

Research Article

Meta-analysis of twin studies highlights the importance of genetic variation in primary school educational achievement

Eveline L. de Zeeuw^{a,b,*}, Eco J.C. de Geus^{a,b}, Dorret I. Boomsma^{a,b}

^a Department of Biological Psychology, VU University, Van der Boechorststraat 1, 1081 BT Amsterdam, The Netherlands

^b EMGO+ Institute for Health and Care Research, VU University Medical Centre, Amsterdam, The Netherlands



ARTICLE INFO

Article history:

Received 20 February 2015

Received in revised form

16 June 2015

Accepted 18 June 2015

Available online 10 July 2015

Keywords:

Educational achievement

Genetic variation

Heritability

Twins

Primary education

ABSTRACT

Children differ in their ability to learn what is taught at school. Evidence from twin studies suggests that genetic effects contribute to such differences. The aim of the present study was to systematically review the existing literature, including 61 studies from 11 cohorts, on twin studies of educational achievement in primary school children. The meta-analysis estimated heritability, based on up to 5330 MZ and 7084 DZ twin pairs, at 73% for reading, 49% for reading comprehension, 57% for mathematics, 44% for spelling, 64% for language and 66% for educational achievement. The importance of genetic effects on educational achievement differed between countries. Heritability was consistently high in the Netherlands across educational domains, while this was not always true for the USA and the UK. It can be concluded that genetic variation is an important contributor to the individual differences in educational achievement, with some indication for interaction with country.

© 2015 Elsevier GmbH. All rights reserved.

1. Introduction

Educational achievement in children can be defined as the extent to which a child has achieved the educational goals corresponding to his or her grade level. Lower educational achievement has an adverse effect on access to higher education and is negatively related to numerous other outcomes later in life, including earnings [1] and health and wellbeing [2]. Research towards the causes of individual differences between children has tended to focus on environmental factors, such as parental educational level, socioeconomic status (SES) and quality of education. Yet, even children from a similar background and attending the same school can differ greatly in their performance at school. This introduces genetic effects as an important additional source of variation in educational achievement. Moreover, parts of the child's environment, like parental educational level, can themselves be influenced by genes [3,4]. In keeping, general cognitive ability is the most important predictor of educational achievement [5], explaining roughly half of the variation [6]. A major role for genetic effects on general cognitive ability has already been well recognized [7] and is characterized by an increase during childhood [8,9]. Here we systematically review twin studies on educational achievement of children in primary school, aiming to provide, based on the existing literature, an

estimate of the heritability and the influence of the environment by meta-analyzing the twin correlations.

Twin studies are the most often used design to analyze the causes of variation in complex phenotypes, such as educational achievement [10]. Monozygotic (MZ) twin pairs are genetically (nearly) identical while dizygotic (DZ) twin pairs share approximately 50 per cent of their segregating genes [11]. If the larger genetic resemblance of MZ twin pairs is mirrored in a larger resemblance for a phenotype, i.e. when the correlation between MZ twin pairs is higher than between DZ twin pairs, this observation is consistent with the phenotype being influenced by genetic effects. Genetic effects are the sum of the additive effects of all genetic variants with an influence on educational achievement. Environmental effects often are distinguished into common environmental and unique environmental effects. Common environmental effects are influences that are shared between twins or siblings who grow up in the same environment and enhance their similarity beyond the similarity due to shared genes. There are other effects that also make offspring from the same parents more similar, including the effects of assortative mating, the similarity between spouses, which will in the classical twin design also be detected as common environmental effects [12]. When the correlation between DZ twin pairs is more than half the correlation between MZ twin pairs there is an indication for the influence of the common environment. Unique environmental effects are influences that are not shared between twins, and make children less similar. When the correlation between MZ twin

* Corresponding author. Tel.: +31 20 598 27 24; fax: +31 20 598 88 32.

E-mail address: el.de.zeeuw@vu.nl (E.L. de Zeeuw).

pairs is not equal to unity the unique environment has an influence. The unique environmental effects also include measurement error.

The twin method assumes that MZ twins are more similar in educational achievement than DZ twins because of their larger genetic resemblance and not because MZ twins are treated more alike than DZ twins. The equal environment assumption can be violated if similarity in treatment relates to similarity in a phenotype. However, MZ twins may be exposed to more similar treatment because of their larger genetic resemblance. For instance, if children that learn easily get treated differently than children that struggle more at school, the higher genetic resemblance in educational achievement of MZ twins causes them to experience more similar environments than DZ twins, as a secondary effect of the genetic effects on educational achievement. In contrast, when there is a similar environment unrelated to the genetic make-up of the twins, e.g. MZ twins are dressed more alike than DZ twins this could lead to a violation of the assumption, but only if similarity in appearance relates to similarity in the outcome. Such violations of the equal environments assumption have been tested by empirical approaches in large scale studies [13–15] which show that the assumption holds for, amongst others, educational achievement.

In order to generalize the outcome of twin studies to the general population, twins should be representative of the general population for the phenotype of interest. With regard to most characteristics, this assumption will be met as twins are born in all strata of society [16]. Nonetheless, twins differ from singletons with regard to birth conditions. Twins are born, on average, 3–4 weeks prematurely and have ~1 kg lower birth weights [17]. These differences dissipate fairly early on, however, and, already in childhood, twins and singletons have very similar body composition [18] and educational achievement [19], especially when birth order within family is taken into account [20,21].

Twin studies have mainly focused on reading and, more recently, mathematics. Most studies are from English speaking countries, such as the USA, the UK and Australia. Studies from other countries with different educational systems are relatively scarce [22–24]. Studies are characterized by differences in age, sample size, cohort and measurement instrument. Therefore, it is difficult to draw clear conclusions regarding the relative contribution of genetic and environmental influences on educational achievement. Here we aim to provide a review of all studies that addressed the heritability of educational achievement in primary school and carry out a meta-analysis of the correlations within MZ and DZ twin pairs. This review does not include twin studies of selected samples (low or high performance) or of learning disabilities, such as dyslexia and dyscalculia, as there are excellent recent reviews describing twin studies (e.g. [25–28]) and molecular genetic studies (e.g. [29,30]).

2. Methods

A search of the published literature was conducted in PubMed to find all relevant papers describing twin studies on the heritability of educational achievement in primary school children published before September 2014. Searches were performed to find any paper in English that contained the words genetics, heritability or twin study combined with educational achievement, educational attainment, school achievement, academic achievement, scholastic achievement, school performance or academic performance or combined with reading, mathematics, arithmetic, spelling, language or science in its title, key words, abstract or main text. Abstracts of these search results were evaluated and relevant full text articles were retrieved from the internet. The reference lists of all these papers were examined to identify additional studies that had not been located in the initial database search and searches on names of authors who previously

published twin studies on educational achievement were performed. Criteria for inclusion were determined a priori and assessed. Only original research reports published in peer-reviewed journals were included in the review. Twin studies including a sample of primary school aged children (6–13 years) were selected. Studies were included when they contained information on heritability estimates for a measure of educational achievement in a specific educational domain, for example, reading or mathematics, or a measure of general educational achievement. Studies were selected when they used standardized tests or teacher assessments to measure educational achievement. Studies reporting on estimates from univariate analyses as well as studies containing univariate estimates from multivariate analyses were included. Only twin studies from unselected genetically sensitive samples were included. From each study, when available, the first author, year of publication, country, cohort, age, sample size, measurement instrument, educational domain and heritability estimates were extracted.

A meta-analysis of studies that provided sample size, separate for MZ and DZ twin pairs, and twin correlations was conducted for both educational achievement in specific educational domains and general educational achievement. The meta-analysis was carried out to estimate heritability across multiple datasets when at least two independent studies from different cohorts were available. The decision which study to select and include in the analysis when studies reported twin correlations from the same cohort was based on the largest sample size. The educational domain science was only available for one cohort which made meta-analyzing the results not possible.

A variance decomposition model was fitted to the twin correlations, weighted by sample size, to estimate the influence of genetic and common environmental effects [31–33] on educational achievement using the structural equation modeling program Mx [34]. With Mx it is possible to analyze the twin correlations from multiple studies in a multi-group analysis and obtain a maximum likelihood estimate of heritability across all studies. It was tested whether the heritability estimate could be constrained to be equal across studies. The difference in goodness of fit between the nested models was assessed with hierarchic chi-squared tests. The difference in the χ^2 -statistic is evaluated with the difference in the number of estimated parameters between the nested models as degrees of freedom. A *p*-value smaller than .01 was considered significant.

3. Results

The PubMed search retrieved 61 studies that were published between 1991 and 2014. Table S1 summarizes the characteristics and results of these twin studies from 6 different, mostly English speaking, countries (mainly Northern Europe, the UK and the US, but also Australia and China). The studies include heritability estimates for a number of specific educational domains or for general educational achievement. Table S1 also gives an overview of the heritability estimates as reported by the included studies. Studies providing separate estimates for the heritability in boys and girls did not report any gender differences [35–40]. Some studies took into account that the members of a twin pair could be assessed by the same or different teachers and reported separate heritability estimates for these groups [41,42]. Studies used teacher assessments, standardized tests taken at school or tests that had been administered by the researchers through the internet, telephone or during a home-visit. Teacher assessments were based on the evaluation by the teacher of the overall proficiency of a student or on criteria that are listed in national guidelines stating what a student should be able to do or know with respect to a certain educational domain.

The cohorts that are described in the studies were the Colorado Learning Disabilities Research Center (CLDRC), UK government's Department of Children, Schools and Families (DSCF), Environmental Risk Longitudinal Twin Study (ERLTS), Florida Twin Project (FTP), International Longitudinal Twin Study (ILTS), Netherlands Twin Register (NTR), Primair Onderwijs en Speciaal Onderwijs Cohort (PRIMA), Twins Early Development Study (TEDS), Virginia Twin Study of Adolescent Behavioral Development (VTSABD) and the Western Reserve Twin Project (WRTP). Most of the studies focused on the so called core educational domains, i.e. reading and mathematics. Other educational domains that we came across in the literature search and that are included in the review are reading comprehension, spelling, language and science. Some of the studies used a measure of general educational achievement. The measurement instruments differ substantially across country and cohort.

Estimates of the heritability of reading (.10–.94), reading comprehension (.32–.87), mathematics (.04–.75), spelling (.33–.84), language (.21–.81), science (.32–.64) and general educational achievement (.27–.57) varied considerably across the studies reported in this review. The same is true for the environmental effects on reading (.00–.74), reading comprehension (.00–.50), mathematics (.00–.81), spelling (.00–.46), language (.10–.25), science (.08–.39) and general educational achievement (.08–.67). Reported heritability estimates may vary due to large differences in sample sizes, different countries, different age groups and variation in measurement instruments. We explore some of these explanations in the meta-analysis.

A meta-analysis was carried out for reading, reading comprehension, mathematics, language, spelling and general educational achievement. The MZ and DZ correlations of all studies included in the meta-analysis are given in Table 1. The number of included studies in the meta-analysis was 11 for reading with a total of 5330 MZ and 7084 DZ twin pairs. For reading comprehension a total of 6 studies provided data on 3042 MZ and 5218 DZ twin pairs. For mathematics, language and spelling, there were fewer studies. Three studies on mathematics included a total of 3419 MZ and 6247 DZ twin pairs, 3 studies on language included 2740 MZ and 4951 DZ twin pairs and 3 studies on spelling had 1093 MZ and 1692 DZ twin pairs. In primary school aged children we retrieved 2 studies for general educational achievement with large sample sizes, totaling 4341 MZ and 7808 DZ twin pairs. The heritability estimates for each study, based on the sample sizes and twin correlations, and the overall estimate of the heritability based on all available studies are displayed in Fig. 1.

We next investigated the heterogeneity between studies for heritability estimates by comparing the fit of the meta-analysis models in which all estimates across studies were constrained to be equal to a model in which all estimates were free. The differences in chi-squared statistics for reading ($\Delta\chi^2=25.46$, $\Delta df=20$, $p=.184$) and general educational achievement ($\Delta\chi^2=6.68$, $\Delta df=2$, $p=.035$) were not significant. For the educational domains reading comprehension ($\Delta\chi^2=73.76$, $\Delta df=14$, $p<.001$), mathematics ($\Delta\chi^2=15.58$, $\Delta df=4$, $p=.004$), language ($\Delta\chi^2=19.82$, $\Delta df=4$, $p<.001$) and spelling ($\Delta\chi^2=30.74$, $\Delta df=8$, $p<.001$) the constrained model fitted worse, pointing to heterogeneity. Estimates for the influence of the genetic effects, based on the weighted twin correlations, were 73% for reading, 49% for reading comprehension, 57% for mathematics, 64% for language, 44% for spelling and 66% for general educational achievement. The influence of the common environmental effects was smaller with estimates of 10% for reading, 13% for reading comprehension, 10% for mathematics, 15% for language, 23% for spelling and 12% for general educational achievement. (see Fig. 2).

The contributions of the included studies to the difference in the chi-squared statistics between the models with all estimates freely estimated and the models where the estimates were

constrained to be equal across the different studies are displayed in Table 1 and inform on the degree and sources of heterogeneity across the different samples. The studies that contributed most to the increase in chi-square statistics were, for reading, a study from the Netherlands [40] and the UK [43], for reading comprehension, a study from the USA [44], for language, a study from the USA [45] and, for spelling, a study from Australia [23]. The included studies contributed approximately the same to the increase in chi-square statistic for mathematics and general educational achievement.

The studies included in the meta-analysis are mainly from cohorts from the USA, the UK and the Netherlands (NL), providing the opportunity to explore gene–environment ($G \times E$) interaction across those countries for the educational domains with available studies from all three countries, i.e. reading, reading comprehension, language and mathematics (Table 1). These countries have different teaching methods, educational systems and societies and the expression of the genotype could depend on differences in the environment (Eaves, 1984). Heritability and the influence of the common environment were first estimated separately for each country. The fit of the model did not deteriorate significantly after equating the estimates across countries for reading ($\Delta\chi^2=10.55$, $\Delta df=4$, $p=.032$), but did so for reading comprehension ($\Delta\chi^2=49.80$, $\Delta df=4$, $p<.001$), language ($\Delta\chi^2=19.82$, $\Delta df=4$, $p<.001$) and mathematics ($\Delta\chi^2=15.58$, $\Delta df=4$, $p=.004$). Heritability of reading was equally high across these countries (USA: 69%; UK: 76%; NL: 66%), but heritability of reading comprehension was larger in the Netherlands (64%) and the USA (67%) compared to the UK (38%), heritability of mathematics was low in the USA (26%), moderate in the UK (46%) and high in the Netherlands (71%) and heritability of language was high in the UK (62%) and the Netherlands (66%) compared to the USA (32%) (Fig. 1). The influence of the common environmental effects was approximately equal for reading (USA: 12%; UK: 9%; NL: 8%) while there were some differences between countries for reading comprehension (USA: 13%; UK: 18%; NL: 3%), mathematics (USA: 32%; UK: 16%; NL: 3%) and language (USA: 55%; UK: 18%; NL: 12%).

4. Discussion

The current paper presents a review on the heritability of educational achievement estimated from twin studies in primary school children. Heritability estimates varied considerably across studies as did the influence of the environmental effects. The differences in sample size, different countries, different age groups and the variety of measurement instruments are probably the main reasons for the broad range of estimates observed in this review. The smallest sample size was 32 MZ and 28 DZ twin pairs [46] and the largest was 2292 MZ and 4184 DZ twin pairs [47]. Some studies used multiple measures to assess educational achievement in a certain domain while others used only one. This resulted in differences between studies with regard to the quality of the measurement instruments. Possibly given rise to larger measurement errors and a higher estimate of the unique environmental effects, which includes measurement error. Even though teacher assessments are correlated with standardized tests they might be less reliable measures of educational achievement. A study with the largest sample size available for a certain cohort often used a less detailed measurement instrument, i.e. web-based test or teacher assessments. Overall, the results suggest that educational achievement is highly heritable and the common environment has a small influence.

A meta-analysis of twin correlations was performed for reading, reading comprehension, mathematics, language, spelling and general educational achievement. Many of the studies included in the review used data from the same cohorts. Consequently, the meta-analysis of twin correlations for most educational domains

Table 1
Descriptives of the studies included in the meta-analysis.

Study	Country	Mean age	Sample size	MZ correlation	DZ correlation	$\Delta\chi^2$ (df)
Reading						
Byrne et al. [67]	USA Scandinavia Australia	8	433 MZ+437 DZ	.81	.43	1.51 (2)
Chow et al. [24]	China	–	228 MZ+84 DZ	.90	.54	1.70 (2)
Harlaar et al. [47]	UK	7	1067 MZ+1039 DZ (boys) 1225 MZ+1111 DZ (girls)	.86 .84	.52 .51	.59 (6)
Hart et al. [68]	USA	6	128 MZ+175 DZ	.82	.50	.45 (2)
Hart et al. [69]	USA	7	486 MZ+468 DZ 442 DOS	.82	.47 .45	.23 (3)
Hohnen and Stevenson [46]	UK	7	34 MZ+32 DZ	.92	.61	1.41 (2)
Olson et al. [70]	USA	11	81 MZ+189 DZ	.91	.50	.83 (2)
Reynolds et al. [39]	USA	11	292 MZ+179 DZ (boys) 380 MZ+184 DZ (girls)	.79 .81	.44 .52	1.40 (5)
			284 DOS		.39	
Trzesniewski et al. [43]	UK	7	285 MZ+244 DZ	.88	.59	7.81 (2)
de Zeeuw et al. [40]	The Netherlands	8	199 MZ+182 DZ (boys) 215 MZ+174 DZ (girls)	.73 .75	.38 .48	8.49 (5)
			369 DOS		.39	
Zumberge et al. [71]	USA	10	139 MZ+84 DZ (boys) 138 MZ+97 DZ (girls)	.80 .78	.50 .52	1.05 (5)
			147 DOS		.43	
Reading comprehension						
Byrne et al. [23]	USA Australia Scandinavia	8	185 MZ+220 DZ 86 MZ+49 DZ 32 MZ+43 DZ	.72 .71 .76	.45 .33 .46	4.88 (2) 1.06 (2) 1.37 (2)
Harlaar et al. [72]	USA	10	89 MZ+131 DZ	.73	.25	7.37 (2)
Harlaar et al. [73]	UK	12	1748 MZ+3117 DZ	.56	.37	12.85 (2)
Hart et al. [44]	USA	8	189 MZ+388 DZ	.83	.53	31.23 (2)
Olson et al. [70]	USA	11	81 MZ+189 DZ	.88	.47	9.42 (2)
de Zeeuw et al. [40]	The Netherlands	8	305 MZ+285 DZ (boys) 327 MZ+261 DZ (girls)	.67 .67	.41 .30	5.58 (5)
			535 DOS		.34	
Mathematics						
Harlaar et al. [73]	UK	11	1627 MZ+2902 DZ	.62	.39	5.52 (2)
Hart et al. [68]	USA	8	128 MZ+175 DZ	.58	.45	3.47 (2)
de Zeeuw et al. [40]	The Netherlands	12	757 MZ+787 DZ (boys) 907 MZ+765 DZ (girls)	.70 .76	.37 .41	6.59 (5)
			1618 DOS		.37	
Language						
Haworth et al. [74]	UK	10	929 MZ+1650 DZ	.80	.49	2.00 (2)
Thompson et al. [45]	USA	10	146 MZ+132 DZ	.87	.71	13.98 (2)
de Zeeuw et al. [40]	The Netherlands	12	757 MZ+787 DZ (boys) 908 MZ+765 DZ (girls)	.77 .78	.46 .42	3.85 (5)
			1617 DOS		.45	
Spelling						
Byrne et al. [23]	USA Australia Scandinavia	8	185 MZ+220 DZ 86 MZ+49 DZ 32 MZ+43 DZ	.79 .74 .68	.41 .10 .24	3.63 (2) 12.79 (2) 3.92 (2)
Olson et al. [70]	USA	11	81 MZ+189 DZ	.91	.48	4.96 (2)
de Zeeuw et al. [40]	The Netherlands	6	344 MZ+316 DZ (boys) 365 MZ+281 DZ (girls)	.62 .57	.40 .40	5.43 (5)
			594 DOS		.53	
Educational achievement						
Haworth et al. [75]	UK	12	1892 MZ+3250 DZ	.75	.47	3.85 (2)
de Zeeuw et al. [40]	The Netherlands	12	1112 MZ+1129 DZ (boys) 1337 MZ+1149 DZ (girls)	.80 .83	.47 .43	2.83 (5)
			2280 DOS		.44	

was based on only a few studies. When studies from the same cohort reported on the same educational achievement domain the only selection criteria for the meta-analysis was the largest sample size and this must be kept in mind when evaluating the mean overall heritability estimates. It was not possible to equate the estimates across the studies included in the meta-analysis without a significant drop in model fit for reading comprehension, mathematics, language and spelling. If we nevertheless estimated the overall heritability, based on the twin correlations, weighted by sample size, across all studies, 73% of the variation in reading, 49% in reading comprehension, 57% in mathematics, 64% in language, 44% in spelling and 66% in the variation of general

educational achievement could be explained by genetic effects. Common environmental effects explained 10% of the variation in reading, 13% in reading comprehension, 10% in mathematics, 15% in language, 23% in spelling and 12% in general educational achievement.

The overall high heritability of educational achievement implies that innate individual differences between children will be highlighted. Even though the mean level of educational achievement can be enhanced by changes in the environment, the variation between individual children will still mainly be due to genetics. This means that children with a predisposition for lower educational achievement may have to struggle while

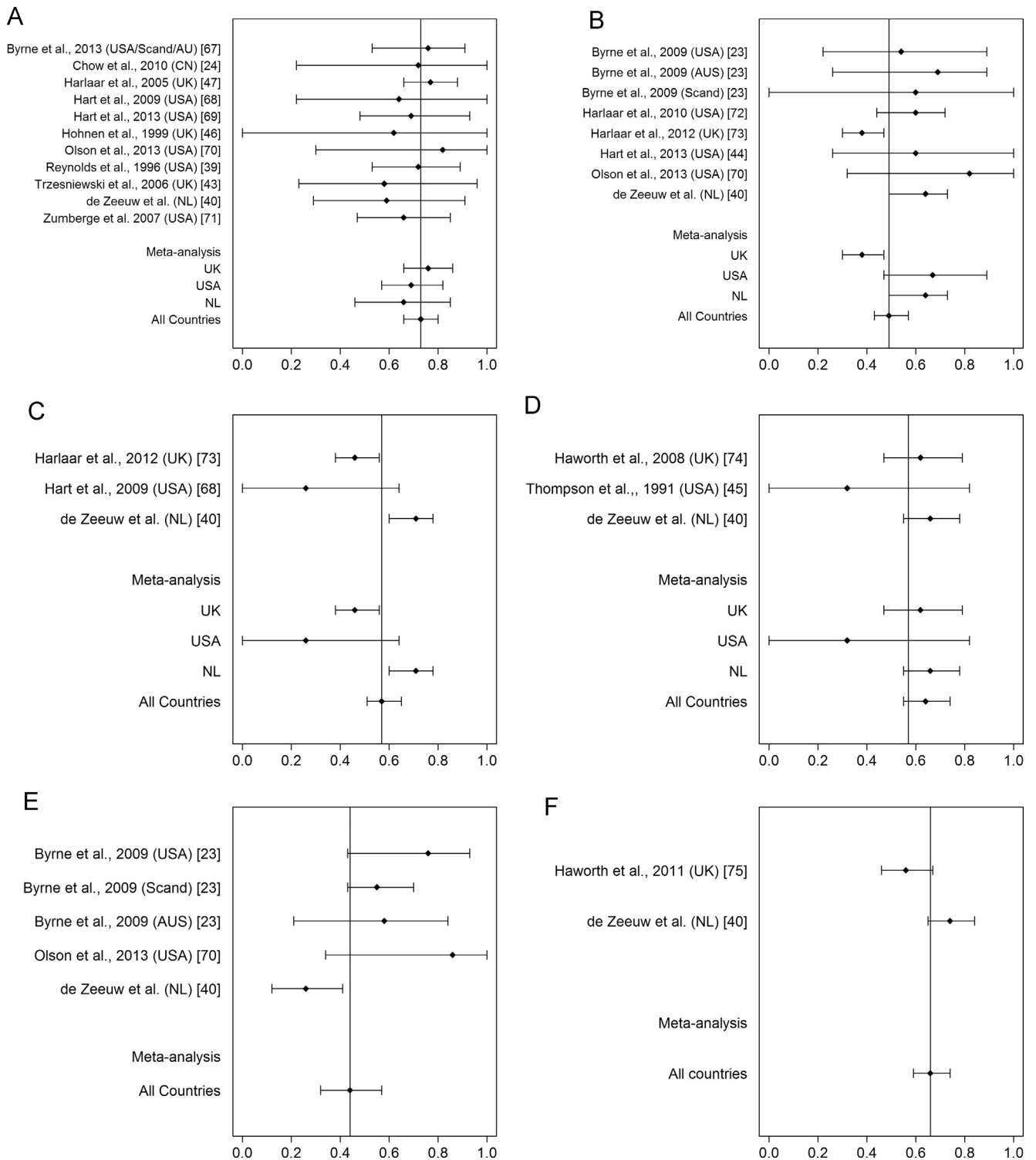


Fig. 1. Heritability estimates (95% confidence intervals) for each study, by country and overall, as estimated in the meta-analysis and based on the reported twin correlations and sample sizes for reading (A), reading comprehension (B), mathematics (C), language (D), spelling (E) and educational achievement (F).

children with a genetic advantage can excel at school without ever tapping their full potential. It implies that teachers should take into account that expectations might differ between children in their class. The challenge for teachers is to make sure that each child can reach its true genetic potential while having the children with a lower potential outperform their genetic make-up. Classroom teaching might not be the best method to achieve this goal and a more personalized approach to education will be necessary.

The heritability of educational achievement in reading comprehension, mathematics and language, but not reading, seems to be moderated by country, i.e. the USA, the UK and the Netherlands. Heritability was consistently high in the Netherlands while this was not always true for the USA and the UK. It must be noted that the sample sizes included in the studies from the USA are much smaller, making the estimates less reliable. Differences in heritability of educational achievement between countries might be explained by differences in educational opportunities. In the USA

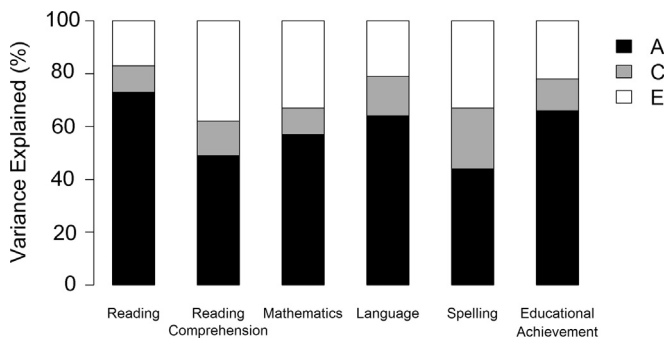


Fig. 2. Estimates for the genetic (A), common environmental (C) and unique environmental (E) effects from the meta-analysis of educational achievement.

and the UK there are private schools and public schools which are supported by the state [48]. Private schools in these countries have the right to select their students and charge tuition. In the Netherlands nearly all public as well as private schools are funded by the government [49] and have to comply to the same standards. The educational system in the Netherlands is more similar to the one implemented in the UK, both countries have a national curriculum, while the educational system in the USA is more decentralized. The equal opportunities in the relatively homogeneous education environment in the Netherlands may restrict the variation in school environments making differences in educational achievement between children to a greater extent due to genetic differences [50,51]. The difference in heritability could also be due to differences in society. The inequality in income is larger in the USA and UK compared to the Netherlands [52]. There has been some indication for the presence of a moderating effect of SES on general cognitive ability although evidence is not yet conclusive. The hypothesis is that children from high SES families have more opportunities to realize their differences in genetic make-up. For example, several studies from the USA found that the heritability of general cognitive ability is larger in children from middle and upper class families while environmental effects have a larger influence in children from lower income families [53,54]. However, a study from the UK concluded that the genetic influence on general cognitive ability was equal in children from low and high SES families while the shared environmental variation was larger in the low SES families [55]. If SES moderates the heritability of educational achievement, a lower percentage of children from disadvantaged groups will lead to a higher heritability of educational achievement.

There are several limitations of this review on the literature of twin studies on educational achievement in primary school children that should be noted. A rather large number of studies included in the review suffer from a lack of power which has an effect on the reliability of the obtained heritability estimates in these studies. Another limitation is the heterogeneity in the age of the samples and in the measures used to assess educational achievement. Teacher assessments are used to assess educational achievement in some studies while others use objective tests. The studies with the largest sample sizes were included in the meta-analysis and these larger available sample sizes might be due to the use of a less detailed measurement instrument. Although the association between teacher assessments and standardized tests is relatively strong they are likely measuring partly different aspects of a child's educational achievement. Furthermore, the number of studies included in the meta-analysis was rather small compared to the number of studies included in this review due to the fact that many studies were based on the same population cohort.

Molecular genetic studies have tried to identify the genetic variants that are responsible for the high heritability of educational

achievement. A large GWA study of educational attainment in adults revealed genome-wide significant associated genetic variants with a largest estimated effect of .02 per cent [56]. GWA studies analyzing data from children are rather scarce and have not yet resulted in conclusive evidence for an association of specific genetic variants with educational achievement. Although most of the genetic variants in these studies did not reach genome-wide significance and none replicated in an independent sample, some genetic variants implicated genes for reading and spelling, i.e. *ABCC12* and *DAZAP1* (pseudogenes) and *CHD2L1*, *CDC2L2* and *RCAN3* [57], for mathematics, i.e. *MMP7*, *GRIK1* and *DNAH5* [58] and for reading, i.e. *ZNF404*, *ZNF45*, *LYPD5*, and mathematics, i.e. *PGM2L1* [59] and for reading and spelling, i.e. *DCDC2*, *KIAA0319* and *CMIP* [60]. The explanation for the lack of significant findings with regard to specific genes influencing educational achievement is that it is a highly complex phenotype that is caused by many common genetic variants with small effects, which make them difficult to detect and replicate. The non-significant measured genetic variants in the GWA studies probably did capture relevant genetic variation, but sample sizes have not been large enough to detect these small effects [61]. This has been confirmed by the observation that using the distant genetic relatedness between unrelated individuals to estimate the variance explained by all the common single nucleotide polymorphisms (SNPs) represented on a DNA array (GREML analyses) [62] a significant proportion of the variance in educational achievement, i.e. reading (27%) and mathematics (52%), was explained [59]. However, there still is a gap between the variance in educational achievement explained by all SNPs taken together and the heritability as observed in twin studies. This has been called the missing heritability problem [63]. One of the explanations for this difference in heritability might be that some variation in educational achievement is due to other variants that are not among the SNPs on the available DNA arrays [64]. Polygenic scores including information from all genetic variants, also the non-significant ones, and their effect sizes observed in a meta-analysis of educational attainment in adults actually explained part of the variance in educational achievement in a sample of children [65,66]. Taken together, this confirms that common genetic variants explain at least a large proportion of the variance in educational achievement and larger sample sizes would eventually be sufficient to identify the genetic variants associated with educational achievement.

Acknowledgments

We are grateful to the twin families and the teachers for their participation. We thank Prof. Dr. J. Jolles for reading and reviewing the manuscript. This project is part of the research program 'Innovative learning materials and methods' funded by the Netherlands Initiative Brain and Cognition, a part of the Organisation for Scientific Research (NWO) under Grant 056-31-001. This research was supported by 'Spinozapremie' (NWO/SPI 56-464-14192); 'Twin-family database for behavior genetics and genomics studies' (NWO 480-04-004); Genetics of Mental Illness: European Research Council (ERC-230374); and Genetic influences on stability and change in psychopathology from childhood to young adulthood (NWO/ZonMW 91210020).

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at: <http://dx.doi.org/10.1016/j.tine.2015.06.001>.

References

- [1] Julian T, Kominski R. Education and synthetic work-life earnings estimates. US Census Bureau report; 2011. p. 1–14.

- [2] Mackenbach JP, Kunst AE, Cavelaars AE, Groenhouf F, Geurts JJ. Socioeconomic inequalities in morbidity and mortality in western Europe. *The EU Working Group on Socioeconomic Inequalities in Health. Lancet* 1997;349:1655–9.
- [3] Rietveld CA, Medland SE, Derringer J, Yang J, Esko T, Martin NW, et al. GWAS of 126,559 individuals identifies genetic variants associated with educational attainment. *Science*, 340; 2013. p. 1467–71.
- [4] Vinkhuyzen AAE, Van Der Sluis S, De Geus EJC, Boomsma DI, Posthuma D. Genetic influences on 'environmental' factors. *Genes Brain Behav* 2010;9:276–87.
- [5] Deary IJ, Strand S, Smith P, Fernandes C. Intelligence and educational achievement. *Intelligence* 2007;35:13–21.
- [6] Frey MC, Detterman DK. Scholastic assessment or g? The relationship between the scholastic assessment test and general cognitive ability *Psychol Sci* 2004;15:373–8.
- [7] Plomin R. Genetics and developmental psychology. *Merrill-Palmer Q* 2004;50:341–52.
- [8] Haworth CM, Wright MJ, Luciano M, Martin NG, de Geus EJ, van Beijsterveldt CE, et al. The heritability of general cognitive ability increases linearly from childhood to young adulthood. *Mol Psychiatry*, 15; 2010. p. 1112–20.
- [9] Molenaar D, van der Sluis S, Boomsma DI, Haworth CM, Hewitt JK, Martin NG, et al. Genotype by environment interactions in cognitive ability: a survey of 14 studies from four countries covering four age groups. *Behav Genet* 2013;43:208–19.
- [10] Boomsma DI, Vink JM, van Beijsterveldt TC, de Geus EJ, Beem AL, Mulder EJ, et al. Netherlands Twin Register: a focus on longitudinal research. *Twin Res* 2002;5:401–6.
- [11] Plomin R, DeFries JC, McClearn GE, Ps McGuffin. Behavioral genetics, 5th. New York: Worth Publishers; 2008.
- [12] Evans DM, Gillespie NA, Martin NG. Biometrical genetics. *Biol Psychol* 2002;61:33–51.
- [13] Evans DM, Martin NG. The validity of twin studies. *GeneScreen* 2000;1:77–9.
- [14] Loehlin JC. Partitioning environmental and genetic contributions to behavioral development. *Am Psychol* 1989;44:1285–92.
- [15] Van den Oord E, Boomsma D, Verhulst F. A study of genetic and environmental effects on the co-occurrence of problem behaviors in three-year-old-twins. *J Abnormal Psychol* 2000;109:360–72.
- [16] Hoekstra C, Willemsen G, van Beijsterveldt CEM, Lambalk CB, Montgomery GW, Boomsma DI. Body composition, smoking, and spontaneous dizygotic twinning. *Fertil Steril* 2010;93:885–93.
- [17] Martin JA, Hamilton BE, Sutton PD, Ventura SJ, Mathews TJ, Kirmeyer S, et al. Births: final data for 2007. *Natl Vital Stat Rep* 2010;58:1–85.
- [18] Estourgie-van Burk GF, Bartels M, Boomsma DI, Deleamarre-van de Waal H. Body size of twins compared with siblings and the general population: from birth to late adolescence. *J Pediatr* 2010;156:586–91.
- [19] Cohen CC, van Goozen SH, Orlebeke JF, Buitelaar JK, Cohen-Kettenis PT. A comparison of educational achievement in a national sample of Dutch female twins and their matched singleton controls. *Twin Res* 2002;5:273–6.
- [20] Boomsma DI, van Beijsterveldt TC, Beem AL, Hoekstra RA, Polderman TJ, Bartels M. Intelligence and birth order in boys and girls. *Intelligence* 2008;36:630–4.
- [21] de Zeeuw EL, van Beijsterveldt CE, de Geus EJ, Boomsma DI. Twin specific risk factors in primary school achievements. *Twin Res Hum Genet* 2012;15:107–15.
- [22] Bartels M, Rietveld MJ, Van Baal GC, Boomsma DI. Heritability of educational achievement in 12-year-olds and the overlap with cognitive ability. *Twin Res* 2002;5:544–53.
- [23] Byrne B, Coventry WL, Olson RK, Samuelsson S, Corley R, Willcutt EG, et al. Genetic and environmental influences on aspects of literacy and language in early childhood: continuity and change from preschool to Grade 2. *J Neurolinguist*, 22; 2009. p. 219–36.
- [24] Chow BW-Y, Ho CS-H, Wong SW-L, Waye MM, Bishop DV. Genetic and environmental influences on Chinese language and reading abilities. *PLoS One* 2011;6:e16640.
- [25] Grigorenko EL. Genetic bases of developmental dyslexia: a capsule review of heritability estimates. *Enfance* 2004;56:273–88.
- [26] Schulte-Körne G. Annotation – genetics of reading and spelling disorder. *J Child Psychol Psychiatry* 2001;42:985–97.
- [27] Wadsworth SJ, Olson RK, DeFries JC. Differential genetic etiology of reading difficulties as a function of IQ: an update. *Behav Genet* 2010;40:751–8.
- [28] Willcutt EG, Pennington BF, Duncan L, Smith SD, Keenan JM, Wadsworth S, et al. Understanding the complex etiologies of developmental disorders: behavioral and molecular genetic approaches. *J Dev Behav Pediatr* 2010;31:533–44.
- [29] Carrion-Castillo A, Franke B, Fisher SE. Molecular genetics of dyslexia: an overview. *Dyslexia* 2013;19:214–40.
- [30] Kere J. The molecular genetics and neurobiology of developmental dyslexia as model of a complex phenotype. *Biochem Biophys Res Commun* 2014;452:236–43.
- [31] Bartels M, Van den Berg M, Sluyter F, Boomsma DI, de Geus EJ. Heritability of cortisol levels: review and simultaneous analysis of twin studies. *Psychoneuroendocrinology* 2003;28:121–37.
- [32] van Beijsterveldt CEM, Van Baal GCM. Twin and family studies of the human electroencephalogram: a review and a meta-analysis. *Biol Psychol* 2002;61:111–38.
- [33] Verweij KJ, Zietsch BP, Lynskey MT, Medland SE, Neale MC, Martin NG, et al. Genetic and environmental influences on cannabis use initiation and problematic use: a meta-analysis of twin studies. *Addiction* 2010;105:417–30.
- [34] Neale MC, Boker SM, Xie G, MaesHH. Mx: statistical modeling, 5th. Richmond, VA: Department of Psychiatry, Virginia University; 1999.
- [35] Harlaar N, Spinath FM, Dale PS, Plomin R. Genetic influences on early word recognition abilities and disabilities: a study of 7-year-old twins. *J Child Psychol Psychiatry* 2005;46:373–84.
- [36] Haworth CM, Dale P, Plomin R. A twin study into the genetic and environmental influences on academic performance in science in nine-year-old boys and girls. *Int J Sci Educ* 2008;30:1003–25.
- [37] Kovas Y, Haworth CM, Petrill SA, Plomin R. Mathematical ability of 10-year-old boys and girls: genetic and environmental etiology of typical and low performance. *J Learn Disabil* 2007;40:554–67.
- [38] Petrill SA, Thompson LA. The effect of gender upon heritability and common environmental estimates in measures of scholastic achievement. *Personal Individual Diff* 1994;16:631–40.
- [39] Reynolds CA, Hewitt JK, Erickson MT, Silberg JL, Rutter M, Simonoff E, et al. The genetics of children's oral reading performance. *J Child Psychol Psychiatry* 1996;37:425–34.
- [40] de Zeeuw EL, van Beijsterveldt CEM, Glasner TJ, De Geus EJC, Boomsma DI. Arithmetic, reading and writing performance has a strong genetic component: a study in primary school children. *Learn Individ Diff* 2015 (submitted for publication).
- [41] Harlaar N, Dale PS, Plomin R. Telephone testing and teacher assessment of reading skills in 7-year-olds: II. Strong genetic overlap. *Read Writ* 2005;18:401–23.
- [42] Walker SO, Petrill SA, Spinath FM, Plomin R. Nature, nurture and academic achievement: a twin study of teacher assessments of 7-year-olds. *Br J Educ Psychol* 2004;74:323–42.
- [43] Trzesniewski KH, Moffitt TE, Caspi A, Taylor A, Maughan B. Revisiting the association between reading achievement and antisocial behavior: new evidence of an environmental explanation from a twin study. *Child Dev* 2006;77:72–88.
- [44] Hart SA, Soden B, Johnson W, Schatschneider C, Taylor J. Expanding the environment: gene x school-level SES interaction on reading comprehension. *J Child Psychol Psychiatry* 2013;54:1047–55.
- [45] Thompson LA, Detterman DK, Plomin R. Associations between cognitive abilities and scholastic achievement: genetic overlap but environmental differences. *Psychol Sci* 1991;2:158–65.
- [46] Hohnen B, Stevenson J. The structure of genetic influences on general cognitive, language, phonological, and reading abilities. *Dev Psychol* 1999;35:590–603.
- [47] Harlaar N, Hayiou-Thomas ME, Plomin R. Reading and general cognitive ability: a multivariate analysis of 7-year-old twins. *Sci Stud Read* 2005;9:197–218.
- [48] National Center for Education Statistics. Public and private schools: how do they differ? National Center for Education Statistics; 1997. p. 1–39.
- [49] Sturm J, Groenendijk L, Kruihof B, Rens J. Educational Pluralism—a historical study of so-called 'pillarization' in the Netherlands, including a comparison with some developments in South African education. *Comp Educ* 1998;34:281–97.
- [50] Heath AC, Berg K, Eaves LJ, Solaas MH, Corey LA, Sundet J, et al. Education policy and the heritability of educational attainment. *Nature* 1985;314:734–6.
- [51] Kovas Y, Voronin I, Kaydalov A, Malykh SB, Dale PS, Plomin R. Literacy and numeracy are more heritable than intelligence in primary school. *Psychol Sci* 2013;24:2048–56.
- [52] OECD. An overview of growing income inequalities in OECD countries: main findings; 2011. p. 1–25.
- [53] Scarr-Salapatek S. Race, social class, and IQ. *Science* 1971;174:1285–95.
- [54] Turkheimer E, Haley A, Waldron M, d'Onofrio B, Gottesman II. Socioeconomic status modifies heritability of IQ in young children. *Psychol Sci* 2003;14:623–8.
- [55] Hanscombe KB, Trzaskowski M, Haworth CM, Davis OS, Dale PS, Plomin R. Socioeconomic status (SES) and children's IQs: intelligence (IQ): In a UK-representative sample SES moderates the environmental, not genetic, effect on IQ. *PLoS One* 2012;7:e30320.
- [56] Rietveld CA, Medland SE, Derringer J, Yang J, Esko T+, Martin NW, et al. GWAS of 126,559 individuals identifies genetic variants associated with educational attainment. *Science* 2013;340:1467–71.
- [57] Luciano M, Evans DM, Hansell NK, Medland SE, Montgomery GW, Martin NG, et al. A genome-wide association study for reading and language abilities in two population cohorts. *Genes Brain Behav* 2013;12:645–52.
- [58] Docherty SJ, Davis OSP, Kovas Y, Meaburn EL, Dale PS, Petrill SA, et al. A genome-wide association study identifies multiple loci associated with mathematics ability and disability. *Genes Brain Behav* 2010;9:234–47.
- [59] Davis OS, Band G, Pirinen M, Haworth CM, Meaburn EL, Kovas Y, et al. The correlation between reading and mathematics ability at age twelve has a substantial genetic component. *Nat Commun* 2014;5:4204.
- [60] Scerri TS, Morris AP, Buckingham LL, Newbury DF, Miller LL, Monaco AP, et al. DCDC2, KIAA0319 and CMIP are associated with reading-related traits. *Biol Psychiatry* 2011;70:237–45.
- [61] Flint J, Munafò M. Genetics. Heritability, *Science* 2013;340:1416–7.
- [62] Yang J, Benyamin B, McEvoy BP, Gordon S, Henders AK, Nyholt DR, et al. Common SNPs explain a large proportion of the heritability for human height. *Nat Genet* 2010;42:565–9.
- [63] Maher B. Personal genomes: The case of the missing heritability. *Nat News* 2008;456:18–21.

- [64] Cirulli ET, Goldstein DB. Uncovering the roles of rare variants in common disease through whole-genome sequencing. *Nat Rev Genet* 2010;11:415–25.
- [65] de Zeeuw EL, van Beijsterveldt CE, Glasner TJ, Bartels M, Ehli EA, Davies GE, et al. Polygenic scores associated with educational attainment in adults predict educational achievement and ADHD symptoms in children. *Am J Med Genet Part B: Neuropsychiatr Genet* 2014;165:510–20.
- [66] Ward ME, McMahon G, Pourcain St B, Evans DM, Rietveld CA, Benjamin DJ, et al. Genetic variation associated with differential educational attainment in adults has anticipated associations with school performance in children. *PLoS One* 2014;9:e100248.
- [67] Byrne B, Wadsworth S, Boehme K, Talk AC, Coventry WL, Olson RK, et al. Multivariate genetic analysis of learning and early reading development. *Sci Stud Read* 2013;17:224–42.
- [68] Hart SA, Petrill SA, Thompson LA, Plomin R. The ABCs of math: a genetic analysis of mathematics and its links with reading ability and general cognitive ability. *J Educ Psychol* 2009;101:388.
- [69] Hart SA, Logan JA, Soden-Hensler B, Kershaw S, Taylor J, Schatschneider C. Exploring how nature and nurture affect the development of reading: an analysis of the Florida Twin Project on Reading. *Dev Psychol* 2013;49:1971–81.
- [70] Olson RK, Hulslander J, Christopher M, Keenan JM, Wadsworth SJ, Willcutt EG, et al. Genetic and environmental influences on writing and their relations to language and reading. *Ann Dyslexia* 2013;63:25–43.
- [71] Zumberge A, Baker LA, Manis FR. Focus on words: a twin study of reading and inattention. *Behav Genet* 2007;37:284–93.
- [72] Harlaar N, Cutting L, Deater-Deckard K, DeThorne LS, Justice LM, Schatschneider C, et al. Predicting individual differences in reading comprehension: a twin study. *Ann Dyslexia* 2010;60:265–88.
- [73] Harlaar N, Kovas Y, Dale PS, Petrill SA, Plomin R. Mathematics is differentially related to reading comprehension and word decoding: evidence from a genetically sensitive design. *J Educ Psychol* 2012;104:622.
- [74] Haworth C, Kovas Y, Dale PS, Plomin R. Science in elementary school: generalist genes and school environments. *Intelligence* 2008;36:694–701.
- [75] Haworth CM, Asbury K, Dale PS, Plomin R. Added value measures in education show genetic as well as environmental influence. *PLoS One* 2011;6:e16006.