calculated. Next, partial correlations were investigated, that is, the residual correlation between educational attainment and general cognitive ability, controlling for achievement motivation, and the residual correlation between educational attainment and achievement motivation, controlling for general cognitive ability. Comparing full and partial correlations allowed us to investigate whether the relation between general cognitive ability and educational attainment is mediated by achievement motivation and whether the relation between achievement motivation and educational attainment is mediated by general cognitive ability. All (partial) phenotypic correlations were calculated in Mplus' (Muthen & Muthen, 2005), using option 'complex' to correct for familial relatedness between the participants.

Genetic analyses: correlation and moderation

To investigate the underlying mechanisms of the phenotypic associations between educational attainment and general cognitive ability (and between educational attainment and achievement motivation), multivariate genetic moderation models were specified. Within these models, variances of educational attainment and general cognitive ability (or achievement motivation), as well as the covariance between educational attainment and general cognitive ability (or achievement motivation), were modeled as a function of genetic and environmental effects. Additive genetic factors (A), genetic dominance (D) and shared- (C) and non-shared (E) environmental factors were considered. 'A' represents additive genetic effects of alleles summed over all genetic loci. 'D' represents the extent to which the genetic effects of alleles at a locus are not additive but interact with each other. 'C' represents common environmental influences that render offspring of the same family more alike. 'E' represents all environmental influences that result in differences between members of a family, including measurement error. Variance components were allowed to vary as a function of the moderator (i.e., general cognitive ability or achievement motivation).

A sample including twins and siblings only, is not sufficient to model both C and D since the effects of C and D have opposite effects on the difference between MZ twin and DZ twin correlations. The variance of educational attainment, general cognitive ability and achievement motivation was therefore decomposed as due to A, C and E, or due to A, D and E. DZ twin correlations higher than half the MZ twin correlations suggest shared environmental influences; in that case an ACE model was fitted to the data. DZ twin correlations less than half the MZ twin correlations suggest the presence of genetic dominance; in that case an ADE model was fitted to the data.

Phenotypic correlations between educational attainment (the trait) and general cognitive ability or achievement motivation (the moderators) may be due to trait-mediating effects of the moderator(s), but may also be due to genetic or environmental factors that are shared between trait and moderator. A common genetic background between trait and moderator (rG) may appear as gene-by-moderator interaction if rG is not considered in the moderation model. Similarly, a common environmental background (rC or rE) may appear as C-by-moderator or E-by-moderator interaction if rC or rE are not modeled.

Detecting effects of gene-by-moderator in the presence of rG (or C-by-moderator / E-by-moderator in the presence of rC / rE, respectively) requires a bivariate approach in which the moderator features twice in the model: as a dependent variable and as a moderator. Modeled as such, moderating effects of general cognitive ability (or achievement motivation) can be modeled on two types of variance components: the variance components unique to educational attainment, and the variance components shared to educational attainment and the moderator (i.e., general cognitive ability or achievement motivation) (Purcell, 2002).

Figure 6.1 shows a partial path diagram of the bivariate model for one twin.

Figure 6.1: Bivariate model for one individual including linear moderation effects of the environmental moderator (general cognitive ability / achievement motivation) on the variances of educational attainment and on the covariance between educational attainment and the moderator.
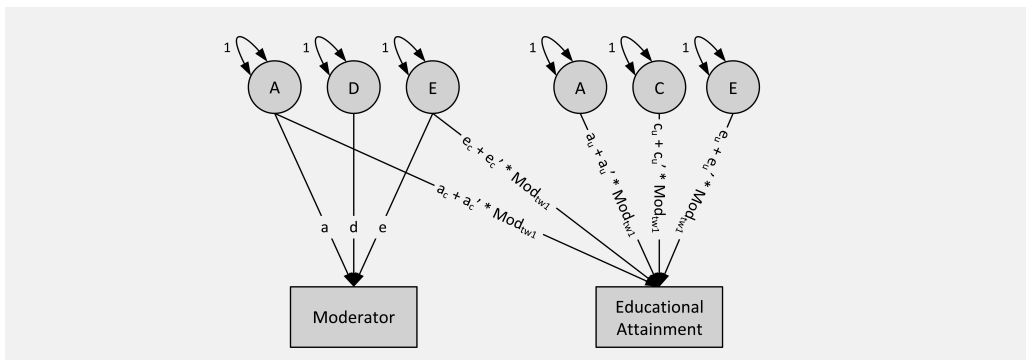
Notes: A = additive genetic effects; D = genetic dominance; C = shared environmental effects; E = non-shared environmental effects; a = unmoderated path coefficient for A; d = unmoderated path coefficient for D; c = unmoderated path coefficient for C; e = unmoderated path coefficient for E; a_c= genetic factors shared between moderator and trait; a_u = genetic factors unique to trait; c_u = shared environmental factors unique to trait; e_c = non-shared environmental factors shared between moderator and trait; e_u = non-shared environmental factors unique to trait; moderator = moderator value. a_c', e_c', a_u', c_u', and e_u' represent linear effects of the moderator.

Under the assumption of an ACE model for educational attainment and an ADE for the moderator, the variance of educational attainment as derived from Figure 6.1 is calculated as:

Var(educational attainment) =
$((a_c+a_c'*Mod_{tw1})^2+(a_u+a_u'*Mod_{tw1})^2) + (c_u+c_u'*Mod_{tw1})^2 + ((e_c+e_c'*Mod_{tw1})^2+(e_u+e_u'*Mod_{tw1})^2)$,

where a_c denotes genetic factors shared between moderator and educational attainment, a_u denotes genetic factors unique to educational attainment, c_u denotes shared environmental factors that are unique to educational attainment, e_c denotes non-shared environmental factors that are shared between moderator and educational attainment, and e_u denotes non-shared environmental factors that are unique to educational attainment.

To examine the significance of linear moderation effects, as well as the significance of unmoderated variance components that were shared between educational attainment and moderator and unmoderated variance components that were unique to educational attainment, a similar series of analyses was conducted for the two bivariate moderation models; (i) moderation effects of general cognitive ability on the variance components of educational attainment and (ii) moderation effects of achievement motivation on the variance components of educational attainment.

For each series of analyses it was first tested whether variance components specific to the moderator were significant (a, d or c). Non-significant variance components were subsequently removed from the model to create a new reference model (reference model 1). Second, it was tested whether linear moderation on the variance components that are common to educational attainment and the moderator (a'_c, d'_c/c'_c and e'_c) were significant. All reduced models were compared to the model including all moderation effects (reference model 1). Non-significant moderation effects were subsequently removed from the model to create a new reference model (reference model 2). Third, significance of linear moderation effects on the variance components of educational attainment that are unique for the trait (a'_u, d'_u/c'_u and e'_u) was tested. The fit of these reduced models was compared to the fit of reference model 2. Again, non-significant moderation effects were subsequently removed from the model to create a new reference model (reference model 3). Fourth, significance of the unmoderated variance components, shared between trait and moderator (a_c, d_c/c_c and e_c), was tested. Fit of these models was compared with the fit of reference model 3. Non-significant unmoderated variance components were subsequently removed from the model to make up a new reference model (reference model 4). Fifth, significance of the unmoderated variance components, unique for the trait (a_u, d_u/c_u, and e_u), was tested. Fit of these models was compared with the fit of reference model 4. Non-significant un-moderated variance components were subsequently removed from the model.

Significance of parameters was tested by comparing the fit of nested (increasingly more restricted) models to the fit of less restricted models. Goodness-of-fit of these sub-models was assessed by likelihood-ratio-tests. The difference in log-likelihoods between two models (which follows a χ^2 distribution) was evaluated. If the χ^2-difference test is significant, the constraints imposed on the nested models are not tenable. If the χ^2-difference test is not significant, the nested, more parsimonious model is to be preferred. When testing the significance of a variance component or moderation coefficient, it is

well established that the null distribution of a suitably parameterized variance component or moderation coefficient is a .5:.5 mixture of a $\chi^2(0)$ and $\chi^2(1)$ (Dominicus et al., 2006; Macgregor et al., 2005). We therefore tested the significance of variance components or moderation coefficient against a critical value of $\chi^2(1)= 2.7055$, given alpha = .05. Analyses were carried out using the raw data option in Mx (Neale, 1994; Posthuma & Boomsma, 2005).

RESULTS

Phenotypic analyses

Means and variances of educational attainment ($\chi^2(2)=.46$, *ns*), general cognitive ability ($\chi^2(2)=.53$, *ns*) and achievement motivation ($\chi^2(2)=2.07$, *ns*) could be constrained to be equal between zygosity groups without a significant deterioration of the model fit, indicating that there was no heterogeneity in these measures as a function of zygosity. Table 6.1 includes information on means and standard deviations of educational attainment, general cognitive ability, and achievement motivation, as well as information on missingness.

Table 6.1 Descriptive statistics for educational attainment, general cognitive ability and achievement motivation

	N	% Missing	Mean (SD)
educational attainment	547	2%	4.91 (.96)
general cognitive ability	859	.6%	99.68 (14.78)
achievement motivation	534	4%	.50 (.13)

Notes: N=number of participants; % Missing=percentage of missingness, this is the percentage of participants that were (i) participated in the present study but did not complete the IQ test or (ii) participants that returned the LEL but did not complete the questions on educational attainment and achievement motivation; Mean = mean score corrected for age and sex effects; SD=standard deviation; p=p-value.

All measures were corrected for age and sex to avoid spuriously increased similarities in MZ and same-sex DZ twin pairs (McGue & Bouchard, Jr., 1984). Table 6.2 shows the sex and age corrected MZ twin, DZ twin, sibling, and pooled DZ/sibling correlations and standardized variance components for educational attainment, general cognitive ability and achievement motivation. Sibling correlations did not differ from DZ twin correlations for educational attainment ($\chi^2(1)=.45$, *ns*), general cognitive ability ($\chi^2(1)=3.72$, *ns*) and achievement motivation ($\chi^2(1)=1.41$, *ns*). MZ twin correlations exceeded the DZ/sibling correlations for educational attainment ($\chi^2(1)=5.20$, p=.02), general cognitive ability ($\chi^2(1)= 77.24$, p<.001), and achievement motivation ($\chi^2(1)=26.59$, p<.001), suggesting the presence of genetic influences. The pooled DZ/sibling correlation for educational attainment is more than half the MZ twin correlation, suggesting the presence of shared environmental factors. Pooled DZ/sibling correlations for general cognitive ability and AAM are less than half the MZ twin correlation, suggesting the absence of common environmental effects and possibly the presence of genetic dominance.

Estimates of the (partial) phenotypic correlations between educational attainment, general cognitive ability and achievement motivation are shown in Table 6.3. Phenotypic correlations of educational attainment with general cognitive ability (r=.47, p<.001) and achievement motivation (r=.31, p<.001) were significantly different from zero.

Table 6.2 Twin and sibling correlations (95% confidence intervals) and standardized variance components (95% confidence intervals) for educational attainment, general cognitive ability and achievement motivation.

	rMZ (95% CI)	rDZ (95% CI)	rSibling (95% CI)	rDZ/rSibling (95% CI)
educational attainment	.52 (.34-.66) N=77	.35 (.10-.54) N=64	.27 (.12-.39) N=297	.28 (.16-.40) N=361
dgeneral cognitive ability	.82 (.77-.86) N=136	.46 (.32-.57) N=152	.32 (.22-.42) N=594	.35 (.26-.44) N=746
achievement motivation	.63 (.48-.74) N=78	-.001 (-.26-.25) N=59	.01 (-.13-.15) N=284	.01 (-.11-.14) N=380

	a^2	d^2	c^2	e^2
educational attainment	.49 (.07-.65)	-	.04 (.00-.31)	.47 (.35-.66)
general cognitive ability	.60 (.24-.85)	.22 (.00-.58)	-	.18 (.14-.23)
achievement motivation	.00 (.00-.21)	.60 (.35-.72)	-	.40 (.28-.57)

Notes: rMZ=MZ twin correlation; rDZ=DZ twin correlation; rSibling=sibling correlation; rDZ/rSibling=combined DZ and sibling correlation; Twin and sibling correlations were corrected for sex and age; N=number of pairs; 95% CI=95% confidence interval; a^2=standardized additive genetic variance; d^2= standardized dominance genetic variance; c^2= standardized shared environmental variance; e^2= standardized non-shared environmental variance. Standardized variance components are based on full models.

Furthermore, the phenotypic correlation between educational attainment and general cognitive ability did not significantly change when the effect of achievement motivation was partialled out ($\chi^2(1)$=.63, *ns*), and the phenotypic correlation between educational attainment and achievement motivation did not significantly change when the effect of general cognitive ability was partialled out ($\chi^2(1)$=2.40, *ns*). As the relation of educational attainment with general cognitive ability was independent of achievement motivation, and vice versa, genetic analyses were performed in a bivariate rather than trivariate context, to avoid unnecessary parameter estimation.

Table 6.3 Full (left) and partial (right) phenotypic correlations and standard errors between educational attainment and general cognitive ability and achievement motivation.

	Educational attainment Full correlation	Educational attainment Partial correlation
general cognitive ability	.47 (.04) p<.001, N=542	.43 (.04) p<.001, N=515
achievement motivation	.31 (.04) p<.001, N=523	.25 (.04) p<.001, N=515

Notes: p=p-value; N=number of individuals; ns=non significant; standard errors are shown between brackets; correlation between general cognitive ability and achievement motivation is .21 (.04), p<.001, N=529; correlation between general cognitive ability and achievement motivation with effects of educational attainment partialled out: .08 (.05) ns, N=515.

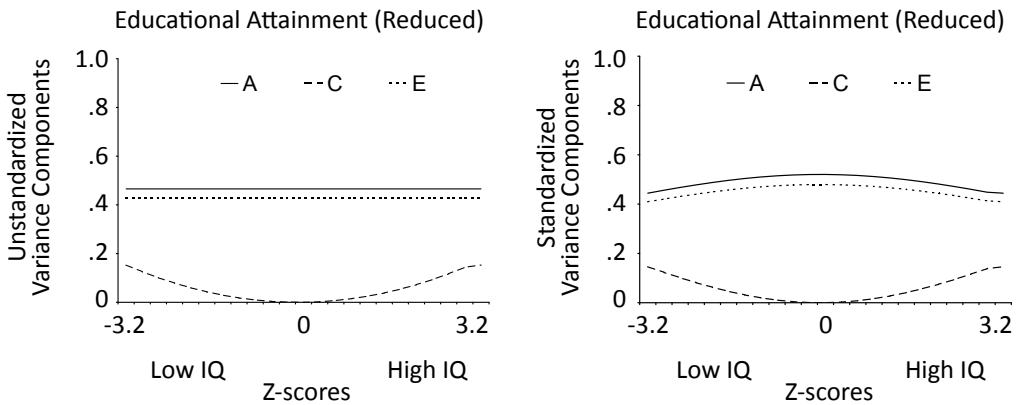***Correlation and moderation: educational attainment and general cognitive ability***
Based on the univariate genetic analyses (not shown), a bivariate model with variance components A, D, and E for general cognitive ability and variance components A, C, and E for educational attainment was specified (see Table 6.2 for twin correlations and variance components based on univariate analyses). Covariance between general cognitive ability and educational attainment was modeled as a function of A and E. Model fitting results are presented in Table 6.4. Analyses of the variance components specific to general cognitive ability showed that broad sense heritability (i.e., additive genetic factors + genetic dominance) was significant ($\chi^2(2)$=231.13, p<.001) (model 2). Please note that models in which the effects of genetic dominance and non-shared environmental factors are estimated but the additive genetic effects are fixed to zero, are not fitted because such models are biologically implausible (Falconer & Mackay, 1989). Genetic dominance (D) on its own, could however be eliminated from the model without a significant worsening of the model fit ($\chi^2(1)$=1.57, *ns*) (model 3). Analyses of moderation effects demonstrated that general cognitive ability significantly moderated the contribution of C unique to educational attainment ($\chi^2(1)$=3.60, p=.03) (model 9). None of the other moderation effects reached significance (models 6, 7, 8, and 10). Analyses also demonstrated significant effects of unmoderated additive genetic (a_c) ($\chi^2(1)$=44.66, p<.001) (model 12) and unique environmental (e_c) ($\chi^2(1)$=10.03, p<.001) (model 13) factors that were shared between general cognitive ability and educational attainment, implying a common genetic and common non-shared environmental background for educational attainment and general cognitive ability. When testing the significance of the variance components unique to educational attainment, additive genetic factors (a_u) ($\chi^2(1)$=2.31, *ns*) (model 15) and shared environmental factors (c_u) ($\chi^2(1)$=1.98, *ns*) (model 16) were non-significant but could not be

dropped simultaneously from the model without a significant deterioration of the model fit ($\chi^2(2)=50.55$, p<.001) (model 17), suggesting strong familial influence, most likely due to genetic factors (based on Akaike's Information Criterion).

Within the preferred model (model 16) standardized estimates of C for educational attainment varied from .00 to.15 as a function of general cognitive ability. C was increased in individuals with either low or high levels of general cognitive ability and was absent in individuals with intermediate levels of general cognitive ability. Although only linear moderation was included in the model, non-linear moderation appears in the final model due to the squaring of the path coefficients. As C is defined as $(c_u+c_u'*Mod_{tw1})^2$ (see Figure 6.1) and c_u is equal to zero, the contribution of c_u' is relatively large, which is why the resulting pattern of moderation appears non-linear. As the heritability is defined as the ratio of the genetic variance to the total variance, the broad sense heritability (h^2) varied concordantly from .52 to .44. Similarly, standardized estimates of E varied concordantly from .48 to .41. Figure 6.2 shows standardized and unstandardized variance components of educational attainment as a function of general cognitive ability.

Table 6.4 shows the genetic (.57) and environmental (.31) correlations between educational attainment and general cognitive ability, as well as the extent to which the phenotypic correlation between educational attainment and general cognitive ability is due to genetic and environmental factors. As the latter coefficient depends on the level of the moderator, percentages are provided for low (mean - 2.5 SD), intermediate (mean ± 0 SD), and high (mean + 2.5 SD) levels of (standardized) general cognitive ability. Results show a decreasing influence of genetic and environmental factors on the phenotypic correlation between educational attainment and general cognitive ability.

Figure 6.2 Unstandardized (left) and standardized (right) variance components of educational attainment as a function of general cognitive ability.

Notes: The figures are based on the most reduced models, i.e., on the models in which all non significant effects were fixed at zero. Unstandardized variance components (left) refer to the absolute contribution of A (additive genetic effects), C (shared environmental effects), and E (non-shared environmental effects); standardized variance components (right) refer to the relative contribution to variation in educational attainment as a function of general cognitive ability.

Table 6.4 Model fitting results for bivariate interaction models of educational attainment with general cognitive ability as moderator variable.

	model	against	-2LL	Par	df	χ^2	Δdf	p	AIC
1	Full model		3520.171	15	1384				752.171
2	**drop a+d**	**1**	**3751.297**	**13**	**1386**	**231.126**	**2**	**.000**	**979.297**
3	drop d	1	3521.736	14	1385	1.565	1	.105	751.736
4	*reference model 1 (= drop d)*	1	3521.736	14	1385	1.565	1	.105	751.736
5	drop a'_c	4	3522.220	13	1386	.484	1	.243	750.22
6	drop e'_c	4	3523.107	13	1386	1.371	1	.121	751.107
7	*reference model 2 (= drop a'_c e'_c)*	4	3523.118	12	1387	1.382	2	.501	749.118
8	drop a'_u	7	3523.206	11	1388	.088	1	.383	747.206
9	**drop c'_u**	**7**	**3526.718**	**11**	**1388**	**3.600**	**1**	**.029**	**750.718**
10	drop e'_u	7	3523.665	11	1388	.547	1	.230	747.665
11	*reference model 3 (=drop a'_u e'_u)*	7	3524.667	10	1389	1.549	2	.461	746.667
12	**drop a_c**	**11**	**3569.323**	**9**	**1390**	**44.656**	**1**	**.000**	**789.323**
13	**drop e_c**	**11**	**3534.697**	**9**	**1390**	**10.030**	**1**	**.001**	**754.697**
14	*reference model 4 (= reference model 3)*	11	3524.667	10	1389	1.549	2	.461	746.667
15	drop a_u	14	3526.980	9	1390	2.313	1	.064	746.98
*16	drop c_u	14	3528.959	9	1390	1.979	1	.080	748.959
17	**drop a_u c_u**	**14**	**3575.215**	**8**	**1391**	**50.548**	**2**	**.000**	**793.215**

			Low	Intermediate	High
rA	.57	%A	80	80	80
rE	.31	%E	20	20	20

	Parameter Estimates Reduced Model (95% CI)	
a_c	.39	(.28, .50)
a_u	-.56	(-.67, .44)
c'_u	.12	(-.29, .29)
e_c	-.21	(-.34, -.08)
e_u	-.62	(-.71, -.54)

Notes: p-values of all 1-df tests are based on a ½:½ mixture of $\chi^2(0)$ and $\chi^2(1)$ distributions (Dominicus et al., 2006); -2LL=minus 2 log likelihood; par=estimated parameters; χ^2=Chi square (difference in -2LL); p=p-value; AIC = Akaike's Information Criterion; r_A=genetic correlation; r_E=non-shared environmental correlation; %A=percentage of phenotypic correlation explained by genetic factors for Low, Intermediate, and High levels of general cognitive ability; %E=percentage of phenotypic correlation explained by non-shared environmental factors for Low, Intermediate, and High levels of general cognitive ability; *=preferred model; significant (moderation) effects are printed in bold font. Path-coefficients correspond to path-coefficients in Figure 6.1. The full model including 15 estimated parameters is described in the 'methods' section.

Correlation and moderation: educational attainment and achievement motivation

Based on the univariate genetic analyses, a bivariate model with variance components A, D, and E for achievement motivation and variance components A, C, and E for educational attainment was specified (see Table 6.2 for twin correlations and variance components based on univariate analyses). Covariance between achievement motivation and educational attainment was modeled as a function of A and E. Model fitting results are presented in Table 6.5. Analyses of the variance components specific to achievement motivation showed significance of additive genetic factors and genetic dominance ($\chi^2(2)$=27.27, p<.001) (model 2) and genetic dominance on its own ($\chi^2(1)$=8.02, p<.01) (model 3). Analyses of moderation effects demonstrated that achievement motivation significantly moderated the contribution of E unique to educational attainment ($\chi^2(1)$=2.81, p=.047) (model 10). None of the other moderation effects reached significance (models 5, 6, 8, and 9). Analyses also demonstrated significant effects of unmoderated additive genetic factors that were shared between achievement motivation and educational attainment (a_c) ($\chi^2(1)$=12.62, p<.001) (model 12). Unique environmental factors that were shared between achievement motivation and educational attainment were non-significant (e_c) ($\chi^2(1)$=2.28, *ns*) (model 13). This implies that the association between achievement motivation and educational attainment is completely due to correlation at the genetic level. When testing the significance of the variance components unique to educational attainment, additive genetic factors (a_u) ($\chi^2(1)$=.00, *ns*) (model 15) and shared environmental factors (c_u) ($\chi^2(1)$=.04, *ns*) (model 16) were non-significant but could not be dropped simultaneously from the model without a significant deterioration of the model fit ($\chi^2(2)$=45.84, p<.001) (model 17), suggesting the presence of strong familial influences, most likely due to common environmental effects (based on Akaike's Information Criterion).

Within the preferred model (model 15) standardized estimates of E varied from .22 to .58, E increased with increasing levels of achievement motivation. As the heritability is the ratio of the genetic variance to the total variance, the broad sense heritability (h^2) varied concordantly from .78 to .42. Shared environmental factors were non-significant and eliminated from the model. Figure 6.3 shows standardized and unstandardized variance components of educational attainment as a function of achievement motivation.

Table 6.5 also shows the genetic (r_A = 1.00) and environmental (r_E = .00) correlations between educational attainment and achievement motivation, as well as the extent to which the phenotypic correlation between educational attainment and achievement motivation is due to genetic and environmental factors. Results show that the genetic and environmental correlations as well as the extent to which the phenotypic correlation between educational attainment and achievement motivation is due to genetic and environmental factors are independent of the level of achievement motivation.

Table 6.5 Model fitting results for bivariate interaction models of educational attainment with achievement motivation as moderator variable.

	model	against	-2LL	est par	df	χ^2	Δdf	p	AIC
1	Full model		2780.813	15	1029				722.813
2	**drop a+d**	**1**	**2808.084**	**13**	**1031**	**27.271**	**2**	**.000**	**746.084**
3	**drop d**	**1**	**2788.830**	**14**	**1030**	**8.017**	**1**	**.002**	**728.83**
4	*reference model 1 (= full model)*	1	2780.813	15	1029				722.813
5	drop a'_c	4	2780.813	14	1030	.00	1	.500	720.813
6	drop e'_c	4	2781.862	14	1030	1.05	1	.153	721.862
7	*reference model 2 (*drop $a'_c e'_c$)	4	2782.225	13	1031	1.41	2	.494	720.225
8	drop a'_u	7	2782.225	12	1032	.00	1	.500	718.225
9	drop c'_u	7	2782.386	12	1032	.16	1	.344	718.386
10	**drop e'_u**	**7**	**2785.033**	**12**	**1032**	**2.81**	**1**	**.047**	**721.033**
11	*reference model 3 (=drop $a'_u c'_u$)*	7	2782.386	11	1033	.16	2	.923	716.386
12	**drop a_c**	**11**	**2795.007**	**10**	**1034**	**12.62**	**1**	**.000**	**727.007**
13	drop e_c	11	2784.661	10	1034	2.28	1	.066	716.661
14	*reference model 4 (=drop e_c)*	11	2784.661	10	1034	2.28	1	.066	716.661
*15	drop a_u	14	2784.661	9	1035	.00	1	.500	714.661
16	drop c_u	14	2784.703	9	1035	.04	1	.419	714.703
17	**drop $a_u c_u$**	**14**	**2830.496**	**8**	**1036**	**45.84**	**2**	**.000**	**758.496**

rA	1	%A	100
rE	0	%E	0

	Parameter Estimates Reduced Model (95% CI)	
a_c	-.72	(-.84, .50)
d	.15	(-.47, .47)
e_u	-.62	(-.72, -.53)
e'_u	-.08	(-.15, .00)

Notes: p-values of all 1-df tests are based on a ½:½ mixture of $\chi^2(0)$ and $\chi^2(1)$ distributions (Dominicus et al., 2006); -2LL=minus 2 log likelihood; par=estimated parameters; χ^2=Chi square (difference in -2LL); p=p-value; AIC = Akaike's Information Criterion; r_A=genetic correlation; r_E=non-shared environmental correlation; %A=percentage of phenotypic correlation explained by genetic factors; %E=percentage of phenotypic correlation explained by non-shared environmental; *=preferred model; significant (moderation) effects are printed in bold font. Path-coefficients correspond to path-coefficients in Figure 6.1. The full model including 15 estimated parameters is described in the 'methods' section.

Figure 6.3 Unstandardized (left) and standardized (right) variance components of educational attainment as a function of achievement motivation.
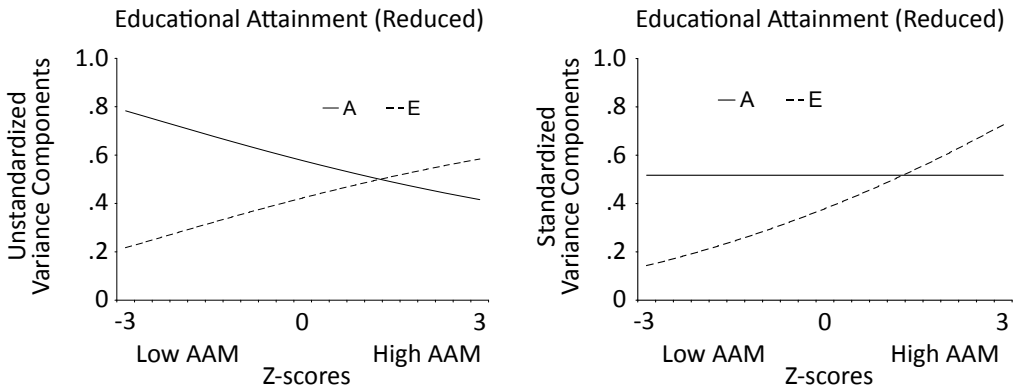
Notes: The figures are based on the most reduced models, i.e., on the models in which all non significant effects were fixed at zero. Unstandardized variance components (left) refer to the absolute contribution of A (additive genetic effects), standardized variance components (right) refer to the relative contribution to variation in educational attainment as a function of achievement motivation.

DISCUSSION

In this study we have confirmed considerable phenotypic correlations between educational attainment and general cognitive ability (r=.47) and between educational attainment and achievement motivation (r=.31). Higher levels of educational attainment coincided with having higher levels of general cognitive ability (independent of achievement motivation) and higher levels of achievement motivation (independent of general cognitive ability). Educational attainment and general cognitive ability were associated through common genetic factors (57%) and common environmental factors (31%), while the relation between educational attainment and achievement motivation was completely of genetic origin.

In addition, results demonstrated small but significant moderation of environmental effects. Contributions of shared environmental factors to individual differences in educational attainment increased in individuals with either low or high levels of general cognitive ability implying that individuals with either low or high levels of general cognitive ability are more vulnerable to those familial environmental influences that cause individual differences in educational attainment. For example, rearing style efforts (an environmental factor that is shared between family members), such as parental attention to their children's educational achievement, could have greater impact in individuals with either low or high levels of general cognitive ability.

Contributions of non-shared environmental factors on educational attainment increased in individuals with higher levels of achievement motivation implying that individuals with higher levels of achievement motivation are more vulnerable to non-shared environmental influences. Note that as non-shared environmental factors also include measurement error, it is plausible that the increasing effect of non-shared environmental factors with increasing levels of achievement motivation is due to increasing measurement error. Since non-shared environmental factors are not measured within the present study, it is not possible to disentangle measurement error and non-shared environmental factors.

Common genetic factors for educational attainment and general cognitive ability and moderation by general cognitive ability were previously reported (e.g. Tambs et al., 1989; Baker et al., 1996; Johnson et al., 2009). Common genetic factors for educational attainment and achievement motivation as well as moderation effects of achievement motivation have not been reported before.

Moderation of variance components of educational attainment by general cognitive ability was previously studied by Johnson et al. (2009), effects as reported in the present study differ somewhat from the results as presented by Johnson et al. Within a sample of 24-years-old, Johnson et al. reported generally decreasing shared environmental influences and generally increasing genetic influences on educational attainment as a function of increasing levels of general cognitive ability (measured at age 17). Non-shared environmental factors were unaltered. Within the present study, data suggested no significant moderation of genetic factors. Shared environmental factors were absent in individuals with mean levels of general cognitive ability and were increased in individuals with lower or higher levels of general cognitive ability. Differences between the two studies may be due to the age differences of the two samples. The majority of the participants in the present study had, given the age range of 23-75 years, completed their educational trajectory. Although information on whether participants aged 24 were enrolled in educational programs at the time of study participation was included in the analyses by Johnson et al. (Johnson et al., 2009), it is possible that particularly higher educated individuals had not completed their education yet. Furthermore, heritability of general cognitive ability tends to increase with increasing age, with larger genetic influences at later age (Haworth et al., 2009). Differences in the genetic and environmental etiology of the moderator may affect the moderator effect on the variance components of educational attainment.

Limitations

A number of limitations of this study should be noted. Effects of sex and age on the relative importance of genetic and environmental factors were not considered within the present study. Earlier studies on educational attainment, however, suggested significant effects of sex and age with higher heritability estimates in males, and higher shared- and non-shared environmental influences in older people (Heath et al., 1985; Tambs et al., 1989; Lichtenstein & Pedersen, 1997). A larger sample size would be required to model variance components as a function of both age and sex in the context of environmental moderation. We did partial out effects of age and sex on the means to avoid potential bias in heritability estimates, we were however unable to investigate possible age and sex effects on the variance components of educational attainment nor on the effects of the moderator.

In our genetic models, absence of parental assortative mating was assumed. The failure to accommodate assortative mating when the assumption of random mating is actually violated, might result in deflated estimates of genetic- and inflated estimates of shared environmental effects (Keller et al., 2009). Estimates of the moderator are however not seriously affected (Loehlin et al., 2009). A large sample that includes twins with their spouses or parents of the twins and siblings would allow the modeling of genetic and environmental moderation in the presence of assortative mating.

Within the present study, moderation effects were modeled as a linear function

of the moderator. It is however conceivable that genetic or environmental effects are attenuated or exaggerated at extreme high and extreme low levels of the moderator. Such non-linear effects can be facilitated by including a quadratic moderation term in the model (Purcell, 2002). Within the present sample, an ordinal variable (educational attainment, 7 categories of increasing attainment level) was used in combination with a continuous moderator. A larger sample size, preferably in combination with a continuous measurement level of the trait and an ordinal measurement level of the moderator, is necessary to reliably model non-linear moderation.

In the present paper we have shown that educational attainment and general cognitive ability, and educational attainment and achievement motivation, are associated through common genetic and common non-shared environmental factors, and that the extent to which environmental effects cause individual differences in educational attainment is not randomly distributed across the entire population, but varies as a function of general cognitive ability and achievement motivation. These results increase our understanding of underlying mechanisms of associations between educational attainment and general cognitive ability, and between educational attainment and achievement motivation. Understanding these mechanisms may be useful in social and political programs concerning education. Efforts to optimize educational attainment should consider levels of general cognitive ability and achievement motivation as both traits control the effect of environmental factors on individual differences in educational attainment. Finally, results of the present study may also be useful in future efforts in gene finding for educational attainment. For example, association studies may consider shared genetic influences for educational attainment and general cognitive ability and for educational attainment and achievement motivation. Association studies may also consider the relatively increased effect of genetic factors in individuals with intermediate levels of general cognitive ability or in individuals with low levels of achievement motivation (due to decreased environmental influences).

Chapter 7

Life Events

Life events moderate variation in general cognitive ability in adults

ABSTRACT

Heritability estimates of general cognitive ability in adults range from 75-85%. These estimates are based on the assumption that genes and environment act in an additive manner. This assumption has, however, not been extensively tested. We set out to test this assumption for general cognitive ability by studying gene by environment interaction. To this end, moderation effects of different *positive*, *negative* and *neutral* Life Events on the variance components of general cognitive ability were investigated in a sample of adult twins and siblings (N=560). Results demonstrated modest moderation of genetic influences and considerable moderation of environmental influences; heritability estimates ranged from 32% to above 90%. We conclude that the extent to which genetic and environmental factors influence individual differences in general cognitive ability in adults is partly dependent on exposure to Life Events.

INTRODUCTION

Heritability estimates of general cognitive ability in adults vary between ~75% and ~85% (Bouchard, Jr. & McGue, 1981; Plomin et al., 1994a; Plomin, 1999; Posthuma et al., 2001a; Haworth et al., 2009). These estimates are derived from twin studies in which it is generally assumed that genes and environment act in an additive manner. For a number of traits and disorders this assumption works well in practice. For complex polygenic traits, such as general cognitive ability, this assumption may, however, not hold and could lead to biased estimates of the relative importance of genetic and environmental influences, which in turn may seriously frustrate attempts at gene finding.

Two different forms of non-additivity between genes and environment are generally recognized: gene-environment correlation ($r_{(GE)}$) and gene by environment interaction (GEI). In $r_{(GE)}$, the environmental influences are not a random sample of the entire range of possible environments but are correlated with, or a function of, the genotype of an individual. In GEI, genes control an individual's sensitivity to an environmental factor, or the environment controls the expression of genes.

At present, several studies have provided evidence of GEI in the context of general cognitive ability. Most studies focused on childhood and adolescent general cognitive ability (Rowe et al., 1999; Turkheimer et al., 2003; Caspi et al., 2007; Harden et al., 2007; Loehlin et al., 2009). Rowe et al. (1999) investigated the heritability of general cognitive ability stratified by low and high parental education. Results demonstrated higher heritability of general cognitive ability in children from more highly educated families, compared to children from less well-educated families. Related to this, Turkheimer et al. (2003) reported increasing heritability of general cognitive ability with higher socio-economic status. Data collected in the Netherlands Twin Register (NTR, Boomsma et al., 2006) demonstrated an increasing heritability across the life span (GxAge) within a partly cross-sectional, partly longitudinal sample (Boomsma & van Baal, 1998; Posthuma et al., 2001a; van Leeuwen et al., 2008; Polderman et al., 2009).

Few studies have investigated GEI in general cognitive ability in adults (Kremen et al., 2005; van der Sluis et al., 2008b). These studies did not provide evidence for moderation of genetic influences on general cognitive ability, although they did report moderation of shared environmental effects. Kremen et al. (2005) showed decreased shared environmental variation in 'word recognition' in an adult male sample with highly educated parents. More recently, Van der Sluis et al. (2008b) showed increased shared environmental variation in older men whose parents were highly educated and increased non-shared environmental variation in older men living in more affluent areas.

In the context of psychiatric dysfunctioning, significant moderation effects of life events, such as childhood adversity, violence, and health problems, have been reported on genetic influences on depression (Wichers et al., 2009; Caspi et al., 2003), anxiety (Silberg et al., 2001), and borderline personality disorder (Distel et al., 2009a). Life events may also affect the variance decomposition of general cognitive ability. For example, positive life events may function as "proximal processes" (Bronfenbrenner & Ceci, 1994) that actualize genetic potential, while negative life events may cause negative emotional stress resulting in reduced genetic potential and a (relative) increase of the effects of environmental factors.

In the present study, we investigate moderation effects of life events on the variance

components of general cognitive ability in adults (age 23-75) (i.e., GxLife Events, CxLife Events, ExLife Events). Moderation effects of *individual* Life Events as well as composite measures of *Positive*, *Negative* and *Neutral* Life Events will be examined.

METHODS

Sample

This study is part of a large ongoing project on the genetics of cognition (Posthuma et al., 2001a) performed with understanding and written consent of each participant and approved by the Central Committee on Research Involving Human Subjects in the Netherlands. Information on environmental factors was gathered using the Life Experiences List (LEL), which is described in more detail below. Data were available for 560 twins and siblings (58.9% female) from 256 different families that were registered in the Netherlands Twin Register (NTR, Boomsma et al., 2006). The sample consisted of 150 complete twin pairs (55.33% MZ), 87 incomplete twin pairs (32.10% MZ) and 172 siblings (47.1% men, 0-5 per siblings per family). From 19 families, only sibling data were available. The average age of the participants was 47.11 years (SD=12.40, range: 23–75) at the time they completed the LEL. All five zygosity groups were reasonably well represented: monozygotic males (MZM: 21.5%, 119 participants), monozygotic females (MZF: 26.8%, 150 participants), dizygotic males (DZM: 11.8%, 66 participants), dizygotic females (DZF: 23.4%, 131 participants), and dizygotic opposite sex (DOS: 16.8%, 94 participants). Zygosity of same-sex twins was based on DNA polymorphisms (97 pairs, 74.1%) or, if DNA markers were not available, on questions about physical similarity and confusion of the twins by family members and strangers. Agreement between zygosity diagnoses from survey and DNA was 97% (Willemsen et al., 2005). The sample was representative for the general Dutch population with regard to educational level (see Posthuma et al., 2001a for details).

Measures

General cognitive ability

General cognitive ability was assessed with the Dutch version of the WAIS-IIIR. Data collection occurred at one of two time points. In the first wave of data collection (1997-2001), participants (N=484) completed eleven subtests of the WAIS-IIIR: Block design, Letter-number sequencing, Information, Matrix reasoning, Similarities, Picture completion, Arithmetic, Vocabulary, Digit symbol-coding, Digit-symbol pairing and Digit symbol-free recall. In the second wave of data collection (2007-2009), participants (N=67) completed seven subtests of the WAIS-IIIR: Block design, Letter-number sequencing, Information, Matrix reasoning, Arithmetic, Vocabulary and Digit symbol-coding. Full scale IQ (FSIQ) was derived from these subtests, and is the unit of analysis in this study. The correlation between FSIQ assessed with eleven or seven subtests was high (Pearson's r = .95, N = 484, p<.001). 59 participants completed the WAIS twice with an interval of ~10 years (first and second wave of data collection) to evaluate test-retest reliability (Pearson's r=.85, N=59, p<.001).

Life Events

Information on Life Events was collected using 19 questions from the List of Threatening Experiences (Brugha & Cragg, 1990) that was incorporated in the Life Experiences List (LEL) (Vinkhuyzen et al., 2010a). The LEL was sent out to participants by mail (overall response rate 76%).

Participants were asked how often, and at what time in their life (before age 12, between age 12 and age 18; after age 18 but more than five years ago; less than five years ago), a particular Life Event had taken place. In the present study, we only used information on whether or not a Life Event took place. Moderation effects of Life Events were studied in two ways: by using composite measures of *positive*, *negative,* and *neutral* Life Events and by looking at the moderation effects of *individual* Life Events.

Composite measures of Life Events represented the number of different *positive*, *negative* or *neutral* Life Events a subject had been exposed to in his/her life. *Positive Life Events* was a sum score of events concerning *Graduation, Promotion, Marriage, Driving license,* and *Birth of a child* (range 0-5). *Neutral Life Events* was a sum score of *Changing schools in childhood, Moving house,* and *Retirement* (range 0-3). *Negative Life Events* was a sum score of S*evere illness/violent assault, Divorce, Falling-out/Breaking up with friends/ relatives, Severe trouble with friends/relatives, Death of friends/relatives, Receiving mental health treatment, Severe offence, Robbery, Sexual abuse, Being fired,* and *Unemployment* (range 0-11). Since few subjects (<8%) were exposed to seven or more different *negative* Life Events, scores 7-11 were collapsed (i.e., recoded as 7). Classification of individual Life Events into categories of positive, negative or neutral Life Events was in line with Kendler and Baker (2007).

Individual measures of Life Events were specified as ordinal measures representing categories 'never experienced', 'experienced once or twice', and 'experienced more than twice'. The second and third category were collapsed if the third category comprised less than 3% of the sample.

Test-retest reliability of the Life Events items was investigated in an independent sample of 62 participants who completed the LEL twice within a period of two months (31 parent-offspring pairs, 75.4% women; age range 17-71, mean: 39.95, SD: 16.19). Test-retest reliability was calculated in PRELIS (Joreskog & Sorbom, 2006) and indicated good reliability for both *composite* and *individual* measures of Life Events (mean = .82; range .61-1.00).

Statistical analyses

The variance of FSIQ was decomposed into additive genetic factors (*A*), shared environmental factors (*C*), and non-shared environmental factors (*E*). *A* represents additive effects of alleles summed over all genetic loci. *C* represents environmental influences that render members of the same family more alike. *E* represents all environmental influences that result in differences between members of a family, including measurement error. The choice of an ACE-model was based on previous research on individual differences in general cognitive ability (Bouchard, Jr. & McGue, 1981; Plomin, 1999; Posthuma et al., 2001a; van der Sluis et al., 2008b). *A*, *C* and *E* were allowed to vary as a function of exposure to Life Events. Genetic or environmental effects may be attenuated or exaggerated at extreme high and extreme low levels of the moderator. Including a quadratic interaction term in the model facilitates detecting such non-linear effects (Purcell, 2002). We therefore included both

linear and non-linear moderation effects of life events on the variance components of FSIQ, except when the life event was dichotomous (since squaring does not affect dichotomous measures).

Figure 7.1 shows the full univariate interaction model for one twin pair. When available, data of additional siblings were included in the analyses. Within the full univariate model, conditional on the twins' moderator M_1, the expected trait mean for twin i is: $E(Y_i) = m+m'M_{1i}$ where m represents the part of the mean that is independent of the moderator (grand mean), and m' the linear effect of the moderator on the mean.

The expected variance of FSIQ is calculated as:
$Var(FSIQ)=(a+a'M_{1i}+a''M_{1i}{}^2)^2+ (c+c'M_{1i}+c''M_{1i}{}^2)^2+ (e+e'M_{1i}+e''M_{1i}{}^2)^2$,where **a**, **c**, and **e** represent the path coefficients of A, C, and E that are independent of the moderator, a', c', and e' represent linear, and a'', c'', and e'' represent non-linear effects (on the path coefficients) of the moderator[7].

Causes of individual differences in general cognitive ability and Life Events in a largely overlapping sample have been described previously. Genetic factors accounted for ~86% of the phenotypic variance of general cognitive ability (Posthuma et al., 2001a) and for ~30% of the phenotypic variance of Life Events (Vinkhuyzen et al., 2010a). As both FSIQ and (subjective report of) exposure to Life Events have been reported to be under genetic control, these variables may share a common genetic background ($r_{(GE)}$) or a common environmental background ($r_{(CE)}$, $r_{(EE)}$). Ignoring genetic or environmental factors that are shared between trait and moderator in an interaction model, may lead to biased estimates of the effect of the moderator (Purcell, 2002). However, as phenotypic correlations between Life Events and FSIQ were very close to zero (see Table 7.1), shared genetic and environmental factors are not expected to be substantial. Explicitly modeling of moderation of genetic and environmental influences that are shared between trait and moderator was therefore deemed unnecessary. Linear effects of the moderator were, however, included on the means, to correct for any – unmoderated – correlation between Life Events and FSIQ (see Purcell, 2002).

A series of univariate interaction models was fitted for each moderator (3 *composite* measures and 19 *individual* measures of Life Events) separately. To avoid multicollinearity and related computational problems, the composite measures were mean-centered around 0 such that *positive* Life Events ranged from -2.5 to 2.5, *negative* Life Events from -3.5 to 3.5, and *neutral* Life Events from -1.5 to 1.5. Ordinal *individual* Life Events were coded as: -1 (never experienced), 0 (experienced once or twice), and 1 (experienced more than twice). Dichotomous moderators were coded as: 0 (never experienced) and 1 (experienced once or more). As many studies have shown that shared environmental factors do not explain

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7   When a moderator X is coded as a variable with a mean of 0, then the interaction term X^2, created by squaring X, is completely uncorrelated with X because high values of X^2 go with low as well as high values of X. In contrast, if we would use the raw scores of the composite measures (ranging between 0-5, 0-11, and 0-3 for Positive, Negative, and Neutral Life Events respectively), then the interactions terms of these composite measures would be correlated .98, .94, and .96, respectively, with the original measures because low/high scores on the original measures always go with low/high scores on the interaction terms. Such multicollinearity results in computational problems.

Figure 7.1 Full univariate interaction model for one twin pair
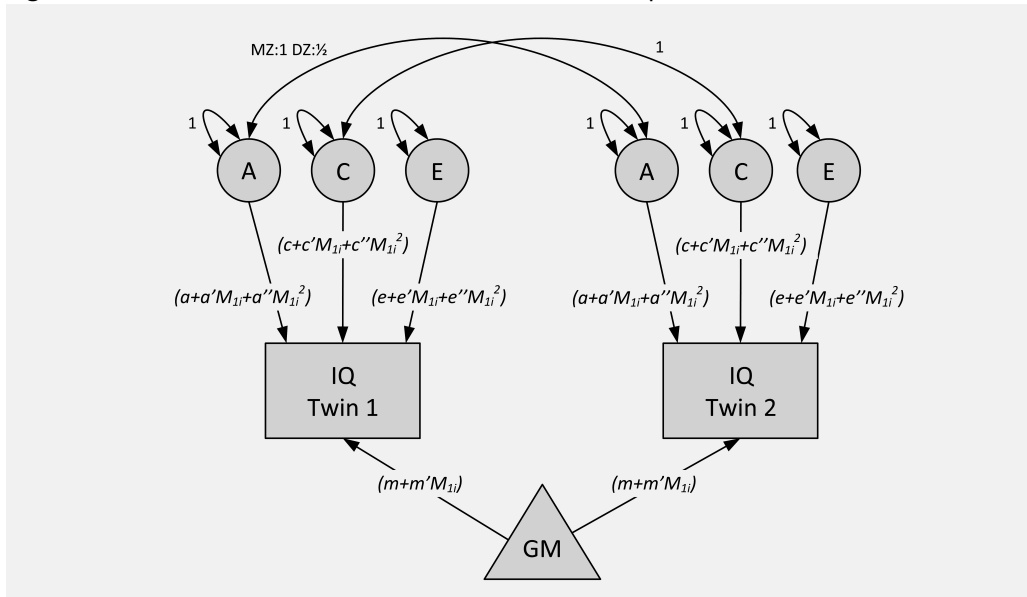
Notes: Univariate model including linear- and non-linear moderation effects of the observed environmental moderator on the variances of twin 1 and twin 2; linear moderation effects of the observed environmental moderator on the means of twin 1 and twin 2. Parameters a, c, and e represent the parts of A (additive genetic effects), C (shared environmental effects), and E (non-shared environmental effects) that are independent of the moderator, a', c', and e' represent linear, and a'', c'', and e'' represent non-linear effects of the moderator. Within in the means model, GM represents the observed grand mean, m represents the part of the mean that is independent of the moderator (intercept) and m' represents the linear effect on the mean (slope). Note that c is not incorporated in the full GEI interaction model but is illustrated for ease of interpretation.

individual differences in general cognitive ability in adults (Luciano et al., 2001; Posthuma et al., 2001a; Wright et al., 2001; Rijsdijk et al., 2002), **c** (i.e., part of *C* that is independent of the moderator) was fixed to zero within the full model. Note that although *C* is absent within the general population, effects of *C* may be substantial under certain environmental conditions. Moderation effects on *C* were therefore included in the model. We note that similar results were established in case **c** was incorporated in the model.

Significance of the non-linear (*a''*, *c''* and *e''*) and linear (*a'*, *c'* and *e'*) moderation effects on the variance components was established by comparing the fit of nested (increasingly more restricted) models to the fit of less restricted models. Goodness-of-fit of these sub-models was assessed by likelihood-ratio-tests. When testing the significance of a variance component, it is well established that the null distribution of a suitably parameterized variance component is a .5:.5 mixture of a $\chi^2(0)$ and $\chi^2(1)$ (Macgregor et al., 2005; Dominicus et al., 2006). We therefore tested against a critical value of $\chi^2(1)= 2.7055$, given alpha = 0.05, when testing for the significance of moderation effects on the variance components.

Age and sex corrected FSIQ measures were used to ensure that moderation effects were unaffected by age and sex. All analyses were carried out using the raw data option in Mx (Neale, 1994).

RESULTS

Main effects
The upper part of Table 7.1 shows FSIQ scores and means (SD) of composite measures of Life Events. Correlations between FSIQ and composite measures of Life Events were close to zero.

Ȃ The lower part of Table 7.1 lists the prevalence of exposure to each individual Life Event, as well as the regression coefficients (β) for the regression of FSIQ on these Life Events. For 12 individual Life Events, endorsement rates in the third category were below 3% (see Table 7.1), second and third categories of these Life Events were collapsed in subsequent analyses.

Ȃ Six individual Life Events were significantly related to FSIQ scores: increasing exposure to *Graduation, Driving license, Birth of child, Death of friends/relatives,* and *Moving house* was related to a higher FSIQ score.

Gene-environment interaction – Composite measures of Life Events
Table 7.2 shows the model fitting results of the three composite measures of Life Events.

Ȃ *Positive* Life Events significantly moderated the contribution of shared environmental factors (*C*). *C* was considerably increased in individuals not exposed to *positive* Life Events or exposed to many different *positive* Life Events, while shared environmental effects were absent in individuals exposed to some *positive* Life Events. Standardized estimates of C varied from .62 at the low and high end of the moderator distribution (i.e., no or frequent exposure) to .00 at the center (i.e., occasional exposure). As the heritability is the ratio of the genetic variance to the total variance, the broad sense heritability (h^2) varied concordantly from .32 (no or frequent exposure) to .83 (occasional exposure).

Ȃ *Negative* Life Events significantly moderated the effects of non-shared environmental effects (*E*). *E* was estimated at .11 in individuals hardly exposed to *negative* Life Events, while *E* increased to .26 in subjects frequently exposed to *negative* Life Events.

Ȃ Moderation effects of *Neutral* Life Events were non significant. Figure 7.2 shows standardized and unstandardized variance components of FSIQ as a function of composite measures of *positive* and *negative* Life Events. Note that all figures are based on the most reduced models, i.e., on the models in which all non significant effects were fixed at zero.

Table 7.1 Prevalences of exposure to Life Events, FSIQ (grand mean, corrected for age and sex effects) and regression coefficients (effect of Life Event on FSIQ).

Composite measures of Life Events	Mean LE	Spearman Rho LE*FSIQ	grand mean FSIQ	β (p-value)
Life Events Positive	2.80 (1.01)	.01 (ns)	100.50	.85 (p=.16)
Life Events Negative	3.18 (2.32)	-.02 (ns)	100.73	-.17 (p=.53)
Life Events Neutral	1.37 (.66)	.08 (ns)	101.12	.79 (p=.21)

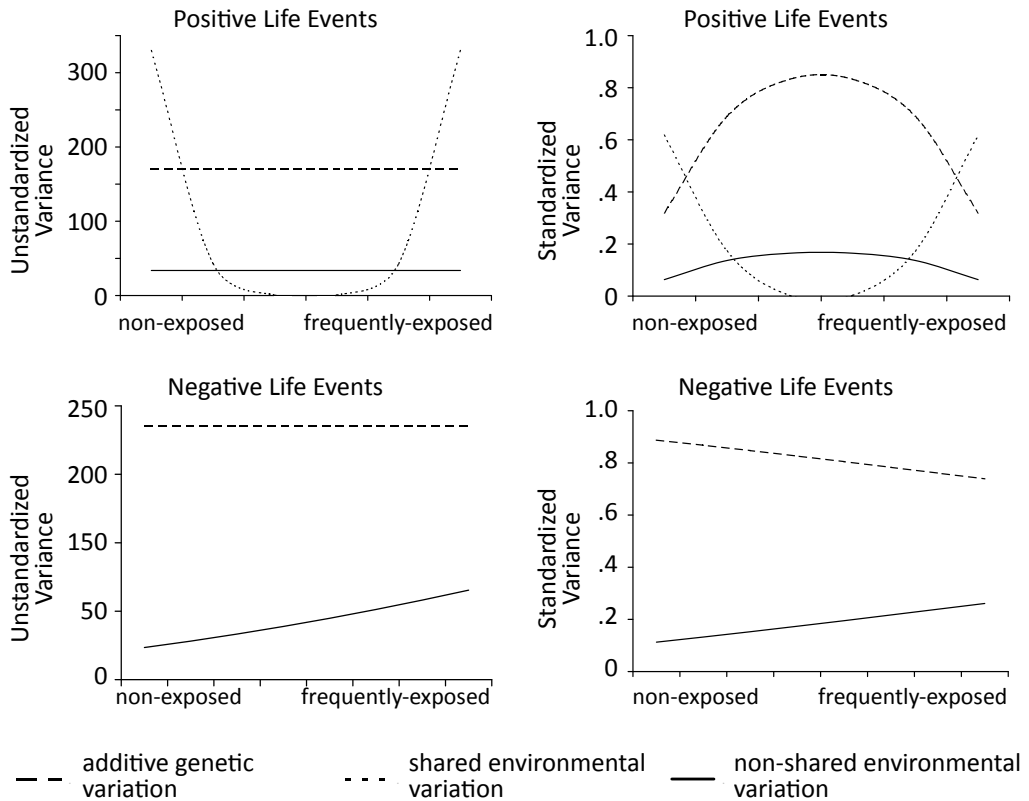| Individual Life Events	Non-exposed N(%)	Exposed once (or twice) N(%)	Exposed > twice N(%)	grand mean FSIQ	β (p-value)
Positive individual Life Events					
Graduation	56 (10%)	280 (51%)	218 (39%)	100.36	1.88 (p=.04)
Promotion	399 (72%)	98 (18%)	57 (10%)	100.23	.63 (p=.48)
Marriage*	216 (39%)	331 (60%)	7 (1%)	100.03	1.32 (p=.14)
Driving license*	69 (13%)	472 (85%)	13 (2%)	96.31	5.22 (p=.01)
Birth of child	253 (46%)	194 (35%)	107 (19%)	101.41	2.21 (p=.004)
Negative individual Life Events					
Severe illness/ Violent assault *	459 (83%)	81 (15%)	14 (2%)	100.74	.33 (p=.80)
Divorce*	438 (79%)	105 (19%)	11 (2%)	100.93	-.41 (p=.78)
Falling-out/Breaking up with friends/relatives*	439 (79%)	101 (18%)	14 (3%)	101.14	-1.23 (p=.38)
Severe trouble with friends/ relatives*	463 (84%)	85 (15%)	6 (1%)	101.23	-1.26 (p=.30)
Death of friends/relatives	239 (43%)	167 (30%)	148 (27%)	101.14	1.95 (p=.002)
Receiving mental health treatment *	453 (82%)	90 (16%)	11 (2%)	100.86	-.19 (p=.80)
Severe offence*	503 (91%)	48 (9%)	3 (1%)	100.82	.12 (p=.94)
Robbery	355 (64%)	170 (31%)	29 (5%)	101.89	1.61 (p=.08)
Sexual abuse*	517 (93%)	36 (7%)	1 (0%)	100.82	-.25 (p=.90)
Being fired*	487 (88%)	64 (11%)	3 (1%)	100.07	-2.06 (p=.14)
Unemployment*	492 (89%)	57 (10%)	5 (1%)	100.97	-1.13 (p=.42)
Neutral individual Life Events					
Changing schools in childhood	389 (70%)	136 (25%)	29 (5%)	100.96	.32 (p=.73)
Moving house	102 (18%)	186 (34%)	266 (48%)	99.69	3.98 (p<.001)
Retirement*	524 (95%)	30 (5%)	0 (0%)	100.62	2.99 (p=.30)

*Notes: If the 3rd category contained <3% of the data, the 2nd and 3rd categories were collapsed in subsequent analyses; * = moderator variables of which the 2nd and 3rd categories are collapsed; β = regression coefficient of FSIQ on Life Events; LE = Life Events; FSIQ = Full Scale Intelligence Quotient; ns = non significant. Grand mean of FSIQ and regression coefficients (β) are based on models in which the 3rd and 2nd categories were collapsed in case the 3rd category contained <3% of the data.*

Table 7.2 Model fitting results for interaction models of FSIQ with composite measures of Life Events as moderator variables.

model		-2LL	par	χ^2	p
Positive Life Events					
1	AE-model	4356.31	10		
2	drop non-linear moderation A	4356.35	9	.04	.42
3	**drop non-linear moderation C**	**4359.66**	**9**	**3.35**	**.03**
4	drop non-linear moderation E	4356.62	9	.31	.29
5	drop linear moderation A	4357.63	9	1.31	.13
6	drop linear moderation C	4358.05	9	1.73	.09
7	drop linear moderation E	4356.39	9	.07	.39
Negative Life Events					
1	AE-model	4358.28	10		
2	drop non-linear moderation A	4359.05	9	.77	.19
3	drop non-linear moderation C	4358.75	9	.47	.25
4	drop non-linear moderation E	4360.24	9	1.96	.08
5	drop linear moderation A	4359.15	9	.87	.18
6	drop linear moderation C	4358.31	9	.03	.43
7	**drop linear moderation E**	**4361.76**	**9**	**3.48**	**.03**
Neutral Life Events					
1	AE-model	4359.25	10		
2	drop non-linear moderation A	4360.10	9	.85	.18
3	drop non-linear moderation C	4359.40	9	.15	.35
4	drop non-linear moderation E	4359.34	9	.09	.38
5	drop linear moderation A	4359.33	9	.08	.39
6	drop linear moderation C	4359.95	9	.69	.20
7	drop linear moderation E	4359.56	9	.30	.29

Notes: p-values are based on a ½:½ mixture of chi-square distributions (Dominicus et al., 2006); models 2-7 were compared to the AE-model (½:½ mixture of $\chi^2(0)$ and $\chi^2(1)$); -2LL = minus 2 log likelihood; par = estimated parameters; χ^2 = Chi square (difference in -2LL); p = p-value; significant moderation effects are printed in bold font.

Figure 7.2 Unstandardized (left) and standardized (right) variance components of FSIQ as a function of the composite measures of Positive and Negative Life Events.

Notes: The figures are based on the most reduced models, i.e., on the models in which all non significant effects were fixed at zero. Unstandardized variance components (left) refer to the absolute contribution of A (additive genetic effects), C (shared environmental effects), and E (non-shared environmental effects); standardized variance components (right) refer to the relative contribution to variation in FSIQ as a function of the composite measures of Positive and Negative Life Events.

GENE-ENVIRONMENT INTERACTION – INDIVIDUAL LIFE EVENTS
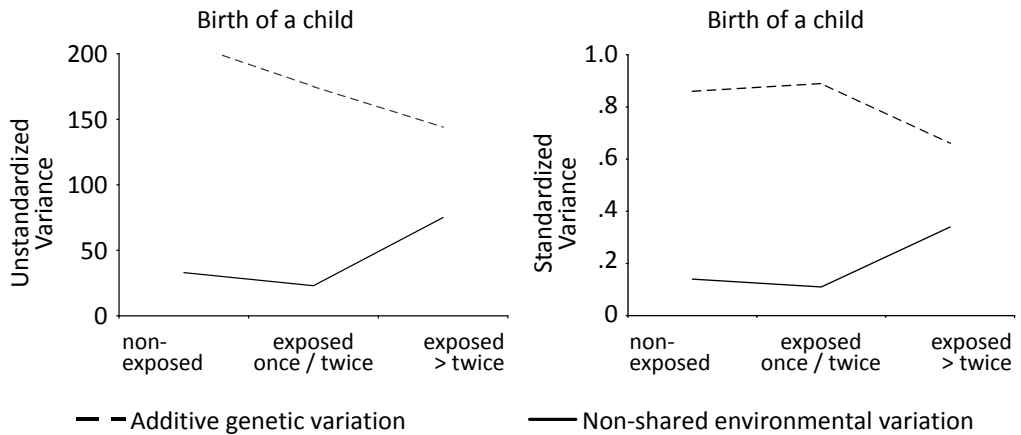
Positive individual Life Events

Table 7.3 shows the model fitting results of the *positive* individual Life Events. Only *Birth of a child* significantly moderated the variance components of FSIQ: *A* was decreased in individuals who had children (.86 vs .66) while *E* was considerably increased in individuals who had more than two children (.14 vs .34). Figure 7.3 shows standardized and unstandardized variance components of FSIQ as a function of *Birth of a child*.

Table 7.3 Model fitting results for interaction models of FSIQ with positive individual Life Events as moderator variable.

model		-2LL	par	χ^2	p
Graduation					
1	AE-model	4350.06	10		
2	drop non-linear moderation A	4350.34	9	.28	.30
3	drop non-linear moderation C	4350.07	9	.01	.46
4	drop non-linear moderation E	4352.09	9	2.03	.08
5	drop linear moderation A	4352.66	9	2.60	.05
6	drop linear moderation C	4350.94	9	.88	.17
7	drop linear moderation E	4350.24	9	.18	.34
Promotion					
1	AE-model	4359.45	10		
2	drop non-linear moderation A	4359.45	9	.00	incalc.
3	drop non-linear moderation C	4359.96	9	.51	.24
4	drop non-linear moderation E	4359.45	9	.00	incalc.
5	drop linear moderation A	4359.58	9	.14	.36
6	drop linear moderation C	4360.96	9	1.51	.11
7	drop linear moderation E	4361.19	9	1.74	.09
Marriage					
1	AE-model	4365.46	7		
2	drop linear moderation A	4365.47	6	.01	.47
3	drop linear moderation C	4365.46	6	.00	incalc.
4	drop linear moderation E	4365.50	6	.04	.42
Driving License					
1	AE-model	4356.34	7		
2	drop linear moderation A	4356.38	6	.04	.42
3	drop linear moderation C	4356.34	6	.00	incalc.
4	drop linear moderation E	4357.10	6	.76	.19
Birth of child					
1	AE-model	4347.53	10		
2	drop non-linear moderation A	4347.99	9	.46	.25
3	drop non-linear moderation C	4347.53	9	.00	incalc.
4	**drop non-linear moderation E**	**4352.44**	**9**	**4.91**	**.01**
5	**drop linear moderation A**	**4350.96**	**9**	**3.43**	**.03**
6	drop linear moderation C	4347.53	9	.00	incalc.
7	**drop linear moderation E**	**4351.92**	**9**	**4.39**	**.02**

Notes: p-values are based on a ½:½ mixture of chi-square distributions (Dominicus et al., 2006); models 2-7 were compared to the AE-model (½:½ mixture of $\chi^2(0)$ and $\chi^2(1)$); -2LL = minus 2 log likelihood; par = estimated parameters; χ^2 = Chi square (difference in -2LL); incalc. = incalculable; p = p-value; significant moderation effects are printed in bold font.

Figure 7.3 Unstandardized (left) and standardized (right) variance components of FSIQ as a function of the individual Life Event Birth of a Child.

Notes: Positive Life Events: Unstandardized (left) and standardized (right) variance components of FSIQ as a function of Birth of a child. The figures are based on the most reduced models, i.e., on the models in which all non significant effects were fixed at zero. Unstandardized variance components (left) refer to the absolute contribution of A (additive genetic effects) and E (non-shared environmental effects); standardized variance components (right) refer to the relative contribution to variation in FSIQ for individuals "non-exposed", "exposed once or twice" and "exposed more than twice".

Negative individual Life Events

Table 7.4 shows the model fitting results of the *negative* individual Life Events. *Falling out/ Breaking up with friends/relatives, Severe trouble with friends/relatives, Death of friends/ relatives, Severe offence, Being fired,* and *Unemployment* showed significant moderation effects on the variance components of FSIQ. *A* was slightly decreased in individuals exposed to *Falling out/Breaking up with friends/relatives* and *Death of friends/relatives. E* was increased in individuals exposed to *Severe trouble with friends/relatives* and *Severe offence,* and decreased in individuals who had been *Fired* or *Unemployed*.

Note that moderation effects on unstandardized variance components can be significant while *standardized* variance components remain virtually unchanged. As the standardized estimates are a function of both the individual unstandardized variance components and the total unstandardized variance (i.e., the sum of all unstandardized components), moderator-related fluctuations in the unstandardized components are not always mirrored in the standardized components. For example, the estimated unstandardized additive genetic variance decreased from 198 to 155 (with total variances of 238.12 and 195.18, respectively) in subjects frequently exposed to *Death of friends/ relatives,* while the standardized additive genetic effects decreased only slightly from .83 to .80.

Figure 7.4 shows the standardized and unstandardized variance components of FSIQ as a function of the six *negative* individual Life Events that significantly moderated the variance decomposition of FSIQ.
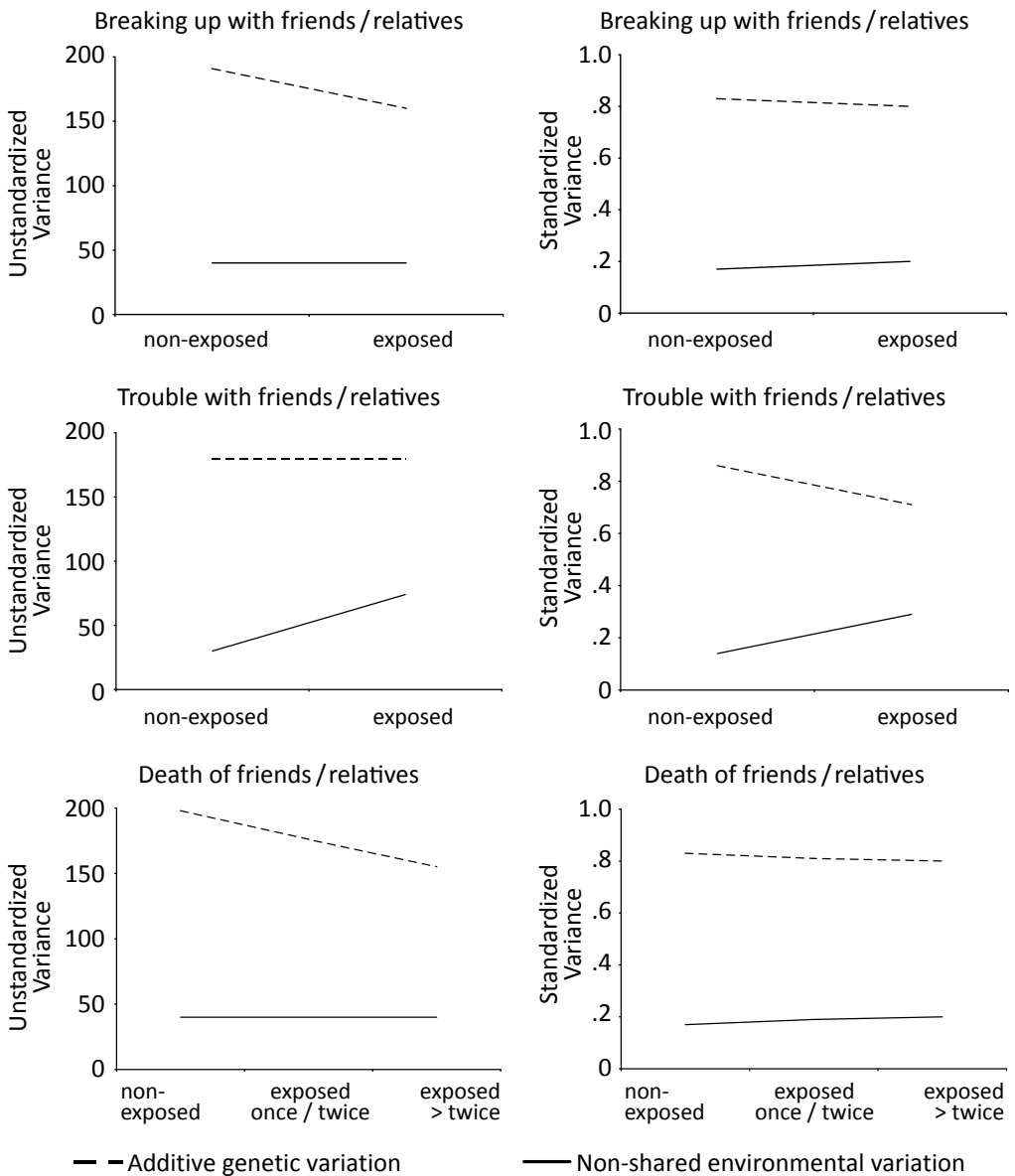
Table 7.4 Model fitting results for interaction models of FSIQ with negative individual Life Events as moderator variables.
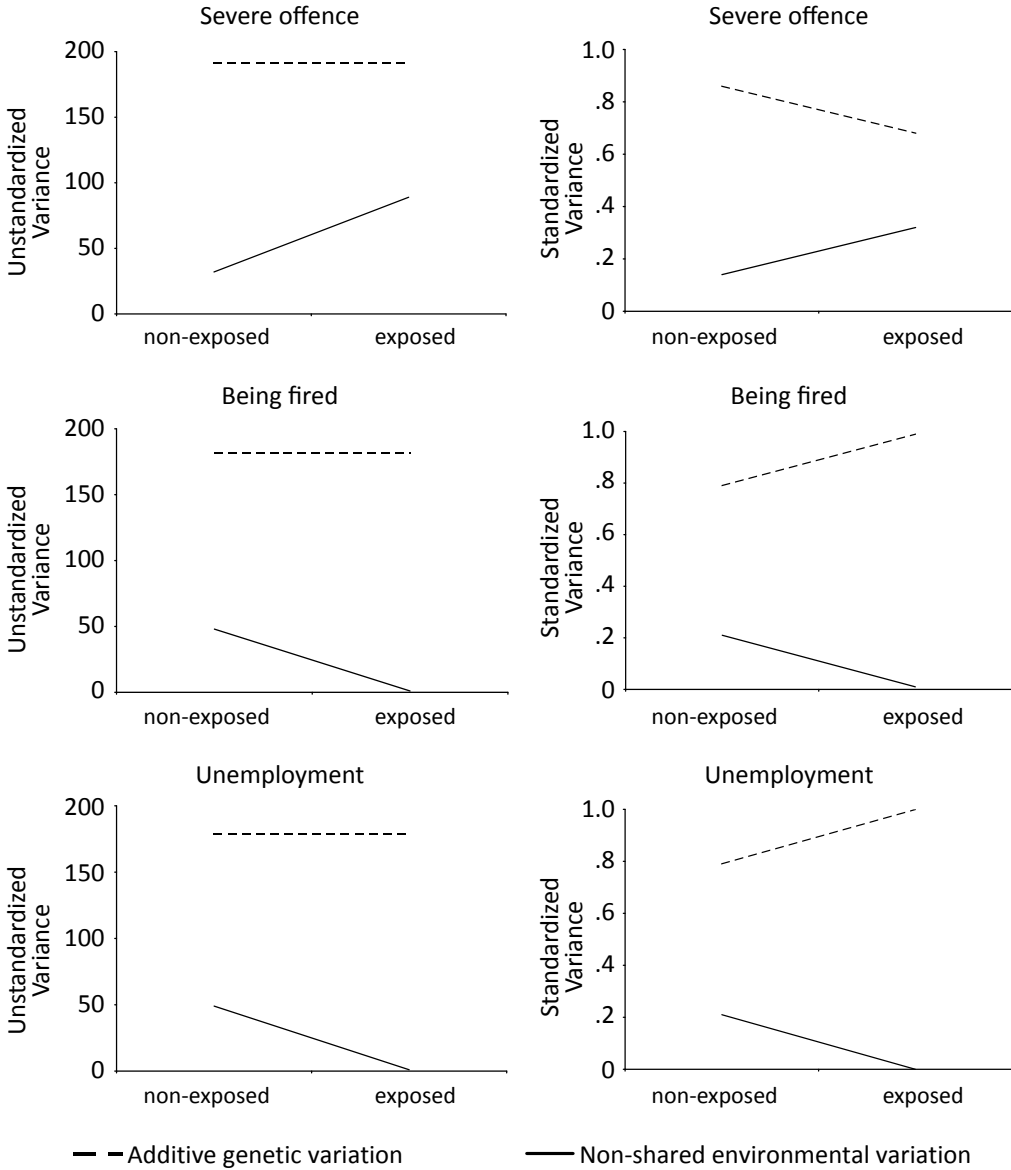
model		-2LL	par	χ^2	p
Severe illness / Violent assault					
1	AE-model	4366.03	7		
2	drop linear moderation A	4366.67	6	.64	.21
3	drop linear moderation C	4366.03	6	.00	incalc.
4	drop linear moderation E	4366.35	6	.32	.29
Divorce					
1	AE-model	4364.16	7		
2	drop linear moderation A	4365.71	6	1.55	.11
3	drop linear moderation C	4364.53	6	.38	.27
4	drop linear moderation E	4364.19	6	.04	.42
Falling out/Breaking up with friends/relatives					
1	AE-model	4361.51	7		
2	**drop linear moderation A**	**4364.47**	**6**	**2.96**	**.04**
3	drop linear moderation C	4361.72	6	.21	.32
4	drop linear moderation E	4362.40	6	.89	.17
Death of friends/relatives					
1	AE-model	4352.80	10		
2	drop non-linear moderation A	4352.80	9	.00	incalc.
3	drop non-linear moderation C	4352.80	9	.00	incalc.
4	drop non-linear moderation E	4353.07	9	.27	.30
5	**drop linear moderation A**	**4356.47**	**9**	**3.67**	**.03**
6	drop linear moderation C	4352.80	9	.00	incalc.
7	drop linear moderation E	4355.47	9	2.67	.05
Severe trouble with friends/relatives					
1	AE-model	4358.57	7		
2	drop linear moderation A	4359.10	6	.53	.23
3	drop linear moderation C	4358.57	6	.00	incalc.
4	**drop linear moderation E**	**4364.26**	**6**	**5.69**	**.01**
Mental health treatment					
1	AE-model	4361.65	7		
2	drop linear moderation A	4364.21	6	2.56	.05
3	drop linear moderation C	4361.69	6	.04	.42
4	drop linear moderation E	4362.26	6	.60	.22
Severe offence					
1	AE-model	4358.99	7		
2	drop linear moderation A	4361.19	6	2.20	.07
3	drop linear moderation C	4358.99	6	.00	incalc.
4	**drop linear moderation E**	**4361.87**	**6**	**2.87**	**.045**
Robbery					
1	AE-model	4354.29	10		
2	drop non-linear moderation A	4354.30	9	.02	.45
3	drop non-linear moderation C	4354.91	9	.62	.22
4	drop non-linear moderation E	4354.31	9	.02	.45
5	drop linear moderation A	4354.30	9	.01	.46
6	drop linear moderation C	4354.91	9	.62	.22
7	drop linear moderation E	4355.99	9	1.70	.10
Sexual abuse					
1	AE-model	4366.50	7		
2	drop linear moderation A	4366.66	6	.16	.35
3	drop linear moderation C	4366.50	6	.00	incalc.
4	drop linear moderation E	4366.54	6	.03	.43
Being fired					
1	AE-model	4356.64	7		
2	drop linear moderation A	4356.79	6	.15	.35
3	drop linear moderation C	4358.22	6	1.58	.10
4	**drop linear moderation E**	**4364.07**	**6**	**7.43**	**.00**

model		-2LL	par	χ^2	*p*
Unemployment					
1	AE-model	4355.04	7		
2	drop linear moderation A	4356.33	6	1.29	.13
3	drop linear moderation C	4356.24	6	1.19	.14
4	**drop linear moderation E**	**4361.23**	**6**	**6.19**	**.01**

Notes: p-values are based on a ½:½ mixture of chi-square distributions (Dominicus et al., 2006); models 2-7 were compared to the AE-model (½:½ mixture of $\chi^2(0)$ and $\chi^2(1)$); -2LL = minus 2 log likelihood; par = estimated parameters; χ^2 = Chi square (difference in -2LL); incalc. = incalculable; p = p-value; significant moderation effects are printed in bold font.

Figure 7.4 Unstandardized (left) and standardized (right) variance components of FSIQ as a function of negative individual Life Events.

Severe offence

Severe offence

Being fired

Being fired

Unemployment

Unemployment

– – – Additive genetic variation ⎯⎯⎯ Non-shared environmental variation

Notes: Unstandardized (left) and standardized (right) variance components of FSIQ as a function of negative individual Life Events: Falling out/Breaking up with friends/relatives, Severe trouble with friends/ relatives, Death of friends/relatives, Severe offence, Being Fired, and Unemployment. The figures are based on the most reduced models, i.e., on the models in which all non significant effects were fixed at zero. Unstandardized variance components (left) refer to the absolute contribution of A (additive genetic effects) and E (non-shared environmental effects); standardized variance components (right) refer to the relative contribution to variation in FSIQ for "non-exposed" and "exposed" individuals. Note that for the moderator variable Death of friends/relatives three categories were distinguished: "non-exposed", "exposed once or twice" and "exposed more than twice".

Neutral individual Life Events

Table 7.5 shows the model fitting results of the *Neutral* individual Life Events. *Moving house* and *Retirement* showed significant moderation effects. *A* was considerably decreased and

C considerably increased in individuals exposed to *Retirement*. *C* was also slightly increased in individuals who never or very often moved house. Figure 7.5 shows standardized and unstandardized variance components of FSIQ as a function of these two *neutral* individual Life Events.

Table 7.5 Model fitting results for interaction model of FSIQ with neutral individual Life Events as moderator variables.

model		-2LL	par	χ^2	*p*
Changing schools in childhood					
1	AE-model	4364.14	10		
2	drop non-linear moderation A	4364.21	9	0.06	.40
3	drop non-linear moderation C	4364.24	9	0.10	.38
4	drop non-linear moderation E	4365.30	9	1.15	.14
5	drop linear moderation A	4364.15	9	0.00	incalc.
6	drop linear moderation C	4364.29	9	0.15	.35
7	drop linear moderation E	4365.95	9	1.80	.09
Moving house					
1	AE-model	4336.07	10		
2	drop non-linear moderation A	4336.49	9	0.42	.26
3	drop non-linear moderation C	4336.18	9	0.11	.37
4	drop non-linear moderation E	4336.32	9	0.25	.31
5	drop linear moderation A	4337.13	9	1.06	.15
6	**drop linear moderation C**	**4339.01**	**9**	**2.94**	**.04**
7	drop linear moderation E	4336.15	9	0.08	.39
Retirement					
1	AE-model	4358.97	7		
2	**drop linear moderation A**	**4363.02**	**6**	**4.05**	**.02**
3	**drop linear moderation C**	**4365.15**	**6**	**6.18**	**.01**
4	drop linear moderation E	4358.97	6	0.00	incalc.

Notes: p-values are based on a ½:½ mixture of chi-square distributions (Dominicus et al., 2006); models 2-7 were compared to the AE-model (½:½ mixture of $\chi^2(0)$ and $\chi^2(1)$); -2LL = minus 2 log likelihood; par = estimated parameters; χ^2 = Chi square (difference in -2LL); incalc. = incalculable; p = p-value; significant moderation effects are printed in bold font.

Figure 7.5 Unstandardized (left) and standardized (right) variance components of FSIQ as a function of neutral individual Life Events.
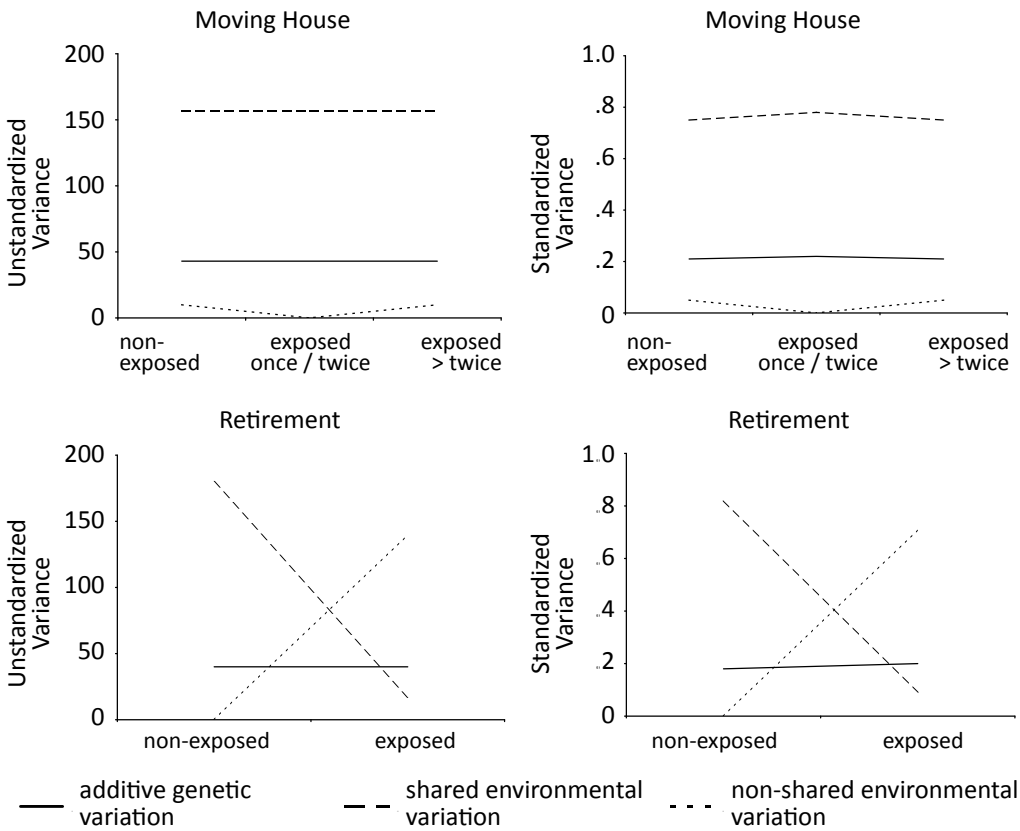
Notes: Unstandardized (left) and standardized (right) variance components of FSIQ as a function of neutral individual Life Event: Moving house and Retirement. The figures are based on the most reduced models, i.e., on the models in which all non significant effects were fixed to zero. Unstandardized variance components (left) refer to the absolute contribution of A (additive genetic effects), C (shared environmental effects), and E (non-shared environmental effects); standardized variance components (right) refer to the relative contribution to variation in FSIQ for "non-exposed" and "exposed" individuals. Note that for the moderator variable Moving house three categories were distinguished: "non-exposed", "exposed once or twice" and "exposed more than twice".

DISCUSSION

The aim of the present study was to identify the extent to which Life Events moderate genetic and environmental influences on individual differences in general cognitive ability in adults. Heritability estimates changed as a function of exposure to Life Events, but this was mainly due to moderation of effects of environmental influences. Analyses of *individual* Life Events showed some modest, but significant decrease of genetic influences as a function of exposure to Life Events (*Birth of a child, Falling out/Breaking up with friends/relatives, Death of friends/relatives,* and *Retirement*) but moderation effects on the environmental factors were generally larger and more frequent (*Birth of a child, Falling out/Breaking up with friends/relatives, Severe trouble with friends/relatives, Death of friends/relatives, Severe offence, Being fired, Unemployment*, and *Retirement*), with the direction of the moderation effect depending on the specific Life Event.

Two theories consider generic mechanisms in the context of environmental moderation of genetic effects (GEI): the '*Diasthesis-stress model*' (Gottesman, 1991) and the '*Bio-ecological model*' (Bronfenbrenner & Ceci, 1994). The '*Diasthesis-stress model*' is based on the assumption that individuals, who are genetically at risk, are more sensitive to environmental risk factors. The model predicts genetic influences to be larger in less advantageous circumstances, e.g., when the number of environmental stressors (e.g., adverse Life Events) is larger. Alternatively, the '*Bio-ecological model*' proposes that environmental factors can act as proximal processes, i.e., processes that enhance effective development. If exposure to Life Events enhances development, i.e., can be considered proximal processes, then an increase in genetic influences is expected with increasing exposure. All significant moderation of genetic influences observed in the present study concerned a decrease of genetic influences with an increase in the number of Life Events. This is difficult to reconcile with either theory, unless exposure to *multiple* Life Events is considered disadvantageous, irrespective of whether these events are positive, negative or neutral.

Theoretical mechanisms of moderation of environmental (risk) factors on latent shared and unshared environmental influences (CxE and ExE) have as yet not been considered in the literature. However, the same mechanisms as proposed for GEI may apply. For example, Life Events may function as proximal processes that enhance an environment's potential to cause individual differences in general cognitive ability, analogous to proximal processes that enhance genetic potential. Exposure to multiple Life Events may also act as a stressor that increases or reduces the extent to which the environment can cause individual differences in general cognitive ability.

This was the first study to investigate moderation of Life Events on individual differences in general cognitive ability in adults. Other studies on gene-environment interaction in adult general cognitive ability focused on parental and partner educational level, urbanization level, and mean real estate price of someone's residential area (van der Sluis et al., 2008b; Kremen et al., 2005). These studies reported significant moderation on environmental influences, and not on genetic influences. Most moderation effects that we observed for Life Events in the present study indeed concerned moderation of environmental factors, although we did observe some moderation of genetic influences as well. The unmoderated heritability of general cognitive ability in adults is generally high (h^2

ranges between 70% and 85%) (Bouchard, Jr. & McGue, 1981; Plomin et al., 1994a; Plomin, 1999; Posthuma et al., 2001a; Haworth et al., 2009), the remaining variance is explained by unshared environmental factors. Unmoderated heritability of general cognitive ability in children, however, is much lower (h^2 ranges between 25% and 60%) (Bouchard, Jr. & McGue, 1981; Boomsma & van Baal, 1998; Haworth et al., 2009), leaving ample room for shared and non-shared environmental influences. As GEI will be part of the unshared environmental influences if it is not modeled explicitly in the classic twin design, the genetic variation that can be moderated by environmental factors such as Life Events is relatively small in adults, compared to children. The statistical power to pick up moderation of genetic effects may therefore be much higher in children. The present study, however, did provide evidence of moderation of genetic effects by some individual Life Events in adults as well.

A number of limitations of this study should be noted. First, the sample size was relatively small. The power to detect significant gene-environment interaction depends on the sample size, but also on the frequency of exposure to the environmental moderator, the magnitude of the interaction effect, and the magnitude and nature of the correlation between trait and moderator (i.e., the power to detect moderation effects decreases with increasing genetic or environmental correlation between trait and moderator (Purcell, 2002)). To increase power in future studies, researchers should not only focus on larger sample sizes, but also on clever sample selection (i.e., the distribution of the moderator within the sample should be maximally informative), and accurate measurement of trait and moderator.

Second, due to the large age range within the current sample, we could not distinguish between moderation effects of Life Events that took place recently or many years ago. Possibly, the specific effects of the moderators depend on the age at which the Life Event takes place. For example, exposure to Life Events in childhood may lead to moderation of genetic factors, or environmental factors that are involved in the *development* of general cognitive ability, while exposure to the same Life Events at a later age may affect environmental factors only. Such differential moderation effects can only be studied if the sample is stratified with respect to the age at which the Life Events took place.

Third, as this is the first study on moderation effects of Life Events on variance components of general cognitive ability. The novelty of the study, in combination with the relatively small sample size, let us to adopt a criterion level α of .05, without correction for multiple testing, in order to reduce the number of Type II errors; i.e., missing out on small interaction effects that are actually present. A disadvantage of this strategy is that we may have picked up some false positive effects, although the number of significant findings was higher than that expected by chance alone.

In the present paper we have shown that the extent to which genetic and environmental effects cause individual differences in adult general cognitive ability is not stable across the entire population, but varies as a function of *positive*, *negative* and *neutral* Life Events. Moderation effects reported in the present study are small, and replication is necessary to establish which effects are genuine. The finding that genetic and environmental influences fluctuate across environments may be of importance in the context of gene finding studies as accounting for environmental stratification may enhance the chance to find genes related to cognition.

Chapter 8

Interaction between experience seeking and genetic and environmental influences underlying general cognitive ability

ABSTRACT

Although it is well established that experience seeking behavior (ES) is positively related to cognitive functioning, the mechanisms underlying this association are not clearly understood. In a large sample of adult twins and siblings (N=864, age range 23-75), we studied the causes of covariation between ES and general cognitive ability and we studied whether ES moderates the genetic and environmental causes of variation in general cognitive ability.

Results demonstrate a common genetic and a common environmental background between general cognitive ability and ES. Moreover, the extent to which genetic and environmental factors are shared between general cognitive ability and ES is increased in individuals with higher levels of ES. In addition, the extent to which genetic and environmental factors influence individual differences in general cognitive ability in adults partly depended on ES. Standardized influences of additive genetic factors on general cognitive ability ranged from 16% to 98% with lower estimates in higher levels of ES, while standardized estimates of environmental factors ranged from 2% to 85%, with higher estimates in higher levels of ES.

Hence, ES and cognitive ability are not only associated through common genetic and environmental factors, but also via moderating effects of genetic and environmental influences on cognitive ability by ES. These findings have implications for future studies on the association between ES and general cognitive ability, and for future research on the genetics of cognitive ability.

INTRODUCTION

Considerable phenotypic correlations (~.30) are consistently reported between the personality trait 'openness to experience' and general cognitive ability (Ackerman & Heggestad, 1997; Moutafi et al., 2003; Phillips et al., 2003; Higgins et al., 2007). In line with this, higher levels of experience seeking behavior (ES), a trait related to openness to experience (Fitzgerald, 1966; Zuckerman et al., 1972), coincide with better focused attention skills (Martin, 1985), increased scientific interests (Kish & Leahy, 1970), better perceptual, arithmetic and spatial ability (Kish & Busse, 1968; Kish & Leahy, 1970), and higher levels of general cognitive ability (Kish & Leahy, 1970; Fagan, 1984; Zuckerman, 1994). Individuals with high levels of ES are curious, open to new experiences and change, and receptive to new ideas and views, which are all qualities that are related to general cognitive ability (Myers & McCaulley, 1985). Moutafi et al. (2003) suggested a reciprocal relation between ES and general cognitive ability, such that individuals with lower levels of general cognitive ability may become less curious, and less appreciative of, or receptive to, unfamiliar experiences due to their lower ability to handle novel information. Restricted ability to benefit from novelty in turn makes exposure to new information and experiences less rewarding. On the other hand, curiosity and openness to experience may evolve in individuals with higher levels of general cognitive ability exactly because they profit from these abilities and experience them as stimulating and rewarding. In addition, experience seekers may create for themselves an enriched environment that stimulates cognitive development (Raine et al., 2002).

To date, the exact nature of the association between general cognitive ability and ES is largely unknown. The association may be reciprocal, as suggested by Moutafi et al. (2003), but may also be driven by a third factor. For example, as both ES and general cognitive ability are under genetic control (in adults ES: h^2 range from 50% to 60% (Koopmans et al., 1995; Wainwright et al., 2008); general cognitive ability: h^2 range from 75% to 85% (Bouchard, Jr. & McGue, 1981; Plomin, 1999)), genes might mediate the relation between ES and general cognitive ability. Substantial genetic covariation has indeed been reported between openness to experience and general cognitive ability in one study in young adults by Wainwright and colleagues (2008) supporting the possibility of genetic covariation between ES and general cognitive ability in adults.

Wainwright et al. assumed that the association between general cognitive ability and openness to experience is homogeneous across different levels of openness to experience. However, increasing evidence suggests that variation in general cognitive ability is not homogenous across the whole range of cognitive abilities but depends on other traits or environmental factors (van der Sluis et al., 2008b; Haworth et al., 2009; Vinkhuyzen et al., 2010b). It is therefore conceivable that covariation between general cognitive ability and ES also fluctuates as a function of ES (and/or general cognitive ability).

If the relative contributions of genetic and environmental influences on general cognitive ability differ as a function of ES (i.e., gene-ES interaction), point estimates of these influences merely reflect the average heritability and environmentability of general cognitive ability across the whole range of ES levels. We refer to gene-ES interaction as 'gene-trait interaction' (GTI) to distinguish this from the term gene-environment interaction in which the moderator is assumed not to be influenced by genetic factors (i.e., is of environmental nature).

Considering GTI may aid our understanding of the role of genetic and environmental influences on individual differences in general cognitive ability, and in our understanding of the underlying mechanisms of the phenotypic correlation between general cognitive ability and ES.

We set up a twin-sibling study (N=864 adults) to investigate (i) whether or not the covariance between ES and general cognitive ability is partly genetic in nature, (ii) whether or not the relative contribution of genetic and environmental influences to this covariance varies as a function of ES, and (iii) whether or not the relative contribution of genetic and environmental influences to general cognitive ability depend on ES.

METHODS

Sample

Data were available for 864 twins and siblings (55.8% women, 288 complete twin pairs, 23 incomplete twin pairs, 265 siblings) from 317 families that were registered at the Netherlands Twin Registry (Boomsma et al., 2006). Mean age of the participants was 46.61 years (SD=12.40, range: 23–75) at the time they completed the Life Experience List (Vinkhuyzen et al., 2010a) (LEL, see *Measures*). Zygosity of same-sex twins was determined using DNA polymorphisms (127 pairs, 88.2%) or, if information on DNA markers was not available, using questions about physical similarity and confusion of the twins by family members and strangers. Agreement between zygosity based on DNA and zygosity based on survey was 97% (Willemsen et al., 2005). The sample was previously shown to be representative of the general Dutch population with regard to educational attainment (Posthuma et al., 2001a). The study was performed with understanding and written consent of each participant, and was approved by the Central Committee on Research Involving Human Subjects of the VU/VUmc Amsterdam, the Netherlands.

Measures

General cognitive ability

General cognitive ability was operationalized as Full Scale Intelligence Quotient (FSIQ) and assessed with the Dutch version of the WAIS-IIIR (Wechsler, 1997). FSIQ was based on seven subtests of the WAIS-IIIR (N=74; Block design, Letter-number sequencing, Information, Matrix reasoning, Arithmetic, Vocabulary, and Digit symbol-coding) or eleven subtests of the WAIS-IIIR (N=785; the above seven plus Similarities, Picture completion, Digit symbol-coding, and Digit-symbol pairing). The correlation between FSIQ assessed with eleven subtests, and FSIQ assessed with seven subtests, was very high (Pearson's *r*=.97, p<.001; N=785). Test-retest reliability, studied in 59 participants who completed the WAIS-IIIR twice with an interval of ~10 years, was also high (*r*=.85, p<.001).

Experience seeking

The Experience Seeking (ES) Scale is one of the four subscales of the Dutch translation of the Sensation Seeking Scale (Zuckerman et al., 1964; Zuckerman, 1971; Zuckerman, 1979; Feij & van Zuilen, 1984) and was incorporated in the Life Experiences List (LEL) (Vinkhuyzen et al., 2010a). The ES scale has been described as the 'hippie factor' (Zuckerman, 1971)

and refers to desired experiences through wanderlust, exhibitionism, use of marijuana and hallucinatory drugs, association with non-conformist friends, and liking of modern and arousing arts and music. The ES scale consists of 14 multiple choice items measured on a 5-point Likert scale with answer categories ranging from 1='definitely disagree' to 5='definitely agree'. All items were scored such that high item scores correspond to high levels of experience seeking behavior. Information on missingness is available in the supplementary information of this chapter. Test-retest reliability of the ES scale, studied in an independent sample of 62 participants (31 parent-offspring pairs, 75.4% women; age range 17-71, mean=39.95, SD=16.19), who completed the LEL twice within a period of two months, was high (.87, p<.001).

Statistical analyses
To start with, the phenotypic correlation between general cognitive ability and ES was calculated in Mplus (Muthen & Muthen, 2005), using option 'complex', to correct for familial relatedness between the participants.

Subsequently, monozygotic (MZ) twin, dizygotic (DZ) twin, and sibling correlations for general cognitive ability and ES were estimated within an unrestrained model. Differences between zygosity groups in means and variances, as well as differences between DZ twin correlations and regular sibling correlations of cognitive ability and ES, were tested using likelihood ratio tests.

To detect moderation effects in the presence of possible shared genetic effects or shared environmental factors, a bivariate interaction model was fitted to the data (Purcell, 2002). Within the bivariate interaction model, variances of cognitive ability and ES, as well as the covariance between cognitive ability and ES, were modeled as a function of genetic and environmental effects. Genetic factors 'A' and 'D' and environmental factors 'C' and 'E' were considered. 'A' represents additive genetic effects of alleles summed over all genetic loci (*additive genetic effects)*. 'D' represents non-additive genetic effects within loci (*genetic dominance*). 'C' represents shared environmental influences that render offspring of the same family more alike (*shared environmental factors*). 'E' represents all environmental influences that result in differences between members of a family, including measurement error (*non-shared environmental factors*). To model GTI, variance components of cognitive ability were allowed to vary as a function of ES. Note that C and D are confounded when only data from twins and siblings are available because C and D have opposite effects on the difference between MZ twin and DZ twin correlations. When DZ twin correlations are less than half the MZ twin correlations, as was the case for both ES and cognitive ability in the present data, dominance genetic effects are expected rather than common environmental effects. In that case, a model including A, D and E is deemed most appropriate.

Within this bivariate interaction model the moderator ES features twice: as a dependent variable and as an actual moderator. Moreover, moderating effects of ES can be modeled on two types of variance components: the variance components unique to cognitive ability, and the variance components shared between cognitive ability and ES (Purcell, 2002). An extensive description of the bivariate interaction model is provided in the supplementary information of this chapter.

Within this bivariate model, we tested whether (1) unmoderated components of genetic dominance, (2) unmoderated components additive genetic variance, and (3) the

unmoderated component of the environmental variance shared between cognitive ability and ES were significant. Subsequently, we tested whether (4) non-linear and (5) linear moderation effects, both shared between trait and moderator and unique to the trait, were significant.

Significance of parameters was tested by comparing the fit of nested (increasingly more restricted) models to the fit of less restricted models. Goodness-of-fit of sub-models was assessed by likelihood-ratio-tests. The difference in log-likelihoods between two models was evaluated. A significant χ^2-difference test implies that the constraints imposed on the nested models are not tenable whereas a non-significant χ^2-difference test implies that the nested, more parsimonious model is to be preferred. Since the null distribution of a variance component or moderation coefficient is a .5:.5 mixture of a $\chi^2(0)$ and $\chi^2(1)$ (Dominicus et al., 2006; Macgregor et al., 2005), significance of distinct variance components and moderation coefficients was tested against a critical value of $\chi^2(1)=2.7055$, given alpha = .05. In contrast, significance of differences in means, variances and twin/sibling correlations were tested against a critical value of $\chi^2(1)=3.8414$, as the null distribution in this case follows the χ^2 distribution. All measures were corrected for age and sex to avoid spuriously increased similarities in MZ and same-sex DZ twin pairs (McGue & Bouchard, Jr., 1984). Analyses were carried out using the raw data option in Mx (Neale, 1994; Posthuma & Boomsma, 2005).

RESULTS

The phenotypic correlation (corrected for familiarity) between cognitive ability and ES in the sample was .17 (p<.001).

Means and variances of cognitive ability ($\chi^2(2)=.53$, *ns*) and ES ($\chi^2(2)=.10$, *ns*) could be considered equal between zygosity groups without a significant deterioration of the model fit, implying that there was no heterogeneity in these measures for MZ and DZ twins and their siblings. Table 8.1 includes information on means and standard deviations of general cognitive ability and ES, as well as information on missingness.

Table 8.1 Descriptive statistics for cognitive ability and experience seeking.

	N	% Missing	Mean (SD)
cognitive ability	859	.6 *	99.68 (14.78)
ES	549	2 **	2.61 (.60)

Notes: N=number of participants; % Missing=percentage of missingness, this is the percentage of participants that (*) participated in the present study but did not complete the IQ test or that (**) returned the LEL but did not complete the questions on experience seeking; Mean=mean score corrected for age and sex effects; SD=standard deviation.

Table 8.2 shows the sex and age corrected MZ twin, DZ twin, sibling, and pooled DZ/sibling correlations and standardized variance components for cognitive ability and ES. Sibling correlations did not differ from DZ twin correlations for cognitive ability ($\chi^2(1)=3.72$, *ns*) and ES ($\chi^2(1)=.25$, *ns*) suggesting no special twin environment. MZ twin correlations exceeded the DZ/sibling correlations for cognitive ability ($\chi^2(1)=77.24$, p<.001) and ES ($\chi^2(1)=13.15$, p<.001), suggesting the presence of genetic influences. As pooled DZ/sibling correlations for cognitive ability (.35) and ES (.28) were less than half the MZ twin correlations (cognitive ability=.82; ES=.60), presence of genetic dominance rather than common environmental effects, was

indicated. Table 8.2 also shows the results of the univariate variance decomposition of both ES and general cognitive ability. For both general cognitive ability and ES, additive genetic influences explained the major part of the variance. Genetic dominance deviations were not significantly different from zero for both ES and general cognitive ability, although the point estimate of .22 suggested moderate effects for general cognitive ability.

Table 8.2 Twin and sibling correlations (95% confidence intervals) and standardized variance components (95% confidence intervals) for cognitive ability and experience seeking

	rMZ (95% CI)	rDZ (95% CI)	rSibling (95% CI)	rDZ/rSibling (95% CI)
cognitive ability	.82 (.77-.86) N=136	.46 (.32-.57) N=152	.32 (.22-.42) N=594	.35 (.26-.44) N=746
ES	.60 (.50-.71) N=83	.31 (.11-.48) N=67	.26 (.13-.39) N=313	.28 (.16-.39) N=380
	a^2	d^2	e^2	
cognitive ability	.60 (.24-.85)	.22 (.00-.58)	.18 (.14-.23)	
ES	.57 (.10-.70)	.03 (.00-.53)	.40 (.30-.53)	

Notes: rMZ=MZ twin correlation; rDZ=DZ twin correlation; rSibling=sibling correlation; rDZ/rSibling=pooled DZ and sibling correlation; Twin and sibling correlations were corrected for sex and age; N=number of pairs; 95% CI=95% confidence interval; a^2=standardized additive genetic variance; d^2=standardized dominance genetic variance; e^2=standardized non-shared environmental variance. Standardized variance components are based on full models.

Correlation and moderation
Model fitting results of a bivariate analysis, in which the variances of cognitive ability and experience seeking as well as their covariance were decomposed into A, D, and E are presented in Table 8.3.

Bivariate analyses excluding interaction effects showed that genetic dominance did not significantly contribute to variation in general cognitive ability and ES, nor to their covariation (models 2-5). Unmoderated additive genetic effects, however, did significantly contribute to variation and covariation of cognitive ability and ES (models 6-8). Unmoderated non-shared environmental effects did not contribute significantly to the covariance between cognitive ability and ES (model 9).

Bivariate analyses including moderation effects demonstrated that neither linear moderation nor non-linear moderation of genetic dominance effects were significant (model 11-16), implying that dominance effects were non-significant across the entire range of ES. Non-linear moderation of additive genetic factors specific to cognitive ability (model 18: $\chi^2(1)=8.21$, p<.01) and linear moderation of additive genetic factors common to cognitive ability and ES (model 19: $\chi^2(1)=2.81$, p<.05) were significant. Furthermore, analyses demonstrated significant non-linear moderation (model 21: $\chi^2(1)=4.25$, p<.05) and linear moderation (model 23: $\chi^2(1)=3.06$, p<.05) on non-shared environmental factors common to cognitive ability and ES, as well as significant non-linear moderation on environmental factors specific to cognitive ability (model 22: $\chi^2(1)=5.30$, p<.05).

Within the preferred model (model 23) standardized estimates of additive genetic factors for cognitive ability varied from 16% to almost 98%, with smaller additive genetic effects observed for higher levels of ES. Standardized estimates of non-shared environmental factors varied concordantly from 84% to almost 2%. Figure 1 shows standardized and unstandardized variance components of cognitive ability as a function of ES.

Figure 8.1. Standardized and unstandardize variance components of cognitive ability as a function of ES
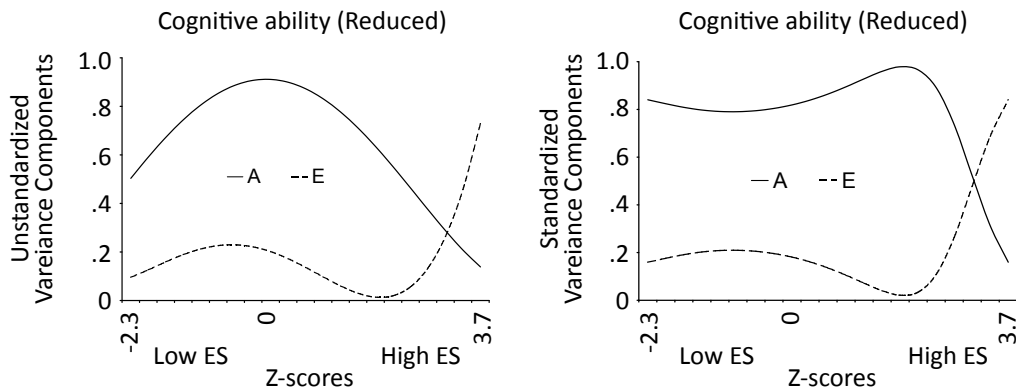
Notes: Unstandardized (left panel) and standardized (right panel) variance components of cognitive ability as a function of experience seeking. The figures are based on the most reduced models, i.e., on the models in which all non significant effects were fixed at zero. Unstandardized variance components (left panel) refer to the absolute contribution of A (additive genetic effects) and E (non-shared environmental effects); standardized variance components (right panel) refer to the relative contribution to variation in cognitive ability as a function of experience seeking. ES=experience seeking.

Table 8.3 shows genetic and environmental correlations between general cognitive ability and ES, as well as the extent to which the phenotypic correlation between cognitive ability and ES is due to genetic and environmental factors, as a function of the level of ES. The coefficients are therefore reported for low (-2 SD), intermediate (± 0 SD), and high (+2 SD) levels of (standardized) ES. Due to positive linear moderation of the genetic factors that were shared between cognitive ability and ES, both the genetic correlation (r_G) and the contribution of genetic factors to the phenotypic correlation between cognitive ability and ES ($\%_A$), was increased in individuals with higher levels of ES.

Due to positive non-linear moderation of the environmental factors that were shared between cognitive ability and ES, both the environmental correlation (r_E) and the contribution of environmental factors to the phenotypic correlation between cognitive ability and ES ($\%_E$), was increased in individuals with either low or high levels of ES. In individuals with intermediate levels of ES, the environmental correlation and the contribution of environmental factors to the phenotypic correlation between ES and general cognitive ability were negligible.

As the contribution of genetic and environmental factors to the phenotypic correlation between ES and general cognitive ability was dependent on the level of the moderator, the phenotypic correlation was also dependent of the moderator. Although the mean phenotypic correlation was .17, the phenotypic correlation was relatively increased in individuals with low (*r*=.19; -2 SD) and high (*r*=.26; +2 SD) levels of ES and decreased in individuals with moderate (*r*=.11; 0 SD) levels of ES.

Table 8.3 Model fitting results for bivariate ADE interaction models of cognitive ability with experience seeking as moderator variable.

	model	against	-2LL	est par	df	χ^2	Δdf	p
1	Full model (no moderation)		2865.268	11	1075			
2	drop d	1	2866.393	10	1076	1.125	1	.144
3	drop d_c	1	2866.121	10	1076	.853	1	.178
4	drop d_u	1	2865.467	10	1076	.199	1	.328
5	drop d, d_c, d_u	1	2867.679	8	1078	2.411	3	.492
6	**drop a**	**5**	**2924.628**	**7**	**1079**	**56.949**	**1**	**.000**
7	**drop a_c**	**5**	**2876.08**	**7**	**1079**	**8.401**	**1**	**.002**
8	**drop a_u**	**5**	**2917.836**	**7**	**1079**	**50.157**	**1**	**.000**
9	drop e_c	5	2867.727	7	1079	.048	1	.413
10	Full model (including moderation)		2843.158	19	1067			
11	drop d_c''	10	2843.158	18	1068	.000	1	.500
12	drop d_u''	10	2843.198	18	1068	.040	1	.421
13	drop d_c'',d_u''	10	2843.198	17	1069	.040	2	.980
14	drop d_c'	13	2843.198	16	1070	.000	1	.500
15	drop d_u'	13	2843.198	16	1070	.000	1	.500
16	drop d_c',d_u'	13	2843.198	15	1071	.000	2	1.000
17	drop a_c''	16	2845.732	14	1072	2.534	1	.056
18	**drop a_u''**	**16**	**2851.404**	**14**	**1072**	**8.206**	**1**	**.002**
19	**drop a_c'**	**17**	**2848.539**	**13**	**1073**	**2.807**	**1**	**.047**
20	drop a_u'	17	2847.143	13	1073	1.411	1	.117
21	**drop e_c''**	**20**	**2851.391**	**12**	**1074**	**4.248**	**1**	**.020**
22	**drop e_u''**	**20**	**2852.444**	**12**	**1074**	**5.301**	**1**	**.011**
23	**drop e_c'**	**20**	**2850.199**	**12**	**1074**	**3.056**	**1**	**.040**
24	drop e_u' (= final model)	20	2848.811	12	1074	1.668	1	.098
		low ES	intermediate ES		high ES			
	r_A	.16	.16		.23			
	r_E	.31	.00		.97			
	$\%_A$	57	100		66			
	$\%_E$	43	0		34			

Notes: p-values of all 1-df tests are based on a ½:½ mixture of $\chi^2(0)$ and $\chi^2(1)$ distributions (Dominicus et al., 2006); -2LL=minus 2 log likelihood; par=estimated parameters; χ^2=Chi square (difference in -2LL); p=p-value; AIC=Akaike's Information Criterion; ES=experience seeking; r_A=genetic correlation; r_E=non-shared environmental correlation; $\%_A$=percentage of phenotypic correlation explained by genetic factors for Low, Intermediate, and High levels of experience seeking; $\%_E$=percentage of phenotypic correlation explained by non-shared environmental factors for Low, Intermediate, and High levels of experience seeking; *=preferred model; significant (moderation) effects are printed in bold font. Path-coefficients correspond to path-coefficients in Figure 1; '=linear effects of the moderator; "=non-linear effects of the moderator. The full model is described in the 'methods' section.

Within the present sample, we were not able to model both genetic dominance (D) and shared environmental factors (C). Instead, an interaction model with additive genetic factors, genetic dominance and non-shared environmental factors was considered (i.e., a bivariate ADE interaction model) assuming shared environmental factors to be absent. The choice of an ADE-model was based on univariate twin correlations for cognitive ability and ES that suggested absence of shared environmental factors and possible presence of genetic dominance deviation. These correlations were however based on the overall sample while moderation was assumed to be absent. Previous studies (Kremen et al., 2005;

van der Sluis et al., 2008b; Vinkhuyzen et al., 2010b), however, demonstrated that shared environmental factors for general cognitive ability can seem absent in the full sample, while they are actually substantial for specific levels of a moderator. We therefore specified a second series of interaction models in which the variances of cognitive ability and ES, as well as their covariance, were specified as a function of additive genetic factors, shared- and non-shared environmental factors (i.e., bivariate ACE interaction model). Within this ACE interaction model, dominance genetic (interaction) effects were assumed to be absent, as is in line with the results presented in Table 8.3. These bivariate ACE interaction analyses (Table S1 supplement), however, showed no significant moderation of shared environmental factors.

DISCUSSION

In order to elucidate the association between experience seeking behavior (ES) and general cognitive ability, we decomposed their covariance into genetic and environmental effects and tested whether ES moderates the causes of variation in general cognitive ability. Within the present study, a positive but modest association between ES and general cognitive ability was confirmed (.17). This phenotypic association between ES and general cognitive ability, however, depended on the level of ES, with highest correlation in individuals with high levels of ES (.26). This was mainly due to an increase in environmental influences, common to ES and general cognitive ability, in higher levels of ES.

Furthermore, ES significantly moderated additive genetic (A) and non-shared environmental (E) variance components of cognitive ability. Standardized heritability estimates were generally high (above 80%) but decreased substantially in individuals with high levels of ES (to 16%) while environmental factors increased (84%). Thus, individual differences in cognitive ability are on average best explained by a large contribution of genetic factors, while environmental factors gain in importance when ES levels are high.

Although moderation effects of ES have not been studied before, these results support previous theories on moderation of variance components of general cognitive ability suggesting that genetic and environmental factors do not simply add up, but have a more complex relation (Eaves et al., 1977; Loehlin & DeFries, 1987). Our analyses suggest that the relative contribution of environmental influences on individual differences in general cognitive ability tend to increase while the genetic contribution tends to decrease with higher levels of ES. That is, environmental factors are more important and genetic influences are less important in explaining individual differences in general cognitive ability in those subgroups that actively seek out exposure to a wide variety of experiences. Individuals with high levels of ES are likely to seek out environments that optimize the probability to be exposed to new experiences; the observation that environmental factors gain in importance in individuals with high levels of ES is therefore expected. Although the relative influence of genetic factors decreases as a function of increasing ES, we also observed a decrease in absolute contribution of genetic factors due to moderation. The decrease of variation due to genetic factors, however, is more complicated. Our results suggest that genetic effects on general cognitive ability are conditional on environmental exposure (i.e., related to ES), but the underlying mechanisms underlying this interaction remain as yet unknown. Future studies may focus e.g. on epigenetic effects; for example,

environmental factors may cause epigenetic changes that may reduce gene-expression.

The genetic overlap between ES and general cognitive ability across different levels of ES is of particular interest in the context of the role of dopamine in both ES and general cognitive ability. For example, the D4 dopamine receptor gene (*D4DR*) is expressed in limbic (Van Tol et al., 1991) and prefrontal (Mrzljak et al., 1996; Primus et al., 1997; De La & Madras, 2000) areas which are involved in general cognitive ability. A positive association has been demonstrated between blockade of dopamine D4 receptors and cognitive impairment. At the same time, an association between novelty seeking and dopamine transmission has been proposed (Cloninger, 1987). Ebstein et al. (1996) and Benjamin et al. (1996) demonstrated an association between higher levels of novelty seeking behavior and the 7 repeat allele in the D4DR gene. As individual differences in general cognitive ability and individual differences in novelty seeking behavior are related to genetic variability in dopamine transmission, future studies may investigate whether the association between ES and cognitive ability is moderated by dopamine receptor genes such as the *D4DR* gene.

To conclude, we demonstrated that general cognitive ability and ES are not only associated through common genetic and environmental factors, but also via moderating effects of the underlying variance components of general cognitive ability by ES. These results are valuable in understanding the underlying mechanisms of the phenotypic association between general cognitive ability and ES as well as in understanding individual differences in general cognitive ability.

SUPPLEMENTARY INFORMATION

Figure S8.1 Partial path diagram of the bivariate model for one twin of a twin pair.
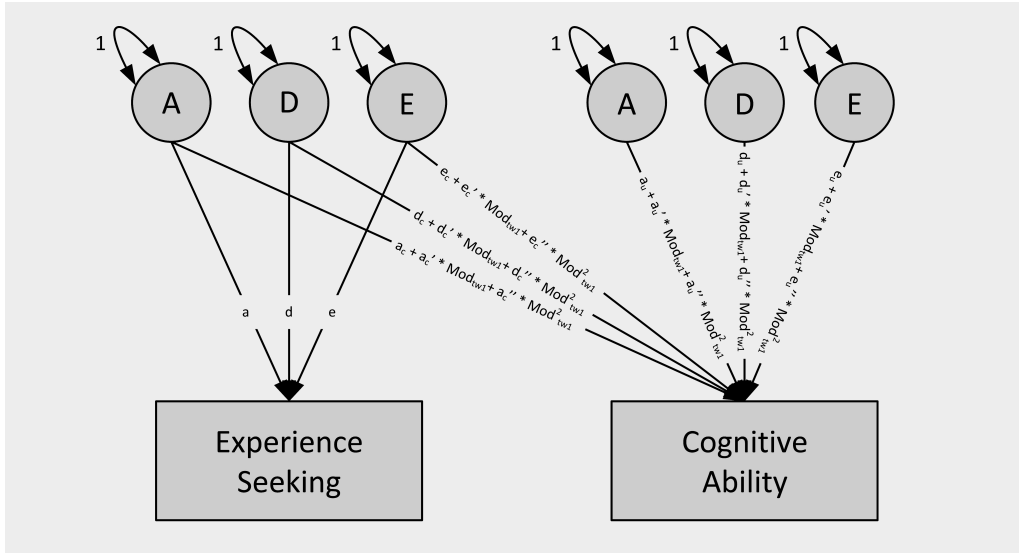
Notes: Partial bivariate model for one twin including linear and non-linear moderation effects of the environmental moderator (experience seeking) on the variances of general cognitive ability and on the covariance between cognitive ability and the experience seeking. A=additive genetic effects; D=genetic dominance; E=non-shared environmental effects; a=unmoderated path coefficient for A; d=unmoderated path coefficient for D; e=unmoderated path coefficient for E; a_c=genetic factors shared between moderator and trait; a_u=genetic factors unique to trait; d_c=genetic dominance effects shared between moderator and trait; d_u=genetic dominance effects unique to trait; e_c=non-shared environmental factors shared between moderator and trait; e_u=non-shared environmental factors unique to trait. a_c', d_c', and e_c' denote linear moderation coefficients for A, D, and E, respectively whereas a_c'', d_c'', and e_c'' denote non-linear moderation coefficients for A, D, and E, respectively.

Description of the bivariate interaction model

Given that the twin correlations for cognitive ability and ES were suggestive of genetic dominance, the variance of ES is calculated as:

$$\text{Var(ES)} = a^2 + d^2 + e^2,$$

where a^2 denotes additive genetic variance, d^2 denotes genetic dominance variance, and e^2 denotes non-shared environmental variance, whereas the variance of general cognitive ability is calculated as follows:

$$\text{Var(general cognitive ability)} =$$
$$(a_c+a_c'*\text{Mod}_{tw1}+a_c''*\text{Mod}^2_{tw1})^2 + (a_u+a_u'*\text{Mod}_{tw1}+a_u''*\text{Mod}^2_{tw1})^2 +$$
$$(d_c+d_c'*\text{Mod}_{tw1}+d_c''*\text{Mod}^2_{tw1})^2 + (d_u+d_u'*\text{Mod}_{tw1}+d_u''*\text{Mod}^2_{tw1})^2 +$$
$$(e_c+e_c'*\text{Mod}_{tw1}+e_c''*\text{Mod}^2_{tw1})^2 + (e_u+e_u'*\text{Mod}_{tw1}+ea_u''*\text{Mod}^2_{tw1})^2,$$

where Mod_{tw1} denotes the value of twin 1 on the moderator, i.e., the ES score of

twin 1, a_c, d_c, and e_c denote unmoderated regression coefficients of additive genetic, genetic dominance and non-shared environmental factors, respectively, that are shared between ES and cognitive ability. a_u, d_u, and e_u denote unmoderated regression coefficients of additive genetic, genetic dominance and non-shared environmental factors that are unique to cognitive ability. a_c', d_c', and e_c' denote linear moderation coefficients, i.e., the regression coefficients of A, D and E that fluctuate as a function of ES. Similarly, a_c'', d_c'', and e_c'' denote non-linear moderation coefficients for A, D, and E, respectively. Coefficients correspond to path-coefficients in Figure S8.1.

To test whether unmoderated variance components (specific to trait and moderator as well shared between trait and moderator) were significant within the full sample (i.e., average levels of ES), a bivariate model without moderation was specified.

A reference model was specified in which non-significant unmoderated variance components were fixed to zero and potential moderation coefficients were freely estimated (model 10 in Table 8.3), to test significance of linear and non-linear moderation effects. Since moderation on D has indirect effects on the additive genetic variance, moderation coefficients on the additive genetic variance (i.e., a' and a'' in Figure S8.1) should be included in the model whenever moderation coefficients on the dominance component are estimated (i.e., d' and d'' in Figure S8.1) (Rebollo et al., 2007). Therefore, we first tested the significance of non-linear and linear dominance related moderation effects (i.e., d_c'', d_u'' and d_c', d_u' in Figure S8.1) before testing non-linear and linear moderation on additive genetic influences (i.e., a_c'', a_u'' and a_c', a_u' in Figure S8.1) and non-shared environmental influences (e_c'', e_u'' and e_c', e_u' in Figure S8.1).
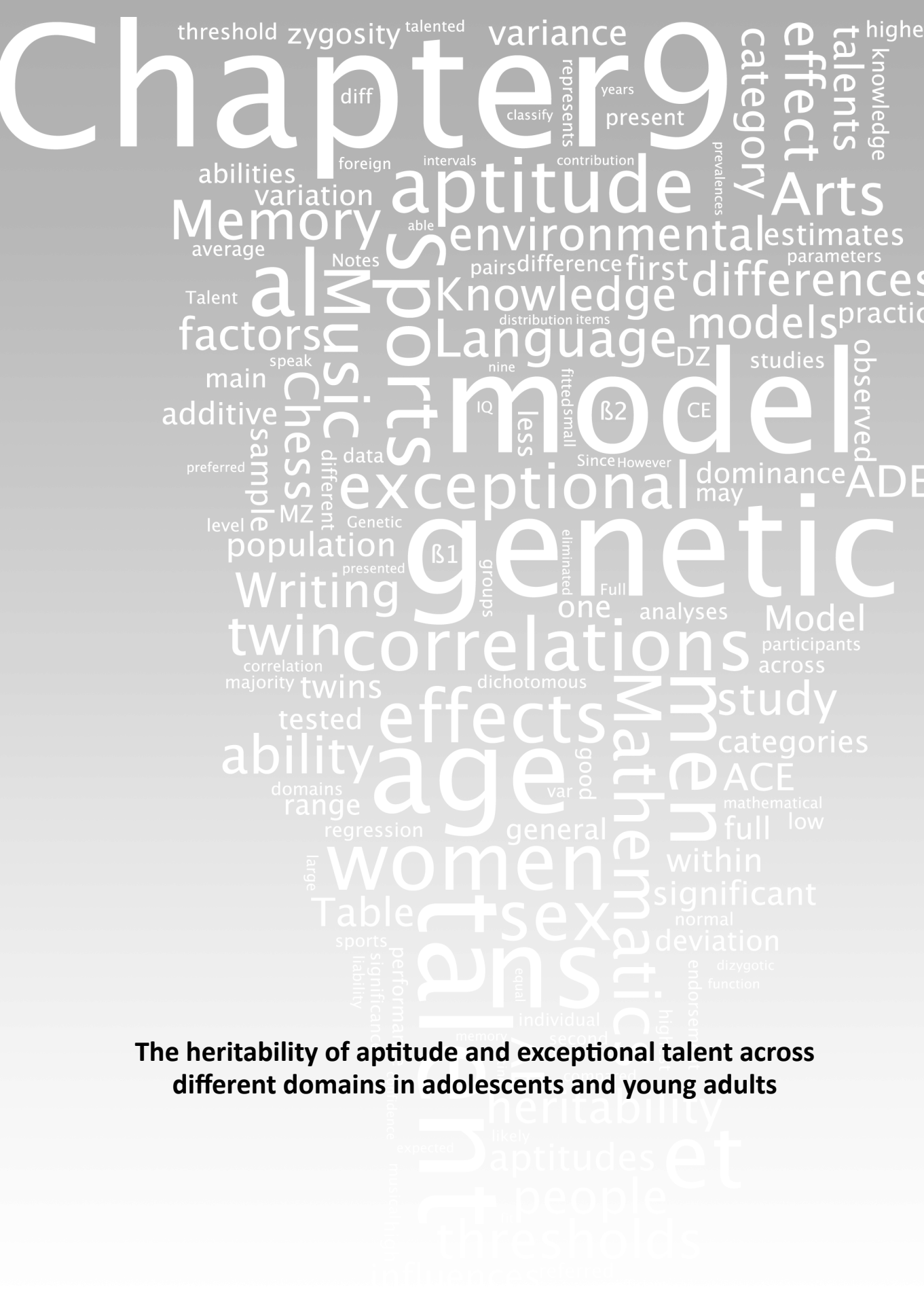
Note on Experience Seeking Scale
If three or more item responses were missing, overall ES scores were considered unreliable, and the ES data were excluded from analysis. Sum scores calculated across all available items, and divided by the number of valid items, were used as unit of analysis in this study, such that the minimum scores was one, and the maximum score was five.

Table S8.I Model fitting results for bivariate ACE interaction models of cognitive ability with experience seeking behavior as moderator variable.

	model	against	-2LL	est par	df	χ2	Δdf	p
1	Full model (no moderation)		2867.679	11	1075			
2	drop c	1	2867.679	10	1076	.000	1	.500
3	drop c_c	1	2867.679	10	1076	.000	1	.500
4	drop c_u	1	2867.679	10	1076	0.000	1	.500
5	drop c, c_c, c_u	1	2867.679	8	1078	0	3	1.000
6	**drop a**	**5**	**2924.628**	**7**	**1079**	**56.949**	**1**	**.000**
7	**drop a_c**	**5**	**2876.08**	**7**	**1079**	**8.401**	**1**	**.002**
8	**drop a_u**	**5**	**2917.836**	**7**	**1079**	**50.157**	**1**	**.000**
9	drop e_c	5	2867.727	7	1079	.048	1	.413
10	Full model (including moderation)		2843.198	19	1067			
11	drop c_c''	10	2843.198	18	1068	.000	1	.500
12	drop c_u''	10	2843.198	18	1068	.000	1	.500
13	drop c_c'', c_u''	10	2843.198	17	1069	.000	2	1.000
14	drop c_c'	13	2843.198	16	1070	.000	1	.500
15	drop c_u'	13	2843.198	16	1070	.000	1	.500
16	drop c_c', c_u'	13	2843.198	15	1071	.000	2	1.000
17	drop a_c''	16	2845.732	14	1072	2.534	1	.056
18	**drop a_u''**	**16**	**2851.404**	**14**	**1072**	**8.206**	**1**	**.002**
19	**drop a_c'**	**17**	**2848.539**	**13**	**1073**	**2.807**	**1**	**.047**
20	drop a_u'	17	2847.143	13	1073	1.411	1	.117
21	**drop e_c''**	**20**	**2851.391**	**12**	**1074**	**4.248**	**1**	**.020**
22	**drop e_u''**	**20**	**2852.444**	**12**	**1074**	**5.301**	**1**	**.011**
23	**drop e_c'**	**20**	**2850.199**	**12**	**1074**	**3.056**	**1**	**.040**
24	drop e_u' (= final model)	20	2848.811	12	1074	1.668	1	.098

	low ES	intermediate ES	high ES	
r_A	.16	.16	.23	
r_E	.31	.00	.97	
$\%_A$	57	1	66	
$\%_E$	43	0	34	

Notes: p-values of all 1-df tests are based on a ½:½ mixture of $\chi^2(0)$ and $\chi^2(1)$ distributions (Dominicus et al., 2006); -2LL = minus 2 log likelihood; par = estimated parameters; χ^2 = Chi square (difference in -2LL); p = p-value; AIC = Akaike's Information Criterion; ES = experience seeking; a_c, c_c, and e_c = unmoderated parts of additive genetic, shared-environmental and non-shared environmental factors, respectively, that are shared between ES and cognitive ability; a_u, c_u, and e_u = unmoderated parts of additive genetic, shared-environmental and non-shared environmental factors that are unique to cognitive ability; a_c', c_c', and e_c' = linear moderation coefficients, i.e., the parts of A, C and E that fluctuate as a function of ES, respectively; a_c'', c_c'', and e_c'' = non-linear moderation coefficients for A, C, and E that fluctuate as a function of ES, respectively; r_A = genetic correlation; r_E = non-shared environmental correlation; $\%_A$ = percentage of phenotypic correlation explained by genetic factors for Low, Intermediate, and High levels of experience seeking; $\%_E$=percentage of phenotypic correlation explained by non-shared environmental factors for Low, Intermediate, and High levels of experience seeking; * = preferred model; significant (moderation) effects are printed in bold font.

Chapter 9

The heritability of aptitude and exceptional talent across different domains in adolescents and young adults

ABSTRACT

The origin of individual differences in aptitude, defined as a domain-specific skill within the normal ability range, and talent, defined as a domain specific skill of exceptional quality, is under debate. The nature of the variation in aptitudes and exceptional talents across different domains was investigated in a population based twin sample. Self-report data from 1685 twin pairs (12-24 years) were analyzed for Music, Arts, Writing, Language, Chess, Mathematics, Sports, Memory and Knowledge. The influence of shared environment was small for both aptitude and talent. Additive and non-additive genetic effects explained the major part of the substantial familial clustering in the aptitude measures with heritability estimates ranging between .32 and .71. Heritability estimates for talents were higher and ranged between .50 and .92. In general, the genetic architecture for aptitude and talent was similar in men and women. Genetic factors contribute to a large extent to variation in aptitude and talent across different domains of intellectual, creative and sports abilities.

INTRODUCTION

Familial clustering of talent and giftedness has been described in various case studies of legendary families. For example, the Bach family showed a remarkable concentration of musical talents. All Bach sons grew up in a musical-social milieu, in which the young boys were trained by older family members. More recently, the Hungarian Polgar sisters became famous as advanced chess players, after being thoroughly instructed in chess by their father. Pedigrees of talented families suggest a strong familial component to exceptional ability. Case studies, however, provide insufficient information to distinguish between genetic and shared familial environmental influences. The question of whether genetic or cultural transmission causes variation in exceptional abilities and the means to develop skills through deliberate practice remains to a large extent unresolved.

In this study, the contribution of genetic influences on individual differences in aptitude and talent was investigated. Aptitude was defined as a domain-specific skill within the normal ability range of the general population. Causes of individual differences in exceptional talent were examined by explicitly distinguishing genuine outstanding ability from aptitude within the normal range. Aptitude and talent were assessed in adolescents and young adult twins from a general population sample. A self-report scale was used which distinguished nine different abilities: Music, Arts, Writing, Language, Chess, Mathematics, Sports, Memory and Knowledge. For some of these abilities, heritability has been studied before (McGue et al., 1993; Sternberg, 1993; Howe et al., 1998; Lubinski et al., 2006; Ruthsatz et al., 2008). In a survey on the determinants of musical ability, Fuller and Thompson (1978) concluded that genetic factors contribute to musical ability in general. Coon and Carey (1989) estimated heritability to range from .10 (nonschool musical performance) to .71 (vocal performance). Based on a longitudinal study on the relation between deliberate practice and performance in Chess, De Bruin et al. (2008) concluded that deliberate practice accounted for most of the variation in performance. However, this finding leaves unresolved whether extensive practice reflects a genetic disposition to, e.g., enjoy and benefit from, playing and practicing chess.

The majority of research on Sports focuses on sports participation, rather than aptitude or talent (e.g. Beunen & Thomis, 1999; De Moor et al., 2007). MacArthur and North (2005) reviewed evidence for genetic factors on human physical performance and concluded that strong genetic influences were present.

Evidence for a biological basis for mathematical talent is reported by Benbow and Lubinski (1993) in a study on sex differences in mathematics. Biological mechanisms such as hormonal influences, medical and bodily conditions and right hemispheric activations tend to correlate with mathematical achievement. Heritability estimates from twin studies range from .19 to .90 (Thompson et al., 1991; Alarcon et al., 2000; Wijsman et al., 2004). Regarding memory function, the majority of studies show heritability estimates around .50 (Finkel et al., 1995; Bouchard, Jr., 1998; Rijsdijk et al., 2002). General Knowledge such as measured in this study is largely comparable to the Information subtest of the WAIS-III (1997). Rijsdijk et al. (2002) reported a heritability of .75 for the Information subtest.

There is consensus on genetic factors playing a role in many, if not all, aspects of language (Stromswold, 2001). This suggests that the ability to fluently speak multiple foreign languages might be under genetic control as well. Heritability studies on the ability

to speak multiple foreign languages are however not available. Similarly, genetic studies on aptitude (normal population) in Writing and Arts, such as measured in the present study, have not been conducted.

Studies on causes of variation in ability in the general population are not necessarily informative about the heritability of talents and the discussion on the etiology of variation in ability is most intense with respect to variation observed in exceptional talent. Performing at an exceptional level may require more or other qualities than performing at a more ordinary level. The genetic architecture of exceptional talents may differ from the genetic architecture of aptitudes in the normal range. Studies on the heritability of exceptional talent are rare. Only a few twin studies reported high heritability estimates for talentedness in Music, Arts, Chess and Mathematics (Coon & Carey, 1989; Walker et al., 2004; Jenkins, 2005), but the genetic origin of talent is still very much under debate (Ericsson et al., 1993; Ericsson & Charness, 1994; Howe et al., 1998; Ruthsatz et al., 2008). The present study concerns an investigation of the genetic and environmental influences on the variation observed in both aptitude and talent across nine different domains in adolescents and young adults.

METHODS

Sample
Since 1991, the Netherlands Twin Register (NTR) (Boomsma et al., 2006) focuses on longitudinal survey research on health, lifestyle, personality and psychopathology. Twins and their family-members receive a questionnaire every 2-3 years. In the present study, data from the first survey are used. Data were available for 3370 twins (54% women, 1685 pairs). Zygosity of same-sex twins was based on DNA polymorphisms (434 same-sex twin pairs) or, if information on DNA markers was not available, on questions about physical similarity and confusion of the twins by family members and strangers. Agreement between zygosity diagnoses from survey and DNA data was 97% (Willemsen et al., 2005). Twelve twin pairs (three complete and nine incomplete) were excluded because zygosity was unknown.

All five zygosity groups were well represented: monozygotic males (MZM: 16,8%), dizygotic males (DZM: 14,5%), monozygotic females (MZF: 22,6%), dizygotic females (DZF: 17,6%) and dizygotic opposite sex (DOS: 28,4%). The geographic distribution of the sample mirrored the geographic distribution of the Dutch population. The sample of participating twins was representative of the general Dutch population with regard to the educational level of the twins (CBS, CBS, 2009) and the parents (Koopmans et al., 1995). Furthermore, prevalences of smoking and sport participation was comparable to other national large scale surveys (Plomp et al., 1991; de Zwart et al., 1993; Sangster & Abrahamse, 1995), implying that the sample mirrored the Dutch population.

Average age of the twins was 17.7 years, (SD=2.3; range: 12.6 - 24.6 years).

Measures
Nine items were selected from the Talent Inventory developed by McGue et al. (1993) which concerned self-report information on Music, Arts, Writing, Language, Chess, Mathematics,

Sport, Memory and Knowledge. These nine items required subjects to rank their own competence, compared to the general population, on an ordinal four-point scale. The first category represents people who classify themselves as less competent than most people. The second category represents the average (as competent as most people), the third category the above average (more competent than most people) and the fourth category represents people who classify themselves at the top-end, i.e., as being exceptionally skilled.

Music referred to singing or playing one or more instruments. Arts referred to artistic and creative activities (painting, acting). Writing referred to creative writing (letters, manuscripts, books). Language referred to the ability to speak one or more foreign languages. Chess referred to the ability to play games like chess, backgammon and mah-jong. Mathematics referred to mathematical and numerical ability. Sports referred to athletic skills. Memory referred to general mnemonic skills (events, numbers and facts). Knowledge referred to general and specific knowledge of facts. A detailed overview of the nine phenotypes is provided in the Supplementary Information of this chapter.

The endorsement rate of the fourth (exceptional) category was very low in most phenotypes (Table 9.1). For the study of <u>aptitude</u>, categories 3 and 4 were therefore merged. For the study of <u>exceptional talent</u>, categories 1, 2 and 3, representing ability within the normal range, were merged and contrasted to category 4, representing a rare and exceptional ability level.

Statistical Analysis

All ordinal variables were assumed to reflect an imprecise measurement of an underlying normal distribution of liability (Falconer & Mackay, 1989). For the studies of aptitude and talent scores on this liability distribution could fall into 3 or 2 categories that were defined by two and one thresholds, which depend on the prevalence of the responses to the items. Since the liability is a theoretical construct, its scale is arbitrary. The liability was assumed to be standard normally distributed with zero mean and unit variance.

Aptitude

To test for differences in prevalences in aptitudes between men and women, thresholds were specified separately in both sexes. Thresholds were allowed to vary as a function of age. The second threshold was modeled as a positive deviation from the first threshold so that the second threshold was always above the first. To obtain age corrected correlations, the effect of age was modeled as a main effect of age on the first threshold and a deviation of this main effect of age on the incremental second thresholds:

$$T_{\female 1} = S_{\female 1} + \beta_{\female 1}\text{Age} \qquad\qquad T_{\male 1} = S_{\male 1} + \beta_{\male 1}\text{Age}$$
$$T_{\female 2} = (S_{\female 1} + \beta_{\female 1}\text{Age}) + (S_{\female 2} + \beta_{\female 2}\text{Age}) \qquad T_{\male 2} = (S_{\male 1} + \beta_{\male 1}\text{Age}) + (S_{\male 2} + \beta_{\male 2}\text{Age})$$

in which $T_{\female 1}$ and $T_{\female 2}$, indicate the first and the second threshold (women). $S_{\female 1}$ denotes the estimate of the first threshold; $S_{\female 2}$ denotes the estimates of the increment of the second threshold (women). $\beta_{\female 1}$ is the regression of age on the first threshold; $\beta_{\female 2}$ reflects the effect of age on the increment. The term $(S_{\female 2} + \beta_{\female 2}\text{Age})$ was restricted to be larger than, or equal to zero to ensure that the second threshold was always higher than the first. A similar model was specified in men.

First, analyses were carried out to test the effect of zygosity, sex and age on the thresholds and to estimate twin correlations. Initially, thresholds were allowed to differ for

the six zygosity-by-sex groups to test for possible sibling interaction effects (model 1). Social interaction is expected to result in differences in prevalences and thus thresholds, across zygosity groups (Carey, 1992). The effects of social interaction were tested within sex. The effect of sex on the thresholds was tested by constraining the thresholds and age regression effects to be equal across sexes (model 2). The effect of age on the thresholds was tested stepwise. Since β_2 was modeled as a deviation of the main effect of age (β_1), significance of β_2 was tested first (model 3: *men* and model 4: *women*). Then, the significance of β_1 was tested (model 5: *men* and model 6: *women*).

Age-corrected twin correlations were derived from the most parsimonious model for liability in aptitude. Analyses were carried out using the raw data option in Mx (Neale, 1994; Posthuma & Boomsma, 2005) and a criterion level α of .05 was adopted for all tests. The Mx script detailing these analyses can be found online at http://psy.vu.nl/mxbib.

Talent

Talent was analyzed as a dichotomous phenotype; exceptional talent versus all other categories. As exceptional talent is rare, the endorsement rate of the fourth category was low and very few twin pairs were concordant for being exceptionally talented. To preserve a sufficient number of concordant twin pairs within the fourth category, just two zygosity groups were distinguished (MZ and DZ). Even then, empty cells were observed for some talents. To overcome this problem, contingency tables were analyzed instead of raw data and empty cells were filled with a small non-zero value (0.5). All other frequencies in the table were adjusted accordingly so that the marginal values remained unaltered (Brown et al., 1983). These adjusted contingency tables were then used as input for Mx. This approach allows the study of heritability of exceptional talent, but does not allow examination of the effect of sex and age on thresholds. Therefore, polyserial correlations (Joreskog & Sorbom, 2006) between age and talent (as a dichotomous phenotype) were estimated. These were all not significantly different from zero; i.e. age does not affect endorsement rates in the highest category. Furthermore, tetrachoric correlations (Joreskog & Sorbom, 2006) between sex and talent (as a dichotomous phenotype) were not significant, i.e. sex does not affect endorsement rates in the highest category. Contingency table analyses do not allow for partial missingness of data. However, the percentage of missingness was small (max 2.5% per trait).

Genetic analyses

Genetic models were specified in which individual differences in liability for aptitude and talent were modeled as a function of genetic and environmental effects. Genetic factors A and D and environmental factors C and E were considered. 'A' represents additive effects of alleles summed over all loci. 'D' represents the extent to which the effects of alleles at a locus are not additive but interact with each other (genetic dominance). 'C' represents common environmental influences that render offspring of the same family more alike. 'E' represents all environmental influences that result in differences between members of a family. E also includes measurement error.

In a classical twin design, the effect of C and D cannot be estimated simultaneously because these factors have opposite effects on the difference between MZ and DZ twin

correlations. As the present study sample only included twins, the variance in liability was decomposed as due to A, C and E, or due to A, D and E. The expected covariance for MZ twins was var(A)+var(C), or var(A)+var(D) in case of genetic dominance; where var(A) and var(D) represent additive genetic and non-additive genetic variance and var(C) represents variance due to C. The expected covariance for DZ twins was ½var(A)+var(C), or ½var(A)+¼var(D) (Falconer 1989). When DZ twin correlations are at least half the MZ twin correlations, additive genetic effects are implied and an ACE model was fitted to the data. DZ twin correlations less than half the MZ twin correlations suggest the presence of genetic dominance. Then an ADE model was fitted to the data.

Quantitative sex differences in genetic and environmental parameters are implied when correlations in same-sex twin pairs differ between men and women. In that case, genetic models were fitted separately in men and women, allowing different parameter estimates of genetic and environmental variance components.

Significance of parameters was tested by comparing the fit of nested models to the fit of less restricted models. Goodness-of-fit of these sub models was assessed by likelihood-ratio-tests. The difference in log-likelihoods between models (which follows a χ^2distribution) was tested. If the test is significant, the constraints imposed on the nested models are not tenable. If the difference test is not significant, the nested, more parsimonious model is to be preferred.

RESULTS

Table 9.1 lists frequencies and percentages of all abilities in the four original categories. In all abilities but Language, the highest category has the lowest endorsement rate. In all abilities, except Arts and Music, the second category (average population level) accommodates the majority of the participants.

Aptitude

Table 9.2 shows tests for zygosity-, sex- and age-effects on the thresholds. In all aptitudes but Sports, no significant differences between zygosity groups within sex were observed (model 1), indicating the absence of social interaction effects. A small zygosity effect on the thresholds was observed for Sports (χ^2=16.46 (8), p=.04). However, equating thresholds in two steps (first within men, then within women) did not result in a significant deterioration of the model fit. Since the difference in model fit (model 1 vs. full model) was rather small, it was decided to equate thresholds in all zygosity groups (within sex) for all variables, including Sports. In model 2, thresholds and age regression coefficients on the thresholds were constrained to be equal between men and women. Sex effects on the thresholds were significant (all aptitudes; model 2). Men endorsed the higher categories of Arts, Chess, Mathematics, Sports, Memory and Knowledge more often than women. Women endorsed the higher categories of Music, Writing and Language more often than men.

Table 9.1 Number of participants and prevalences in the four original categories for men and women

	1		2		3		4		total
	♂	♀	♂	♀	♂	♀	♂	♀	♂/♀
Music	721 (48.4%)	613 (33.7%)	537 (36.0%)	823 (45.3%)	210 (14.1%)	357 (19.6%)	22 (1.5%)	24 (1.3%)	1490/1817
Arts	901 (60.5%)	877 (48.5%)	481 (32.3%)	711 (39.3%)	83 (5.6%)	182 (10.1%)	25 (1.7%)	38 (2.1%)	1490/1808
Writing	354 (23.6%)	238 (13.1%)	923 (61.4%)	1208 (66.4%)	215 (14.3%)	362 (19.9%)	11 (.7%)	10 (.6%)	1503/1818
Language	96 (6.4%)	86 (4.7%)	877 (58.8%)	1007 (55.6%)	201 (13.5%)	209 (11.5%)	317 (21.3%)	510 (28.1%)	1491/1812
Chess	276 (18.4%)	561 (30.9%)	864 (57.8%)	1097 (60.4%)	347 (23.2%)	158 (8.7%)	9 (.6%)	1 (.1%)	1496/1817
Mathematics	308 (20.7%)	708 (39.1%)	796 (53.5%)	852 (47.1%)	325 (21.8%)	232 (12.8%)	60 (4.0%)	18 (1.0%)	1489/1810
Sports	179 (12.1%)	302 (16.7%)	688 (46.6%)	1068 (59.1%)	459 (31.1%)	342 (18.9%)	151 (10.2%)	95 (5.3%)	1477/1807
Memory	56 (3.7%)	84 (4.6%)	719 (47.9%)	1053 (57.9%)	665 (44.3%)	649 (35.7%)	62 (4.1%)	34 (1.9%)	1502/1820
Knowledge	57 (3.9%)	135 (7.5%)	889 (60.1%)	1431 (79.1%)	393 (26.6%)	184 (10.2%)	141 (9.5%)	59 (3.3%)	1480/1809

Notes: 1 = "no curiosity or no knowledge at all; 2 = little knowledge and little interest, aptitude about average; 3 = knowledge, interests and aptitude above average; 4 = a superior or outstanding level

Table 9.2 Model fit of aptitude scores for men and women. For the full model the likelihood and number of degrees of freedom are presented. For all submodels χ^2 scores, difference in degrees of freedom and p-values are presented.

	Full Model	Model 1	Model 2	Model 3	Model 4	Model 5	Model 6
	-2 LL (*df*)	Test for differences in thresholds between zygosity within sex	Test for differences in thresholds between sex	Test for significance of the deviation of age effect (β_2) men	Test for significance of the deviation of age effect (β_2) women	Test for significance of the main effect of age (β_1) men	Test for significance of the main effect of age (β_1) women
Music	6279.29 (3286)	1.93 (8), *ns*	72,05 (4), p<.001	.90 (1), ns	**.01 (1), *ns***	7.44 (1), p<.01	31.52 (1), p<.001
Arts	5854.87 (3297)	4.80 (8), *ns*	48,34 (4), p<.001	**.06 (1), *ns***	8.35 (1), p<.01	4.93 (1), p<.05	16.01 (1), p<.001
Writing	5805.49 (3320)	5.67 (8), *ns*	69,87 (4), p<.001	3.64 (1), *ns*	1.44 (1), *ns*	**.075 (1), *ns***	4.43 (1), p<.05
Language	5289.95 (3282)	14.42 (8), *ns*	14,22 (4), p<.01	1.83 (1), *ns*	1.06 (1), *ns*	1.439 (1), *ns*	**.54 (1), *ns***
Chess	5990.41 (3292)	14.74 (8), *ns*	145,64 (4), p<.001	.89 (1), *ns*	.03 (1), *ns*	3.02 (1), *ns*	**.22 (1), *ns***
Mathematics	6336.94 (3306)	10.51 (8), *ns*	130,84 (4), p<.001	**1.46 (1), *ns***	6.59 (1), p<.05	4.117 (1), p<.05	18.15 (1), p<.001
Sports	5869.37 (3283)	**16.46 (8), p<.05**	80,46(4), p<.001	7.10 (1), p<.01	10.55 (1), p<.01	24.90 (1), p<.001	22.20 (1), p<.001
Memory	5381.67 (3301)	6.45 (8), *ns*	34,09 (4), p<.001	.78 (1), *ns*	1.23 (1), *ns*	4.04 (1), p<.05	**2.49 (1), *ns***
Knowledge	4566.16 (3268)	8.40 (8), *ns*	208,83 (4), p<.001	.082 (1), *ns*	1.75 (1), *ns*	1.49 (1), *ns*	**.78 (1), *ns***

Notes: -2LL = minus 2 log likelihood; β_1 = coefficient of main age effect; β_2 = deviation of the regression coefficient of age; ns = non significant; p = p-value. Full model: All parameters estimated: 2 thresholds for all 6 zygosity groups; main age effects men/women; deviation age effect men/women. Model 1: model wherein thresholds are constrained equal for all zygosity groups within sex. Estimated parameters: 2 thresholds for men/women; main age effects men/women; deviation age effect men/ women. Model 2: model wherein thresholds and age coefficients are constrained equal for men and women. Estimated parameters: 2 thresholds; main age effects; deviation age effect. Model 3: model wherein deviation of the regression coefficient of age (β_2) is eliminated from the model for men. Model 4: model wherein deviation of the regression coefficient of age (β_2) is eliminated from the model for women. Model 5: model wherein regression coefficient of the main age effect (β_1) is eliminated from the model for men. Model 6: model wherein regression coefficient of the main age effect (β_1) is eliminated from the model for women. Subsequent models are tested against its previous model, provided that the fit of that previous model is acceptable. For clarity of the presentation, the most parsimonious model for all aptitudes is presented in bold font.

Significance of both β_2 and β_1 was tested for men and women. Since β_2 was modeled as a deviation of the main effect of age (β_1), significance of β_2 was tested first (model 3 and 4). Next, significance of β_1 was tested (model 5 and 6). Significant age effects were all negative, i.e. older participants were less inclined to endorse the higher categories. β_2 was significant for Sports in men (model 3) and for Arts, Mathematics and Sports in women. β_1 was significant for Music, Arts, Mathematics, Sports and Memory in men and for Music, Arts, Writing, Mathematics and Sports in women. Regression coefficients of age range from .03 to -.10. on the first threshold and from -.04 to -.06 on the increment. Although the age range in this sample was not large (12.6–24.6 years), age influences self reported aptitudes. Maturation effects during puberty (e.g. fast maturation may lead to higher aptitudes at a relatively earlier age), or the ability to assess one's own aptitude, may be of importance within this age range. Non-significant age effects were eliminated from the genetic models. The most parsimonious model for all aptitudes is presented in bold.

Table 9.3 Sex and age corrected polychoric twin correlations (95% confidence intervals) for aptitude

	rMZM n = 283, 16.8%	rDZM n = 245, 14.5%	rMZF n = 381, 22.6%	rDZF n = 297, 17.6%	rDOS n = 479, 28.4%
Music	.74 (.65 - .81)	.45 (.30 - .58)	.80 (.74 - .85)	.63 (.53 - .71)	.42 (.32 - .51)
Arts	.54 (.40 - .66)	.36 (.19 - .51)	.64 (.55 - .71)	.29 (.14 - .42)	.23 (.10 - .34)
Writing	.47 (.33 - .59)	.11 (.01 - .26)	.46 (.33 - .57)	.09 (.01 - .23)	.23 (.12 - .33)
Language	.63 (.50 -.73)	.42 (.26 - .55)	.76 (.67 - .82)	.39 (.25 - .51)	.31 (.20 - .42)
Chess	.48 (.34 - .59)	.20 (.05 - .35)	.51 (.38 -.62)	.07 (.01 - .22)	.01 (.01 - .11)
Mathematics	.66 (.56 - .74)	.19 (.03 - .33)	.68 (.60 - .75)	.30 (.16 - .43)	.14 (.03 - .25)
Sports	.62 (.51 - .72)	.38 (.23 - .52)	.80 (.74 - .85)	.66 (.55 - .75)	.16 (.05 - .27)
Memory	.43 (.27 - .57)	.15 (.01 - .32)	.51 (.40 - .62)	.01 (.01 - .07)	.19 (.06 - .31)
Knowledge	.58 (.45 - .69)	.30 (.11 - .46)	.51 (.37 - .63)	.25 (.07 - .42)	.31 (.19 - .42)

Notes: rMZM = correlation monozygotic males; rDZM = correlation dizygotic males; rMZF = correlations monozygotic females; rDZF = correlation dizygotic females; rDOS = correlation opposite sex twins; n = number of twin pairs. For each aptitude, correlations were obtained from the most parsimonious model (Table 9.3).

Table 9.3 lists the polychoric twin correlations and their confidence intervals. For all variables, MZ twin correlations exceeded the DZ twin correlations suggesting the presence of genetic influences. In Chess, Mathematics, Writing and Memory, DZ correlations were smaller than half the MZ correlations, implying the presence of genetic dominance. ADE models were fitted to these four aptitudes, while ACE models were fitted to the other five. Twin correlations were equal in men and women for all aptitudes but Sports ($\Delta\chi^2(2)=19.027$, p<.001). Higher heritability was implied in men, while a larger influence of shared environmental factors was implied in women. Correlations of A and C were fixed to .5 and 1 respectively, in DZ same-sex and in DZ opposite-sex pairs.

Table 9.4 Model fitting results for aptitude

	Models	vs	-2LL	Estimated parameters	χ^2	Δdf	*p*
Music							
1	**ACE**		**6303.93**	**10**			
2	ACE no sex diff.	1	6314.59	8	10.66	2	<.01
3a	AE men	1	6311.95	9	8.02	1	<.01
4a	CE men	1	6319.73	9	15.80	1	<.001
3b	AE women	1	6322.01	9	18.08	1	<.001
4b	CE women	1	6314.20	9	10.27	1	<.01
Arts							
1	ACE		5861.56	11			
2	ACE no sex diff.	1	5865.16	9	3.60	2	*ns*
3	**AE**	**2**	**5865.16**	**8**	**0**	**1**	***ns***
4	CE	2	5898.00	8	32.84	1	<.001
5	E	2	6057.93	7	192.77	2	<.001
Writing							
1	ADE		5818.64	9			
2	ADE no sex diff.	1	5818.68	7	.04	2	ns
3	**AE**	**2**	**5821.42**	**6**	**2.75**	**1**	**ns**
4	E	2	5909.02	5	87.60	2	<.001
Language							
1	ACE		5309.25	8			
2	ACE no sex diff.	1	5314.18	6	4.93	2	ns
3	**AE**	**2**	**5314.20**	**5**	**.20**	**1**	**ns**
4	CE	2	5357.59	5	43.39	1	<.001
5	E	2	5589.30	4	275.10	2	<.001
Chess							
1	ADE		6009.91	8			
2	**ADE no sex diff.**	**1**	**6015.46**	**6**	**5.55**	**2**	**ns**
3	AE	2	6029.33	5	13.87	1	<.001
Mathematics							
1	ADE		6338.03	11			
2	**ADE no sex diff.**	**1**	**6341.02**	**9**	**2.99**	**2**	**ns**
3	AE	2	6353.47	8	12.45	1	<.001
Sports							
1	ACE		5891.81	12			
2	ACE no sex diff.	1	5935.82	10	44.00	2	<.001
3a	**AE men**	**1**	**5892.26**	**11**	**.45**	**1**	**ns**
4a	CE men	1	5910.68	11	18.42	1	<.001
5a	E men	1	5990.60	10	79.92	2	<.001
3b	AE women	3a	5920.64	10	28.38	1	<.001
4b	CE women	3a	5907.27	10	15.01	1	<.001
Memory							
1	ADE		5405.179	9			
2	**ADE no sex diff.**	**1**	**5405.263**	**7**	**.08**	**2**	**ns**
3	AE	2	5416.659	6	11.396	1	<.001
Knowledge							
1	ACE		4578.864	8			
2	ACE no sex diff.	1	4579.644	6	.78	2	ns
3	**AE**	**2**	**4579.807**	**5**	**.16**	**1**	**ns**
4	CE	2	4595.169	5	15.36	1	<.001
5	E	2	4713.440	4	133.63	2	<.001

Notes: vs = compared to model; -2LL = minus 2 log likelihood; χ^2 = Chi square (difference in -2LL); Δdf = difference in degrees of freedom; p = p-value

Table 9.4 lists the genetic model fitting results; preferred models are presented in bold. First, a full ACE or ADE model was evaluated with different parameter estimates for men and women (model 1). Next, the difference between men and women in magnitude of the genetic and environmental components was tested (model 2). Significance of A and C or D was tested by constraining the relevant parameters to zero (models 3 to 5).

A full ACE model was preferred for Music and Sports (women). A full ADE model was preferred for Chess, Mathematics and Memory. An AE model was preferred for Arts, Language, Sports (men) and Knowledge. Quantitative sex differences were observed in Music and Sports (model 2).

Table 9.5 Proportions of variance for the best fitting models and full models for aptitude in Dutch twins across 9 domains of intellectual, creative and sports abilities. For Music and Sports, parameter estimates are shown for men and women separately.

Variable	a^2	d^2	c^2	e^2
Music (men)	.66 (.52 - .77)	-	.08 (.04 - .16)	.25 (.19 - .34)
Music (women)	.30 (.16 - .36)	-	.54 (.48 - .68)	.16 (.12 - .22)
Arts *Full model*	.60 (.53 - .66) *.60 (.53 - .66)*	*-*	- *.00 (.00 - .13)*	.40 (.34 - .47) *.40 (.34 - .47)*
Writing *Full model*	.43 (.35 - .50) *.18 (.00 - .44)*	- *.27 (.00 - .52)*	*-*	.57 (.50 - .65) *.55 (.47 - .63)*
Language *Full model*	.71 (.65 - .76) *.70 (.50 - .76)*	*-*	- *.01 (.00 - .17)*	.29 (.24 - .35) *.29 (.24 - .36)*
Chess	.01 (.00 - .17)	.48 (.28 - .56)	-	.52 (.44 - .61)
Mathematics	.11 (.00 - .41)	.56 (.25 - .73)	-	.33 (.27 - .39)
Sports (men) *Full model*	.64 (.51 - .72) *.57 (.41 - .68)*	*-*	- *.06 (.01 - .18)*	.36 (.28 - .47) *.37 (.28 - .48)*
Sports (women)	.29 (.09 - .53)	-	.51 (.29 - .69)	.20 (.15 - .26)
Memory	.01 (.00 - .20)	.47 (.25 - .55)	-	.52 (.45 - .62)
Knowledge *Full model*	.56 (.47 - .63) *.51 (.26 - .63)*	- *.04 (.00 - .23)*	*-*	.44 (.37 - .53) *.45 (.37 - .55)*

Notes: a^2 = additive genetic effects; d^2 = dominance genetic effects; c^2 = common environmental effects; e^2 = unique environmental effects.

The proportion of variance explained by additive genetic factors was low in Chess (.01), Mathematics (.11) and Memory (.01), while the proportion of variance accounted for by dominance genetic factors was high for Chess (.48), Mathematics (.56) and Memory (.47) (see Table 9.5). Since dominance deviation are not generally expected without a contribution of additive genetic factors, relatively low proportions of additive genetic variance in Chess, Mathematics and Memory are not eliminated from the model.

The proportion of variance explained by additive genetic factors was relatively high in Music (.66, men), Arts (.60) and Sports (men: .64). Shared environmental variance components were not significant in Arts, Language, Sports (men) and Knowledge, whereas this components were significant in Music (men: .09, women: .48) and in Sports (women: .51).

Talent

As stated, contingency tables were analyzed for exceptional talent. Genetic analysis was not conducted for Chess due to the very low endorsement rate of the exceptional ability category (Table 9.1). Table 9.6 lists tetrachoric twin correlations and their confidence intervals. For all talents, MZ twin correlations exceeded the DZ twin correlations implying genetic influences. For Arts, Writing, Mathematics, Sports, Memory and Knowledge, DZ correlations were smaller than half the MZ correlations, implying the presence of genetic dominance. ADE models were fitted to these abilities, while ACE models were fitted to Music and Language.

Table 9.6 Tetrachoric twin correlations (95% confidence intervals) for talent

	rMZ	rDZ
Music	.92 (.73- .98)	.49 (.11 - .76)
Arts	.61 (.27 - .84)	.05 (-.45 - .48)
Writing	.83 (.28 - .98)	.38 (-.25 - .79)
Language	.72 (.64 - .80)	.48 (.37 - .57)
Mathematics	.89 (.74 - .96)	.04 (-.48 - .48)
Sports	.85 (.74 - .92)	.40 (.23 - .55)
Memory	.59 (.23- .82)	.24 (-.06 - .49)
Knowledge	.65 (.47 - .79)	.20 (-.02 - .41)

Notes: rMZ = correlation monozygotic twins;
rDZ = correlation dizygotic twins

Table 9.7 Model fitting results for talent

Models		vs	χ^2	Estimated parameters	$\Delta\chi^2$	Δdf	p
Music							
1	ACE		.35	3			
2	**AE**	**1**	**.38**	**2**	**.03**	**1**	**ns**
3	CE	1	9.378	2	9.03	1	<.01
4	E	2	49.222	1	48.84	1	<.001
Arts							
1	ADE		2.95	3			
2	**AE**	**1**	**3.82**	**2**	**.87**	**1**	**ns**
3	E	2	13.73	1	9.91	1	<.01
Writing							
1	ADE		17.64	3			
2	**AE**	**1**	**17.64**	**2**	**0**	**1**	**ns**
3	E	2	85.71	1	68.07	1	<.001
Language							
1	**ACE**		**5.67**	**3**			
2	AE	1	9.96	2	4.30	1	*<.05 (.038)*
3	CE	1	20.40	2	10.44	1	<.01
Mathematics							
1	ADE		6.18	3			
2	**AE**	**1**	**8.77**	**2**	**2.59**	**1**	**ns**
3	E	2	67.66	1	58.89	1	<.001
Sports							
1	ADE		2.3	3			
2	**AE**	**1**	**2.49**	**2**	**.10**	**1**	**ns**
3	E	2	116.60	1	114.11	1	<.001

Models		vs	χ²	Estimated parameters	Δχ²	Δdf	p
Memory							
1	ADE		3.59	3			
2	**AE**	**1**	**3.74**	**2**	**.15**	**1**	***ns***
3	E	2	15.64	1	11.90	1	<.001
Knowledge							
1	ADE		2.96	3			
2	**AE**	**1**	**4.17**	**2**	**1.21**	**1**	***ns***
3	E	2	42.71	1	38.54	1	<.001

Notes: vs = compared to model; χ² = Chi square test statistic; Δχ² = difference Chi square; Δdf = difference degrees of freedom; p = p-value

Table 9.7 lists the genetic model fitting results; preferred models are presented in bold. None of the dominance genetic effects were statistically significant. Variation in all talents is explained by additive genetic and non-shared environmental factors (table 9.8). Shared environmental factors were only significant for Language, explaining 23% of the variation. Noticeable are the high heritability estimates for Music (.92), Writing (.83), Mathematics (.87) and Sports (.85).

Table 9.8 Proportions of variance (95% confidence intervals) of the best fitting models and full models for talent across 8 domains of intellectual, creative and sports abilities.

Variable	a^2	d^2	c^2	e^2
Music	.92 (.74 - .98)		-	.08 (.02 - .26)
full model	*.86 (.22 - .98)*		*.06 (.00 - .62)*	*.08 (.02 - .27)*
Arts	.56 (.22 - .80)	-		.44 (.20 - .78)
full model	*.00 (.00 - .78)*	*.60 (.00 - .83)*	-	*.40 (.17 - .74)*
Writing	.83 (.33 - .98)	-		.17 (.02 - .67)
full model	*.88 (.00 - .95)*	*.00 (.00 - .95)*	-	*.12 (.05 - .26)*
Language	.50 (.25 - .75)	-	.23 (.01 - .43)	.27 (.20 - .36)
Mathematics	.87 (.72 - .95)	-		.13 (.05 - .28)
full model	*.00 (.00 - .93)*	*.88 (.00 - .96)*	-	*.12 (.04 - .26)*
Sports	.85 (.74 - .92)	-		.15 (.08 - .26)
full model	*.74 (.07 - .92)*	*.10 (.00 - .80)*	-	*.15 (.08 - .26)*
Memory	.56 (.26 - .79)	-		.44 (.21 - .75)
full model	*.35 (.00 - .79)*	*.25 (.00 - .82)*	-	*.41 (.18 - .74)*
Knowledge	.62 (.44 - .76)	-		.38 (.24 - .56)
full model	*.14 (.00 - .74)*	*.51 (.00 - .79)*	-	*.35 (.21 - .53)*

Notes: a^2 = additive genetic effects; d^2 = dominance genetic effects; c^2 = common environmental effects; e^2 = unique environmental effects.

DISCUSSION

The aim of this study was to investigate causes of human variation observed in self-reported aptitude and talent across nine different domains. For aptitudes, sex differences in prevalences were observed across nearly all domains. Women were more inclined to classify themselves into higher categories in Music, Writing and Language, while men classified their own performance more often as above average in Arts, Chess, Mathematics, Sports, Memory and Knowledge.

Despite the small age range (12-24 years), age effects on aptitudes were significant in Music, Arts, Writing (women), Mathematics, Sports and Memory (men). Older participants were less inclined to classify themselves in the highest categories. The age effect might be attributable to differences in the ability to compare oneself with other people. Younger participants may be less capable in comparing themselves with other people of similar age. Alternatively, individual differences in maturation could create true differences among adolescents and young adults. Sex and age effects were observed in the study of aptitude, while no sex or age effects were observed in the study of talent. Polychoric correlations between sex and talent and polyserial correlations between age and talent were not significant, suggesting that age is not related to the expression of rare talents.

Results of the genetic analyses clearly demonstrate that in both aptitude and talent, genetic factors contribute to a large extent to the observed variation. Moreover, a comparison between the relative contribution of genetic and environmental factors on aptitudes and talents showed a highly similar contribution of genetic factors for Arts and a decreased genetic contribution for Language. Increased contribution of genetic factors in exceptional talent was observed for Music, Writing, Mathematics, Sports, Memory and Knowledge: heritability estimates of the majority of these talents exceed the upper bound of the confidence intervals around the heritability estimates of aptitude. These outcomes suggest that genetic factors are essential for outstanding levels of ability.

Some methodological limitations regarding the comparison between aptitude and talent should be noted. First, the low endorsement rates of the exceptional category and the use of contingency tables precluded the simultaneous investigation of sex and age effect in the genetic analyses of talent. Neglecting possible effects of sex and age could bias estimates of additive genetic effects and shared environmental effects, respectively. However, non-significant correlations between talent (as a dichotomous phenotype) and sex and age were found.

The dominance genetic effects reported for aptitudes were not seen for talent. This might be due to a reduction in statistical power in the dichotomous analyses of talent. In general, of the use of dichotomous measures requires a larger sample size to detect genetic dominance. Furthermore, a low prevalence (i.e. rare talent) requires a much larger sample size compared to an 'optimal' prevalence (50%) (Neale et al., 1994). Given the present sample size with a prevalence of 5%, genetic dominance must explain at least 78% of the total variance (additive genetic variance = 10%) to reject an AE model with a power of 80% when the true world model is ADE. Third, estimates of E are generally lower in the analyses of talent, compared to the analyses of aptitude, suggesting that unique environment contributes less to variation or that measurement error is lower. For dichotomous measures, more measurement error might be expected. Yet, classifying

oneself as either exceptionally talented or not, may not be that prone to misclassification, resulting in a relatively reliable dichotomous measure of talent.

Any trait with a heritability of less then unity (Eysenck & Gudjonsson, 1989), will show regression towards the mean. Highly talented people are therefore less likely to have similarly talented children. In his theory of genius and creativity, Eysenck (1989) argues that *"genius would be seen as a highly unlikely segregation of genes, occurring very rarely for a few individuals only"* and that complex human traits such as genius and talent are likely to be controlled by combinations of interacting genes called epistasis or emergenesis (Lykken et al., 1992). Such traits may be heritable but resemblance will not be seen in first degree relatives while MZ twins do bear a resemblance to each other. Although we observe some DZ correlations that are relatively low compared to MZ correlations for a few talents, for most talents substantial additive genetic variance is also suggested.

It is possible that individual differences in aptitudes and talents are associated with IQ and that part of the heritability is shared with genetic influences on IQ. For 295 participants from this sample, information on IQ was available (Rijsdijk & Boomsma, 1997). Participants with high IQ were slightly overrepresented in the highest category of the Talent Inventory. Polyserial correlations (Joreskog & Sorbom, 2006) between talents and IQ ranged from .12 (Sport*IQ, *ns*) to .28 (Mathematics*IQ, p<.001).

Findings about genetic influences on individual differences in aptitude from the present study are in line with findings from previous heritability studies on Music (Coon & Carey, 1989), Mathematics (Thompson et al., 1991; Alarcon et al., 2000), Sports (Bouchard & Malina, 1983; Boomsma et al., 1989; Beunen & Thomis, 1999; Maia et al., 2002; Macarthur & North, 2005; Stubbe et al., 2005; Stubbe et al., 2006), Memory (Bouchard, Jr., 1998; Finkel et al., 1995) and Knowledge (Rijsdijk et al., 2002).

In contrast to the majority of research on aptitude and talent, self-report questionnaires were used in the present study. Self-report questionnaires can easily be administered to a large sample, representative of the general population. Since it is not the ability itself that is studied, but its etiology in terms of genetic and environmental influences, a good representation of the general population, in which all levels of aptitude and talent are present, is required. The validity of self-report data might, however, be questioned. People may differ in the extent to which they are capable of comparing their own ability to that of others, a capacity which may be related to age and in their readiness to portray themselves as more or less talented then others. In addition, people are likely to compare their own competence with that of people in their proximity. If one's environment is correlated with one's phenotype, people will be less likely to classify themselves in the lower or higher end of the population. Yet, the distribution of the prevalences of the majority of the traits in this study was in line with the expected distribution for the general population, with mean scores for the majority of the participants and exceptional scores for only a very small part of the sample. Regarding Language, the majority of the participants classified themselves into the two highest categories.

No information is available on the reliability of the single items that were analyzed. However, heritability cannot exceed the reliability of a trait. As heritability for most items is not low, we conclude that reliability is not low either (Bouchard, Jr. et al., 1990) (Bouchard et al. 1990).

The high endorsement rate of the two highest ability levels for Language indicates that this item of the Talent Inventory does not discriminate well within the Dutch population. In the Netherlands, foreign languages are taught in nearly all high schools. As a result, all people who completed high school are likely to endorse one of the two highest categories; this original Language item seems therefore unsuited as a measure of linguistic talent in this sample.

Genetic influences on variation in self-rated talent were earlier described by (1993) (1993). In that study, no distinction was made between aptitude and exceptional talent. The study by McGue et al. as well as the present study report considerable genetic influences on talents and aptitudes. However, other studies (Ericsson & Charness, 1994; Howe et al., 1998; de Bruin et al., 2007; de Bruin et al., 2008) question these findings and emphasize that excelling only occurs after large amounts of deliberate practice. According to Gagne (1999), experts in music are likely to benefit more from deliberate practice than average musicians do, but extensive practice remains indispensable. Such explanations point to the possible importance of gene-environment correlations. Genetic factors that account for higher abilities may also contribute to a more favorable environment for that ability to flourish in (Plomin et al., 1977). In a recent review, (Ruthsatz et al., 2008) proposed a multi-factor view as an explanation for the achievement of outstanding musical abilities. Innate talent, practice and intelligence together accounted for more of the variance in music performance than practice alone.

Giftedness in a particular domain is likely to generate various aspects of being rewarded for personal qualities. Talented people are more rewarded compared to people within the normal range. Reward could possibly lead to more training and practice, more social opportunities, more support and even more rewards. That is, to be rewarded could initiate a reciprocal process of success that leads to even more practice and higher levels of performance (Dickens & Flynn, 2001). This gene-environment correlation view on the variability observed in aptitude and talent thus unites the views that practice is indispensable and that heritability at the same time is clearly of importance as well and merits further research. This also implies that high heritability does not mean environmental influences to be unimportant. To reach exceptional levels of ability, deliberate practice is indispensible even for people with a genetic predisposition to develop a talent. This study does however show that differences in genetic make-up control individual differences in self-reported aptitude and talent.

SUPPLEMENTARY INFORMATION:

Talent Inventory in the 1991 survey

The response items in the questionnaire appear in the reverse order to the categories used in the analyses.

The following questions concern special talents you may possess. The first category describes exceptional talent. The third category describes the mean, not good and not bad. Only few people have an exceptional talent. Most people will classify themselves in the third or fourth category. People that have an exceptional talent are able to explicate their talent. Please choose one possible category.

1. Singing and music
1. You are a professional singer or a professional musician playing one or more instruments.
2. You are able to read music and are a good singer or musician.
3. You sometimes sing a song for fun or play a simple melody on a piano or other musical instrument.
4. You neither sing nor play any musical instrument.

2. Arts
1. You have professional qualities regarding visual arts, dancing or acting.
2. You participate in visual arts, dancing or acting at amateur level.
3. You've average talents in arts
4. You are not talented in arts.

3. Writing
1. You are a professional writer, author, journalist or you could have been one.
2. You are able to write comprehensible and interesting letters or tales.
3. You are an average writer.
4. You have difficulties with writing a letter.

4. Language
1. You're able to speak and read three or more languages.
2. You're able to speak and read one foreign language fluently.
3. You're able to speak and read one foreign language good enough to get by.
4. You do not speak or read any foreign language.

5. Chess (Chess, Checkers, Cards)
1. You participate in highly competitive tournaments in one or more of these games.
2. You offer good resistance in this kind of games.
3. You're neither good nor bad in this kind of games.
4. You're not interested in this kind of games.

6. Mathematics

1. You have an exceptional mathematical understanding.

2. You perform better than most people on mathematical and numerical tasks.

3. You mathematical understanding is equivalent to most people.

4. You have difficulties with mathematical and numerical tasks.

7. Sports

1. You are athletically shaped and you are very good in one or more sports.

2. Your performance in sports is better than most people.

3. You do participate in one ore more sports for fun, without any exceptional performances

4. You do not participate in any sport and you don't have any talent.

8. Memory

1. You've an almost photographic memory for facts, numbers or details.

2. You've a good memory function.

3. Your memory function neither better nor worse than most people's memory.

4. You're memory function is not really good.

9. Knowledge

1. You have an exceptional knowledge about one or more subjects (for example: sports, Second World War, wines etc.) besides your everyday knowledge regarding your job.

2. You have good knowledge about one or more subjects and people often ask you questions.

3. Your knowledge is about the same as most people's knowledge.

4. You have less knowledge of facts than most people have.

Chapter 10

Summary and discussion

SUMMARY AND DISCUSSION

At the start of this project, it was well recognized that individual differences in general cognitive ability are to a large extent due to differences at a genetic level (Bouchard, Jr. & McGue, 1981; Plomin, 1999), with increasing heritability estimates from childhood to adulthood (Haworth et al., 2009). These estimates were, however, based on classical twin studies in which the possible interplay between genes and environment, and processes such as assortative mating and cultural transmission, were not always considered. In this PhD-project, I aimed to elucidate causes of individual differences in general cognitive ability in adults beyond the regular sources of additive genetic effects, shared environmental effects, and non-shared environmental effects. I investigated four potential mechanisms that might have an effect on heritability estimates of general cognitive ability, namely gene-environment correlation ($r_{(GE)}$), gene-environment interaction (GEI), assortative mating, and cultural transmission. To this end, I collected measures of general cognitive ability as well as measures of putative environmental factors important for general cognitive ability in a large sample of twins and their extended family members (N=1419). The sample included adult twins and their siblings, the spouses of the twins and siblings, and either the parents or the adult children of the twins and siblings. In addition, in an independent sample of adolescent twins, we investigated whether the variance decomposition differed for aptitude (domain-specific skills within the normal ability range) and talent (domain-specific skills of exceptional quality) across different domains of intellectual, creative and sports abilities.

In Chapter 3 of this thesis, we showed that when relatives of twins are included and more sources of variation can be estimated, individual differences in general cognitive ability in adults are not only due to additive genetic and non-shared environmental effects, but also to genetic dominance and genetic variation caused by positive assortative mating. Although considerable spousal correlations have been reported previously for general cognitive ability (Reynolds et al., 2000; Mascie-Taylor, 1989; Jencks et al., 1972; Loehlin, 1978), we were the first to model their effect on the variance decomposition of general cognitive ability within an adult extended twin family design. The results are a valuable addition to previous theoretical studies (Jinks & Fulker, 1970; Fulker, 1982) in which researchers hypothesized that the presence of positive assortative mating may lead to increased genetic resemblance between dizygotic twins, and, if assortative mating is not considered, to increased estimates of shared environmental factors. Our results, however, showed that in adults, classical twin studies generally underestimated influences of genetic dominance, rather than overestimated shared environmental influences.

In Chapter 4, we studied the extent to which specific, measured environmental factors, which have been hypothesized to contribute to individual differences in cognitive abilities, are under genetic control themselves. Results clearly revealed that individual differences in four environmental domains (i.e., *Childhood Environment*, *Social Environment and Behavior*, *Leisure Time Activities*, and *Influential Life Events*) reflected individual differences at a genetic level. Overall, the mean broad sense heritability of these environmental factors calculated across all domains was 49%, implying that factors we tend to call 'environmental' are generally also under genetic control, rendering the terms $r_{(GE)}$ and GEI not fully unambiguous. The significant heritability of various aspects of the

environment as reported in this thesis, nicely adds to discussions on whether and how people shape their own environment (Scarr & McCartney, 1983; Plomin et al., 1985; Plomin & Daniels, 1987). Scarr and McCartney (1983) proposed a developmental theory in which genetic differences were suggested to affect phenotypic differences via passive, active, and evocative gene-environment correlation. By showing that environmental factors putatively related to cognitive functioning and general cognitive ability are not randomly distributed across the population but reflect individual differences at a genetic level, our results stress the role of genetic factors in determining exposure to environmental factors as was suggested by Scarr and McCartney (1983).

Prior to Chapter 6, in which we studied moderation effects of achievement motivation on the variance components underlying general cognitive ability, we studied the factor structure of the Dutch Achievement Motivation Test (DAMT), and the presence of sex-related bias in Chapter 5. Two main underlying factors in the DAMT were distinguished: General Achievement Motivation (with subscales Dedication and Persistence) and Academic Achievement Motivation (with subscales Pressure, Accomplishment, Work Approach, Future Orientation, and Competition). Sex differences were reported for the Dedication subscale, with women reporting higher levels of dedication to their academic work than men, and for the Future Orientation subscale, with women reporting lower levels of future orientation than men. Sex differences were marginally significant for the Competition subscale, with women reporting to be less actuated by competitive motives than men. Furthermore, sex bias was observed for five of the twenty-eight achievement motivation items. These biased items were subsequently eliminated from the analyses in Chapter 6.

In Chapter 6, we studied whether academic achievement motivation and general cognitive ability moderated genetic and environmental variance components underlying educational attainment. Educational attainment was selected as a dependent variable because it is often considered to be influenced by both academic achievement motivation and general cognitive ability, and not the other way around. Results demonstrated that environmental variance components of educational attainment were moderated by general cognitive ability (shared environmental influences were slightly increased in individuals with either low or high levels of cognitive ability) and academic achievement motivation (non-shared environmental influences were considerably increased in individuals with higher levels of achievement motivation). Moderation of genetic variance components was not significant.

In Chapters 7 and 8, we studied whether variance components underlying general cognitive ability were moderated by exposure to influential life events and experience seeking behavior, respectively. Results demonstrated that both genetic and environmental variance components were moderated by exposure to several influential life events (i.e., Retirement, Being fired, Unemployment, Severe offence, Breaking up with friends/ relatives, Trouble with friend/relatives, Birth of a child, Death of friends/relatives, and Moving house) and by experience seeking behavior.

The results presented in Chapters 6, 7 and 8 led us to conclude that the relative contribution of genetic and environmental factors to individual differences in general cognitive ability and educational attainment in adults, is not stable across the entire population, but varies as a function of exposure to environmental conditions

and personality factors. These results corroborate to earlier studies that investigated moderation effects on the variance components of general cognitive ability. Moderation effects on genetic influences have been reported in studies in children (e.g., moderation of parental educational level and social economic status; Rowe et al., 1999; Turkheimer et al., 2003; Harden et al., 2007), but had not been replicated in studies based on adults (Kremen et al., 2005; van der Sluis et al., 2008b). We were the first to show significant moderation on genetic influences underlying general cognitive ability in adults.

In Chapter 9, we studied causes of individual differences in aptitude and talent across different domains of intellectual, creative, and sports abilities in a sample of adolescent twins. Results showed that genetic influences explained the major part of the substantial familial clustering in the aptitude measures, heritability estimates ranged from 32% to 71%. Heritability estimates for talents were higher and ranged between 50% and 92%.

All in all, these results imply that the well known large influence of additive genetic effects on individual differences in general cognitive ability in adults partly reflects more complex processes such as gene-environment correlation ($r_{(GE)}$), gene-environment interaction (GEI), genetic dominance, and positive phenotypic assortment.

IMPLICATIONS OF THE RESULTS OF THIS STUDY

This PhD project started in 2006, some years after the completion of the human genome project which greatly facilitated gene finding studies (Collins et al., 2003). In 2006, researchers had investigated a number of genetic variants associated with individual differences in general cognitive ability. The few variants that were putatively associated with general cognitive ability, together explained a very small proportion of the variance (i.e., < 2%). In addition, the majority of those genetic variants had not been replicated, with the exception of the apolopoprotein E (*APOE*) gene (Small et al., 2004), the catechol-O-methyltransferase (*COMT*) gene (Savitz et al., 2006), the cholinergic muscarinic receptor 2 (*CHRM2*) gene (Comings et al., 2003; Gosso et al., 2006b), and the *SNAP25* gene (Gosso et al., 2006a; Gosso et al., 2008). (For an overview, see Posthuma et al., 2009; Deary et al., 2010).

Major advances in genotyping technology led to the start of the so-called 'GWAS' era in 2006/2007. GWAS refers to genome wide association studies, in which hundreds of thousands of genetic variants are genotyped across the entire human genome in thousands of individuals. Together this multitude of genetic variants captures between 60-80% of all genomic variation. At the start of the GWAS era scientists anticipated major results in gene finding studies for highly heritable traits, including general cognitive ability. Four years and ~900 GWAS studies later, the general conclusion of GWAS is that with the exception of some major genes for nearly Mendelian disorders, most GWAS studies detected very few genetic variants and most of these variants explain only a very small proportion of the variance in complex traits (Hardy & Singleton, 2009). This observation has become known as the case of the missing heritability (Maher, 2008). Missing heritability is as true for general cognitive ability as it is for most other heritable, complex traits. Hitherto, no large scale GWAS for general cognitive ability has been conducted. Recently, Ruano et al. (2010) showed in a relatively small GWAS sample of 627 individuals that there were no genome-

wide significant genetic variants associated with general cognitive ability. However, when these researchers looked at the joint effect of multiple genes that were grouped according to cellular function (functional gene group analysis) they were able to demonstrate that the group of genes that code for G proteins (synaptic heterotrimeric guanine nucleotide binding proteins) explained 3.3% of the observed variation in general cognitive ability. Although this effect is larger than any previously reported effect of a single gene on general cognitive ability, 3.3% is still small compared to heritability estimates based on classical twin studies for general cognitive ability around 40% in children and around 80% in adults. The 'missing heritability' thus remains a challenging problem.

The results presented in this thesis may, however, provide important clues for the case of the missing heritability. First, the well recognized large contribution of additive genetic factors (~80%) to individual differences in general cognitive ability seems overrated. Using an extended twin-family design, estimates of additive genetic effects were adjusted downwards when positive assortative mating was taken into account. Additive genetic factors explained no more that 47% of the individual differences in general cognitive ability, while genetic dominance, that was previously assumed to be absent, explained at least 27%. GWAS studies generally assume an additive model as inclusion of non-additive effects in GWAS increases the multiple testing problem and thereby decreases the statistical power to detect association effects. However, if non-additive genetic influences are known to be of importance, such genetic influences should be taken into account in GWAS studies for general cognitive ability.

Second, the estimates of genetic and environmental influences vary as a function of exposure to environmental factors. When this is observed, genes determine an individual's vulnerability to environmental influences which in turn affect general cognitive ability, or vice versa, environmental influences may affect the regulation of gene expression. Statistical associations between genetic variants and general cognitive ability are then diluted. To this end, future research should not merely focus on associations between genetic variants and levels of general cognitive ability, but also on the influence of environmental factors on these gene-trait associations. Alternatively, when particular environmental factors, such as influential life events, control the expression of particular genes, some genes have large effects on individuals exposed to an environmental factor while the same genes may have small or no effects in individuals that are not exposed to this environmental factor. Consequently, associations between these genes and general cognitive ability in the total population may be very low, while associations are expected to be higher in a subpopulation that is exposed to the environmental factor. In this situation, researchers might consider stratifying their study population for GWAS analyses according to the participants' exposure to particular environmental factors (such as life events or experience seeking behavior).

FUTURE PERSPECTIVES
The results presented in this thesis provide recommendations for future study designs (as discussed above), but may also guide future projects that take these results one step further. For example, we showed moderation of genetic effects for cognitive ability genetic correlations between *'environmental'* factors and general cognitive ability. However, we did

not investigate the exact mechanism underlying the moderation and correlation. Questions such as why and on which level moderation occurs (e.g., genes, proteins, neurons), and what kind of biological processes are involved, remain as yet unanswered. A first step to elucidate these processes would be to study moderation effects of reported environmental moderators on influences of a priori selected genes (i.e., candidate genes). Thus far, 'measured gene - measured environment' interaction with respect to general cognitive ability has been reported in one study in children (Caspi et al., 2007). In this study, which is still awaiting replication, the positive association between breastfeeding and general cognitive ability was moderated by a variant in the *FADS2* gene, which is involved in the genetic control of fatty acid pathways. In the context of attention in children, interaction has been reported between the catechol-O-methyltransferase (*COMT*) gene and parenting (Voelker et al., 2009), whereas in the context of adolescents' reading comprehension, interaction has been reported between the *COMT* gene and maternal rejection (Grigorenko et al., 2007). Future moderation studies may focus on genes that previously have been associated with general cognitive ability, such as the *FADS2, COMT, APOE, CHRM2*, *SNAP25* and G-protein genes, and include some of the environmental moderators identified in this thesis. Furthermore, technological progress in microarray technology allows us to identify genes whose expression has changed in response to exposure to environmental influences by comparing gene expression in exposed and non-exposed individuals. Studying genetic variants and gene expression in the context of environmental moderation may clarify underlying mechanisms of interaction and as such increase our understanding of the relation between genes, environment and general cognitive ability.

Alternatively, heritable differences may not only be due to structural differences in the DNA, but also to epigenetic effects (Johnston & Edwards, 2002; Fraga et al., 2005). Recent findings from epigenetic studies may help us to understand the underlying mechanisms of moderation. Epigenetic differences may reveal how environmental influences can affect genetic influences on general cognitive ability (e.g., gene expression or gene methylation levels may be altered by environmental influences). Future studies may focus on whether environmental factors cause epigenetic changes, and how these changes affect individual differences underlying general cognitive ability.

GENERAL CONCLUSION

Based on an extended twin-family study, we showed that the well recognized high influence of additive genetic factors on individual differences in general cognitive ability in adults partly reflects more complex processes such as genetic dominance, positive phenotypic assortment, gene-environment correlation ($r_{(GE)}$) and gene-environment interaction (GEI). The outcomes of the studies presented in this thesis increase our understanding of causes of individual differences in general cognitive ability. Considering the complex interplay between genes and environment in future studies may help us to reveal neurobiological pathways underlying variation in general cognitive ability and understand why people differ in general cognitive ability.
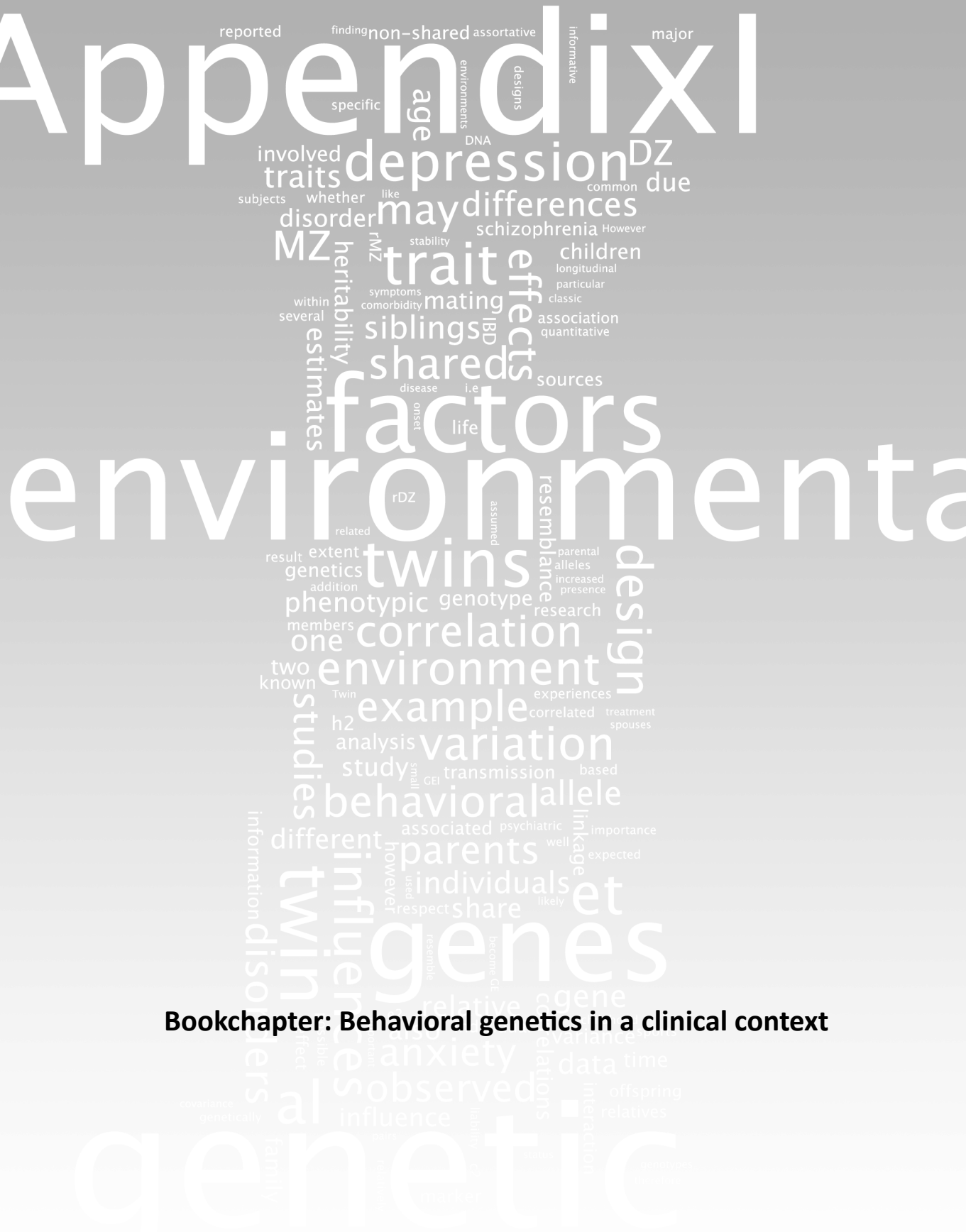
Bookchapter: Behavioral genetics in a clinical context

INTRODUCTION

Large individual differences exist among people in behavioral traits such as personality, cognitive ability, and psychiatric disorders. Some people are more sociable or more learned than others, some people are more likely to suffer from psychiatric disorders, and some are more likely to become addicted to stimulants like nicotine, alcohol, and drugs. Research in the field of behavioral genetics aims to understand the causes of these variations in behavior and disease. Behavioral geneticists distinguish two major sources of inter-individual variation: genetic sources and environmental sources. The nature-nurture debate is founded on this duality and is concerned with determining the relative importance of innate abilities, versus the importance of personal experiences or environmental influences. The view that *nurture* is the single source of the observed variation in behavioral traits was favored by developmentalists in the 17th century. For example, John Locke (1632–1704) described the new born baby as a tabula rasa ("blank slate") to emphasize his belief that humans are born "blank" and then shaped by their experiences and sensory perceptions of the environment. The *nature* view, on the other hand, emphasizes the relative importance of the innate variation in ability (i.e., of genetic factors). If a trait is heritable, then the closer the genetic relatedness of two individuals, the more these individuals will resemble each other in terms of that trait. This observation forms the basis of behavioral genetics research. Although the nature-versus-nurture debate is still ongoing, it is generally accepted and has been shown for many clinical traits that both genetic and environmental factors are important in explaining individual differences. In this chapter we describe how the relative importance of genetic and environmental influences can be quantified and how the actual genetic risk factors for a clinical trait can be detected. In addition, we describe a few more complex mechanisms that may underlie individual differences in complex traits, such as gene-environment interaction and correlation. We provide examples in the context of anxiety and depression, although similar methods can be applied to any other clinical trait.

SOURCES OF PHENOTYPIC VARIATION

In behavioral genetics it is assumed that the total variance (V_T) of a trait, also called the phenotypic or observed variance, can be decomposed into three sources of variation: one source of genetic variation (V_G) and two sources of environmental variation: shared (or common) environmental variation (V_C) and unshared (or unique) environmental variation

$$(V_E): V_T = V_G + V_C + V_E$$

V_G reflects all possible genetic contributions to the observed variation of a trait in the population—additive genetic factors, dominance genetic factors, and effects of multi-gene interaction (*epistasis*; Bateson, 1909). Shared environmental influences (V_C) are environmental factors that are shared by family members and render members of the same family more alike. The environments of individuals from the same family are more alike than the environments of individuals from different families. Shared environmental influences include shared experiences such as diet, socioeconomic status, and residential area. Non-shared environmental influences (V_E) are environmental factors that create differences between members of the same family. In fact, it is the part of the phenotypic variation that cannot be explained by either genetic or shared environmental factors. Non-shared environmental influences include unique experiences such as relationships with friends and teachers and sports participation that are not shared with other family members. In addition, non-shared environmental influences may also be due to measurement error. By dividing the estimates of the genetic or environmental variance components by the total variance V_T, we can standardize the three variance components. The standardized components are represented as: $h^2 + c^2 + e^2 = 1$ where h^2 denotes the proportion of the phenotypic variation that is due to genetic factors (broad-sense heritability), c^2 denotes the proportion of the phenotypic variation that is due to the shared environment (factors shared by family members), and e^2 denotes the proportion of phenotypic variation that is due to the non-shared environment (factors not shared by family members). Determining the relative proportions of different sources of variations for multiple traits has long been the major goal of behavioral genetics. Due to the rapid advances in genotyping technology, however, the goal has shifted toward detection of the actual genes that are important for a trait. Below, we briefly describe the classic research designs and methods applied in behavioral genetics as well as some of the more recently applied methods.

CLASSIC RESEARCH DESIGNS IN THE FIELD OF BEHAVIORAL GENETICS

Determining the relative proportion of different sources of variation

To determine the relative influence of genetic and environmental factors on a trait, data are required from individuals who are genetically and/or environmentally informative. Since actual gene finding or gene identification (or identification of influential environmental factors) is not the aim, there is no need to actually genotype individuals, as long as their genetic and environmental relationships are known. Three research designs are commonly used: the family design, the adoption design, and the twin design. Several extensions of the twin design allow researchers to deal with specific research questions. In the *family design,*

variation within families is compared to variation between families. The main question is, for example, whether biological brothers and sisters living in the same household are more alike than unrelated children of similar age. If family members resemble each other more with respect to a particular trait than unrelated individuals, then familial factors are expected to affect the individual differences in a particular trait. Family members, however, share both genes and common environmental factors, and therefore the family design does not allow for the disentanglement of these sources of variation. In the *adoption design,* a distinction is made between genetic relatives and environmental relatives. Genetic relatives in the adoption design are family members who share (part of their) genes but do not live together. Environmental relatives are individuals who do not share genes but do share environmental factors as they share the same home environment. Phenotypic resemblance between genetic relatives living apart is evidence of genetic influences, while phenotypic resemblance between environmental relatives who do not share genes is evidence of shared environmental influences. The phenotypic resemblance, quantified as a correlation, between genetic relatives and environmental relatives can thus be used to determine the extent to which phenotypic variation is due to genetic or environmental factors. Adoption studies are particularly informative when the adoptees are twins. Imagine the case of monozygotic (MZ) twins, that is, genetically identical twins who are adopted by two different families soon after birth. Although fairly rare, this situation is ideal for the estimation of the heritability of a trait: as the twins are genetically identical but reared in different environments, any resemblance between them is entirely attributable to genetic influences (h^2). The correlation between adopted MZ twins reared apart is therefore a direct estimate of heritability. In contrast, the correlation between MZ twins reared together is the result of both shared genes and a shared environment. The difference between the correlation of MZ twins reared together and the correlation of MZ twins reared apart is therefore a direct estimate of the influence of the shared environment (c^2). The extent to which MZ twins reared together do not resemble each other is an estimate of the influence of non-shared environmental factors (e^2). In addition, the correlation between adopted children and their adoption parents provides a direct estimate of shared environmental effects, while the correlation between adopted children and their biological parents provides a direct estimate of heritability. Comparing individuals from different generations is, however, not always optimal. As a result of cultural and age-related changes in environment and genetic expression, correlations between parents and children are likely to be lower than correlations between contemporaries. Such changes create differences between individuals from different generations, and as a result, genetic influences may be underestimated. The *twin design* obviates the drawbacks of both the family design and the adoption design. The twin design makes use of the differences in genetic resemblance between MZ and dizygotic (DZ) twin pairs. MZ twins share 100% of their genetic material, while DZ twins, like pairs of regular sibs, share on average 50% of their genetic material. At the same time, when growing up in the same household, both MZ twins and DZ twins share 100% of their common environment. The correlation (i.e., the standardized measure of resemblance) between MZ twins can therefore be written as a function of the heritability and shared environmental factors: $r_{MZ} = h^2 + c^2$ while the correlation between DZ twins, or regular siblings, equals: $r_{DZ} = \frac{1}{2}h^2 + c^2.$ From this, it follows that if the MZ twin correlation is

larger than the DZ twin correlation, at least part of the resemblance must be attributed to genetic factors (see also Table A1.1). Based on the observed MZ and DZ twin correlations as well as their known genetic and environmental relatedness, the relative proportions of genetic factors (h^2), shared environmental factors (c^2), and non-shared environmental factors (e^2) can be estimated as follows (Falconer & Mackay, 1989):

$$h^2 = 2*(r_{MZ} - r_{DZ})$$
$$c^2 = 2* r_{DZ} - r_{MZ} = r_{MZ} - h^2$$
$$e^2 = 1 - r_{MZ}$$

Extensions of the twin design

The twin design is the most commonly used design in the field of behavioral genetics to evaluate the relative influence of genetic and environmental factors on a trait. This research design does, however, rely on several assumptions. First, it is assumed that DZ twins share on average 50% of their genes. This assumption is only tenable if both parents are random subjects from the population and do not have more genetic variants in common than would be expected by chance alone. In other words, it is assumed that mating occurs at random in the population and that partners do not select each other based on the trait under study. Second, it is assumed that MZ twins do not share more environmental factors than DZ twins; this is the so-called equal environment assumption. Third, it is assumed that all genes act in an additive way (i.e., that dominance genetic influences are absent). Fourth, it is assumed that genes and environment do not interact. In other words, genes do not affect an individual's sensitivity to an environmental factor, and the environment does not affect the expression of the genes. The phenomenon of gene-environment interaction will be discussed in more detail later in this chapter.

Table A1.1: Illustration of MZ and DZ twin correlations and calculated estimates of genetic effects and common environmental and unique environmental effects.

Twin correlations		rMZ	rDZ	h^2	c^2	e^2
rMZ = rDZ = 0	→ E	.00	.00	0	0	1
rMZ = rDZ > 0	→ E+C	.40	.40	0	.40	.60
rMZ = 2*rDZ	→ E+G	.60	.30	.60	0	.40
rMZ < 2*rDZ	→ E+C+G	.80	.65	.30	.50	.20

Notes: rMZ = twin correlation MZ twins; rDZ = twin correlation DZ twins; E = unique environmental effects; C = common environmental effects; G = genetic effects; h^2 = heritability; c^2 = proportion of the phenotypic variation due to shared environment; e^2 = proportion of phenotypic variation due to non-shared environment

To illustrate, significant differences between MZ and DZ twin correlations were reported in a summary of early twin studies on the genetics of depression and bipolar disorder. For depression, average correlations of .40 and .11 were observed for MZ and DZ twins, respectively, suggesting the influence of genetic factors (Allen, 1976). For bipolar disorder, average correlations of .72 and .40 were observed for MZ and DZ twins, respectively, suggesting involvement of both genetic and common environmental influences. Several extensions of the classic twin design have been proposed to deal with these assumptions, such as study designs that include the siblings, partners, or spouses of twins. Adding non-twin siblings to a classic twin design allows researchers to investigate whether means and

variances are equal in regular siblings and twins and whether the covariance between DZ twins equals the covariance between non-twin siblings. If the DZ covariance is different from the covariance between regular siblings, a special twin environment is implicated, which means that the shared environmental influences of twins differ from the shared environmental influences of regular siblings. These tests are important because only when twins are not different from siblings findings from twin-based research can be generalized to the general population. Moreover, including non-twin siblings in twin studies enhances statistical power to detect sources of variance due to genetic and environmental effects (Posthuma & Boomsma, 2000). To test the assumption of random mating, the parents and spouses of twins can be included in a research design. Two types of non-random mating can be distinguished, both of which occur in human populations. The first form of non-random mating is known as inbreeding and refers to mating between biological relatives. The second form of non-random mating is known as assortative mating and occurs when mate selection is based on traits that may themselves be under genetic pressure. It is known that for several traits, individuals prefer to choose mates whom they resemble phenotypically (Crow & Felsenstein, 1968). Assortative mating implies that spouses are more similar with respect to a trait than would be expected by chance alone, which will affect the level of that trait in their offspring. For example, an increased percentage of disorders in spouses of patients, compared to controls, is indicative of non-random assortment. Assortative mating has been shown to take place with respect to biological factors such as body height (Silventoinen et al., 2003), but also for behavioral traits such as intelligence (Plomin & Loehlin, 1989), as well as for several psychiatric disorders. To illustrate, Maes et al. (1998) investigated assortative mating in the context of alcoholism, generalized anxiety disorder, major depression, panic disorder, and phobias. Findings suggested considerable associations between partners for most psychiatric diagnoses, and assortment was observed both within and between classes of psychiatric disorders. Variables that were correlated with the psychiatric diagnoses, such as age, religious attendance, and education, did explain part, but not all, of the assortment between partners. Since assortative mating increases the genetic and environmental correlations between mates, estimates of the relative influence of genetic and environmental factors within a twin design will be biased if assortative mating is not appropriately accounted for. When parents are more genetically alike than expected by chance, the DZ twins genetic resemblance will on average be more than 50% due to transmission of the correlated parental genes. As a result, the resemblance of DZ twin pairs will increase relatively to MZ twin pairs. Unmodeled assortative mating will therefore result in artificially inflated estimates of the shared environmental component and an underestimation of heritability. The presence of assortative mating can be studied by calculation of the phenotypic correlation between the parents of twins, or the phenotypic correlation between twins and their spouses, when spouses of the twins are included in the study, assuming that the extent of assortative mating does not change across generations. Thus, in an attempt to discern the relative contribution of the sources of variance of a particular trait, including parents or spouses of twins in the study design allows one to accommodate the effects that assortative mating may have on the estimates of the relative influences of genetic and environmental factors. In the classic twin design, which includes only data from MZ

and DZ twins, the influence of non-additive or dominance genetic factors and shared environmental factors are confounded. Inclusion of parental data, or data from cousins of twins or children of twins, for example, allows for the simultaneous estimation of shared environmental effects (C) and dominance genetic effects (D). Collecting data of parents or children of twins has several additional advantages. First, it enables one to distinguish between *genetic transmission* from parents to offspring and *cultural transmission* from parents to offspring. Genetic transmission refers to resemblance between parents and offspring that is caused by the genes that are transmitted from parents to their offspring, while cultural transmission refers to the resemblance between parents and offspring that is due to a home environment that is created by the parents. Cultural transmission increases resemblance between parents and offspring but also increases resemblance between twins and siblings. To complicate things even more, parents may create an environmental situation that is correlated with their own genotype or phenotype. For example, parents with a genetic liability to be anxious may create an overprotective home environment, which in turn may have a disadvantageous effect on the development of anxiety in their children. When cultural transmission exists in the presence of genetic transmission, environmental influences become correlated with genetic influences. In a classic twin design, where parental data are not available, cultural transmission cannot be modeled or estimated explicitly, and the effects of cultural transmission will end up as shared environmental variation. When parental information is available, the effects of genetic transmission and cultural transmission on familial resemblance can be explicitly distinguished. Second, when parental data are available, researchers can test for the presence of correlations between genes and environment (gene-environment correlations). In the classical twin design, it is assumed that genetic effects and environmental effects act independently on the phenotype. When genes and environment are correlated, however, the effects of genes cannot be considered independent of the effects caused by environmental factors. Third, comparing the estimates of the genetic and environmental effects obtained in studies in which parental data were or were not included, provides information about possible developmental changes in genetic and environmental influences between childhood and adulthood. For example, when the estimates of the additive genetic effects are not equal across the two designs, this may indicate that genes are of importance in adulthood, while they have no function in childhood, or vice versa.

INTERPLAY BETWEEN GENES AND ENVIRONMENT
The classic twin design assumes that genes and environment act in an additive manner. It is, however, conceivable that individuals seek out, or grow up in, environmental situations that are somehow correlated to their genotype. For example, parents who are fond of sports will transmit their athletic genes to their offspring and in addition are likely to stimulate their children by joining a sports club or providing them with sports equipment such as a football or a baseball bat. In such a case, the environment that is created by the parents is correlated with the genotype of the children. Similarly, children who are genetically predisposed to become good athletes are likely to actively select environmental conditions in which their genetic disposition can become manifest. It is even possible that genes and environment interact. In that case, the effect that a certain environmental factor

has depends on someone's genotype, or the extent to which genes come to expression depends on environmental conditions.

Gene-environment correlation

In general, in the presence of gene-environment correlation ($r_{(GE)}$), the environmental factors that influence an individual's phenotype are not a random sample of the entire range of possible environments but are correlated with, or caused by, the genotype of an individual. Usually, three different types of gene-environment correlation are distinguished (Plomin et al., 1977): passive, evocative, and active $r_{(GE)}$. Passive $r_{(GE)}$ refers to the situation in which parents transmit both genotypes and relevant environmental factors. For example, athletically gifted parents transmit genes that influence physical attributes such as strong muscles, a well-functioning hemoglobin system, and a healthy respiratory system. In addition, these parents also provide their children with an athletically stimulating environment, such as sports equipment and training facilities. Since the environment that is created by the parents is a function of the parents' genotypes, and each parent transmits 50% of his/her genes to the offspring, a correlation between the environment and the child's genotype is implicated. We speak of evocative $r_{(GE)}$ when the genetic predispositions of an individual evoke certain reactions from the environment. For example, a child who shows talent for sports may be treated differently by his/her high school trainer than a child whose sports ability is average. Active $r_{(GE)}$ occurs when individuals create, or seek out, their own environments based on their genetic predisposition. For example, the child with the predisposition for being a good basketball player may seek out a high school or university with good sports facilities and a lively sports culture, because this will allow him/her to exercise, develop, and improve. That is, individuals with a certain genetic predisposition will select environments that fit their predisposition, that is, environments in which they can thrive and that are optimal for their predisposition to become manifest. When $r_{(GE)}$ is actually present, ignoring the gene environment correlation in statistical genetic models and analyses may lead to biased estimates of the relative importance of both genetic and environmental factors (Eaves et al., 1977).

Gene-environment interaction

Besides the possibility that genes and environment are correlated, it is also possible that environmental factors modify or trigger gene expression, or that someone's genetic makeup determines the effect that environmental stressors can have (Gene-environment interaction, GEI). For example, traumatic experiences like life-threatening illness, molestation, and assault do in some victims cause severe depression, but not in all. It is conceivable that the actual effect of such extreme experiences depends on someone's genotype, that is, on one's genetic liability to become depressed. When GEI interaction is present, sample-based estimations of the additive genetic effects (A), the shared environmental effects (C), and the non-shared environmental effects (E) do not accurately reflect what is going on. After all, the relative contribution of genetic and environmental factors to the explanation of the observed individual differences in the phenotype may be different for subjects with different experiences, or for subjects with different genotypes. GEI is one possible explanation for discordance observed between MZ twins with respect to disease (e.g., one

twin suffers from depression or schizophrenia, while the other twin does not). As MZ twins are genetically identical, they have, in theory, the same genetic predisposition, or the same genetic liability for disease. This liability could, however, be increased or decreased as a consequence of specific life experiences. In other words, it is conceivable that differences in life experiences create differences in the extent to which genes come to expression, which in turn results in phenotypic differences. Just like disregarding gene-environment correlation, ignoring the effects of existing GEI leads to biased estimates of the relative importance of genetic and environmental determinants. When GEI interaction concerns the interaction between genes and *shared* environmental influences, ignoring its presence results in overestimation of the effect of genetic factors on the phenotype. If GEI interaction concerns the interaction between genes and non-shared environmental factors, ignoring its presence will result in overestimation of the effects of the non-shared environmental factors (Eaves et al., 1977; Jinks & Fulker, 1970). To illustrate, an increasing body of evidence supports the presence of $r_{(GE)}$ and GEI in the context of complex psychiatric disorders (Caspi & Moffitt, 2006; Kendler et al., 2005). Caspi et al. (2003) reported an interaction between the 5-HT transporter gene (5-HTT) and stressful life events that appears to determine liability to depressive illness. Individuals with one or two copies of the short allele of the 5-HTT gene exhibited more depressive symptoms after experiencing traumatic life events than subjects who were homozygotes for the long allele. This finding has been replicated in several studies (Eley et al., 2004; Kendler et al., 2005; Wilhelm et al., 2006; Zalsman et al., 2006). Recently, Wichers et al. (2009) reported an interaction between the BDNF Met allele, the short allele of the 5-HTTLPR gene, and childhood adversity in a model of depressive symptoms. Childhood adversity had a greater impact on depression scores in adulthood among BDNF "Met" carriers than among BDNF "non- Met" carriers. Moreover, this interaction effect between BDNF and childhood adversity was more pronounced in subjects who were carriers of the short repeat allele of the *5-HTTLPR* gene. In addition, carriers of the Met allele also reported significantly more childhood adversity than non-carriers, which suggests gene- environment correlation.

STATISTICAL METHODS APPLIED TO THE (CLASSIC) TWIN DESIGN

Although calculating the relative proportion of genetic and environmental influences on a trait based on comparisons of MZ and DZ twin correlations is straightforward, this simple framework has some disadvantages. First of all, it does not allow for a test of the statistical significance of the genetic and environmental influences. For example, when the comparison of MZ and DZ twin correlations suggests a heritability of 10%, then one would want to know whether this 10% deviates significantly from 0%. Twin correlations provide neither confidence intervals of the estimated parameters nor a description of how well the twin model describes the observed data. In addition, missing data cannot be accommodated if estimates are based on twin correlations, and the information of family members other than twins cannot be accommodated in the model. In behavioral genetic studies it is therefore customary to use estimation procedures implemented in structural equation modeling. Structural equation modeling is a flexible statistical technique for testing and estimating linear relationships between observed and latent variables, where latent variables are not measured directly but are estimated based on observed information. The

latent variables are the unmeasured sources of variation, denoted by G, C, and E. Their regression on the trait can be deducted from the known relations between the G, C, and E factors in MZ and DZ twins (see figure A1.1). How well the model depicted in figure A1.1 describes the observed data is evaluated through the use of an iterative model fitting procedure (see, e.g., Neale & Cardon, 1992), which returns parameter estimates and their confidence intervals.

Figure A1.1 path diagram for univariate twin data
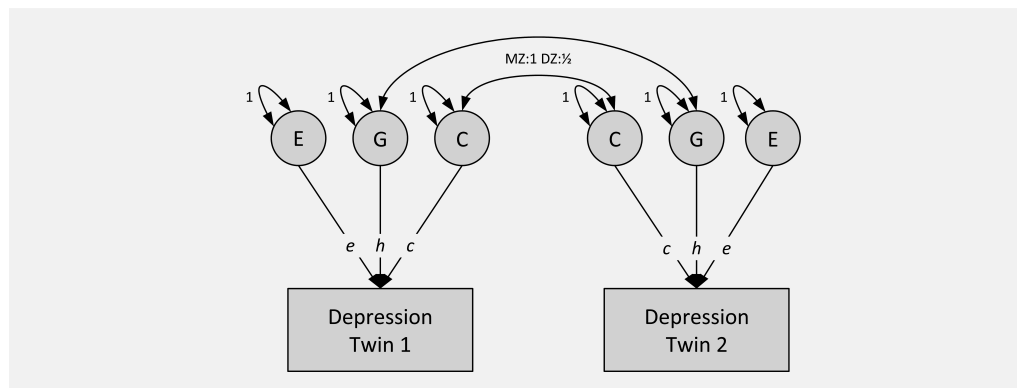
Notes: In this path diagram, the latent factors (the sources of variance) are scaled by fixing their variance to 1. As described above, the correlation between the shared environmental variance components (C) of twin 1 and twin 2 is fixed to 1, while the correlation between the genetic variance components (G) of twin 1 and twin 2 is fixed to 1 in MZ twin pairs and fixed to .50 in DZ twin pairs. Non-shared environmental factors are not shared between twins, so these variance components are not connected with a double headed arrow.

Multivariate analyses of twin data

For many psychiatric disorders, comorbidity is the rule rather than the exception. An important question is why two traits covary, that is, what is the nature of this covariation? For example, depression and anxiety often coincide, but why is that? Is this comorbidity due to genes that influence both traits, or is it largely due to environmental factors that act as risk factors for both depression and anxiety? Bivariate (or multivariate) twin models can be used to investigate to what extent two (or more) traits are influenced by the same set of genes (genetic correlation) or by the same environmental influences (environmental correlation). That is, not only the variance of a trait but also the covariance between traits can be decomposed into genetic and environmental sources of variation on the basis of twin data. Figure A1.2 shows a path model of bivariate twin data, in which the relationship between depression and anxiety is described in terms of correlation at a genetic and environmental level. If in the example depicted in Figure A1.2, the correlation of the depression scores of one twin with the anxiety scores of the co-twin is higher in MZ twins than in DZ twins, then this suggests that the observed correlation between the two traits is mainly due to genetic factors. To illustrate, much research has focused on the comorbidity of anxiety and depression.

Figure A1.2 Bivariate Twin Design
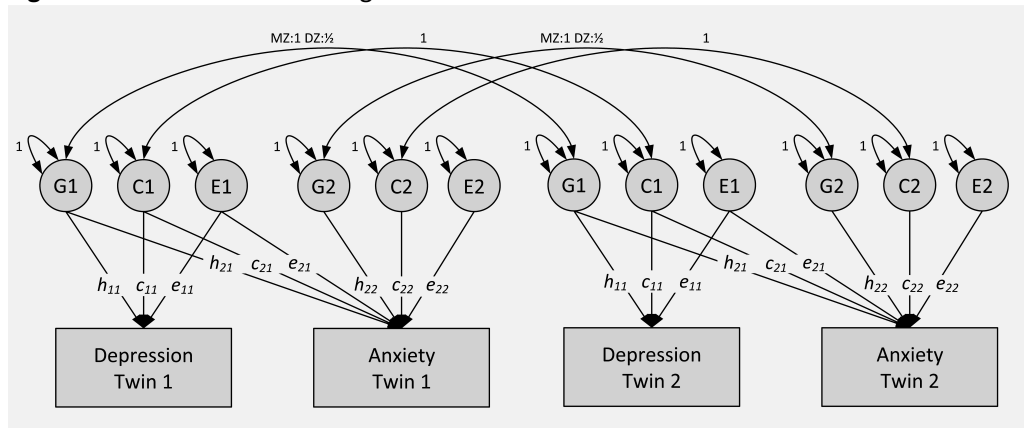
Notes: *A so-called 'Cholesky decomposition' in which, each trait has latent additive genetic (G), shared environmental (C) and non-shared environmental (E) factors. All latent factors have single headed arrows connecting them with the observed traits. Latent factors that are thought to have an effect on the first trait do also have single headed arrows connecting them to the second trait within the same person. The covariance between depression and anxiety is modeled via these diagonal paths.*

According to Gray and McNaughton (2000), comorbidity of anxiety and depression can be explained in two ways. First, one disorder is an epiphenomenon of the other disorder. Second, the disorders partially share a genetic etiology. In a review of a large number of multivariate twin and family studies on comorbidity of anxiety and depression, Middeldorp et al. (2005) support both explanations for the covariance observed between anxiety and depression. Depression and anxiety are genetically closely related; the two traits are 86%– 100% influenced by the same genetic factors.

Longitudinal analyses of twin data

When it has been established that genetic factors do to some extent explain individual differences observed in a certain trait or multiple traits, a next question could be are these genetic influences stable over time and are the same genes involved at different stages of life? Costly longitudinal studies would be needed to answer this question. However, the stability of genetic influences over time is sometimes investigated by analyzing data at one point in time with a *cohort design.* In such a design, subjects from different age cohorts are assessed phenotypically. Analyzing the relative influence of genetic and environmental factors in different age cohorts gives information about stability of the magnitude of genetic and environmental influences along those age cohorts. An advantage of the cohort design is that longitudinal data collection within one single-population sample is not required, which saves researchers a lot of time waiting for their subjects to grow older. A major disadvantage, however, is that this design does not allow for any conclusions on whether the genetic factors that explain variation in one cohort are the same as the genetic factors explaining variation in another cohort. Moreover, differences due to age are confounded with any other differences between the cohorts. An example of a cohort-design is a study on the diagnosis of early- and late-onset major depression, as defined by the *DSM-III-R* (Lyons et al., 1998). Early onset (before age 30 years) and late-onset (after age 30 years)

major depression were both significantly affected by genetic factors (early onset h^2 = .47; late onset h^2 = .10) and non-shared environmental factors (early onset e^2 = .53; late onset e^2 = .90). The size of genetic effects was larger for early-onset major depression, while non-shared environmental effects explained more variance in late-onset major depression. When longitudinal twin data are available, it is possible to investigate to what extent the contribution of genetic and environmental factors to the observed phenotypic variability is stable over time, and to what extent genetic and environmental variation is time specific.

However, longitudinal analysis has several disadvantages: the design is relatively expensive, data collection takes more effort and time compared to the cohort design, and longitudinal designs are prone to dropout. That is, participants are asked to participate in the study over a longer period of time, and considerable numbers of participants tend to withdraw from the study for reasons that may or may not be related to the study object itself. To illustrate, in a longitudinal study of 3- to 12-year old children, Boomsma et al. (2008a) determined the relative stability and change of genetic and environmental influences on anxiety and depression. Mother and father ratings of their child's behavioral, emotional, and social problems were collected at five different time points. Stability of anxiety and depression in childhood was relatively low from age 3 to later ages ($r \approx$ .30 from age 3 to later ages); after age 7, the stability increased (r = .67 between ages 10 and 12). With age, the heritability of anxiety and depression decreased and the influence of shared environmental factors increased. Heritability estimates diminished from around 60% at age 3 to around 40% at age 12. Shared environmental factors accounted for only 8% of the observed variation at age 3 but increased to about 23% at age 12. The contribution of non-shared environmental factors increased from 29% at age 3 to 36% at age 12. Genetic factors accounted for about 50% of the phenotypic stability of anxiety and depression over time. Results suggested a relatively small overlap of genes that influence anxiety and depression in younger children (age 3–5) and an increased genetic overlap at later ages. Shared environmental influences on the stability of anxiety and depression were relatively large in younger children (around 50% for age 3–5) and reduced after age 7. This example of a longitudinal twin study shows that genetic and environmental variation may to some extent be time specific. It also shows that stability of traits such as anxiety and depression can be analyzed in terms of genetic and environmental factors. This example shows a decrease in genetic influences on the variability observed in depression and anxiety across the life span. An explanation could be that life events such as accidents and illnesses and home-, education-, and occupation-related incidents accumulate over time. Such environment-related life events increasingly contribute to differences between individuals, and as a consequence, the relative influence of genetic factors decreases over time. In contrast, studies on the heritability of cognitive abilities repeatedly show an increase in genetic influences across the life span (Ando et al., 2001; Bartels et al., 2002; Boomsma & van Baal, 1998; Luciano et al., 2001; Petrill et al., 2004; Plomin, 1999; Posthuma et al., 2001a). Increasing heritability over the life span could be due to genes that become active later in life, or to a decrease in the influence of environmental factors, as a result of which the relative contribution of genetic influences increases. Otherwise, relatively small genetic influences in childhood may have large effects later in life. While parents and teachers are important with respect to the intellectual development of a child, adults are likely to

seek out their own intellectually stimulating environment, which may reinforce genetic differences.

RECENT DEVELOPMENTS IN BEHAVIORAL GENETICS: GENE FINDING

The behavioral genetics methods discussed so far are informative about the extent to which genes explain variability in human behavior. These family-based designs give information about the relative influence of genes on variation observed in a particular trait. However, these designs are not informative about which specific genes are involved, how many genes are involved, or even where the genes are that are involved, that is, in which (part of the) chromosome. After it has been established that genes are involved (i.e., that the trait under study is heritable), a reasonable next step is to verify which part of the human genome is involved (linkage analysis) and, more precisely, which specific genes are involved (association analysis).

Linkage analysis

Once genetic factors have been shown to be of importance in explaining variation in a trait, the next goal is to localize the genes that are involved. The aim of linkage analysis is to discover the rough location of a gene region on the chromosome. Linkage analysis is based on the comparison of genetic relatives, such as siblings. The assumption of linkage analysis is that relatives who resemble each other more phenotypically will also resemble each other more genetically. In other words, siblings who resemble each other with respect to a particular trait, like depression, personality, intelligence, or weight, will share more alleles on the genes that are actually involved in the trait under study than would be expected by chance alone. Two types of allele sharing are distinguished: identical-by-state (IBS) and identical-by-descent (IBD). Alleles are IBS if they have the same DNA sequence (i.e., have the same form). Alleles are IBD if they have the same DNA sequence *and* the same ancestral origin (i.e., they are inherited from the same ancestor). Alleles that are IBD must be IBS, but alleles that are IBS are not necessarily IBD. Since offspring receive one allele from each parent, siblings can share zero, one, or two alleles IBD at a locus. For example, suppose a mother has genotype A1A2 and a father has genotype A3A3. Sibling 1 inherits A1 from his mother and the first A3 allele from his father, while sibling 2 inherits the same allele A1 from the mother, but the other A3 allele from the father. Both siblings have genotype A1A3, so their IBS status is 2. However, as the A3 allele is not exactly the same A3 allele, their IBD status is 1. In behavioral genetics studies of quantitative traits, a causal gene is called a *quantitative trait locus* (QTL). However, rather than comparing siblings with respect to all QTLs on the genome, linkage analysis makes use of genetic markers. This genetic marker, or DNA marker, is a unique DNA sequence (segment of DNA) with a known position on the chromosome. For each participant, a number of markers are typed on each chromosome. These markers are not only informative about their own specific DNA sequence but indirectly also give information about genes lying close to this marker on the chromosome. Markers are indicative of adjacent genes because the marker alleles and the alleles of genes in close proximity are often inherited together, that is, as a block. So siblings who share marker alleles IBD, that is, they inherited the same allele from the same parent, most likely also share alleles on adjacent genes because they inherited the

entire block of alleles from the same parent. If, however, the siblings only share the marker allele IBS, that is, the allele is physically the same, but it is not exactly the same allele, then the marker is less informative about the siblings' likeness with respect to adjacent genes, because the siblings did not inherit the same block of information. We will not go into this in more detail, but it is important to understand that information about genes adjacent to the marker can be obtained from knowledge about siblings' IBD status at the marker: the IBD status at the marker reflects the IBD status at QTLs that are close to the marker. Differences observed between siblings with respect to the trait will be smaller if they share the same variant of a marker, obtained from the same ancestor (IBD) (Haseman & Elston, 1972). If parental genotypes are not available, probabilities of IBD status of the offspring can be estimated based on allele frequencies in the population. In many complex traits that are (highly) heritable, a large number of genes are expected to be involved, all with small effect. The shortcoming of linkage analysis with respect to the study of the genetic basis of quantitative traits is that it lacks power to detect genes of small effect. Another shortcoming of linkage is that it only gives information about an area in which a QTL may lie. These areas, however, are often still very large, covering hundreds of base pairs and often hundreds of genes. Linkage analysis thus provides a rough indication for where to look for the QTLs, but does not actually identify the QTLs. To illustrate, results from linkage studies on anxiety and depression show significant linkage signals on several chromosomes (Boomsma et al., 2008c). However, the replication rate of these studies is relatively low. This might be due to the relatively small sample sizes and different definitions of the phenotypes. For example, Holmans et al. (2007) reported linkage regions on chromosomes 8, 15, and 17; McGuffin et al. (2005) reported regions on chromosomes 1, 12, 13, and 15; and Middeldorp et al. (2009) reported linkage regions on chromosomes 2, 8, and 17. All these regions may thus contain one (or more) gene that contributes to susceptibility to anxiety or depression.

Association analysis

Once the rough location of a gene region on the chromosome is identified, candidate genes can be selected from this region. In association analysis, it is subsequently tested whether these candidate genes are actually involved in the trait under study. This is done by testing whether the trait means are the same for all possible genotypes. For example, if a gene is diallelic, three genotypes A1A1, A1A2, and A2A2 can be distinguished, and one can test whether the trait means are the same across these three genotype groups. A commonly used approach in association analysis is the case-control design. Here, allele frequencies in a group of unrelated, affected individuals (i.e., patients or cases) are compared to the allele frequencies observed in a group of unrelated controls (healthy subjects). Alleles that are statistically more frequent in cases than in controls are thought to be involved in the disorder under study. Further research into the function of the gene is then required to establish whether the relationship between the allele and the disorder is causal in nature. Association analysis is statistically powerful and therefore allows for the detection of genes with small effect. While linkage analysis is conducted within families, association studies are usually performed at a population level, which facilitates data collection. Furthermore, while linkage is usually genome wide, association studies were until recently limited to

candidate genes or candidate regions, as detected within a linkage study. Presently, however, completion of the Human Genome Project in 2003, the International Hap-Map Project in 2005, the 1000genomes project in 2009, and the decline in genotyping costs has made genome wide association analysis feasible. In this approach, hundred thousands of DNA markers across the entire genome are scanned to find genetic variations associated with a particular trait or disorder. It is important to note that although association studies are theoretically straightforward, they come with their own shortcomings. There are several reasons why genes can be statistically associated with a trait without being functionally related to the trait (this is called spurious association). Especially in genome-wide association, problems related to statistical power (e.g., sample size, multiple testing) are serious. Finally, practice shows that results obtained through association studies are often hard to replicate. This can be due to various reasons, such as difference between studies in the definition or measurement of the phenotype, differences between studies related to the sampling of participants, differences between studies of the origin of the participants (i.e., allele frequencies may differ between the countries in which the studies are conducted), and sample size. Finally, once a gene has been statistically linked to a trait, it still remains to be seen how the gene is functionally related to the trait. The link between proteins and enzymes, on the one hand, and observed behavioral traits, on the other hand, is often far from clear, and the road from DNA sequences that code for specific enzymes and proteins to the behavioral trait under study is in itself a very long and very complicated one.

Behavioral genetics and clinical practice

Discoveries in the field of human genetics have changed the general view on behavioral disorders dramatically. For example, until the 1970s, the development of ADHD was thought to be caused by poor upbringing. Nowadays, ADHD is known to be one of the most heritable childhood disorders, with heritability estimates around 70% (Jepsen & Michel, 2006). Likewise, liability to mood disorders such as depression and anxiety is influenced by genetic factors as well (Hettema et al., 2001; Kendler et al., 2006b; Kendler et al., 2006a; Sullivan et al., 2000). Studies have been conducted on the genetic influences on many other behavioral disorders, of which schizophrenia is the most widely studied. Twin studies show heritability estimates of liability to schizophrenia of around 80% (Sullivan et al., 2003). Since the completion of the Human Genome Project in 2003 and the International HapMap Project in 2005, countless studies have focused on gene finding for behavioral diseases. To date, many genes have been reported to be associated with bipolar disorder. The two most replicated genes in bipolar disorder are the same genes that are associated with schizophrenia (Farmer et al., 2007). Up to now, gene finding results for major depression and anxiety have been less encouraging. One of the reasons for this failure to detect and replicate genes might be that multiple genes of small effect are involved in these behavioral disorders (Harrison & Law, 2006; Jonsson et al., 2004; Li et al., 2006a; Straub et al., 2002). Understanding the genetic architecture of behavioral diseases is expected to have two major benefits. First, an individual's genetic makeup provides information about his or her risk of developing a particular disease. This information is useful in prevention. For example, individuals known to have a greater risk of developing schizophrenia may be

advised to avoid the use of hallucinogenic drugs. Second, an individual's genetic makeup may be of interest in the choice of treatment. Nowadays treatment is adapted to several factors, such as personality, gravity of the disease, and motivation and cooperation of the patient. Success of treatment may, however, also depend on individuals' genetic makeup, and adapting treatment to the genetic characteristics of patients may lead to higher improvement rates. In physical diseases, selection of treatment based on genotype has already been introduced. Studies on breast cancer, for example, have shown that specific gene variants affect therapy outcome. For example, recurrence after tamoxifen therapy, a widely used endocrine therapy for estrogen-receptor-positive breast cancer, is dependent on genes that are related to metabolic enzymes (Wegman et al., 2005). Identifying genes that are associated with behavioral disorders will allow us to gain insight into the etiology of the disease. Hopefully, this will lead to development of therapies that are maximally tailored to the clients' characteristics, including their genotype. Furthermore, identifying genes that are associated with effects of medical treatment may lead to genotype-adjusted pharmacotherapy. For example, molecular genetic research on ADHD focused on candidate genes involved in the dopamine system that is associated with treatment with methylphenidate. Stimulant medications such as methylphenidate act primarily by inhibiting the dopamine transporter that is responsible for the dopamine reuptake. Small but significant associations have been reported for two dopamine receptor genes (Li et al., 2006b).

CONCLUDING REMARKS

In the majority of behavioral disorders, individual differences observed in liability for disease have been shown to relate to individual differences in genetic architecture. Heritability estimates range from very low (sleep problems $h^2 \approx 20\%$ (Boomsma et al., 2008b) to very high (autism $h^2 \approx 90\%$; Freitag, 2007). Many studies report higher heritability estimates for more severe manifestations of disorders and for early onset manifestations of disorders. For example, both depression and anxiety show higher heritability estimates for more severe forms and for early- onset forms (Hettema et al., 2001; McGuffin et al., 1996; Scherrer et al., 2000). Higher heritability estimates were also reported for more severe manifestations of schizophrenia (Gottesman, 2001). Moreover, genetic influences are larger for type 2 schizophrenia, which is known for passive symptoms such as withdrawal and lack of emotion, than for type 1 schizophrenia, which is known for active symptoms such as delusions and hallucinations (Dworkin & Lenzenweger, 1984). In general, type 1 schizophrenia has a better prognosis and a better response to medication. The finding that more severe manifestations of disorders are more heritable raises questions on whether, for example, the same genes are associated with different manifestations of a disorder. Since development is a result of a constant interplay between genetic and environmental factors, neurodevelopmental disorders like schizophrenia, especially the late-onset type, might be the result of interplay between genes and environment. Insight into this interplay will lead to a better understanding of the expression of genes. In recent years, behavioral disorders are assessed as a quantitative feature instead of a dichotomous feature. That is, researchers have focused on a continuum from mild to severe depression symptoms, rather than on a dichotomous distinction between participants with and without depression. When focusing

on continua, behavioral disorders are considered the quantitative extreme of the same genetic and environmental factors that contribute to the phenotypic variation observed within the normal range of behavior. Analyzing behavioral disorders as a quantitative feature may require the inclusion of individuals who are not actually diagnosed for the disorder but do suffer from some of its symptoms. These individuals can be informative since they are expected to be carriers of associated genotypes. A quantitative view on disorders is also useful in finding genes that are associated with multiple disorders. It has been shown that phenotypic, but also genetic, comorbidity is common in numerous behavioral disorders. For example, genes associated with bipolar disorder are known to be associated with schizophrenia as well. However, according to *DSM* criteria, bipolar disorder is only diagnosed when schizophrenia is not, which precludes comorbidity studies if diagnostic dichotomies are used as input, rather than quantitative measures. When participants with symptoms of both disorders are neglected in gene-finding studies, a lot of potentially valuable information is lost. In addition, it is possible that analyzing disorders as a continuum may lead to the identification of QTLs that contribute to individual differences in the disorder itself. The recent technological improvements, available financial funding, and intended close cooperation with fields like molecular biology and functional genomics make behavioral genetics at present one of the most rapidly changing and evolving fields in science.

Appendix II

Overview of all possible relations between relatives in the extended twin family design as applied in this thesis

Table A2.1 Overview of all possible relations between relatives in the extended twin family design as applied in this thesis.

Group and acronym	Description
Twins/Nuclear families	
MZ: MM	Monozygotic male - male
DZ: MM	Dizygotic male - male
MZ: FF	Monozygotic female - female
DZ: FF	Dizygotic female - female
DOS: MF	Dizygotic male - female
Spouses	
sibs: MM	Male – male sibling pairs
sibs: FF	Female – female sibling pairs
sibs: MF	Male – female sibling pairs
Fath-son	Father – son
Fath-dau	Father – daughter
Moth-son	Mother – son
Moth-dau	Mother – daughter
Avuncular	
PatSIBavMM	Nephew with father's brother
PatSIBavMF	Niece with father's brother
MatSIBavFM	Nephew with mother's sister
MatSIBavFF	Niece with mother's sister
PatSIBavFM	Nephew with father's sister
PatSIBavFF	Niece with father's sister
MatSIBavMM	Nephew with mother's brother
MatSIBavMF	Niece with mother's brother
PatDZavMM	Nephew with father's DZ brother
PatDZavMF	Niece with father's DZ brother
MatDZavFM	Nephew with mother's DZ sister
MatDZavFF	Niece with mother's DZ sister
PatDZavFM	Nephew with father's DZ sister
PatDZavFF	Niece with father's DZ sister
MatDZavMM	Nephew with mother's DZ brother
MatDZavMF	Niece with mother's DZ brother
PatMZavMM	Nephew with father's MZ twin
PatMZavMF	Niece with father's MZ twin
MatMZavFM	Nephew with mother's MZ twin
MatMZavFF	Niece with mother's MZ twin

Group and acronym	Description	Parent's relation
Spouses of uncles and aunts		
SPaSIBavFM	Male with wife of father's brother	
SPaSIBavFF	Female with wife of father's brother	
SMaSIBavMM	Male with husband of mother's sister	
SMaSIBavMF	Female with husband of mother's sister	
SPaSIBavMM	Male with husband of father's sister	
SPaSIBavMF	Female with husband of father's sister	
SMaSIBavFM	Male with wife of mother's brother	
SMaSIBavFF	Female with wife of mother's brother	
SPaDZavFM	Male with wife of father's male twin	
SPaDZavFF	Female with wife of father's male twin	
SMaDZavMM	Male with husband of mother's female twin	
SMaDZavMF	Female with husband of mother's female twin	
SPaDZavMM	Male with husband of father's female twin	
SPaDZavMF	Female with husband of father's female twin	
SMaDZavFM	Male with wife of mother's male twin	
SMaDZavFF	Female with wife of mother's male twin	
SPaMZavFM	Male with wife of father's twin	
SPaMZavFF	Female with wife of father's twin	
SMaMZavMM	Male with husband of mother's twin	
SMaMZavMF	Female with husband of mother's twin	
Spouses of twins/siblings		
SPMZM	Spouses of MZ male twins	
SPMZF	Spouses of MZ female twins	
SPDZM	Spouses of DZ male twins	
SPDZF	Spouses of DZ female twins	
SPDMF	Spouses of DZ male-female twins	
SPSIBMM	Spouses of SIB male twins	
SPSIBFF	Spouses of SIB female twins	
SPSIBMF	Spouses of SIB male-female twins	
Cousins	Sex of cousins	Parent's relation
MZMCsMM	Male - male	MZ male
MZMCsFF	Female - female	MZ male
MZMCsMF	Male – female	MZ male
MZFCsMM	Male – male	MZ female

Group and acronym	Description
Siblings-in-law	
SIBInlawMF	Wife with husband's brother
SIBInlawFM	Husband with wife's sister
SIBInlawMM	Husband with wife's brother
SIBInlawFF	Wife with husband's sister
DZInlawMF	Wife with husband's male cotwin
DZInlawFM	Husband with wife's female cotwin
DZInlawMM	Husband with wife's male cotwin
DZInlawFF	Wife with husband's female cotwin
MZInlawMF	Wife with husband's MZ male cotwin
MZInlawFM	Husband with wife's MZ female cotwin
MZInlawFM	Husband with wife's MZ female cotwin
MZInlawFF	Wife with wife's MZ female cotwin
MZInlawMM	Husband with husband's MZ male cotwin
Parent-in-law	
Fa-DInlaw	Father with daughter-in-law
Fa-SInlaw	Father with son-in-law
Mo-SInlaw	Mother with daughter-in-law
Mo-DInlaw	Mother with son-in-law

Group and acronym	Description	
MZFCsFF	Female - female	MZ female
MZFCsMF	Male – female	MZ female
DZMCsMM	Male – male	DZ male
DZMCsFF	Female - female	DZ male
DZMCsMF	Male – female	DZ male
DZFCsMM	Male – male	DZ female
DZFCsFF	Female - female	DZ female
DZFCsMF	Male – female	DZ female
DZMFCsMM	Male – male	DZ male-female
DZMFCsFF	Female - female	DZ male-female
DZMFCsMF	Male – female	DZ male-female
DZMFCsFM	Female – male	DZ male-female
SIBMMCsMM	Male – male	SIB male
SIBMMCsFF	Female - female	SIB male
SIBMMCsMF	Male – female	SIB male
SIBFFCsMM	Male – male	SIB female
SIBFFCsFF	Female - female	SIB female
SIBFFCsMF	Male – female	SIB female
SIBMFCsMM	Male – male	SIB male-female
SIBMFCsFF	Female - female	SIB male-female
SIBMFCsMF	Male – female	SIB male-female
SIBMFCsFM	Female – male	SIB male-female

Notes: Three-generational relationships were omitted since none of the participating families within the present study comprised all three generations. Homosexual relationships were omitted because sample sizes were small. Since sex may have an effect on familial transmission, relationships involving men are distinguished from relationships involving women. The relationships within MZ kinships are biologically different from relationships within DZ and sibling kinships. Relationships involving MZ twins are therefore distinguished from relationships involving DZ twins and regular siblings.

Description of cognitive data additionally collected within this PhD project

EXECUTIVE FUNCTIONING

Executive functioning was measured with the *Trail Making Test* (Reitan, 1955). During this test, subjects were required to connect numbers and letters that were randomly printed on a sheet of A4-sized paper. A standardized written instruction (which was displayed on an instruction sheet and, at the same time, read aloud by the test-administrator) was provided. To start with, subjects were asked to connect displayed numbers *one* to *twenty-two* as fast as possible (part A). Subsequently, subjects were asked to connect the numbers *one* to *eleven* and letters *A* to *K*. Numbers and letters had to be connected alternately, such that numbers were in ascending order while letters were in alphabetical order (part B). The time taken to complete the chains of part A and part B is generally used as a measure of visuo-motor speed and task-switching skills, respectively. The difference in time that is required to complete part A and part B is generally interpreted as a measure of executive functioning in which a relatively large increase (i.e., part B > part A) is related to less optimal executive functioning.

VERBAL LEARNING AND MEMORY

Verbal learning and memory was measured with the *Verbal Learning & Memory Task* (Mulder et al., 1996). During part one of this task, a list of sixteen items from a general shopping list was presented five times. Items were equally classified into four distinct categories (fruits, herbs & spices, clothing, and handy tools); each series was orally presented in a standardized order by the test administrator. After each presentation, subjects were required to recall as many items as possible. Subsequently, an interference list of sixteen different items was presented. Again, items were equally classified into four distinct categories (fruits, herbs & spices, fish and kitchen tools). Subjects were required to recall as many items from this interference list as possible. Immedeately afterwards, subjects were required to respectively recall from the first list as many items as possible (short delay free recall) and from each of the four semantic categories from the first list as many items as possible (short delay cued recall). After a 20 minutes time interval (part two), subjects were again asked to recall as many items from the first list as possible (long delay free recall) and as many items from each of the four semantic categories (long delay cued recall). Finally, subjects were provided with a recognition list of 44 items. Performance on the first five trials was used as a measure of learning ability; performance on the short and long delay free and cued recall was used as a measure of memory, and performance on recognition was used as a measure of recognition ability.

LINGUISTIC ABILITY: NON WORDS

Subjects' linguistic ability (reading aloud and repeating non-words) was measured in the *Non-Words Test*. Subjects were required to read aloud 40 non-words (e.g., bisjoeda, trola and, brosati etc.) that appeared on a computer screen, while trying to avoid errors. Subsequently, subjects were required to repeat the same 40 non-words that were read aloud by a recorded voice. A standardized test instruction was displayed on the computer screen previously to the test (and at the same time read aloud by the test administrator). The amount of errors and type of error (i.e., wrong pronunciation of vowel, consonant, and word stress) were used as measures of performance in reading out and repeating non-words.

LINGUISTIC ABILITY: WORD STRESS

Subjects' ability to recognize the correct lexical stress of drawings of common objects is measured with the *Word Stress Task* (Schiller, 2006). Subjects were, one by one, provided with four repeats of a series of 40 pictures (e.g., giraffe, canoe, and castle), corresponding to bisyllabic nouns on a computer screen. Within the first series, subjects were provided with the pictures together with the corresponding written bisyllabic noun, to get familiar with the pictures and corresponding nouns. Within the second series, subjects were provided with the pictures without the name and were asked to say aloud each picture name. In case the subject gave the wrong name, the test administrator provided the subject with the correct name. Within the third series, subjects were required to press the spacebar as fast as possible in case the lexical stress location of the word corresponding to the picture was on the first syllable (half of the trials). Within the fourth series, subjects were required to press the spacebar as fast as possible in case the lexical stress location was on the second syllable (half of the trials). Accuracy and response time within the third and fourth series were used as measures of linguistic ability.

VISUO-SPATIAL MEMORY

Visuo-spatial memory was assessed with the *Corsi Block Tapping Task* (Corsi, 1972). During this task, nine white blocks were displayed randomly on a computer screen. During the illustration, the blocks turn red one by one, after that, the screen turned blank. Subjects were required to mimic a sequence of blocks by tapping the blocks in exactly the same order as the blocks turned red in the illustration. The sequence started simple with two blocks, and became more complex, depending on the accuracy of the subject. The total span lasted up to nine blocks. The length of the span was increased by one block after every five runs; the test was however terminated when the subject responded incorrectly to three out of five runs of the same length. Instruction was read by each participant from the computer screen (and at the same time read aloud by the test-administrator). Subjects were provided with two practice trials. The total number of correct runs (maximum is 40) and the best set size (maximum is 9) were used as measures of visuo-spatial memory.

TIME PERCEPTION

Time perception was measured with the *Time Perception Task* (Barkley, 1998). During this task, subjects were asked to reproduce visual temporal intervals with interval lengths of 1, 2, 3, 4, or 5 seconds. After a standardized written instruction (which was displayed on an instruction sheet and, at the same time, read aloud by the test-administrator), three practice trials and twenty experimental trials were administered. Each different interval length was provided four times, in a randomized order. Within each trial, subjects were provided with two light bulbs on a screen. To start with, the left light bulb switched on for a particular time interval length (i.e., 1, 2, 3, 4, or 5 seconds), subsequently subjects were required to light the right light bulb for the same time interval length by pressing the space bar. Subjects were not informed about the length of the intervals and did not receive feedback. The precision of the reproduction (operationalized as the absolute discrepancy between the response length and the stimulus length) was used as a measure of time perception.

INSPECTION TIME

Inspection Time was measured using the *Inspection Time Task* (extensively described by Luciano et al., 2001). During this task subjects were provided with a π–shaped figure with, at appearance, unequal legs. After a short interval, the two legs of the π–shaped figure were covered with a mask. Subsequently, subjects were required to denote the longest leg of the π–shaped figure (by pressing the M or Z button on a computer keyboard for the right or left leg, respectively). The stimulus duration was altered based on the correctness of the subjects' response. After a correct response, the stimulus duration within the next trial was decreased while after an incorrect response, the stimulus duration within the next trial was increased. The amount of decrease or increase depended on the number of previous reversals and became smaller as the task continued, such that the interval converged at the subjects' inspection time and the Parameter Estimation by Sequntial Testing procedure (PEST) estimates became consistent. The protocol was stopped when the interval was converged, or when the maximum of 96 trials was reached. The last measured pi-duration was used as a measure of inspection time.

Appendix IV

Descriptives of cognitive measures collected within this PhD project

Table A4.1 Descriptives of cognitive measures collected within this PhD project

	Grand mean	SD	β_{sex}	β_{age}	N
Full scale IQ	100.00	15.00	6.05	.16	1340
Verbal IQ	100.00	15.00	2.03	.14	1340
Performance IQ	99.81	14.81	7.81	.15	1336
Trail Making Test, Version A Time in seconds	10.89	5.21	-1.34	-.18	537
Trail Making Test, Version B Time in seconds	16.73	8.09	-1.47	-.30	492
Trail Making Test, Interference Absolute Time difference Version A vs Version B	5.96	5.63	-.10	-.11	474
Trail Making Test, Interference Percentage Time difference Version A vs Version B	57.00	38.20	3.24	-.18	479
VLGT: Sum score list 1 to 5	59.10	9.32	-6.37	.32	551
VLGT: Short Term Free Recall	13.21	2.74	-1.60	.09	550
VLGT: Short Term Cued Recall	13.06	2.47	-1.38	.06	548
VLGT: Long Term Free Recall	13.48	2.66	-1.71	.08	547
VLGT: Long Term Cued Recall	13.43	2.47	-1.55	.06	548
VLGT: Recognition	43.22	1.87	-.82	.05	536
Non Words, reading Percentage incorrect total	26.86	10.93	-.37	-.10	554
Non Words, reading Percentage incorrect word stress	18.55	6.01	-.98	-.02	557
Non Words, reading Percentage incorrect vowels	3.32	3.28	.22	.00	550
Non Words, reading Percentage incorrect consonants	.96	2.06	-.29	-.01	543
Non Words, reading Percentage incorrect multiple errors	2.96	4.47	.21	-.04	536
Non Words, repeating Percentage incorrect total	8.75	7.51	.09	-.09	551
Non Words, repeating Percentage incorrect word stress	1.129	1.53	.44	.00	544
Non Words, repeating Percentage incorrect vowels	3.02	2.89	.14	-.01	548
Non Words, repeating Percentage incorrect consonants	2.44	3.59	-.80	-.05	546
Non Words, repeating Percentage incorrect multiple errors	.89	1.95	-.16	-.02	533
Word Stress Percentage correct syllable 1	58.47	18.06	-.52	-.04	575
Word Stress Time syllable 1 in milliseconds	1010.04	133.57	11.11	-1.45	570
Word Stress Percentage correct syllable 2	70.12	17.86	2.19	-.03	564
Word Stress Time syllable 2 in milliseconds	1043.92	138.17	1.54	-1.62	561

	Grand mean	SD	β_{sex}	β_{age}	N
Corsi Blocks: Best set size	6.23	1.00	.44	.04	607
Corsi Blocks: Total score	23.04	4.61	2.10	.17	607
Time Test: Absolute discrepancy	.51	.21	-.08	.00	590
Pi task: Pi-duration last in milliseconds	77.59	35.88	-2.82	-.61	552
Pi task: Number of trials	83.65	9.19	-.38	-.05	579

Notes: SD = standard deviation; β_{sex} = beta coefficient sex (regression weight); β_{age} = beta coefficient age (regression weight); N = number of participants excluding outliers. Negative β_{sex} coefficients indicate that men have generally lower scores than women. Negative β_{age} coefficients indicate that older individuals have generally lower scores than younger individuals.

AppendixV

Recall Word Test Interference correct total difference Short task size Cued Full Long Words seconds milliseconds vs stress reading ns incorrect consonants Trail VLGT Stress Time Version IQ Making Term vowels Performance Free Corsi Absolute syllable errors repeating score Percentage

Phenotypic correlations between cognitive measures collected within this PhD project

Table A5.1 Phenotypic correlations (standard errors).

	Full Scale IQ	Verbal IQ	Performance IQ
Full scale IQ	1		
Verbal IQ	.92 (.01)***	1	
Performance IQ	.83 (.01)***	.57 (.02)***	1
Trail Making Test, Version A Time in seconds	-.37 (.04)***	-.27 (.04)***	-.42 (.04)***
Trail Making Test, Version B Time in seconds	-.44 (.04)***	-.39 (.04)***	-.42 (.04)***
Trail Making Test, Interference Absolute Time difference Version A vs Version B	-.27 (.05)***	-.28 (.05)***	-.21 (.05)***
Trail Making Test, Interference Percentage Time difference Version A vs Version B	-.10 (.05)*	-.15 (.05)**	-.01 (.05), ns
VLGT: Sum score list 1 to 5	.41 (.04)***	.36 (.04)***	.38 (.04)***
VLGT: Short Term Free Recall	.35 (.04)***	.32 (.04)***	.30 (.04)***
VLGT: Short Term Cued Recall	.40 (.04)***	.37 (.04)***	.33 (.04)***
VLGT: Long Term Free Recall	.39 (.04)***	.36 (.04)***	.31 (.04)***
VLGT: Long Term Cued Recall	.39 (.04)***	.37 (.04)***	.31 (.04)***
VLGT: Recognition	.30 (.04)***	.27 (.04)***	.24 (.04)***
Non Words, reading Percentage incorrect total	-.31 (.04)***	-.30 (.04)***	-.24 (.04)***
Non Words, reading Percentage incorrect word stress	.11 (.05)*	.13 (.05)**	.05 (.04), ns
Non Words, reading Percentage incorrect vowels	-.27 (.05)***	-.29 (.04)***	-.20 (.05)***
Non Words, reading Percentage incorrect consonants	-.28 (.04)***	-.30 (.04)***	-.19 (.04)***
Non Words, reading Percentage incorrect multiple errors	-.38 (.04)***	-.38 (.04)***	-.28 (.04)***
Non Words, repeating Percentage incorrect total	-.28 (.04)***	-.27 (.04)***	-.19 (.04)***
Non Words, repeating Percentage incorrect word stress	-.19 (.04)***	-.18 (.04)***	-.14 (.04)**
Non Words, repeating Percentage incorrect vowels	-.03 (.04), ns	-.01 (.04), ns	-.03 (.05), ns
Non Words, repeating Percentage incorrect consonants	-.22 (.04)***	-.24 (.04)***	-.13 (.04)**
Non Words, repeating Percentage incorrect multiple errors	-.23 (.04)***	-.24 (.04)***	-.16 (.04)***
Word Stress Percentage correct syllable 1	.40 (.03)***	.36 (.03)***	.34 (.04)***
Word Stress Time syllable 1 in milliseconds	-.16 (.05)**	-.11 (.05)*	-.16 (.05)***
Word Stress Percentage correct syllable 2	.50 (.03)***	.49 (.03)***	.37 (.04)***
Word Stress Time syllable 2 in milliseconds	-.22 (.05)***	-.16 (.05)***	-.21 (.05)***
Corsi Blocks: Best set size	.35 (.04)***	.28 (.04),*	.36 (.04)***

	Full Scale IQ	Verbal IQ	Performance IQ
Corsi Blocks: Total score	.37 (.04)***	.30 (.04)***	.38 (.04)***
Time Test: Absolute discrepancy	-.11 (.04)**	-.08 (.04)***	-.12 (.04**
Pi task: Pi-duration last in milliseconds	-.28 (.04)***	-.23 (.04)***	-.25 (.04)***
Pi task: Number of trials	-.13 (.04)***	-.09 (.04)*	-.15 (.04)**

Notes: Phenotypic correlations were calculated in Mplus' (Muthen & Muthen, 2005), using option 'complex' to correct for familial relatedness between the participants. Standard errors are displayed between brackets; measures are corrected for age and sex effects; p = p-value; all scores are corrected for age and sex effects; ***=significant at α of .001; **=significant at α of .01; *=significant at α of .05; ns = not significant at α of .05.

AppendixVI

Letter to the editor:

Life events moderate variation in cognitive ability (g) in adults

Letter to the editor: Life events moderate variation in cognitive ability (g) in adults

The heritability of general cognitive ability (*g*) in adults is estimated to lie approximately between 75% and 85% (Plomin, 1999). Despite this overwhelming indirect evidence of 'genes for *g*', only a handful of genes have been identified so far, together explaining less than ~5% of the genetic variation (Posthuma & de Geus, 2006). Several reasons have been suggested for this 'missing heritability' (Maher, 2008), including the presence of gene-environment interactions (GEI). We have investigated the presence of GEI for measured Life Events and *g*, in a population-based sample of adult twins and their siblings (N=560).

The reported large heritability estimates for *g* are derived from classical twin studies, in which additivity of genetic and environmental effects is assumed; implying heritability estimates are equal across environmental conditions. Non-additivity of genetic and environmental effects (i.e., GEI), conversely, implies that genes control an individual's sensitivity to environmental influences, or environmental factors moderate gene expression. If GEI is present, the extent to which genes and environment cause variation in *g* varies across environmental conditions, and a single heritability estimate is no longer accurate (Purcell, 2002). Consequently, assuming the absence of GEI may lead to biased estimates of the relative importance of genetic and environmental influences (Purcell, 2002). Moreover, when genetic effects vary across environmental conditions, an environmentally stratified design might seriously improve gene finding success when researchers focus on those environmental conditions where genetic effects are largest. Gene finding attempts for *g* would thus benefit from studies that elucidate the environmental circumstances for which genetic effects are largest.

Few studies have provided evidence of GEI in the context of *g* in children and adolescents, demonstrating increased heritability in children from highly educated parents and in children with socio-economic background. To date, studies on GEI in adults, where heritability estimates of *g* are largest (Haworth et al., 2009), are rare, with two studies hitherto showing evidence of modest moderation on environmental influences but not on genetic influences (Kremen et al., 2005; van der Sluis et al., 2008b).

We first determined whether there is a correlation between intrapair sum and intrapair difference scores for *g* in 136 complete adult MZ twin pairs, as such a correlation would imply non-additivity of latent genetic and environmental factors (Jinks & Fulker, 1970). This correlation was .20 (p=.02) suggesting that adults of higher cognitive ability are more sensitive to the environment. We then focused on moderation effects of *measured* environmental effects, i.e., 19 measures of positive, negative, and neutral Life Events on genetic and environmental influences of *g* within a population-based sample of 560 twins and their non-twin siblings (age 23-75 years) (for a sample description see Vinkhuyzen et al., 2010a). Statistical analyses were conducted in which linear and non-linear moderation by the 19 Life Events on genetic and environmental influences was tested. Results demonstrated modest negative moderation of genetic factors by several Life Events (i.e., genetic influences were smaller for subjects who experienced *Birth of a child, Breaking up with friends/relatives, Death of friends/relatives,* and *Retirement*), and considerable moderation of these Life Events on the overall environmental influence (*Birth of a child, Breaking up with friends/relatives, Severe trouble with friends/relatives, Death of friends/*

relatives, Severe offence, Being fired, Unemployment, and *Retirement*), with direction depending on the specific Life Event. Estimates of genetic and environmental influences, as a function of the exposure to a particular Life Event, are depicted in Figure AVI.1 (unstandardized) and AVI.2 (standardized). Exposure to *Severe illness*, *Divorce*, *Receiving mental health treatment*, *Robbery*, *Sexual abuse*, *Marriage*, *Drivers license*, *Graduation*, *Promotion*, and *Changing schools in childhood* did not moderate the variance components of *g*.

Although these results need replication, the broad heritability of *g* ranged from only 9% to above 90% across levels of positive, negative, and neutral Life Events, suggesting that the extent to which genetic and environmental influences affect individual differences in *g* in adults is not equal across the entire population, but varies with exposure to Life Events.

This conclusion is important in the context of gene finding studies for *g* as linkage and association studies generally assume additivity of genetic and environmental factors, implying that genetic effects are equal under various environmental circumstances. We show that this assumption does not always hold. Ignoring the complex interplay between genes and environment in gene finding studies may partly explain the lack of success in the identification of genes for *g*. Gene finding studies should thus include GEI effects to increase their chances of success.

Figure A6.1 Unstandardized variance components of g as a function of the exposure to different Life Events.
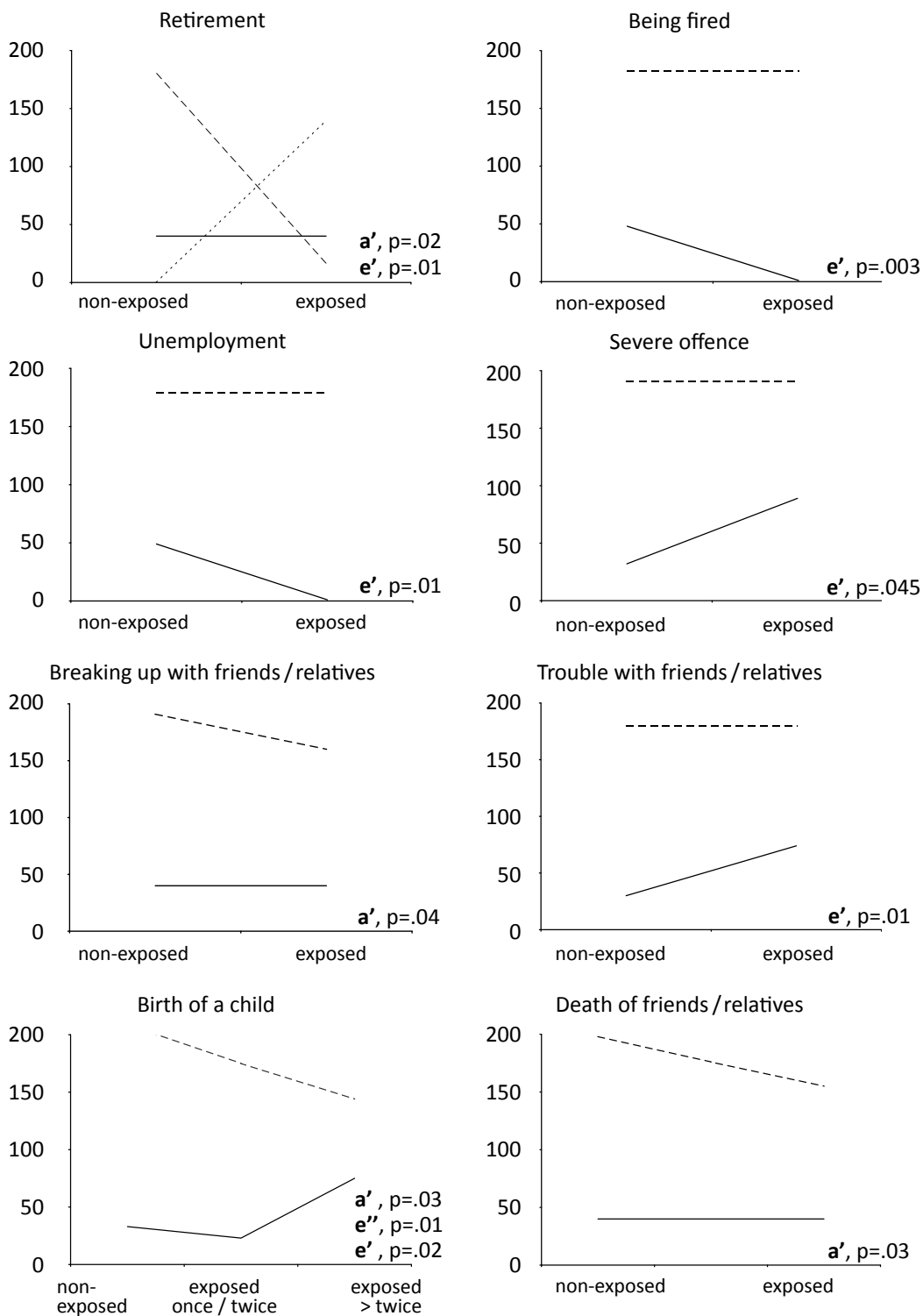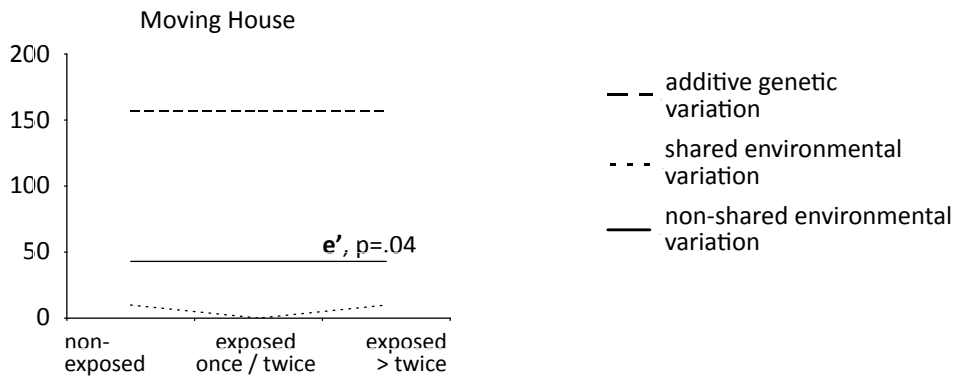
Notes: Unstandardized variance components of g as a function of the exposure to different Life Events. The figures are based on the most reduced models, i.e., on models in which all non significant effects were eliminated from the model. Unstandardized variance components refer to the absolute contribution of additive genetic effects, shared environmental effects, and non-shared environmental effects to variation in g. Additive genetic variation represents additive effects of alleles summed over all genetic loci. Shared environmental variation represents environmental influences that render members of the same family more alike. Non-shared environmental variation represents all environmental influences that result in differences between members of a family, including measurement error. P-values correspond to significance levels of non-linear moderation of additive genetic effects (**a''**), shared- (**c''**) and non-shared environmental effects (**e''**) and significance levels of linear moderation of additive genetic effects (**a'**), shared- (**c'**) and non-shared environmental effects (**e'**). Please note that the heritability (h^2) is defined as the ratio of the genetic variance to the total variance.

Figure A6.2 Standardized variance components of g as a function of the exposure to different Life Events.
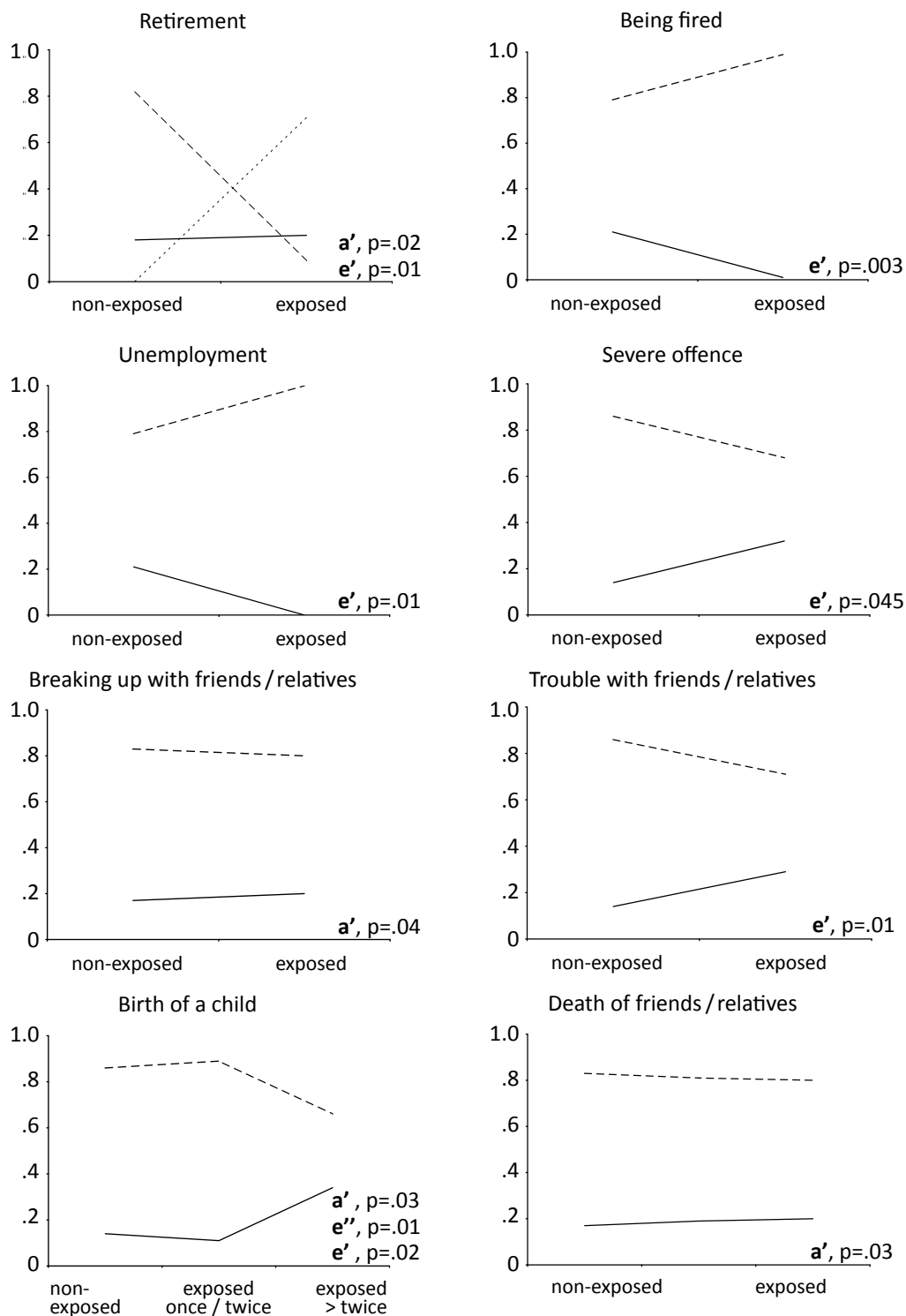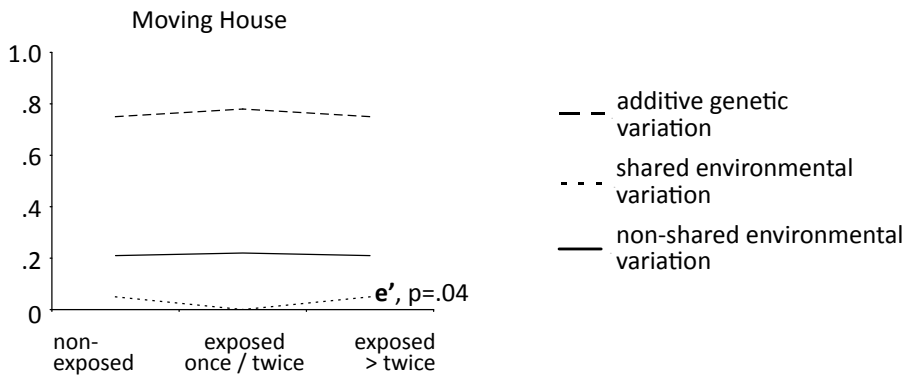
Notes: The figures are based on the most reduced models, i.e., on models in which all non significant effects eliminated from the model. Standardized variance components refer to the relative contribution of additive genetic effects, shared environmental effects, and non-shared environmental effects to variation in g. Additive genetic variance represents additive effects of alleles summed over all genetic loci. Shared environmental variance represents environmental influences that render members of the same family more alike. Non-shared environmental variance represents all environmental influences that result in differences between members of a family, including measurement error. P-values correspond to significance levels of non-linear moderation of additive genetic effects (a''), shared- (c'') and non-shared environmental effects (e'') and significance levels of linear moderation of additive genetic effects (a'), shared- (c') and non-shared environmental effects (e'). The heritability (h^2) is defined as the ratio of the genetic variance to the total variance.

Nederlandse Samenvatting

De onderzoeken beschreven in dit proefschrift zijn onderdeel van een grootschalig onderzoek naar individuele verschillen in algemene cognitieve vaardigheden. Algemene cognitieve vaardigheden is een verzamelnaam voor concentratie, geheugen, redeneren en denkvermogen. Al lange tijd is bekend dat een belangrijk deel van de verschillen tussen mensen in algemene cognitieve vaardigheiden wordt verklaard door verschillen tussen mensen op genetisch niveau. Bij 5 jaar oude kinderen verklaren genen ongeveer een kwart van de geobserveerde individuele verschillen, bij kinderen van 10 jaar oud is dit ongeveer twee keer zo veel. De invloed van genen stijgt verder tot ongeveer het 18^e levensjaar (80%), waarna de invloed van genen ongeveer stabiel blijft.

Deze gegevens zijn gebaseerd op een groot aantal tweelingstudies. Met behulp van tweelingstudies kan op basis van de gelijkenis van eeneiige tweelingparen en de gelijkenis van twee-eiige tweelingparen een uitspraak worden gedaan over de mate waarin geobserveerde verschillen tussen mensen kunnen worden verklaard door genen of door omgevingsinvloeden. Hierbij worden twee typen omgevingsinvloeden onderscheiden: omgevingsinvloeden die een individu deelt met zijn of haar familieleden, de *gedeelde omgeving* (bijvoorbeeld dezelfde woonomgeving, dezelfde opvoeding) en omgevingsinvloeden die een individu niet deelt met zijn of haar familieleden, de *unieke omgeving* (bijvoorbeeld eigen vrienden, eigen hobby's).

Eeneiige tweelingen zijn genetisch identiek, twee-eiige tweelingen daarentegen, delen gemiddeld de helft van hun genetisch materiaal. Per definitie delen zowel eeneiige als twee-eiige tweelingen 100% van hun gedeelde omgeving en delen zij niets van hun unieke omgeving. Uit tweelingonderzoek naar individuele verschillen in algemene cognitieve vaardigheden blijkt dat de scores op een intelligentietest van twee leden van

een eeneiig tweelingpaar over het algemeen veel dichter bij elkaar liggen dan scores van twee leden van een twee-eiige tweelingpaar. Met de kennis die we hebben over de mate van genetische gelijkenis tussen eeneiige en twee-eiige tweelingparen, kunnen we berekenen in hoeverre verschillen in scores op een intelligentietest kunnen worden toegeschreven aan genetische invloeden, gedeelde omgevingsinvloeden en unieke omgevingsinvloeden.

Deze klassieke tweelingmethode berust echter op een aantal aannamen die mogelijk niet houdbaar zijn als het gaat om algemene cognitieve vaardigheden. Ten eerste wordt er aangenomen dat partners elkaar willekeurig uitkiezen terwijl onderzoek heeft aangetoond dat partners elkaar selecteren op basis van enigzins vergelijkbare cognitieve vaardigheden. In de literatuur worden er twee processen genoemd die ten grondslag kunnen liggen aan deze partner selectie: sociale homogeniteit en actieve partner selectie op basis van het fenotype. Bij sociale homogeniteit ontmoeten partners elkaar in een omgeving die gecorreleerd is met algemene cognitieve vaardigheden. In het geval van actieve partner selectie zoeken partners elkaar uit op basis van geobserveerde gelijkenis. Ten tweede wordt in het klassieke tweeling design de gelijkenis die ouders en kinderen vertonen volledig toegeschreven aan het feit dat zij gemiddeld 50% van hun genetisch materiaal delen, terwijl invloeden van bijvoorbeeld opvoeding worden verwaarloosd. Ten derde wordt aangenomen dat de invloed van genetische effecten en omgevingseffecten additief zijn. Het is echter mogelijk dat genetische effecten en omgevingseffecten elkaar beïnvloeden en dat dit samenspel van invloed is op individuele verschillen in algemene cognitieve vaardigheden. Zo is het mogelijk dat een bepaald onderwijssysteem niet voor iedereen dezelfde weerslag heeft op cognitieve ontwikkeling,

maar dat dit effect afhangt van een bepaalde genetische aanleg van de leerling. In het geval dat deze aannamen niet houdbaar zijn zullen schattingen van de invloed van genen en omgeving zoals verkregen in een klassieke tweelingstudie mogelijk niet accuraat zijn.

Om een beter beeld te krijgen van de mate waarin genetische invloeden en omgevingsinvloeden de verschillen tussen mensen in algemeen cognitief functioneren bepalen, zijn data verzameld in een grote groep tweelingen en hun broers en zussen, partners, en ouders of kinderen. Al deze mensen hebben een aantal cognitieve taken uitgevoerd, waaronder een IQ test (Wechsler, 1997). Daarnaast hebben zij de levenservaringenlijst (LEL) ingevuld. In deze lijst staan vragen over verscheidene omgevingsfactoren die van invloed kunnen zijn, of zijn geweest, op cognitieve ontwikkeling, zoals type school of soort werk, het bespelen van een muziekinstrument, of het beoefenen van een sport.

Deze gegevens maakten het mogelijk te onderzoeken in hoeverre processen als actieve partnerselectie en het samenspel tussen genen en omgeving verklaren waarom mensen van elkaar verschillen in algemene cognitieve vaardigheden.

In het eerste empirische hoofdstuk van dit proefschrift (hoofdstuk 3) hebben we IQ-scores geanalyseerd van tweelingen en hun familieleden. De aanwezigheid van partners en ouders maakt het mogelijk om te onderzoeken in hoeverre partners gelijkenis vertonen in algemene cognitieve vaardigheden, de aanwezigheid van ouders maakt het tevens mogelijk om invloeden van genetische dominantie te schatten. Dominantie is de genetische invloed die ontstaat door interactie tussen allelen van een gen. We vonden, net als in eerdere studies was aangetoond, dat de IQ scores van partners inderdaad enigszins op elkaar lijken, Het was echter moeilijk statistisch onderscheid te maken tussen de twee

onderliggende processen: sociale homogeniteit en actieve partner selectie. Een model waarin actieve partner selectie het onderliggende proces was leek beter te passen bij de geobserveerde data. Daarnaast lieten onze analyses zien dat als je deze gelijkenis door actieve partner selectie mee modelleert, dat behalve additieve genetische factoren en unieke omgevingsfactoren, ook genetische dominantie van belang is. Deze resultaten laten zien dat in voorgaande klassieke tweelingstudies (waarin de gelijkenis tussen eeneiige en twee-eiige tweelingparen wordt vergeleken, maar informatie van partners, ouders en kinderen ontbreekt) de invloed van genetische dominantie in volwassenen is onderschat. Additieve genetische factoren verklaren 44%, genetische dominantie 27%, actieve partner selectie 11% en unieke omgevingsfactoren verklaren 18% van de geobserveerde individuele verschillen in algemene cognitieve vaardigheden.

Van factoren zoals opleiding, opvoeding en levensgebeurtenissen die mogelijk verband hebben met algemeen cognitief functioneren wordt over het algemeen gezegd dat ze kunnen worden toegeschreven aan de 'omgeving'. Om te toetsen of dit ook werkelijk 'omgeving' is hebben we in hoofdstuk 4 gekeken in hoeverre genetische factoren van invloed zijn op de mate waarin mensen blootgesteld worden aan deze omgevingsfactoren. Hierbij hebben we ons gericht op vier domeinen: omgeving in de kindertijd, sociale omgeving en gedrag, vrijetijdsbesteding, en belangrijke levensgebeurtenissen (zoals geboorte van een kind, of het verlies van een familielid of dierbare). Het blijkt dat genetische factoren gemiddeld bijna de helft (49%) van de van de geobserveerde verschillen tussen mensen in de mate waarin ze blootgesteld worden aan deze omgevinsgfactoren verklaren. Genetische factoren verklaren gemiddeld 66% van de individuele verschillen in blootstelling aan omgevingsfactoren in de kindertijd, voor

vrijetijdsbesteding gemiddeld 52%, voor sociale omgeving en gedrag 52%, en voor levensgebeurtenissen 36%. Dit betekent dat invloeden die over het algemeen puur worden toegeschreven aan de omgeving, voor een deel kunnen worden toegeschreven aan verschillen op genetisch niveau. Het is mogelijk dat mensen actief hun omgeving uitzoeken op basis van hun genotype, slimme mensen zullen bijvoorbeeld vaker naar de bibliotheek gaan of een hoge opleiding volgen dan minder slimme mensen. De blootstelling aan opvoeding of onderwijs is daardoor gerelateerd aan genen die van invloed zijn op individuele verschillen in algemene cognitieve vaardigheden.

In hoofdstuk 5 hebben we bestudeerd in hoeverre de Prestatie Motivatie Test (Hermans, 2004) dezelfde latente factoren meet in mannen en in vrouwen. In de LEL zijn twee subschalen van de Prestatie Motivatie Test opgenomen, de Academische Prestatie Motivatie schaal en de Algemene Prestatie Motivatie schaal. Het bleek dat vijf van de 28 vragen sekse-bias lieten zien, wat betekent dat de scores van mannen en vrouwen op deze vragen niet direct vergelijkbaar zijn. In vervolganalyses waarin de Prestatie Motivatie Test een rol speelde, zijn deze vragen verwijderd. Tevens vonden we dat mannen en vrouwen gemiddeld verschillend scoorden op sommige onderliggende factoren van de beide schalen. Bijvoorbeeld, vrouwen gaven aan minder toekomstgericht te zijn dan mannen, terwijl vrouwen op school meer toewijding aan de dag legden met betrekking tot hun schoolwerk.

In hoofdstuk 6 is onderzocht in hoeverre genetisch factoren en omgevingsfactoren individuele verschillen in opleidingsniveau verklaren. Hierbij hebben we ook bestudeerd of de invloed van deze factoren afhangt van het niveau van algemeen cognitief functioneren en/of van het niveau van academische prestatie motivatie. Dit onderzoek liet

zien dat de relatieve invloed van gedeelde omgevingsfactoren iets groter was voor mensen die laag of juist hoog scoorden op een intelligentietest. Schattingen van de relatieve invloed van gedeelde omgevingsinvloeden liepen van 0% tot 15%. De relatieve invloed van unieke omgevingsfactoren nam behoorlijk toe bij mensen met een hoog opleidingsniveau. Schattingen van de unieke omgevingsinvloeden liepen van 22% tot 58%.

In hoofdstukken 7 en 8 hebben we bestudeerd in hoeverre levensgebeurtenissen (zoals geboorte van een kind, of het verlies van een familielid of dierbare) en spanningsbehoefte (gemeten met de Spanningsbehoeftelijst; Feij & van Zuilen, 1984) van invloed zijn op de relatieve invloed van genen en omgeving op individuele verschillen in algemeen cognitief functioneren. Het bleek dat zowel het meemaken van levensgebeurtenissen als de mate van spanningsbehoefte van invloed zijn op de mate waarin genen en omgevingsfactoren individuele verschillen in algemeen cognitief functioneren verklaren. De relatieve genetische invloed is veel kleiner bij mensen die met pensioen zijn in vergelijking met mensen die nog niet met pensioen zijn. Relatieve invloeden van gedeelde omgevingsfactoren zijn echter juist van groter belang bij mensen die met pensioen zijn. Schattingen van de relatieve invloed van genen liepen van 32% tot boven de 90%, afhankelijk van de levensgebeurtenis. De relatieve genetische invloed neemt ook af bij mensen met een zeer hoge spanningsbehoefte (schattingen liepen van 16% tot 98%), terwijl de relatieve invloed van de unieke omgeving bij deze mensen juist heel groot is (schattingen liepen van 2% tot 84%). Het gegeven dat de relatieve invloed van genen en omgevingsfactoren afhankelijk is van blootstelling aan verschillende

omgevingsfactoren, zou van belang kunnen blijken te zijn in de zoektocht naar de daadwerkelijke genen die ten grondlag liggen aan individuele verschillen in cognitie.

In hoofdstuk 9 hebben we op basis van vragenlijstgegevens van adolescente tweelingen bestudeerd wat de relatieve invloed van genen en omgevingsfactoren is op individuele verschillen prestatie op een normaal niveau en op prestatie op een zeer hoog niveau. De tweelingen werd gevraagd aan te geven hoe goed hun prestatie was in vergelijking met andere mensen op intellectueel, kunstzinnig en sportieve vlak. De resultaten lieten zien dat genetische factoren een groot deel van de individuele verschillen in prestatie op een normaal niveau bepalen (schattingen lopen van 32% tot 71%) en dat dit aandeel nog groter is als prestatie op een normaal niveau vergeleken wordt met prestatie op een uitzonderlijk hoog niveau (schattingen lopen van 50% tot 92%).

Uit de onderzoeken gebundeld in dit proefschrift blijkt dat de welbekende grote invloed van additieve genetische factoren (~80%) deels wordt verklaard door complexe processen zoals actieve partner selectie, genetische dominantie, en het samenspel van genen en omgevingsfactoren.

Deze uitkomsten kunnen van groot belang zijn voor toekomstige studies naar individuele verschillen in algemeen cognitief functioneren. De substantiële invloed van genetische factoren suggereert dat er specifieke genen zijn die individuele verschillen in algemene cognitieve vaardigheden verklaren. De zoektocht naar deze genen is echter veel moeilijker dan gedacht; de genen die tot nu toe zijn gevonden bepalen maar een heel klein deel van de genetische variantie. Mogelijk zal het complexe samenspel tussen genen en omgeving een deel van deze niet-verklaarde variante bepalen. De resultaten van die zijn beschreven in dit proefschrift laten zien dat genetische invloeden en

omgevingsinvloeden niet onafhankelijk zijn van elkaar. Bij de zoektocht naar oorzaken van individuele verschillen in algemene cognitieve vaardigheden zullen onderzoekers zich daarom meer moeten richten op het samenspel van deze twee componenten.

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Dutch summary

De onderzoeken beschreven in dit proefschrift zijn onderdeel van een grootschalig onderzoek naar individuele verschillen in algemene cognitieve vaardigheden. Algemene cognitieve vaardigheden is een verzamelnaam voor concentratie, geheugen, redeneren en denkvermogen. Het is al lange tijd bekend dat een belangrijk deel van de verschillen tussen mensen in algemene cognitieve vaardigheiden wordt verklaard door verschillen tussen mensen op genetisch niveau. Bij kinderen op de leeftijd van 5 jaar verklaren genen ongeveer een kwart van de geobserveerde individuele verschillen, bij kinderen van 10 jaar oud is dit ongeveer twee keer zo veel. De invloed van genen stijgt verder tot ongeveer het 18^e levensjaar (80%), waarna de invloed van genen ongeveer stabiel blijft.

Deze gegevens zijn gebaseerd op een groot aantal tweelingstudies. Met behulp van tweelingstudies kan op basis van de gelijkenis van eeneiige tweelingparen en de gelijkenis van twee-eiige tweelingparen een uitspraak worden gedaan over de mate waarin geobserveerde verschillen tussen mensen kunnen worden verklaard door genen of door omgevingsinvloeden. Hierbij worden twee typen omgevingsinvloeden onderscheiden: omgevingsinvloeden die een individu deelt met zijn of haar familieleden, de *gedeelde omgeving* (bijvoorbeeld dezelfde woonomgeving, dezelfde opvoeding) en omgevingsinvloeden die een individu niet deelt met zijn of haar familieleden, de *unieke omgeving* (bijvoorbeeld eigen vrienden, eigen hobby's).

Eeneiige tweelingen zijn genetisch identiek, twee-eiige tweelingen daarentegen, delen gemiddeld de helft van hun genetisch materiaal. Per definitie delen zowel eeneiige als twee-eiige tweelingen 100% van hun gedeelde omgeving en delen zij niets van hun unieke omgeving. Uit tweelingonderzoek naar individuele verschillen in algemene cognitieve vaardigheden blijkt dat de scores op een intelligentietest van twee leden van een eeneiig tweelingpaar over het algemeen veel dichter bij elkaar liggen dan scores van twee leden van een twee-eiige tweelingpaar. Met de kennis die we hebben over de mate van genetische gelijkenis tussen eeneiige en twee-eiige tweelingparen, kunnen we berekenen in hoeverre verschillen in scores op een intelligentietest kunnen worden toegeschreven aan genetische invloeden, gedeelde omgevingsinvloeden en unieke omgevingsinvloeden.

Afgezien van de schat aan informatie die klassieke tweelingmodellen heeft opgeleverd is het mogelijk dat schattingen voor bepaalde eigenschappen, waaronder algemene cognitieve vaardigheden, vervormd zijn omdat voldaan is aan bepaalde aannamen van het klassieke tweelingmodel. Ten eerste wordt er aangenomen dat partners elkaar willekeurig uitkiezen terwijl onderzoek heeft aangetoond dat partners elkaar selecteren op basis van enigszins vergelijkbare cognitieve vaardigheden. In de literatuur worden er twee processen genoemd die ten grondslag kunnen liggen aan deze partner selectie: sociale homogeniteit en actieve partner selectie op basis van het fenotype. Bij sociale homogeniteit ontmoeten partners elkaar in een omgeving die correleert met algemene cognitieve vaardigheden. In het geval van actieve partner selectie zoeken partners elkaar uit op basis van geobserveerde gelijkenis. Ten tweede wordt in de klassieke tweeling methode de gelijkenis die ouders en kinderen vertonen volledig toegeschreven aan het gegeven dat zij gemiddeld 50% van hun genetisch materiaal delen, terwijl invloeden van bijvoorbeeld opvoeding worden verwaarloosd. Ten derde wordt aangenomen dat de invloed van genetische effecten en omgevingseffecten additief zijn. Het is echter mogelijk dat genetische effecten en omgevingseffecten elkaar beïnvloeden en dat dit samenspel

van invloed is op individuele verschillen in algemene cognitieve vaardigheden. Zo is het mogelijk dat een bepaald onderwijssysteem niet voor iedereen dezelfde weerslag heeft op cognitieve ontwikkeling, maar dat dit effect afhangt van een bepaalde genetische aanleg van de leerling. In het geval dat deze aannamen niet houdbaar zijn zullen schattingen van de invloed van genen en omgeving zoals verkregen in een klassieke tweelingstudie mogelijk niet accuraat zijn.

Om een beter beeld te krijgen van de mate waarin genetische invloeden en omgevingsinvloeden de verschillen tussen mensen in algemeen cognitief functioneren bepalen, zijn data verzameld in een grote groep tweelingen en hun broers en zussen, partners, en ouders of kinderen. Al deze mensen hebben een aantal cognitieve taken uitgevoerd, waaronder een IQ test (Wechsler, 1997). Daarnaast hebben zij de Levens Ervaringen Lijst (LEL) ingevuld. In deze lijst worden vragen gesteld over verscheidene omgevingsfactoren die van invloed kunnen zijn, of zijn geweest, op cognitieve ontwikkeling, zoals type school of soort werk, het bespelen van een muziekinstrument, of het beoefenen van een sport.

Deze gegevens maakten het mogelijk te onderzoeken in hoeverre processen als actieve partnerselectie en het samenspel tussen genen en omgeving verklaren waarom mensen van elkaar verschillen in algemene cognitieve vaardigheden.

In het eerste empirische hoofdstuk van dit proefschrift (hoofdstuk 3) zijn IQ-scores geanalyseerd van tweelingen en hun familieleden. De aanwezigheid van partners en ouders maakte het mogelijk om te onderzoeken in hoeverre partners gelijkenis vertonen in algemene cognitieve vaardigheden, de aanwezigheid van ouders maakte het tevens mogelijk om invloeden van genetische dominantie te schatten. Dominantie is de genetische invloed die ontstaat door interactie tussen allelen van een gen. We vonden, zoals al in eerdere studies is aangetoond, dat IQ scores van partners inderdaad enigszins op elkaar lijken. Het was echter moeilijk statistisch onderscheid te maken tussen de twee onderliggende processen: sociale homogeniteit en actieve partner selectie. Een model waarin actieve partner selectie het onderliggende proces was leek net iets beter te passen bij de geobserveerde data. Daarnaast lieten de analyses zien dat als je deze gelijkenis door actieve partner selectie mee modelleert, dat behalve additieve genetische factoren (de genetische invloed die ontstaat door een optelsom van het effect van beide allelen van een gen) en unieke omgevingsfactoren, ook genetische dominantie van belang is. Deze resultaten laten zien dat in voorgaande klassieke tweelingstudies de invloed van genetische dominantie in volwassenen is onderschat. Additieve genetische factoren verklaren 44%, genetische dominantie 27%, actieve partner selectie 11% en unieke omgevingsfactoren verklaren 18% van de geobserveerde individuele verschillen in algemene cognitieve vaardigheiden.

Van factoren zoals opleiding, opvoeding en levensgebeurtenissen die mogelijk verband hebben met algemeen cognitief functioneren wordt over het algemeen gezegd dat ze kunnen worden toegeschreven aan de 'omgeving'. Om te toetsen of dit ook werkelijk 'omgeving' is hebben we in hoofdstuk 4 gekeken in hoeverre genetische factoren van invloed zijn op de mate waarin mensen blootgesteld worden aan deze omgevingsfactoren. Hierbij hebben we ons gericht op vier domeinen: omgeving in de kindertijd, sociale omgeving en gedrag, vrijetijdsbesteding, en belangrijke levensgebeurtenissen (zoals geboorte

van een kind, of het verlies van een familielid of dierbare). Het blijkt dat geobserveerde verschillen in de mate waarin mensen blootgesteld worden aan deze omgevingsfactoren, gemiddeld voor bijna de helft (49%) wordt verklaard door genetische factoren. Genetische factoren verklaren gemiddeld 66% van de individuele verschillen in blootstelling aan omgevingsfactoren in de kindertijd, voor vrijetijdsbesteding gemiddeld 52%, voor sociale omgeving en gedrag 36%, en voor levensgebeurtenissen 29%. Dit betekent dat invloeden die over het algemeen puur worden toegeschreven aan de omgeving, voor een deel kunnen worden toegeschreven aan verschillen op genetisch niveau. Het is mogelijk dat mensen actief hun omgeving uitzoeken op basis van hun genotype; mensen die makkelijk leren zullen bijvoorbeeld vaker naar de bibliotheek gaan of een hoge opleiding volgen dan mensen die minder makkelijk leren. De blootstelling aan opvoeding of onderwijs is daardoor gerelateerd aan genen die van invloed zijn op individuele verschillen in algemene cognitieve vaardigheden.

In hoofdstuk 5 hebben we bestudeerd in hoeverre de Prestatie Motivatie Test (Hermans, 2004) dezelfde latente factoren meet bij mannen en bij vrouwen. In de LEL zijn twee subschalen van de Prestatie Motivatie Test opgenomen, de Academische Prestatie Motivatie schaal en de Algemene Prestatie Motivatie schaal. Het bleek dat vijf van de 28 vragen sekse-bias lieten zien, wat betekent dat de scores van mannen en vrouwen op deze vragen niet direct vergelijkbaar zijn. In vervolganalyses waarin de Prestatie Motivatie Test een rol speelde, zijn deze vragen verwijderd. Tevens vonden we dat mannen en vrouwen gemiddeld verschillend scoorden op sommige onderliggende factoren van de beide schalen. Bijvoorbeeld, vrouwen gaven aan minder toekomstgericht te zijn dan mannen, terwijl vrouwen op school meer toewijding aan de dag legden met betrekking tot hun schoolwerk.

In hoofdstuk 6 is onderzocht in hoeverre genetische factoren en omgevingsfactoren individuele verschillen in opleidingsniveau verklaren. Hierbij hebben we ook bestudeerd of de invloed van deze factoren afhangt van het niveau van algemeen cognitief functioneren en/of van het niveau van academische prestatie motivatie. Dit onderzoek liet zien dat de relatieve invloed van gedeelde omgevingsfactoren iets groter was voor mensen die laag of juist hoog scoorden op een intelligentietest. Schattingen van de relatieve invloed van gedeelde omgevingsinvloeden liepen van 0% tot 15%. De relatieve invloed van unieke omgevingsfactoren nam behoorlijk toe bij mensen met een hoog opleidingsniveau. Schattingen van de unieke omgevingsinvloeden liepen van 22% tot 58%.

In hoofdstukken 7 en 8 is bestudeerd in hoeverre levensgebeurtenissen (zoals geboorte van een kind, of het verlies van een familielid of dierbare) en spanningsbehoefte (gemeten met de Spanningsbehoeftelijst; Feij & van Zuilen, 1984) van invloed zijn op de relatieve invloed van genen en omgeving op individuele verschillen in algemeen cognitief functioneren. Het bleek dat zowel het meemaken van levensgebeurtenissen als de mate van spanningsbehoefte van invloed zijn op de mate waarin genen en omgevingsfactoren individuele verschillen in algemeen cognitief functioneren verklaren. Bijvoorbeeld, de relatieve genetische invloed is veel kleiner bij mensen die met pensioen zijn in vergelijking met mensen die nog niet met pensioen zijn. Relatieve invloeden van gedeelde omgevingsfactoren zijn echter juist van groter belang bij mensen die met pensioen zijn. Schattingen van de relatieve invloed van genen liepen van 32% tot boven de 90%,

afhankelijk van de levensgebeurtenis. De relatieve genetische invloed neemt ook af bij mensen met een zeer hoge spanningsbehoefte (schattingen liepen van 16% tot 98%), terwijl de relatieve invloed van de unieke omgeving bij deze mensen juist heel groot is (schattingen liepen van 2% tot 84%). Het gegeven dat de relatieve invloed van genen en omgevingsfactoren afhankelijk is van blootstelling aan verschillende omgevingsfactoren, zou van belang kunnen blijken te zijn in de zoektocht naar de daadwerkelijke genen die ten grondslag liggen aan individuele verschillen in cognitie.

In hoofdstuk 9 is op basis van vragenlijstgegevens van adolescente tweelingen bestudeerd wat de relatieve invloed van genen en omgevingsfactoren is op individuele verschillen in prestatie op een normaal niveau en in prestatie op een zeer hoog niveau. De tweelingen werd gevraagd aan te geven hoe goed hun prestatie was in vergelijking met andere mensen op intellectueel, kunstzinnig en sportieve vlak. De resultaten lieten zien dat genetische factoren een groot deel van de individuele verschillen in prestatie op een normaal niveau bepalen (schattingen lopen van 32% tot 71%) en dat dit aandeel nog groter is als prestatie op een normaal niveau vergeleken wordt met prestatie op een uitzonderlijk hoog niveau (schattingen lopen van 50% tot 92%).

Uit de onderzoeken gebundeld in dit proefschrift blijkt dat de welbekende grote invloed van additieve genetische factoren (~80%) deels wordt verklaard door complexe processen zoals actieve partner selectie, genetische dominantie, en het samenspel tussen genen en omgevingsfactoren.

Deze uitkomsten kunnen van groot belang zijn voor toekomstige studies naar individuele verschillen in algemeen cognitief functioneren. De substantiële invloed van genetische factoren suggereert dat er specifieke genen zijn die individuele verschillen in algemene cognitieve vaardigheden verklaren. De zoektocht naar deze genen is echter veel moeilijker dan gedacht; de genen die tot nu toe zijn gevonden bepalen maar een heel klein deel van de genetische variantie. Mogelijk zal het complexe samenspel tussen genen en omgeving een deel van deze niet-verklaarde variante bepalen. De resultaten die zijn beschreven in dit proefschrift laten zien dat genetische invloeden en omgevingsinvloeden niet onafhankelijk zijn van elkaar. Bij de zoektocht naar oorzaken van individuele verschillen in algemene cognitieve vaardigheden zullen onderzoekers zich daarom meer op het samenspel van deze twee componenten moeten richten.

List of publications

ARTICLES AND BOOKCHAPTERS

Vinkhuyzen, AAE., van der Sluis, S., & Posthuma, D. Interaction between experience seeking and genetic and environmental influences underlying general cognitive ability. Under review.

Vinkhuyzen, AAE., van der Sluis, S., Maes, HHM., & Posthuma, D. Reconsidering the heritability of general cognitive ability in adults: taking into account assortative mating and cultural transmission. In revision.

Vinkhuyzen, AAE., van der Sluis, S., & Posthuma, D. Environmental variation in educational attainment is moderated by cognitive ability and by achievement motivation. In revision.

Hoekstra, RA., Vinkhuyzen, AAE., Wheelwright, S., Bartels, M., Boomsma, DI, Baron-Cohen, S., Posthuma, D., & van der Sluis, S. Brief report: the construction and validation of an abridged version of the autism-spectrum quotient (AQ-short). Published online: doi: 10.1007/s10803-010-1073-0.

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Vinkhuyzen, AAE., van der Sluis, S., Maes, HHM., & Posthuma, D. Reconsidering the heritability of general cognitive ability in adults: taking into account assortative mating and cultural transmission. *Behavior Genetics*. In press.

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