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THEME ARTICLE

A Genetic Study on Attention Problems and Academic Skills: Results of a Longitudinal Study in Twins

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Abstract

Objective: Several studies reported a negative association between ADHD symptoms and academic achievement. We investigated the etiology of the association between Attention Problems (AP, one of the core symptoms in ADHD) in early childhood and four academic skills across childhood in a genetically informative design. **Method:** Academic skills (mathematics, spelling, reading and comprehension) were measured with standardized tests performed at school in grade 2, 4, and 6. AP were measured with mother ratings of the Devereux Child Behavior Rating Scale at age 5 and the Child Behavior Checklist at age 7. Subjects were 767 Dutch twins from 445 families. **Results:** AP were negatively associated with most academic skills in each grade, and this association was stable over time. Correlations of AP with mathematics and comprehension were around -0.20, and with spelling around -0.15. Correlations with reading were not significant. A significant genetic correlation (-0.40) between AP and mathematics across time indicated that shared genes play a role for these measures. The genetic correlations of AP with spelling and comprehension (both -0.28, p= 0.09) were non-significant. **Conclusions:** More complex academic skills, requiring higher cognitive processes, like mathematics and comprehension, are especially negatively associated with attention problems. The association between AP and mathematics is partly due to shared genes, while the association with comprehension, and spelling was driven by unique environmental factors.

Key words: *attention problems, ADHD, academic achievement, genetics, children*

Résumé

Objectif: Étudier l'étiologie génétique et environnementale de la concomitance des symptômes du TDAH et des difficultés de lecture dans le plus vaste échantillon étudié à ce jour, en distinguant deux dimensions dans le TDAH et dans la lecture. **Méthodologie:** Analyse des données tirées de l'étude populationnelle Twins Early Development Study portant sur 6 428 paires de jumeaux âgés de 12 ans. Les symptômes du TDAH (type mixte, type inattentif et type hyperactif/impulsif) ont été consignés à partir les notes des parents. La lecture a été évaluée au moyen d'une batterie de tests de compréhension et de décodage. **Résultats:** L'héritabilité est élevée: elle est d'environ 70 % pour les symptômes du TDAH et de 45 à 65 % pour la lecture. Certains gènes identiques affectent le TDAH de type mixte et la lecture, avec une corrélation génétique de—0,31. La constatation la plus notoire a été que la corrélation génétique-lecture était significativement plus élevée dans le type inattentif (- 0,31) que dans le type hyperactif-impulsif (- 0,16), ce qui permet de penser que le recoupement génétique entre le TDAH mixte et la lecture est surtout motivé par l'inattention. En outre, les résultats montrent que le décodage, et non la compréhension, est relié, de manière différentielle, au TDAH (corrélation génétique moins marquée avec le TDAH de type hyperactif-impulsif qu'avec le type inattentif). **Conclusion:** Le recoupement génétique entre le TDAH et la lecture est davantage motivé par l'inattention que par l'hyperactivité-impulsivité.

Mots clés: *étude de jumeaux, TDAH, lecture, compréhension, décodage*

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Attention Deficit/Hyperactivity Disorder (ADHD) is one of the most common childhood developmental disorders, with a prevalence of 8-12% worldwide (Polanczyk et al., 2007). Developmentally inappropriate levels of hyperactive/impulsive behavior and inattentive problems characterize ADHD. It is commonly agreed now that ADHD symptoms are normally distributed in the population with ADHD at the extreme end of this distribution (Levy et al., 1997; Hay et al., 2006; Polderman et al., 2007; Lubke et al., 2009). ADHD is a great burden for affected families; the disorder not only gives rise to significant clinical and psychosocial problems (Mannuzza & Klein, 2000), but is also associated with cognitive problems such as executive functioning deficits (Barkley, 1997; Bidwell et al., 2007; Willcutt et al., 2005a), lower IQ scores (Frazier et al., 2004; Friedman et al., 2007), and academic problems at school (Frazier et al., 2007; Polderman et al., 2010a). Regarding the high prevalence of ADHD and the predictive value of academic achievement for future functioning (Mackenbach et al., 2008) including health (Groot & van den Brink, 2007; Batty et al., 2010), the association between ADHD and academic abilities has been subject to an increasing amount of research in the past decade (for a systematic review, see Polderman et al. 2010a).

In a population sample of almost 700 children, Breslau et al. (2009) assessed academic skills with the Woodcock-Johnson Test of Achievement-Revised (WJ-R) (Woodcock & Johnson, 1990) when they were 17 years old. At the age of 6 years, ADHD characteristics were assessed with the Attention Problem scale (AP) of the Child Behavior Check List (CBCL) (Achenbach, 1991a) and Teacher Report Form (TRF) (Achenbach, 1991b). Measures of AP are often used in population studies and represent important characteristics of ADHD symptoms. Reading and mathematics correlated respectively -0.09 and -0.10 with AP while IQ was included as covariate in the analyses. Duncan et al. (2007) investigated the prospective relation between AP and academic achievement in six population cohorts (n total > 34.000 children). They observed that AP, assessed between ages 4 and 6 with various behavior checklists and raters, significantly predicted lower academic achievement test scores between ages 8 and 14, with correlations of -0.08 and -0.11 for reading and mathematics respectively. The results applied to all cohorts, to boys and girls, and to children from high and low socio-economic backgrounds.

Clinical studies also reported significant differences in academic achievement between ADHD affected children and normal controls. Lee and Hinshaw (2006) studied the association between academic achievement and ADHD in 209 girls (ADHD cases and controls) aged 6 to 13 years old. The Wechsler Individual Achievement test (Wechsler, 1992), assessed five years after the ADHD diagnosis, was used as outcome variable. The results showed a negative association of academic achievement with inattentive symptoms but not with hyperactive/impulsive symptoms after the inclusion of IQ as covariate. In a case-control study by Massetti et al. (2008), DSM diagnoses were assessed in 255 children (80% boys), at age 4 to 6 years old. Eight years later academic achievement was measured with the WJ-R. Also in this study, a negative association was found with inattentive symptoms but not with hyperactive/impulsive symptoms after the inclusion of covariates such as IQ and comorbid disorders.

An important question is which underlying factor explains the association between ADHD symptoms and academic achievement. Twin and family studies enable to investigate whether variation in a trait is driven by genetic or environmental factors, and can also unravel the etiology of covariance between traits (Boomsma et al., 2002a). It is widely established that ADHD is highly heritable (Freitag et al., 2010) with about 75% of the variation explained by genetic factors across childhood. Only a handful of twin studies examined the influence of genetic and environmental factors on academic skills. Bartels et al. (2002a) reported a heritability of 60% for an academic achievement test in a sample of 12-year-old Dutch twins, while a heritability of 70% was found in an Australian sample of 15 to 18 years old twins (Wainwright et al., 2005). For mathematics and reading heritability estimates vary between 19% and 65% in school aged children (Kovas et al., 2007a; Kovas et al., 2007b; Wadsworth et al., 2001; Davis et al., 2008; Hart et al. 2010) to 90% in adolescent twins (Markowitz et al., 2005). The large variation in heritability estimates may reflect an age effect but is probably also due to different measures of academic skills (such as web testing (Davis et al., 2008), teacher ratings (Kovas et al., 2007a), mother ratings (Markowitz et al., 2005), and achievement tests (Hart et al. 2010) across studies. Two older studies showed heritability estimates for spelling around 65% (DeFries et al., 1991; Stevenson et al., 1987), and more recent studies by Friend et al. (2007) and Bates et al. (2007) showed similar results. Genetic influences on comprehension are estimated in the range of 41 to 76% (Harlaar et al., 2007; Keenan et al., 2006; Betjemann et al., 2008).

Twin studies that investigated the etiology of the association between AP and cognitive problems have mostly focused on IQ so far. Results showed that the negative relation between AP and IQ at age 5 (Kuntsi et al., 2004), age 9, and age 12 (Polderman et al., 2009b) was influenced by a shared genetic factor. In addition, Polderman et al. (2006a) found that a prospective relation between early AP (i.e., at age 5) and IQ performance at age 12 was also explained by genetic factors. This means that partly the same genes have an influence on IQ performance and on AP, indicating a shared underlying biological mechanism. Regarding the genetic correlations that were found between IQ and AP and the fact that IQ and academic achievement are genetically correlated, (Bartels et al., 2002a) one would expect that AP and academic achievement share genetic factors as well.

In a recent study Hart et al. (2010) investigated the etiology of ADHD symptoms and reading and mathematics performance in a sample of 10-year-old twins. Their outcomes suggested that the associations among measures were influenced by both genetic and shared environmental factors.

In the current study, we aim to investigate the genetic architecture of the association between AP and academic achievement over time. We used data of AP assessed at age 5 and age 7, and academic achievement in grade 2 (age 8), 4 (age 10) and 6 (age 12) of the primary school. We distinguished four academic skills, namely reading, mathematics, comprehension and spelling because the association between AP and academic achievement may vary across skills. In addition, we examined the genetic factor structure within the academic skills over time and modeled this as such in the analyses with AP. We used data of 445 twin families that were followed longitudinally. Mother ratings of AP were assessed with the Devereux Child Behavior Rating Scale (Spivack & Spotts, 1966) at age 5, and with the CBCL at age 7. Academic skills in grade 2, 4 and 6 were measured with standardized tests assessed at school.

Methods

Participants and Procedure

All twins were registered with the Netherlands Twin Register (NTR), established in 1986 by the Department of Biological Psychology at the VU University in Amsterdam (Boomsma et al., 2002b). Parents of the twins completed behavior questionnaires when twins were 1, 2, 3, 5, 7, 10 and 12 years old (Bartels et al., 2007). Behavioral data on AP at age 5 were adapted from the Attention Problem scale (five items) of the Devereux Child Behavior Rating Scale (DCB, Spivack & Spotts, 1966), filled in by the mother. Mothers are instructed to rate the severity of their child's behavior over the last six months on a 5-point scale. The DCB is described in detail by Van Beijsterveldt et al. (2004). At age 7, maternal ratings of AP were collected with the Child Behavior Checklist (CBCL) (Achenbach, 1991a). The Attention Problem scale of the CBCL consists of 11 items that are rated on a 3 point scale (not true; somewhat or sometimes true; very true or often true). The two week test-retest correlation and the internal consistency of this scale at age 7 are 0.83 and 0.67, respectively (Verhulst et al., 1996).

About 95% of all schools in the Netherlands use the Pupil Monitoring System (PMS) to track the academic development of their pupils. Schools are free to use the PMS, and are free in their choice of tests they want to use. PMS tests are administered at fixed time points (i.e., beginning, half way, and/or end of the school year) in each grade.

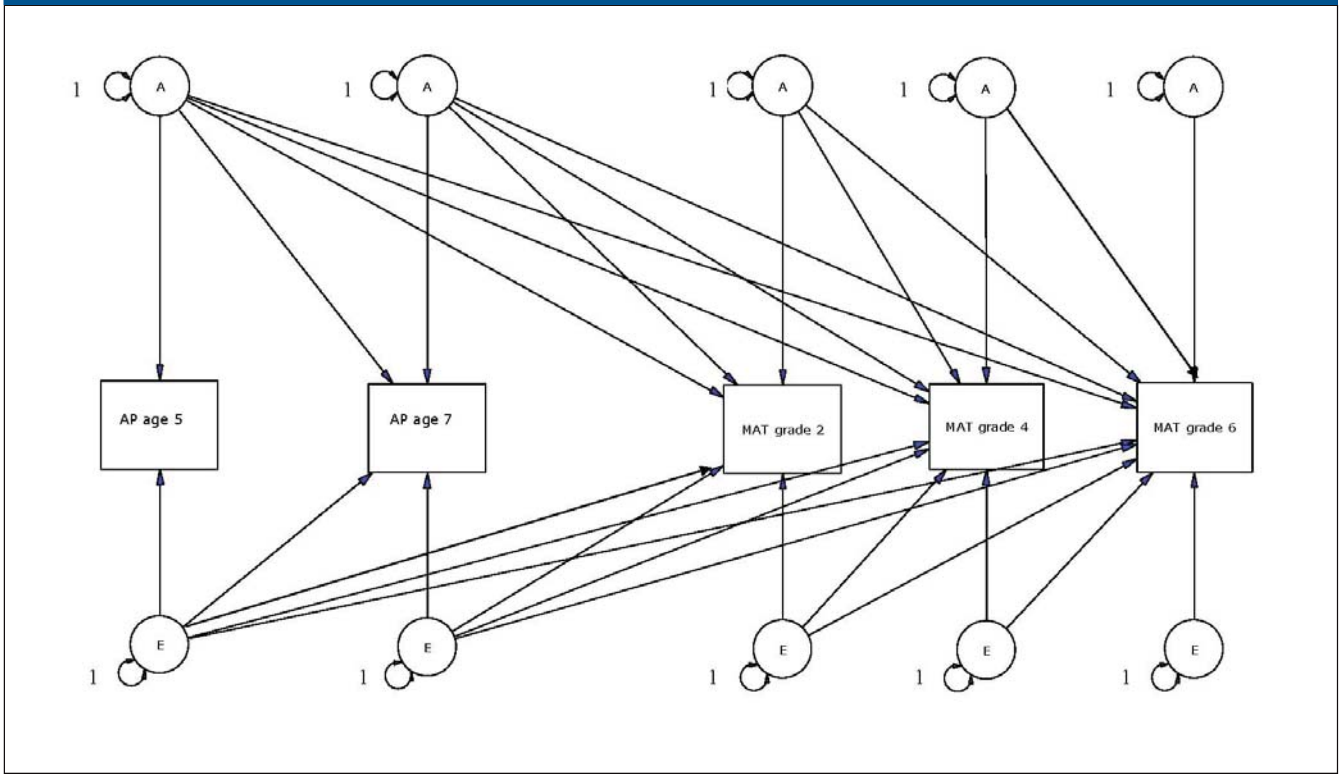
For the current study PMS data were collected in 2008 and 2009 as part of the ongoing survey study of the NTR in 12-years-old twins. After parental consent teachers are invited to complete a Teacher Report Form (TRF), and to provide all available PMS data of the complete primary school period. For the current analyses, we used PMS data, delivered by the schools, obtained half way the school year, on reading comprehension (COM, grade 4 and 6; not many data were available for grade 2, probably because children at that point are still learning how to read, and less attention is paid to comprehension), mathematics (MAT, grade 2, 4 and 6), word reading (READ, grade 2 and 4; not many data were available for grade 6, probably because it is assumed that the level of reading at that point is sufficient), and spelling (SPEL, grade 2, 4 and 6). The choice of academic skills was based on a pilot study in which teachers indicated that these tests were most informative about the cognitive development of pupils (Polderman et al., 2009a).

For COM children had to read short texts and answer related questions, or fill in certain parts of the text themselves, individually without particular time limits. This test measures the capability to interpret and process information from a text read out. MAT included a dictation in which children had to solve simple MAT problems within a short time, and more complex problems that children had to solve individually without particular time limits. The READ score was comprised by the total amount of words children could read aloud (correct) in 3 minutes. SPEL was administered by a dictation in which children had to write down separate words within a certain time limit.

Covariates

We tested whether sex and socio economic status (SES) had a main effect on the mean scores. Boys tend to have more AP than girls (Derks et al., 2007; Rietveld et al., 2003). Furthermore, reading deficits (Rutter et al., 2004; Berninger et al., 2008) and verbal fluency problems (Berninger & Fuller, 1992) are more common in boys than in girls. Second, children from low-income families enter school with lower mean academic skills and this gap might increase during childhood

Figure 1. The Cholesky model with Attention Problems (AP) and mathematics (MAT) as example measures. Observed measures are shown in squares and latent variables in circles. The figure includes latent genetic factors (A) and latent unique environmental factors (E). Latent shared environmental factors (C) follow the same factor structure but are not shown for the sake of clarity.



(Miech et al., 2001). Also, several studies showed a moderating effect of SES on the association between AP and academic achievement (Polderman et al., 2010a).

Data on Socio Economic Status (SES) were collected from surveys mailed out when the twins were 3, 7 and 10 years old. Since SES scores between age 3, 7 and 10 correlated highly (varying from 0.70 to 0.78), we used the SES score of age 7 when age 10 was not available and the SES score of age 3 when scores at age 7 and 10 were not available. SES was based on a full description of the occupation of the parents and classified using a 5-point scale (1=lowest, 5=highest), according to the system used by Statistics Netherlands (Fengler et al., 1997). For the SES assessment at age 10 the EPG-classification scheme was used (Erikson et al., 1979) in combination with information on parental education. In both cases the highest SES score of the two parents determined the SES of the twin pair. The distribution of SES (from low to high) was 1%, 17%, 49%, 20% and 13%.

Included subjects

The response rate of parental consents for the TRF, including PMS measures, was 50% in 2008 and 37% in 2009. For the TRF the response rate was 43% in 2008 and 57% in 2009. In respectively 92% and 95% of completed TRFs a PMS form was included. This resulted in one or more PMS data points of 845 subjects. Five subjects were excluded because of handicap or severe illness, and of 68 subjects no information on SES was available resulting in 767 included subjects. Of these subjects, AP data were present for 683 subjects at age 5 and for 672 subjects at age 7.

The number of subjects and the number of complete twin pairs differed per measure (see Table 1 and Table 2) because the number of assessed PMS measures differed per school and grade. In addition, about 50% of the twin pairs did not share the same classroom. It is reported that this has no effect on their cognitive performance (Polderman et al., 2010a).

Included subjects came from 445 twin families with the following zygosity distribution: 172 monozygotic (MZ) and 273 dizygotic (DZ) pairs, of which 124 pairs were of opposite sex.

Zygosity of same sex twin pairs was determined by DNA or blood group polymorphisms for 41 pairs. For 280 pairs zygosity was based on questionnaire items; zygosity determination using this questionnaire is 93% accurate (Rietveld et al., 2000).

Analyses

Data analyses were performed in the structural equation modeling program Mx (Neale et al., 2006). Mx provides parameter estimates by maximizing the raw data likelihood, so that all available data, also when some observations for subjects are missing, can be included. Estimates of means, variances and correlations were obtained from a so-called saturated model. This is a fully parameterized model in which the covariance structure among relatives is allowed to take any value, and is not modeled as a function of latent traits such as genetic and environmental factors. Correlations were estimated between traits (phenotypic correlations), and between twins per trait (twin correlations). Correlations between phenotypes were constrained to be equal across zygosity, and first and second born twins. We tested per phenotype if means and variances were equal between MZ and DZ twins and we tested whether the covariates gender and SES had a significant effect on the means.

Nested models were evaluated by hierarchic likelihood ratio (χ^2) tests. The χ^2 statistic is computed by taking twice the difference between the log-likelihood of the fully saturated model and the log-likelihood of a sub model with certain constraints, for example with the constraint that SES has no influence on the mean of AP at age 5. The associated degrees of freedom are computed as the difference in degrees of freedom between the two hierarchic models (Rijsdijk, 2007).

Twin method

Information of MZ and DZ twins is used to decompose the variance of a trait, as well as the covariance between traits, into additive genetic influences (A), environmental influences that are shared among family members (C), and environmental influences that are unique for a person (E). A first impression of the relative importance of genetic and environmental influences on phenotypic trait variance is obtained by inspecting the (intra pair) MZ correlations and DZ correlations. MZ twins share all their genes while DZ twins share on average half of their segregating genes. All twins grew up in the same family, and thus share their family environment. Therefore, MZ correlations twice as high as DZ correlations indicate additive genetic influences. DZ correlations higher than half the MZ correlations designate shared environmental influences, while MZ correlations that are of similar magnitude as DZ correlations indicate that only environmental influences play a role (Boomsma et al., 2002a).

Table 1. Numbers, and observed means and variances of AP at age 5 and at age 7, and PMS data in grade 2, 4 and 6

	n	mean	sd
AP age 5	683	11.63	3.42
AP age 7	672	2.58	2.67
COM 4	622	41.17	14.25
COM 6	493	62.17	16.63
MAT 2	558	70.67	13.28
MAT 4	580	96.18	12.42
MAT 6	412	119.34	12.54
READ 2	391	44.77	20.38
READ 4	393	74.21	17.55
SPEL 2	558	119.69	7.89
SPEL 4	630	136.87	7.22
SPEL 6	466	149.68	8.25

Note: AP= Attention Problems; COM= Comprehension; MAT= Mathematics; READ= Reading; SPEL= Spelling

Genetic analyses

A decomposition of the phenotypic matrix into genetic (A) and environmental (C,E) covariance matrices was considered by means of Cholesky decomposition with four observed variables (i.e., AP at age 5 and age 7 and COM grade 4 and grade 6; AP at age 5 and age 7 and READ grade 2 and grade 4) or with five variables (i.e., AP at age 5 and age 7 and MAT grade 2, 4 and 6; AP at age 5 and 7 and SPEL grade 2, 4 and 6). An example of the 5-variate Cholesky decomposition is shown in Figure 1. Since a Cholesky decomposition is fully parameterized and gives the best possible fit to the data, it serves as a reference model to evaluate the fit of more constrained models. First, AE and CE models were fitted. E includes measurement error and is therefore always included in the models. Second, genetic and environmental covariance patterns were inspected to see whether these indicated a more constrained factor model.

As the power to detect effects of covariates on the variance decomposition was rather low with the current sample size (Polderman et al., 2006b), SES was not included as

Table 2. Left part: Estimated phenotypic correlations of AP at age 5 and 7 with PMS measures in grade 2, 4 and 6 including confidence intervals Right part: Estimated MZ and DZ twin correlations of AP at age 5 and 7 and of PMS data in grade 2, 4 and 6 including confidence intervals

	r with AP5 (n twins)	*r* with AP7 (n twins)	MZ (n complete pairs)	DZ (n complete pairs)
AP age 5			0.61 (116) .48 -.70	0.16 (174) .02 -.29
AP age 7	0.39 (615) .31 -.46		0.66 (118) .55 -.74	0.30 (166) .16 -.43
COM 4	-0.17 (559) -.08—.25	-0.10 (544) -.01—.20	0.66 (104) .56 -.74	0.40 (149) .26 -.52
COM 6	-0.23 (435) -.13—.32	-0.22 (428) -.12—.32	0.68 (88) .56 -.76	0.37 (105) .21 -.50
MAT 2	-0.18 (493) -.09—.27	-0.17 (479) -.08—.26	0.67 (91) .54 -.75	0.42 (141) .28 -.55
MAT 4	-0.22 (517) -.13—.30	-0.23 (497) -.14—.32	0.63 (97) .51 -.73	0.43 (145) .28 -.55
MAT 6	-0.17 (367) -.07—.26	-0.17 (357) -.06—.28	0.71 (76) .57 -.80	0.43 (92) .27 -.56
READ 2	-0.09 (358) .00—0.19	-0.11 (335) .00—.22		
READ 4	-0.11 (352) .00—.21	-0.05 (330) .00—.16		
SPEL 2	-0.14 (494) -.05—.23	-0.14 (484) -.05—.23	0.48 (87) .33 -.61	0.32 (140) .15 -.46
SPEL 4	-0.13 (560) -.05—.22	-0.09 (550) .00—.18	0.59 (107) .47 -.68	0.30 (155) .15 -.44
SPEL 6	-0.07 (411) .00—.19	-0.15 (407) -.04—.25	0.74 (86) .62 -.81	0.61 (98) .44—.72

Note: AP= Attention Problems; COM= Comprehension; MAT= Mathematics; READ= Reading; SPEL= Spelling

moderating effect on the variance components and male and female data were combined for both zygosities.

Results

Descriptives

Table 1 summarizes the descriptive statistics of AP at age 5 and age 7 and reading, mathematics, comprehension and spelling in grade 2, 4 and 6. PMS scores lower or higher than four SD from the mean were coded as missing (COM 6 n=1; MAT 2 n=2; MAT 4 n=3, MAT 6 n=4; SPEL 2 n=17; SPEL 4 n=17; SPEL 6 n=15).

Sex had a significant main effect on AP at age 5 and age 7 (boys having more AP), on MAT and COM in all grades (boys having higher scores), on READ in grade 4 (boys having lower scores), but not in grade 2, and on SPEL in grade 2 and 4 (boys having lower scores), but not in grade 6. SES had significant effects on AP at age 5 and age 7, COM and MAT, across grades, but not on READ and SPEL (except for SPEL in grade 6). Higher SES was associated with less AP, and

Table 3. Left part: Relative contributions of additive genetic (A), common environmental (C) and unique environmental (E) variance to Attention Problems (AP) at age 5, and at age 7, Comprehension (COM), Mathematics (MAT), Reading (READ), and Spelling (SPEL) across grades Right part: genetic (rg) and unique environmental (re) correlations among AP at age 5 and at age 7 and each PMS measure across grades

	A	C	E	r^{g} / re with AP5	r^{g} / re with AP7	r^{g} / re	r^{g} / re
AP5	57	0	43				
AP 7	62	3	35	0.60 / 0.15		COM 4	
COM 4	54	13	33	-0.11 / -0.13	-0.18 / -0.07		
COM 6	62	6	32	-0.42 / 0.07	-0.22 / -0.14	0.94 / 0.12	
						MAT 2	MAT 4
MAT 2	51	17	31	-0.20 / -0.09	-0.29 / -0.06		
MAT 4	45	20	34	-0.38 / -0.07	-0.28 / 0.04	0.95 / 0.20	
MAT 6	52	18	29	-0.19 / -0.16	-0.16 / -0.07	0.44 / 0.39	0.66 / 0.63
						SPEL 2	SPEL 4
SPEL 2	29	19	52	-0.18 / -0.10	-0.47 / -0.08		
SPEL 4	50	10	40	-0.22 / -0.01	-0.28 / 0.03	0.93 / 0.31	
SPEL 6	38	38	24	-0.18 / 0.09	-0.35 / 0.01	0.94 / 0.01	0.99 / -0.03

higher PMS scores. Significant covariates were included in the subsequent genetic analyses as fixed effects on the means.

Phenotypic correlations

Table 2 (left part) shows the phenotypic correlations between AP at age 5 and at age 7, and PMS data. Noteworthy is that the correlations with AP do not vary much across grades (within academic skills); in other words, the correlation between AP and academic skills seems rather robust over time. For instance, correlations of AP at age 5 and 7 with MAT in grade 2, 4 and 6 vary between 0.17 and 0.23. The correlations with READ were all non-significant and therefore READ was excluded from the genetic analyses.

Scores across grades within academic skills correlated moderate to high: for COM grade 4-6 this was 0.59, and for READ grade 2-4 this was 0.69. Correlations within MAT varied between 0.50 and 0.71 and within SPEL between 0.35 and 0.61 across grades (not in Table).

Twin correlations

The right part of Table 2 presents the twin correlations of AP and PMS measures. MZ correlations were higher than DZ correlations for AP and all PMS measures, indicating that genetic influences play a role in AP at ages 5 and 7 and in PMS measures across grades. As for academic skills the DZ correlations were not half the MZ correlations, it is suggested that common environmental influences might also play a role here.

Heritability estimates

Relative estimates of genetic (A), common environmental (C) and unique environmental (E) variances, based on the Cholesky model, are shown in the left part of Table 3. Individual differences in all measures were for the largest part explained by genetic influences. Common environmental influences were moderate for the academic skills but absent for AP.

The fit statistics in Table 5 show that models with common environmental influences (C) for the academic skills fitted the data well, but it was also allowed to drop the total variance and covariance of C. It was not allowed to drop the variance and covariance of A. Therefore we continued the analyses without C in the models.

Genetic associations

Inspection of the genetic and unique environmental correlations between measures (see the right part of Table 3) showed that genetic correlations were high within academic skills across grades, and between both AP measures, but low between AP and PMS measures. This suggested that the genetic variance could be constrained to two factors, one for AP and one for PMS. Since we were interested in the genetic association between AP and academic measures, these latent

Table 4. Model fitting results of multivariate genetic analyses for Attention Problems (AP) at age 5 and at age 7, Comprehension (COM), Mathematics (MAT), and Spelling (SPEL), across grades

	-2 LL	X2	df	p	r
COM					
ACE	15406.247				
CE	15350.153	56.094	10	0.000	
AE	15408.848	2.601	10	0.989	
2 factor model					
r free	15418.166	11.919	13	0.534	-0.28
r = 0	15427.412	21.165	14	0.097	
r = 1	15441.789	35.542	14	0.000	
MAT					
ACE	18116.007				
CE	18176.047	60.040	15	0.000	
AE	18128.208	12.201	15	0.664	
2 factor model					
r free	18141.068	25.061	22	0.294	-0.40
r = 0	18161.127	45.120	23	0.003	
r = 1	18182.685	66.676	23	0.000	
SPEL					
ACE	17509.073				
CE	17454.409	54.664	15	0.000	
AE	17516.467	7.394	15	0.946	
2 factor model					
r free	17530.806	21.733	22	0.536	-0.28
r = 0	17541.518	32.445	23	0.091	
r = 1	17569.775	60.702	23	0.000	

Note: Constrained models were compared to Cholesky model; A = additive genetic factors, C = common environmental factors, E = unique environmental factors; r = correlation between the latent genetic factors

genetic factors were allowed to correlate, while uncorrelated genetic factors were represented by genetic factors that were specific for each measure. For the purpose of model identification factor loadings for each genetic factor were set equal. Unique environmental correlations between AP measures and between AP and PMS measures were low; therefore the Cholesky decomposition was kept for the latent factors of E. In Figure 2 an example of this so called correlated factor model is given.

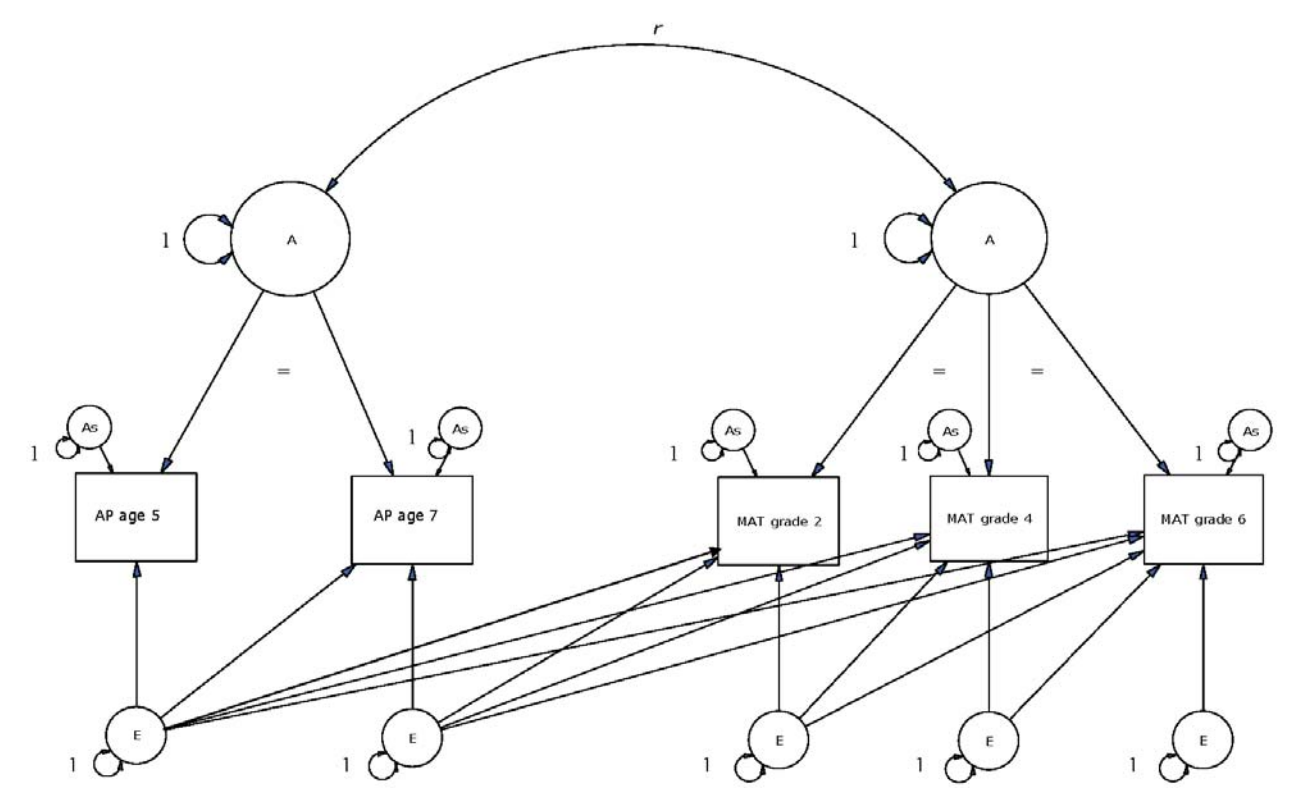
Table 4 shows that the correlated factor model fitted the data well for each academic skill. A significant correlation between the genetic latent factors was found for AP and MAT (r = -0.40). The genetic correlation between AP and COM, and between AP and SPEL was estimated as -0.28, and non-significant. Thus, for these academic skills unique environmental factors explained the association with AP.

Specific genetic factor loadings were significant for AP at age 5 and at age 7. Measurement specific genetic factor loadings for COM, MAT, and SPEL of grade 4, as well as SPEL of grade 2 were non-significant.

Discussion

Previous studies reported a negative association between ADHD related symptoms and academic achievement (for reviews see Frazier et al. (2007) and Polderman et al. (2010a)). Children with ADHD performed worse on academic achievement tests, completed fewer years of education, had a lower grade point average, or more often failed to

Figure 2. The correlated factor model with ADHD symptoms (AP) and mathematics (MAT) as example measures. Observed measures are shown in squares and latent variables in circles. The figure includes latent genetic factors (A) that are allowed to correlate (r), measurement specific latent genetic factors (As), and latent unique environmental factors (E).



complete high school. In the current study we investigated the phenotypic association between Attention Problems (AP) and four academic skills, as well as the etiology of these associations in a longitudinal design.

Our phenotypic analyses confirmed previous work with a negative association between AP at age 5 and 7 and academic skills later in life. Notable was the similar pattern of correlations between AP at age 5 and 7 and each academic skill across grades. These patterns show that the association between AP and academic skills is rather robust over time and that the association is already established at the age of 5.

The strongest associations between AP and academic skills were found for MAT and COM. This may be because READ and SPEL are based on automatized processes and fluency rather than complex cognitive abilities (Schatschneider et al., 2002). Moreover, the way READ and SPEL were measured in this study (i.e., with dictations) demand less attention and concentration. Solving a difficult mathematic problem or interpreting a complicated text relies on higher cognitive processes, and will subsequently require much attentional skills and concentration. In line with this, correlations between AP and IQ are consistently higher, around -0.30 across childhood (Kuntsi et al., 2004; Polderman et al., 2006a; Polderman et al., 2009b). However, a number of clinical studies reported an association between ADHD and Reading Disabilities (Willcutt et al., 2005b; de Jong et al., 2009; Willcutt & Pennington, 2000). In addition, Hart et al. (2010) found correlations around -0.30 between reading and ADHD symptoms.

It is widely established that heritabilities of AP are moderate to high and very stable across childhood (Rietveld et al., 2004; Larsson et al., 2004) and the current estimates of around 60% confirm these previous findings. Genetic studies on academic skills are rather limited so far, especially for spelling and comprehension. A strength of the current study is that we present estimates of longitudinal data based on the same standardized tests across time. In general, our estimates of genetic and environmental influences for reading and mathematics were similar to those presented in earlier studies. The estimates for common environmental influences were absent for AP, and overall low and non-significant for PMS measures in the multivariate models. However, for instance, for SPEL grade 6 it was estimated at 38%, and for MAT around 18% in the full model. Shared environmental influences on academic skills that have been suggested in the literature are for example impoverished environments, in terms of resources (i.e., low income) or in terms of cognitive stimulation (i.e., low parental education) (Flouri, 2007).

Genetic covariance clustered high within AP measures and within academic skills across grades and to a lesser extent between AP and academic measures. We modelled these covariance patterns by two latent genetic factors (one for AP and one for resp. COM, MAT, and SPEL) that were allowed to correlate. The correlation between the latent genetic factors of AP and MAT was significant, indicating a shared set of genes influencing early AP and mathematic skills later in life.

Neuropsychological theories that addressed the causal mechanisms for ADHD and cognitive impairments point to neurological dysfunctions in prefrontal regions that have an influence on regulatory control (Barkley, 1997; Pennington & Ozonoff, 1996), effort, arousal and motivation (Sergeant, 2000), and learning and conditioning (Sagvolden et al., 2005). Each of these processes might have an effect on academic performance. Several brain imaging studies confirmed that ADHD is associated with abnormalities in prefrontal neural circuits (Durston, 2008; Mulder et al., 2008; Castellanos et al., 2002). Shaw et al. (2006a) reported an association between cognition and the trajectory of cortical development, primarily in frontal regions. In a second study they (2006b) showed that children with ADHD have relative cortical thinning in regions important for attentional control (i.e., medial and superior prefrontal and precentral regions).

Candidate genes having an influence on ADHD and complex cognitive functioning like MAT might be involved in the dopaminergic pathways of the prefrontal cortex. These suggestions are based on studies on general cognitive functioning as so far, no studies focused on ADHD and the association with academic functioning. Mill et al. (2006) reported an association for the DRD4 seven-repeat allele and the DAT1 ten-repeat allele with variation in intelligence among children with ADHD in two independent samples. However, a replication of these findings by Genro et al. (2006) and Sonuga-Barke et al. (2008) failed. Recently, Bellgrove et al.(2009) reported that DAT1 haplotype status predicted spatial reorienting deficits in a sample of 50 ADHD cases and 65 age matched controls. The greatest spatial attention impairments were present in children with ADHD homozygous for the DAT1 haplotype.

The genetic correlation with COM and SPEL was not significant suggesting that unique environmental factors explain the association with AP. As half of the twin pairs in this sample did not share the classroom a unique environmental influence could be school conditions, and particularly the qualification of the teachers. A good teacher achieves a climate in which children are engaged and motivated for learning, leading to positive school adjustments (Greenberg et al., 2003).

This study has some limitations. Because no IQ data were available for the current sample, we could not correct for cognitive differences among subjects. Also the interpretation of the shared genetic risk of AP and MAT is uncertain. However, we included SES in our analyses and the correlation between SES and intelligence is substantial (Deary et al., 2005). A second limitation involves the relatively small sample size of complete twin pairs, especially for the academic skills. This made the power to detect significant effects somewhat limited, although the multivariate design of this study compensated for this. Lastly, the causal relation between AP and academic skills could not be investigated in the current design. An important question is whether biological mechanisms that cause AP also cause academic deficits, or whether this is vice versa. Larger twin samples with longitudinal data can clarify this question.

In summary, our findings add to the growing body of evidence supporting the observation that ADHD symptoms are associated with diminished achievement. More complex academic skills, requiring higher cognitive processes, like mathematics and comprehension, are especially negatively associated with attention problems. Furthermore, our results strengthen the suggestion that the association between ADHD symptoms and educational problems later in life originates in early childhood. We found a genetic overlap between AP and mathematics. Possible biological mechanisms underlying the association may be based in the prefrontal cortex and related dopaminergic brain processes.

Acknowledgements / Conflicts of Interest

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References

Achenbach, T. M. (1991a). *Manual for the Child Behavior Checklist/4-18*. Burlington, VT: University of Vermont, Department of Psychiatry.

Achenbach, T. M. (1991b). *Manual for the Teacher Report Form*. Burlington, VT. University of Vermont, Department of Psychiatry.

Barkley, R. A. (1997). Behavioral inhibition, sustained attention, and executive functions: constructing a unifying theory of ADHD. *Psychological Bulletin, 121,* 65-94.

Bartels, M., Rietveld, M. J., van Baal, G. C., & Boomsma, D. I. (2002a). Heritability of educational achievement in 12-year-olds and the overlap with cognitive ability. *Twin Research, 5,* 544-553.

Bartels, M., Rietveld, M. J. H., van Baal, G. C. M., & Boomsma, D. I. (2002b). Genetic and environmental influences on the development of intelligence. *Behavior Genetics, 32,* 237-249.

Bartels, M., van Beijsterveldt, C. E., Derks, E. M., Stroet, T. M., Polderman, T. J., Hudziak, J. J., et al. (2007). Young Netherlands Twin Register (Y-NTR): a longitudinal multiple informant study of problem behavior. *Twin Research and Human Genetics, 10,* 3-11.

Bates, T. C., Castles, A., Luciano, M., Wright, M. J., Coltheart, M., & Martin, N. G. (2007). Genetic and environmental bases of reading and spelling: A unified genetic dual route model. *Reading and Writing, 20,* 147-171.

Batty, G. D., Kivimaki, M., & Deary, I. J. (2010). Intelligence, education, and mortality. *BMJ, 340,* 563.

Bellgrove, M. A., Johnson, K. A., Barry, E., Mulligan, A., Hawi, Z., Gill, M., et al. (2009). Dopaminergic haplotype as a predictor of spatial inattention in children with attention-deficit/hyperactivity disorder. *Archives of General Psychiatry, 66,* 1135-1142.

Berninger, V. W. & Fuller, F. (1992). Gender Differences in Orthographic, Verbal, and Compositional Fluency: Implications for Assessing Writing Disabilities in Primary Grade Children. *Journal of School Psychology, 30,* 363-382.

Berninger, V. W., Nielsen, K. H., Abbott, R. D., Wijsman, E., & Raskind, W. (2008). Gender differences in severity of writing and reading disabilities. *Journal of School Psychology, 46,* 151-172.

Betjemann, R. S., Willcutt, E. G., Olson, R. K., Keenan, J. M., DeFries, J. C., & Wadsworth, S. J. (2008). Word reading and reading comprehension: stability, overlap and independence. *Reading and Writing, 21,* 539-558.

Bidwell, L. C., Willcutt, E. G., DeFries, J. C., & Pennington, B. F. (2007). Testing for neuropsychological endophenotypes in siblings discordant for attention-deficit/hyperactivity disorder. *Biological Psychiatry, 62,* 991-998.

Boomsma, D., Busjahn, A., & Peltonen, L. (2002a). Classical twin studies and beyond. *Nature Reviews Genetics, 3,* 872-882.

Boomsma, D. I., Vink, J. M., van Beijsterveldt, T. C. E. M., de Geus, E. J. C., Beem, A. L., Mulder, E. J. C. M., et al. (2002b). Netherlands Twin Register: A focus on longitudinal research. *Twin Research, 5,* 401-406.

Breslau, J., Miller, E., Breslau, N., Bohnert, K., Lucia, V., & Schweitzer, J. (2009). The impact of early behavior disturbances on academic achievement in high school. *Pediatrics, 123,* 1472-1476.

Castellanos, F. X., Lee, P. P., Sharp, W., Jeffries, N. O., Greenstein, D. K., Clasen, L. S., et al. (2002). Developmental trajectories of brain volume abnormalities in children and adolescents with attention-deficit/hyperactivity disorder. *JAMA, 288,* 1740-1748.

Davis, O. S. P., Kovas, Y., Harlaar, N., Busfield, P., McMillan, A., Frances, J., et al. (2008). Generalist genes and the Internet generation: etiology of learning abilities by web testing at age 10. *Genes Brain and Behavior, 7,* 455-462.

de Jong, C. G., Van, D., V, Roeyers, H., Raymaekers, R., Oosterlaan, J., & Sergeant, J. A. (2009). How distinctive are ADHD and RD? Results of a double dissociation study. *Journal of Abnormal Child Psychology, 37,* 1007-1017.

Deary, I. J., Taylor, M. D., Hart, C. L., Wilson, V., Smith, G. D., Blane, D., et al. (2005). Intergenerational social mobility and mid-life status attainment: Influences of childhood intelligence, childhood social factors, and education. *Intelligence, 33,* 455-472.

DeFries, J. C., Stevenson, J., Gillis, J. J., & Wadsworth, S. J. (1991). Genetic etiology of spelling deficits in the Colorado and London twin studies of reading disability. *Reading and Writing: An interdisciplinary Journal, 3,* 271-283.

Derks, E. M., Dolan, C. V., Hudziak, J. J., Neale, M. C., & Boomsma, D. I. (2007). Assessment and etiology of attention deficit hyperactivity disorder and oppositional defiant disorder in boys and girls. *Behavior Genetics, 37,* 559-566.

Duncan, G. J., Dowsett, C. J., Claessens, A., Magnuson, K., Huston, A. C., Klebanov, P. et al. (2007). School readiness and later achievement. *Developmental Psychology, 43,* 1428-1446.

Durston, S. (2008). Converging methods in studying attention-deficit/hyperactivity disorder: What can we learn from neuroimaging and genetics? *Development and Psychopathology, 20,* 1133-1143.

Erikson, R., Goldthorpe, J. H., & Portocarero, L. (1979). Intergenerational Class Mobility in 3 Western European Societies - England, France and Sweden. *British Journal of Sociology, 30,* 415-441.

Fengler, M., Joung, I., & Mackenbach, J. P. (1997). Sociaal demongrafische kenmerken en gezondheid: Hun relatief belang en onderlinge relaties (Social demographic characteristics and health: Their relative importance and mutual relations). In J.P.Mackenbach & H. Verkleij (Eds.), *Volksgezondheid Toekomst Verkenning 1997, II Gezondheidsverschillen* (pp. 49-67). Maarssen, The Netherlands: Elsevier/De Tijdstroom.

Flouri, E. (2007). Early family environments may moderate prediction of low educational attainment in adulthood: The cases of childhood hyperactivity and authoritarian parenting. *Educational Psychology, 27,* 737-751.

Frazier, T. W., Demaree, H. A., & Youngstrom, E. A. (2004). Meta-analysis of intellectual and neuropsychological test performance in attention-deficit/hyperactivity disorder. *Neuropsychology, 18,* 543-555.

Frazier, T. W., Youngstrom, E. A., Glutting, J. J., & Watkins, M. W. (2007). ADHD and achievement: meta-analysis of the child, adolescent, and adult literatures and a concomitant study with college students. *Journal of Learning Disabilities, 40,* 49-65.

Freitag, C. M., Rohde, L. A., Lempp, T., & Romanos, M. (2010). Phenotypic and measurement influences on heritability estimates in childhood ADHD. *European Child & Adolescent Psychiatry, 19,* 311-323.

Friedman, N. P., Haberstick, B. C., Willcutt, E. G., Miyake, A., Young, S. E., Corley, R. P. et al. (2007). Greater attention problems during childhood predict poorer executive functioning in late adolescence. *Psychological Science, 18,* 893-900.

Friend, A., DeFries, J. C., Wadsworth, S. J., & Olson, R. K. (2007). Genetic and environmental influences on word recognition and spelling deficits as a function of age. *Behavior Genetics, 37,* 477-486.

Genro, J. P., Roman, T., Zeni, C. P., Grevet, E. H., Schmitz, M., de Abreu, P. B. et al. (2006). No association between dopaminergic polymorphisms and intelligence variability in attention-deficit/hyperactivity disorder. *Molecular Psychiatry, 11,* 1066-1067.

Greenberg, M. T., Weissberg, R. P., O'Brien, M. U., Zins, J. E., Fredericks, L., Resnik, H. et al. (2003). Enhancing school-based prevention and youth development through coordinated social, emotional, and academic learning. *American Psychologist, 58,* 466-474.

Groot, W. & van den Brink, H. M. (2007). The health effects of education. *Economics of Education Review, 26,* 186-200.

Harlaar, N., Dale, P. S., & Plomin, R. (2007). From learning to read to reading to learn: substantial and stable genetic influence. *Child Development, 78,* 116-131.

Hart, S. A., Petrill, S. A., Willcutt, E., Thompson, L. A., Schatschneider, C., Deater-Deckard, K., & Cutting, L. E. (2010). Exploring how symptoms of Attention-Deficit/Hyperactivity Disorder are related to reading and mathematics performance: general genes, general environments. *Psychological Science*, e-pub, doi:10.1177/0956797610386617

Hay, D. A., Bennett, K. S., Levy, F., Sergeant, J., & Swanson, J. (2006). A Twin Study of Attention-Deficit/Hyperactivity Disorder Dimensions Rated by the Strengths and Weaknesses of

ADHD-Symptoms and Normal-Behavior (SWAN) Scale. *Biological Psychiatry, 61,* 700-705.

Keenan, J. M., Betjemann, R. S., Wadsworth, S. J., DeFries, J. C., & Olson, R. K. (2006). Genetic and environmental influences on reading and listening comprehension. *Journal of Research in Reading, 29,* 75-91.

Kovas, Y., Haworth, C. M., Harlaar, N., Petrill, S. A., Dale, P. S., & Plomin, R. (2007a). Overlap and specificity of genetic and environmental influences on mathematics and reading disability in 10-year-old twins. *Journal of Child Psychology & Psychiatry, 48,* 914-922.

Kovas, Y., Haworth, C. M., Petrill, S. A., & Plomin, R. (2007b). Mathematical ability of 10-year-old boys and girls: genetic and environmental etiology of typical and low performance. *Journal of Learning Disabilities, 40,* 554-567.

Kuntsi, J., Eley, T. C., Taylor, A., Hughes, C., Asherson, P., Caspi, A., et al. (2004). Co-occurrence of ADHD and low IQ has genetic origins. *American Journal of Medical Genetics Part B- Neuropsychiatric Genetics, 124,* 41-47.

Larsson, J. O., Larsson, H., & Lichtenstein, P. (2004). Genetic and environmental contributions to stability and change of ADHD symptoms between 8 and 13 years of age: A longitudinal twin study. *Journal of the American Academy of Child and Adolescent Psychiatry, 43,* 1267-1275.

Lee, S. S. & Hinshaw, S. P. (2006). Predictors of adolescent functioning in girls with attention deficit hyperactivity disorder (ADHD): the role of childhood ADHD, conduct problems, and peer status. *Journal of Clinical Child and Adolescent Psychology, 35,* 356-368.

Levy, F., Hay, D. A., McStephen, M., Wood, C., & Waldman, I. (1997). Attention-deficit hyperactivity disorder: a category or a continuum? Genetic analysis of a large-scale twin study. *Journal of the American Academy of Child Psychiatry, 36,* 737-744.

Lubke, G. H., Hudziak, J. J., Derks, E. M., van Bijsterveldt, T. C., & Boomsma, D. I. (2009). Maternal ratings of attention problems in ADHD: evidence for the existence of a continuum. *Journal of the American Academy of Child & Adolescent Psychiatry, 48,* 1085-1093.

Mackenbach, J. P., Stirbu, I., Roskam, A. J., Schaap, M. M., Menvielle, G., Leinsalu, M., et al. (2008). Socioeconomic inequalities in health in 22 European countries. *The New England Journal of Medicine, 358,* 2468-2481.

Mannuzza, S. & Klein, R. G. (2000). Long-term prognosis in attention-deficit/hyperactivity disorder. *Child and Adolescent Psychiatric Clinics of North America, 9,* 711-726.

Markowitz, E. M., Willemsen, G., Trumbetta, S. L., van Beijsterveldt, T. C. E. M., & Boomsma, D. I. (2005). The etiology of mathematical and reading (dis)ability covariation in a sample of Dutch twins. *Twin Research and Human Genetics, 8,* 585-593.

Massetti, G. M., Lahey, B. B., Pelham, W. E., Loney, J., Ehrhardt, A., Lee, S. S., et al. (2008). Academic achievement over 8 years among children who met modified criteria for attention-deficit/hyperactivity disorder at 4-6 years of age. *Journal of Abnormal Child Psychology, 36,* 399-410.

Miech, R., Essex, M. J., & Goldsmith, H. H. (2001). Socioeconomic status and the adjustment to school: The role of self-regulation during early childhood. *Sociology of Education, 74,* 102-120.

Mill, J., Caspi, A., Williams, B. S., Craig, I., Taylor, A., Polo-Tomas, M., et al. (2006). Prediction of heterogeneity in intelligence and adult prognosis by genetic polymorphisms in the dopamine system among children with attention-deficit/hyperactivity disorder: evidence from 2 birth cohorts. *Archives of General Psychiatry, 63,* 462-469.

Mulder, M. J., Baeyens, D., Davidson, M. C., Casey, B. J., van den Ban, E., van Engeland, H., et al. (2008). Familial vulnerability to ADHD affects activity in the cerebellum in addition to the prefrontal systems. *Journal of the American Academy of Child and Adolescent Psychiatry, 47,* 68-75.

Neale, M. C., Boker, S. M., Xie, G., & Maes, H. (2006). Mx: Statistical Modeling [Computer software]. VCU, Box 900126, Richmond, VA 23298: Department of Psychiatry.

Pennington, B. F. & Ozonoff, S. (1996). Executive functions and developmental psychopathology. *Journal of Child Psychology & Psychiatry & Allied Disciplines, 37,* 51-87.

Petrill, S. A., Lipton, P. A., Hewitt, J. K., Plomin, R., Cherny, S. S., Corley, R., et al. (2004). Genetic and environmental contributions to general cognitive ability through the first 16 years of life. *developmental psychology, 40,* 805-812.

Polanczyk, G., de Lima, M. S., Horta, B. L., Biederman, J., & Rohde, L. A. (2007). The worldwide prevalence of ADHD: a systematic review and metaregression analysis. *American Journal of Psychiatry, 164,* 942-948.

Polderman, T. J. C., Bartels, M., Verhulst, F. C., Huizink, A. C., Beijsterveldt, T. C. E. M., & Boomsma, D. I. (2010b). No effect of classroom sharing on educational achievement in twins: a prospective, longitudinal cohort study. *Journal of Epidemiology and Community Health, 64,* 36-40.

Polderman, T. J. C., Bartels, M., Verhulst, F. C., Huizink, A. C., & Boomsma, D. I. (2009a). Educational Achievement in children with Attention Problems; results of a pilot study on cognitive data collection by teachers of twins. *Behavior Genetics, 39*.

Polderman, T. J. C., Boomsma, D. I., Bartels, M., Verhulst, F. C., & Huizink, A. C. (2010a). A systematic review of prospective studies on attention problems and academic achievement. *Acta Psychiatrica Scandinavica, 122,* 271-284.

Polderman, T. J. C., Derks, E. M., Hudziak, J. J., Verhulst, F. C., Posthuma, D., & Boomsma, D. I. (2007). Across the continuum of Attention Skills: A twin study of the SWAN ADHD rating scale. *Journal of Child Psychology & Psychiatry, 48,* 1080-1087.

Polderman, T. J. C., Geus, E. J. C., Hoekstra, R. A., Bartels, M., van Leeuwen, M., Verhulst, F. C., et al. (2009b). Attention Problems, inhibitory control and intelligence index overlapping genetic factors: A study in 9, 12 and 18-year-old twins. *Neuropsychology, 23,* 381-391.

Polderman, T. J. C., Gosso, M. F., Posthuma, D., van Beijsterveldt, T. C., Heutink, P., Verhulst, F. C., et al. (2006a). A longitudinal twin study on IQ, executive functioning, and attention problems during childhood and early adolescence. *Acta Neurologica Belgica, 106,* 191-207.

Polderman, T. J. C., Posthuma, D., de Sonneville, L. M. J., Verhulst, F. C., & Boomsma D. I. (2006b). Genetic analyses of teacher ratings of problem behavior in 5-year-old twins. *Twin Research and Human Genetics*.

Rietveld, M. J., Hudziak, J. J., Bartels, M., van Beijsterveldt, C. E., & Boomsma, D. I. (2003). Heritability of attention problems in children: I. cross-sectional results from a study of twins, age 3-12 years. *American Journal of Medical Genetics Part B: Neuropsychiatric Genetics, 117,* 102-113.

Rietveld, M. J., Hudziak, J. J., Bartels, M., van Beijsterveldt, C. E., & Boomsma, D. I. (2004). Heritability of attention problems in children: longitudinal results from a study of twins, age 3 to 12. *Journal of Child Psychology & Psychiatry, 45,* 577-588.

Rietveld, M. J., van, D., V, Bongers, I. L., Stroet, T. M., Slagboom, P. E., & Boomsma, D. I. (2000). Zygosity diagnosis in young twins by parental report. *Twin Research, 3,* 134-141.

Rijsdijk, F. V. (2007). Introduction to statistics. In B.Neale, M. Ferreira, S. Medland, & D. Posthuma (Eds.), *Statistical genetics: Gene mapping through linkage and association*. London: Taylor and Francis.

Rutter, M., Caspi, A., Fergusson, D., Horwood, L. J., Goodman, R., Maughan, B., et al. (2004). Sex differences in developmental reading disability: new findings from 4 epidemiological studies. *JAMA, 291,* 2007-2012.

Sagvolden, T., Johansen, E. B., Aase, H., & Russell, V. A. (2005). A dynamic developmental theory of attention-deficit/hyperactivity disorder (ADHD) predominantly hyperactive/impulsive and combined subtypes. *Behavioral and Brain Sciences, 28,* 397-419.

Schatschneider, C., Carlson, C. D., Francis, D. J., Foorman, B. R., & Fletcher, J. M. (2002). Relationship of rapid automatized naming and phonological awareness in early reading development: Implications for the double-deficit hypothesis. *Journal of Learning Disabilities, 35,* 245-256.

Sergeant, J. (2000). The cognitive-energetic model: an empirical approach to Attention-Deficit Hyperactivity Disorder. *Neuroscience and Biobehavioral Reviews, 24,* 7-12.

Shaw, P., Greenstein, D., Lerch, J., Clasen, L., Lenroot, R., Gogtay, N., et al. (2006a). Intellectual ability and cortical development in children and adolescents. *Nature, 440,* 676-679.

Shaw, P., Lerch, J., Greenstein, D., Sharp, W., Clasen, L., Evans, A., et al. (2006b). Longitudinal mapping of cortical thickness and clinical outcome in children and adolescents with attention-deficit/hyperactivity disorder. *Archives of General Psychiatry, 63,* 540-549.

Sonuga-Barke, E. J., Brookes, K. J., Buitelaar, J., Anney, R., Bitsakou, P., Baeyens, D., et al. (2008). Intelligence in DSM-IV combined type attention-deficit/hyperactivity disorder is not predicted by either dopamine receptor/transporter genes or other previously identified risk alleles for attention-deficit/hyperactivity disorder. *American Journal of Medical Genetics Part B: Neuropsychiatric Genetics, 147,* 316-319.

Spivack, G. & Spotts, J. (1966). *The Devereux Child Behavior Rating Scale*. Devon, A: The Devereux Foundation.

Stevenson, J., Graham, P., Fredman, G., & McLoughlin, V. (1987). A twin study of genetic influences on reading and spelling ability and disability. *Journal of Child Psychology & Psychiatry, 28,* 229-247.

van Beijsterveldt, C. E. M., Verhulst, F. C., Molenaar, P. C. M., & Boomsma, D. I. (2004). The genetic basis of problem behavior in 5-year-old Dutch twin pairs. *Behavior Genetics, 34,* 229-242.

Verhulst, F. C., van der Ende, J., & Koot, H. M. (1996). *Handleiding voor de CBCL/4-18*. Rotterdam: Sophia Kinderziekenhuis/Adfdeling Kinder- en Jeugdpsychiatrie, Erasmus MC, Rotterdam.

Wadsworth, S. J., Corley, R. P., Hewitt, J. K., & DeFries, J. C. (2001). Stability of genetic and environmental influences on reading performance at 7, 12, and 16 years of age in the Colorado Adoption Project. *Behavior Genetics, 31,* 353-359.

Wainwright, M. A., Wright, M. J., Geffen, G. M., Luciano, M., & Martin, N. G. (2005). The genetic basis of academic achievement on the queensland core skills test and its shared genetic variance with IQ. *Behavior Genetics, 35,* 133-145.

Wechsler, D. (1992). *Wechsler Individual Achievement Test*. New York: Psychological Corporation.

Willcutt, E. G., Doyle, A. E., Nigg, J. T., Faraone, S. V., & Pennington, B. F. (2005a). Validity of the executive function theory of attention-deficit/hyperactivity disorder: a meta-analytic review. *Biological Psychiatry, 57,* 1336-1346.

Willcutt, E. G. & Pennington, B. F. (2000). Comorbidity of reading disability and attention-deficit/hyperactivity disorder: differences by gender and subtype. *Journal of Learning Disabilities, 33,* 179-191.

Willcutt, E. G., Pennington, B. F., Olson, R. K., Chhabildas, N., & Hulslander, J. (2005b). Neuropsychological analyses of comorbidity between reading disability and attention deficit hyperactivity disorder: In search of the common deficit. *Developmental Neuropsychology, 27,* 35-78.

Woodcock, R. W. & Johnson, M. B. (1990). *Manual for the Woodcock-Johnson Test of Achievement-Revised*. Allen, TX: RCL Enterprises.