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Evidence for shared genetic risk between ADHD symptoms and reduced mathematics ability: a twin study

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Abstract

Background—Attention-deficit/hyperactivity disorder (ADHD) symptoms and mathematics ability are associated, but little is known about the genetic and environmental influences underlying this association.

Methods—Data came from more than 6,000 12-year-old twin pairs from the U.K. population-representative Twins Early Development Study. Parents rated each twin's behaviour using a DSM-IV-based 18-item questionnaire of inattentive and hyperactive-impulsive ADHD symptoms. Mathematics tests based on the U.K. National Curriculum were completed by each twin. The twins also completed standardised tests of reading and general cognitive ability. Multivariate twin model fitting was applied.

Results—Inattentive and hyperactive-impulsive ADHD symptoms were highly heritable (67% and 73%, respectively). Mathematics ability was moderately heritable (46%). Mathematics ability and inattentiveness showed a significantly greater phenotypic correlation (r_p=−0.26) and genetic correlation (r_A=−0.41) than mathematics ability and hyperactivity-impulsivity (r_p=−0.18; r_A= −0.22). The genetic correlation between inattentiveness and mathematics ability was largely independent from hyperactivity-impulsivity, and was only partially accounted for by genetic influences related to reading and general cognitive ability.

Conclusions—Results revealed the novel finding that mathematics ability shows significantly stronger phenotypic and genetic associations with inattentiveness than with hyperactivity-impulsivity. Genetic associations between inattentiveness and mathematics ability could only partially be accounted for by hyperactivity-impulsivity, reading and general cognitive ability. Results suggest that mathematics ability is associated with ADHD symptoms largely because it

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Supplementary Information

Additional supporting information is provided along with the online version of this article.

Appendix S1. Title of supplementary material Table S1: Fit statistics; Table S2: MZ and DZ CTCT correlations

shares genetic risk factors with inattentiveness, and provide further evidence for considering inattentiveness and hyperactivity-impulsivity separately. DNA markers for ADHD symptoms (especially inattentiveness) may also be candidate risk factors for mathematics ability and vice versa.

Keywords

ADHD; mathematics; twin study; genetics; reading; general cognitive ability

Introduction

The links between ADHD and reading disability, or ADHD and global measures of learning disability are widely studied in the literature (Doyle, Faraone, DuPre, & Biederman, 2001; Willcutt et al., 2010). Less is known about links between ADHD and mathematics disability[1], despite evidence that comorbidity rates between ADHD and mathematics disability may be similar to those between ADHD and reading disability (Capano, Minden, Chen, Schacher, & Ickowicz, 2008; Gross-Tsur, Manor, & Shalev, 1996). Because ADHD and mathematics disability are heritable (Kovas, Haworth, Petrill, & Plomin, 2007; Willcutt et al., 2010), their comorbidity might be due to shared genetic risk factors. However, genetically sensitive research examining links between ADHD and mathematics disability is relatively sparse.

An initial study using familial risk analysis concluded that ADHD and mathematics disability are independently transmitted in families and therefore aetiologically distinct (Monuteaux, Faraone, Herzig, Navsaria, & Biederman, 2005). Subsequent exploratory work contradicted this finding in a selected sample of twins, by suggesting that the association between ADHD and mathematics ability may primarily be explained by shared genetic influences (Willcutt et al., 2010). However, interpretation of these results was constrained because analyses were based only on probands selected for elevations in ADHD symptoms, and not on probands selected directly for mathematics disability or in the unselected population. Moreover, the analyses focused exclusively on genetic factors, and did not test for potential environmental factors underlying this association.

Two twin studies examined the genetic and environmental influences shared between ADHD symptoms and mathematic ability using unselected samples. The first study was based on a U.S. population sample of 271 10-year old twin pairs (Hart et al., 2010). The second study was based on a Dutch population sample of 445 school-age twin pairs (Polderman et al., 2011). Both studies provided evidence that genetic factors are involved in the association between ADHD symptoms and mathematics ability. Only the U.S. study found that this association was also influenced by shared environmental factors (e.g. family or school environments) in addition to genetic factors. However, as these twin studies are inconsistent with the above familial risk analysis, further replication of these results is important.

Inattentiveness and hyperactivity-impulsivity are the two symptom dimensions of ADHD. They are supported by factor analytic evidence, define the constellation of DSM-IV subtypes of ADHD (Willcutt et al., 2012), and show genetic associations in addition to genetic specificity (Greven, Asherson, Rijsdijk, & Plomin, 2011; Greven, Rijsdijk, &

[1]There is no gold-standard, universally applied definition of mathematics disability, and the literature There is no gold-standard, universally applied is additionally complicated by the use of inconsistent labels (e.g., mathematics difficulties/ underachievement/ disability/ disorder, developmental dyscalculia, mathematics ability/ skill), some of which differ conceptually. For the literature reviewed in this paper, we make no differentiation between these labels and concepts. However, for the data shown in this paper, we consider the term mathematics ability to refer to a normally distributed complex trait that ranges from low (disability) to high (ability).

Plomin, 2011; Larsson, Lichtenstein, & Larsson, 2006; McLoughlin, Ronald, Kuntsi, Asherson, & Plomin, 2007). Because of evidence for stronger phenotypic associations of mathematics ability with inattentiveness than hyperactivity-impulsivity (Rodriguez et al., 2007; Willcutt et al., 2012), two of the above papers examined genetic links with mathematics ability separately for the two ADHD symptom dimensions. Hart et al. (2010) concluded that mathematics ability shows similar genetic associations with inattentiveness and hyperactivity-impulsivity. However, the small sample size (N=271) may have limited the statistical power of the study to detect significant differences. In contrast, Willcutt et al. (2010) concluded that mathematics ability is more strongly associated with inattentiveness than hyperactivity-impulsivity, but this difference was not examined statistically. It therefore remains unclear whether mathematics ability also shows stronger genetic associations with inattentiveness than with hyperactivity-impulsivity.

ADHD symptoms and mathematics ability are genetically associated with reading (Davis, Haworth, & Plomin, 2009; Hart et al., 2010; Kovas, Haworth, Dale, & Plomin, 2007), and increasing evidence suggests that phenotypic as well as genetic associations between ADHD symptoms and reading are larger for inattentiveness than hyperactivity-impulsivity (Greven, Harlaar, Dale, & Plomin, 2011; Greven, Rijsdijk, Asherson, & Plomin, 2012; Paloyelis, Rijsdijk, Wood, Asherson, & Kuntsi, 2010; Willcutt, Pennington, Olson, & DeFries, 2007). In addition, ADHD symptoms and mathematics ability are genetically associated with general cognitive ability, referred to as g (Davis et al., 2009; Kovas, Haworth, Dale, et al., 2007; Kuntsi et al., 2004). It is thus possible that associations between ADHD symptoms and mathematics ability are confounded by genetic factors shared with reading or g.

Study aims

The present study addresses three aims using multivariate twin model fitting applied to data from a large population-sample of twins. Aim 1 was to examine the genetic and environmental influences underlying associations between ADHD symptoms and mathematics ability, separately for inattentiveness and hyperactivity-impulsivity.

Aim 2 was to examine the extent to which genetic associations between inattentiveness (or hyperactivity-impulsivity) and mathematics ability can be attributed to genetic factors that inattentiveness (or hyperactivity-impulsivity) and mathematics ability share with hyperactivity-impulsivity (or inattentiveness).

Aim 3 was to examine the extent to which genetic associations between ADHD symptoms and mathematics ability can be attributed to genetic factors that ADHD symptoms and mathematics ability share with reading or g.

Methods

Sample

Participants came from the 12-year assessment of the Twins Early Development Study (TEDS), a U.K. population-representative cohort study of twins born in England and Wales between 1994 and 1996 (Oliver & Plomin, 2007).

Families were excluded from the present study if one or both twins suffered from severe perinatal complications or a severe medical condition such as autism or Down’s syndrome. Uncertain twin sex or zygosity were also grounds for exclusion. The total number of twin pairs included in the analyses was 6121: 982 MZ male, 1209 MZ female, 913 DZ same-sex male, 1082 DZ same-sex female, and 1935 DZ opposite-sex pairs.

Informed parental consent was obtained. Ethical approval for TEDS has been given by the King's College London ethics committee.

Measures

Mathematics ability—Mathematics ability was assessed using mean composites of three web-based tests, completed by each child. The tests were based on the National Foundation for Educational Research 5–14 Mathematics Series, which is closely linked to U.K. National Curriculum criteria for mathematics and the English Numeracy Strategy (nferNelson, 1999). The tests assessed the understanding of numerical and algebraic processes required for problem solving (Understanding Number test), the understanding of non-numerical mathematical processes and concepts including spatial operations such as rotational or reflective symmetry (Non-numerical Processes test), and the ability to perform simple well-rehearsed computations and to recall simple mathematical facts and terminology from memory (Computation and Knowledge test). The tests have demonstrated reliability and validity (Haworth et al., 2007; Kovas, Haworth, Dale, et al., 2007).

ADHD symptom ratings—Parents rated each child's ADHD symptoms using the DSM-IV-based inattentive and hyperactive–impulsive symptom subscales from the Conners' Parent Rating Scale-Revised (Conners, Sitarenios, Parker, & Epstein, 1998). This scale assesses hyperactivity-impulsivity and inattentiveness with nine items each, and the mean of these nine items was taken. The items were sent by postal questionnaire, returned via free-post envelope. The questionnaire uses a 4-point Likert scale from (0) 'not true at all' to (3) 'very much true'. Cronbach's alpha internal consistencies were high for inattentiveness (0.90) and hyperactivity-impulsivity (0.83). A mean composite were created.

Reading—Reading was assessed using a mean composite of four tests. The Test of Word Reading Efficiency (TOWRE; Torgesen, Wagner, & Rashotte, 1999) and the Woodcock-Johnson III Reading Fluency test (Woodcock, McGrew, & Mather, 2001) assessed the twins' ability to read accurately and fluently. The Reading Comprehension Subtest of the Peabody Individual Achievement test (Markwardt, 1997), and the GOAL Formative Assessment in Literacy test (GOAL, 2002) assessed the twins' literal and inferential reading comprehension. The TOWRE was administered via telephone. The other reading tests were web-based. The tests have demonstrated reliability and validity (Haworth et al., 2007; Kovas, Haworth, Dale, et al., 2007).

General cognitive ability (g)—g was assessed using a mean composite of two verbal and two non-verbal web-based tests. The verbal tests were the WISC-III-PI Multiple Choice Information (general knowledge) and the Vocabulary Multiple Choice subtests (Wechsler, 1992). The non-verbal tests were the WISC-III-UK Picture Completion test (Wechsler, 1992), and Raven's Standard and Advanced Progressive Matrices (Raven, Court, & Raven, 1996, 1998). The tests have demonstrated reliability and validity (Haworth et al., 2007).

Statistical analyses

The twin method—The twin method is based on comparisons between identical (monozygotic, MZ) twins, who share 100% of their genes, and fraternal (dizygotic, DZ) twins, who on average share 50% of their segregating genes. Shared environmental influences, which make children in the same family more alike, are equally similar for MZ and DZ twins (100% sharing). There are also individual-specific environments, called non-shared environments, which neither MZ nor DZ twins share with their co-twins (0% sharing).

Based on the genetic and environmental sharing of MZ and DZ twins, conclusions can be drawn about genetic (A), shared environmental (C) and non-shared environmental (E) contributions to individual differences (variance) in a trait, and to associations (covariance) between traits. Standard assumptions of the twin method applied (Plomin, DeFries, Knopik, & Neiderhiser, 2013).

Twin analyses—Phenotypic correlations (trait 1 in twin 1 correlated with trait 2 in twin 1) and cross-twin cross-trait (CTCT) correlations (trait 1 in twin 1 correlated with trait 2 in twin 2) were first obtained. Comparing CTCT correlations between MZ and DZ pairs provided an initial impression of the extent to which genes (A) and environments (C, E) contribute to phenotypic correlations between the measures under investigation.

To address aim 1, a correlated factors solution (Neale & Cardon, 1992) was fitted. This is a standard twin model, and provides genetic (heritability, A), shared environmental (C) and non-shared environmental (E) parameter estimates which represent the proportion of variance in a trait due to A, C, E. It also provides genetic (r_A), shared environmental (r_C) and non-shared environmental ($_{rE}$) correlations. r_A, r_C, $_{rE}$ can range from −1 to 1, and indicate the extent of genetic and environmental associations between two traits. For example, a genetic correlation of 0.50 between inattentiveness and hyperactivity-impulsivity would suggest that 50% of genetic influences are shared between the traits. To obtain a formal confirmation of impressions from CTCT correlations, genetic and environmental contributions to a phenotypic correlation can be obtained from the correlated factors solution by multiplying the product of the square roots of the A, C, E parameter estimates by r_A, r_C, r_E. For example, genetic contributions to the phenotypic correlation between inattentiveness and mathematics ability can be calculated as: $\sqrt{(h^2_{\text{inattentiveness}})}*\sqrt{(h^2_{\text{mathematics}})}*(r_{\text{A inattentiveness-mathematics}})$. Because estimates are multiplied, it is clear that the extent of genetic and environmental contributions to a phenotypic correlation depends not only on the magnitude of r_A, r_C and $_{rE}$, but also of the A, C, E parameter estimates. Dividing genetic and environmental contributions to a phenotypic correlation by the phenotypic correlation gives rise to the proportions of the phenotypic correlation due to A, C, E.

To address aims 2 and 3, Cholesky decompositions (Neale & Cardon, 1992) were fitted, which are mathematically equivalent to a Correlated Factors Solution; however in the Cholesky decomposition the order of variables matters. For example, in Figure 1, phenotypic variance and covariance is accounted for by a set of latent genetic and environmental factors. The first set of latent factors (A_1, C_1, E_1) represents genetic and environmental influences on hyperactivity-impulsivity, as well as genetic and environmental influences shared between hyperactivity-impulsivity, inattentiveness and mathematics ability. The second set of latent factors (A_2, C_2, E_2) represents genetic and environmental influences on inattentiveness and on its covariation with mathematics ability independent of effects shared with hyperactivity-impulsivity. The final set of latent factors (A_3, C_3, E_3) represents genetic and environmental influences specific to mathematics ability and independent of hyperactivity-impulsivity and inattentiveness. Variance and covariance in Figure 2 is partitioned following the same principles, but the order of inattentiveness and hyperactivity-impulsivity is reversed in the model. As a result, Figure 1 allows the examination of genetic and environmental influences shared between inattentiveness and mathematics ability independent of hyperactivity-impulsivity, whereas Figure 2 allows the examination of genetic and environmental influences shared between hyperactivity-impulsivity and mathematics ability independent of inattentiveness. Moreover, extending Figure 1 to include g and reading allows the examination of genetic and environmental influences shared between hyperactivity-impulsivity, inattentiveness and mathematics ability independent of g and reading (see Figure 3).

Twin analysis procedures

Phenotypic correlations, CTCT correlations and twin model results were obtained in the twin model fitting package Mx (Neale, Boker, Xie, & Mae, 2006). The inattentive and hyperactive–impulsive subscales from the Conners' were positively skewed and transformed using the optimised minimal skew command 'lnskew0' in STATA (STATA, 2005). Following standard procedures, raw scores on each measure were regressed for sex and age and residual scores were created. Missing data were handled through full-information maximum-likelihood estimation. Likelihood-based 95% confidence intervals were obtained. Confidence intervals that include zero indicate non-significance of an estimate. Non-overlapping confidence intervals indicate two estimates are significantly different.

Model fit was evaluated using the Bayesian Information Criterion (BIC). Unlike the likelihood ratio χ^2 test, which increases in sensitivity with sample size, the BIC tends to perform better in larger samples and for larger models (Markon & Krueger, 2004). All models in this study had negative BIC values, indicating adequate fit (see online appendix Table S1: Fit statistics).

The question of aetiological sex differences in the present data has previously been addressed, and is therefore not considered here (Davis et al., 2009; Greven, Asherson, et al., 2011; Greven et al., 2012; Greven, Rijsdijk, et al., 2011). Model fitting was guided by these previous studies, e.g., as they found no evidence for significant influences of genetic dominance univariately, the present paper does not test for genetic dominance. Twin correlations (correlations within MZ or DZ pairs for a particular trait) and descriptive statistics are available from these studies.

Results

Phenotypic correlations

Phenotypic correlations, shown in Table 1, revealed that mathematics ability correlated significantly more strongly with inattentiveness (−0.26) than with hyperactivity-impulsivity (−0.18). These phenotypic correlations were significantly different because their confidence intervals did not overlap, and were negative as more inattentive or hyperactive-impulsive symptoms were linked to lower mathematics scores.

Reading also correlated significantly more strongly with inattentiveness (−0.27) than with hyperactivity-impulsivity (−0.18). Inattentiveness and hyperactivity-impulsivity showed modest phenotypic correlations with g (−0.20 and −0.17, respectively).

Cross-twin cross-trait correlations

For hyperactivity-impulsivity, genetic and shared environmental contributions to the phenotypic correlations with mathematics ability, reading and g were implicated, because the DZ CTCT correlations were greater than half the MZ CTCT correlations (see online appendix Table S2: MZ and DZ CTCT correlations). For inattentiveness, the DZ CTCT correlations were less than half the MZ CTCT correlations, which implicated genetic, but no shared environmental contributions to the phenotypic correlations with mathematics ability, reading and g. In addition, modest non-shared environmental contributions to these correlations with inattentiveness were also implicated, as the MZ CTCT correlations deviated somewhat from the phenotypic correlations of inattentiveness with mathematics ability, reading and g.

Twin analysis results

The correlated factors solution (Table 2), which addressed aim 1, confirmed the previous finding of high heritability for inattentiveness (67%) and hyperactivity-impulsivity (73%), and moderate heritability for mathematics ability (46%). Inattentiveness and hyperactivity-impulsivity each showed a significant genetic correlation with mathematics ability (−0.41 and −0.22, respectively). However, the genetic correlation with mathematics ability was significantly larger for inattentiveness than hyperactivity-impulsivity. These genetic correlations were significantly different because their confidence intervals did not overlap. They were negative because phenotypic correlations were negative.

The significant and moderate to high heritabilities of inattentiveness and mathematics ability, together with their significant genetic correlation of −0.41, suggest that the phenotypic correlation between inattentiveness and mathematics ability could significantly and largely be attributed to genetic factors (see Methods description and Table 2). The phenotypic correlation between hyperactivity-impulsivity and mathematics ability could also significantly and largely be attributed to genetic factors (73% due to A; Table 2).

Shared environmental (range from 10% to 23%) and non-shared environmental (12% to 31%) parameter estimates for inattentiveness, hyperactivity-impulsivity and mathematics ability were modest, but significant (Table 2). Inattentiveness demonstrated a significant non-shared environmental (−0.20), but a non-significant shared environmental correlation with mathematics ability. Thus, although the phenotypic correlation between inattentiveness and mathematics ability was largely attributable to genetics, non-shared environmental contributions were also significant, albeit modest. In contrast, hyperactivity-impulsivity showed a significant shared environmental correlation (−s0.27), but a non-significant non-shared environmental correlation (estimated at zero) with mathematics ability. Thus, the phenotypic correlation between hyperactivity-impulsivity and mathematics ability could significantly and modestly be attributed to shared environmental factors, although genetics explained most of this correlation.

These results mirror findings on the aetiological relations between ADHD symptoms and reading. For example, reading also showed a significantly higher genetic correlation with inattentiveness (−0.31) than with hyperactivity-impulsivity (−.12; Table 2). Because genetics explained a large part of variation and covariation in the measures under investigation (Table 2), the remainder of this study will focus on genetic results.

To address aim 2, Cholesky decompositions were fitted to data on ADHD symptoms and mathematics ability. All factor loadings on A_1 in Figure 1 and Figure 2 were significantly greater than zero, which suggests a significant amount of genetic covariance between hyperactivity-impulsivity, inattentiveness and mathematics ability, as already evident from the genetic correlations in Table 2. In addition, the significant factors loadings on A_2 in Figure 1 indicate significant genetic associations between inattentiveness and mathematics ability after controlling for hyperactivity-impulsivity. It can be shown from the paths that link inattentiveness and mathematics ability via latent factors A_1 and A_2 that the genetic association between inattentiveness and mathematics ability was largely independent of hyperactivity-impulsivity.

In contrast, the loading of mathematics ability on latent factor A_2 in Figure 2 was non-significant, which suggests that there were no significant genetic associations between hyperactivity-impulsivity and mathematics ability after controlling for inattentiveness. Finally, most genetic influences on mathematics ability were specific to mathematics ability, that is, not shared with either inattentiveness or hyperactivity-impulsivity (see significant loadings on latent factors A_3 in Figure 1 and Figure 2).

To address aim 3, the Cholesky decomposition in Figure 1 was extended as shown in Figure 3. All loadings on A_1 in Figure 3 were significant, which suggests that there were significant genetic associations between g, reading, hyperactivity-impulsivity, inattentiveness and mathematics ability. Consistent with previous evidence (Paloyelis et al., 2010), there were significant genetic associations between reading and inattentiveness independently of g (see significant factor loadings of reading and inattentiveness on A_2 in Figure 3). For hyperactivity-impulsivity, the modest genetic associations with reading dropped below significance after accounting for g (see non-significant factor loading of hyperactivity-impulsivity on A_2 in Figure 3). The most notable finding from Figure 3 was that there were significant genetic associations between inattentiveness and mathematics ability independent of g, reading and hyperactivity-impulsivity (see significant loadings on A_4 in Figure 3). It can be shown from the paths linking inattentiveness and mathematics ability via latent factors A_1 to A_4 that the genetic correlation between inattentiveness and mathematics ability was moderately independent of hyperactivity-impulsivity, reading and g. Genetic influences specific to mathematics ability remained (see significant loading on A_5 in Figure 3).

Discussion

This study revealed the novel finding that mathematics ability shows significantly stronger phenotypic and genetic associations with inattentiveness than with hyperactivity-impulsivity. This mirrors the pattern of relationships between ADHD symptoms and reading, as reading also shows larger phenotypic and genetic associations with inattentiveness. Independently of inattentiveness, there were no residual genetic associations between hyperactivity-impulsivity and mathematics ability, which suggests that genetic associations between hyperactivity-impulsivity and mathematics ability can fully be explained by inattentiveness. However, genetic associations between inattentiveness and mathematics ability were largely independent of hyperactivity-impulsivity, and could only moderately be accounted for by reading and g. Although the pattern of genetic associations with ADHD symptoms was similar for mathematics ability and reading, genetic factors shared between ADHD symptoms and reading only partially overlapped with those shared between ADHD symptoms and mathematics ability.

Associations between ADHD symptoms and mathematics ability were largely attributable to genetics; however, environmental influences also played a modest role. Non-shared environments also influenced the association between inattentiveness and mathematics ability, whereas shared environments also influenced the association between hyperactivity-impulsivity and mathematics ability.

Strengths and limitations

The present study used continuous assessments of ADHD symptoms in an unselected population-representative sample rather than focusing on the clinical extreme. The focus on the whole distribution of individual differences follows from strong evidence that complex disorders like ADHD, reading and mathematics disability represent the extreme and impairing tail of continuously distributed traits (Larsson, Anckarsater, Rastam, Chang, & Lichtenstein, 2012; Plomin, Haworth, & Davis, 2009). Using an unselected sample facilitated the collection of data from a large number of participants, thereby increasing power, and helped avoid the potential biases associated with referral patterns and ascertainment of clinical samples. Nonetheless, generalisability of results to the clinical extreme remains to be tested, to which considerations relating to an exclusive reliance in this study on parent ratings of ADHD symptoms are also relevant.

Conclusion

The present findings suggest that increased genetic risk for inattentiveness is linked to increased genetic risk for reduced mathematics ability (and vice versa), irrespective of risk for hyperactivity-impulsivity. Genetic results from this study therefore support previous phenotypic work in highlighting the stronger links between academic difficulties and inattentive versus hyperactive-impulsive ADHD symptoms, and provide additional support for the validity of distinguishing between the symptom dimensions in ADHD.

Phenotypic and aetiological associations between inattentiveness and mathematics ability could in part reflect a direct causal link at the cognitive level due to shared neuropsychological deficits. Deficits linked to processing speed, attention, working memory and other executive functions may be suitable candidates (Ashkenazi, Rubinsten, & Henik, 2009; Willcutt et al., 2010). Including such neuropsychological measures in future twin studies will allow researchers to study this hypothesis.

The present finding of shared environmental influences on associations between ADHD symptoms and mathematics ability, in addition to genetic influences, is consistent with a previous finding from a U.S. sample (Hart et al., 2010). An obvious target for the shared environmental factors that link hyperactivity-impulsivity and mathematics ability are the environments children share at home and school.

The non-shared environmental factors found to be in common between inattentiveness and mathematics ability also merit further investigation. Non-shared environments contribute to associations between two traits if environments that are experienced by only one member of a twin pair influence both traits (e.g., differences in the twins' school or home environments, or differences in their perceptions of these environments; see Plomin et al., 2013).

Results also suggest that some genes associated with ADHD symptoms (especially inattentiveness) might also be candidate genes for mathematics ability, with genetic factors specific to mathematics ability also likely. This question remains an important area of enquiry for future research. The present study provides an important first step in illuminating relative genetic and environmental factors that underlie associations between ADHD and children's mathematics ability.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Key points

- The present study examined the association between ADHD symptoms and mathematics ability in a large population sample of twins, separately for inattentive and hyperactive-impulsive ADHD symptoms.
- Mathematics ability and inattentiveness showed a significantly greater phenotypic and genetic correlation than mathematics ability and hyperactivity-impulsivity.
- The genetic correlation between inattentiveness and mathematics ability could only partially be accounted for by hyperactivity-impulsivity, reading and g.
- Results provide further evidence for considering inattentiveness and hyperactivity-impulsivity separately. Genes previously implicated in ADHD (especially inattentiveness) may be suitable candidate genes for reduced mathematics ability.

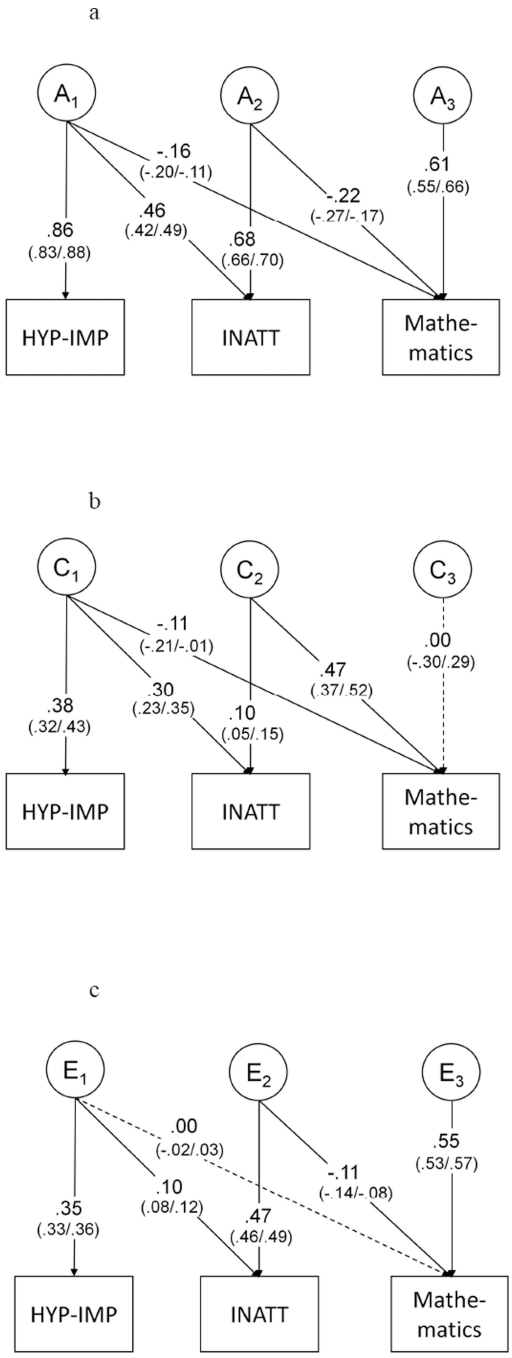


Figure 1.

Cholesky decomposition of hyperactivity-impulsivity (HYP-IMP), inattentiveness (INATT) and mathematics ability. Panels (**a**), (**b**) and (**c**) show genetic, shared environmental, and non-shared environmental results, respectively. Path estimates are standardised. Non-significant paths are shown as dashed lines.

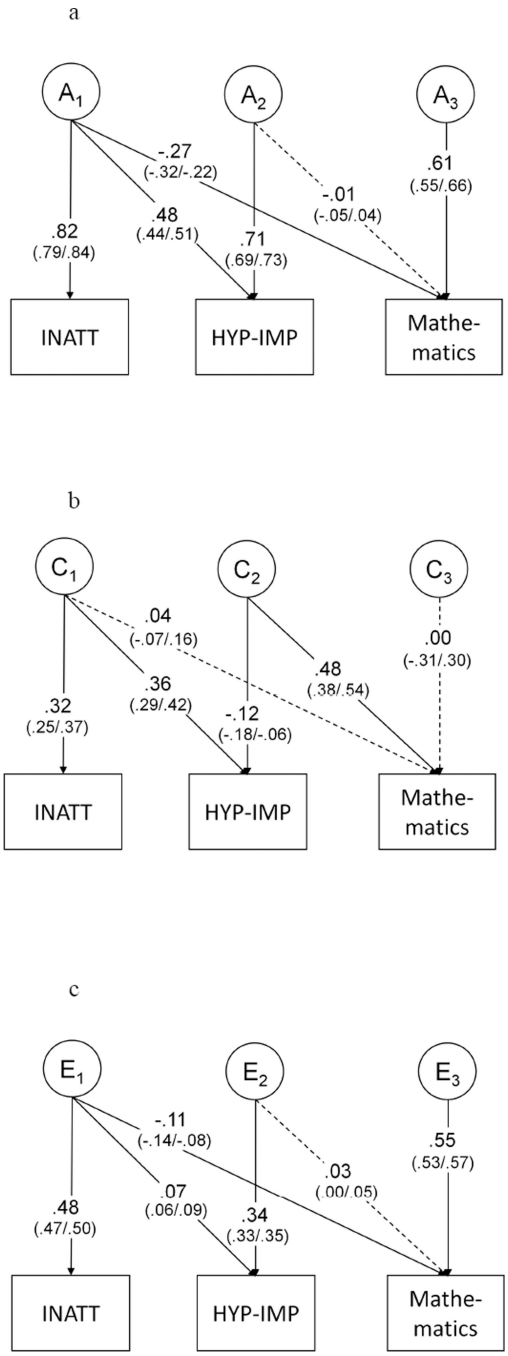
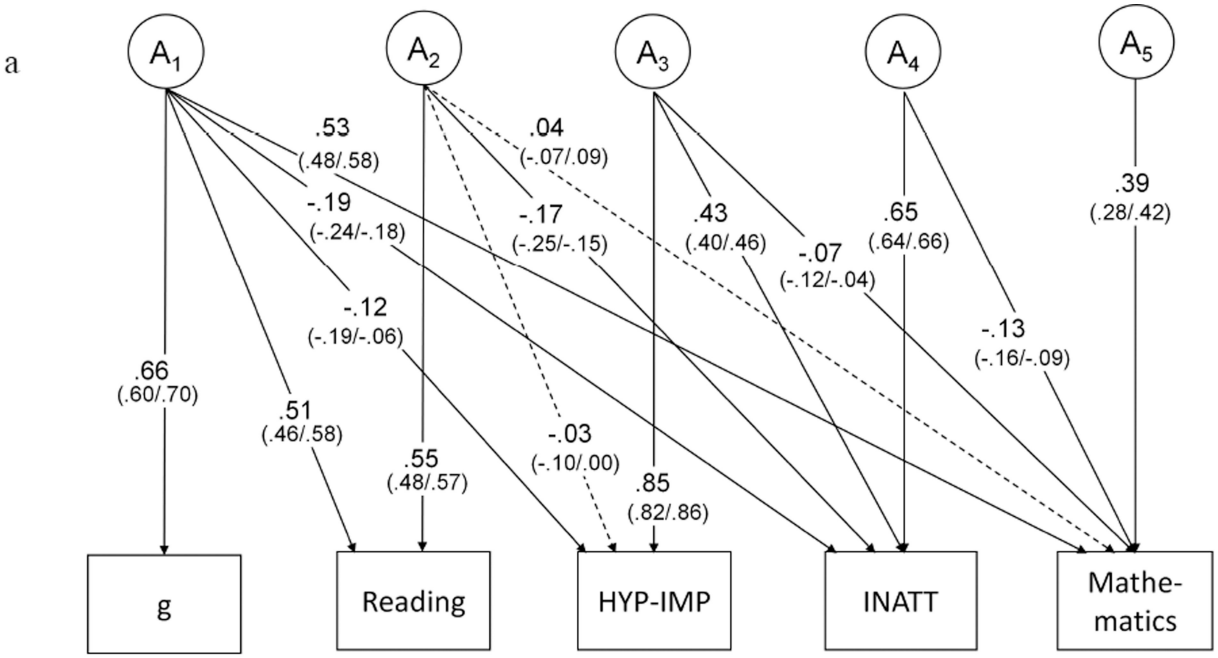
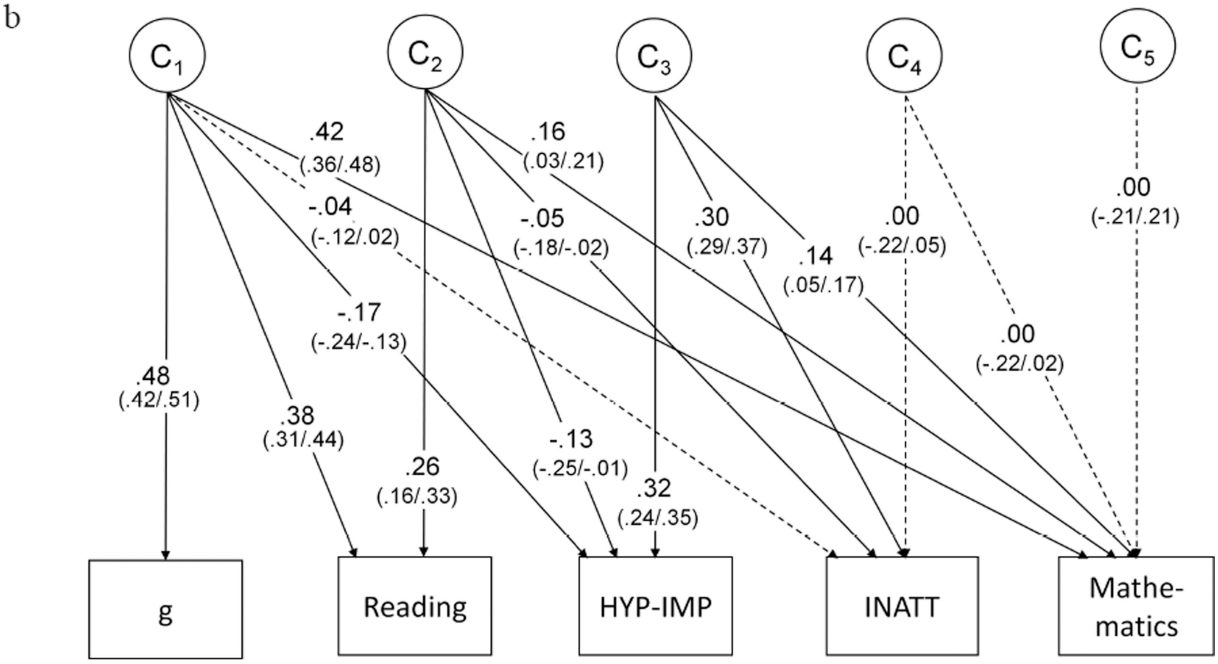


Figure 2.
Cholesky decomposition of inattentiveness (INATT), hyperactivity-impulsivity (HYP-IMP) and mathematics ability. Path estimates are standardised.

a



b



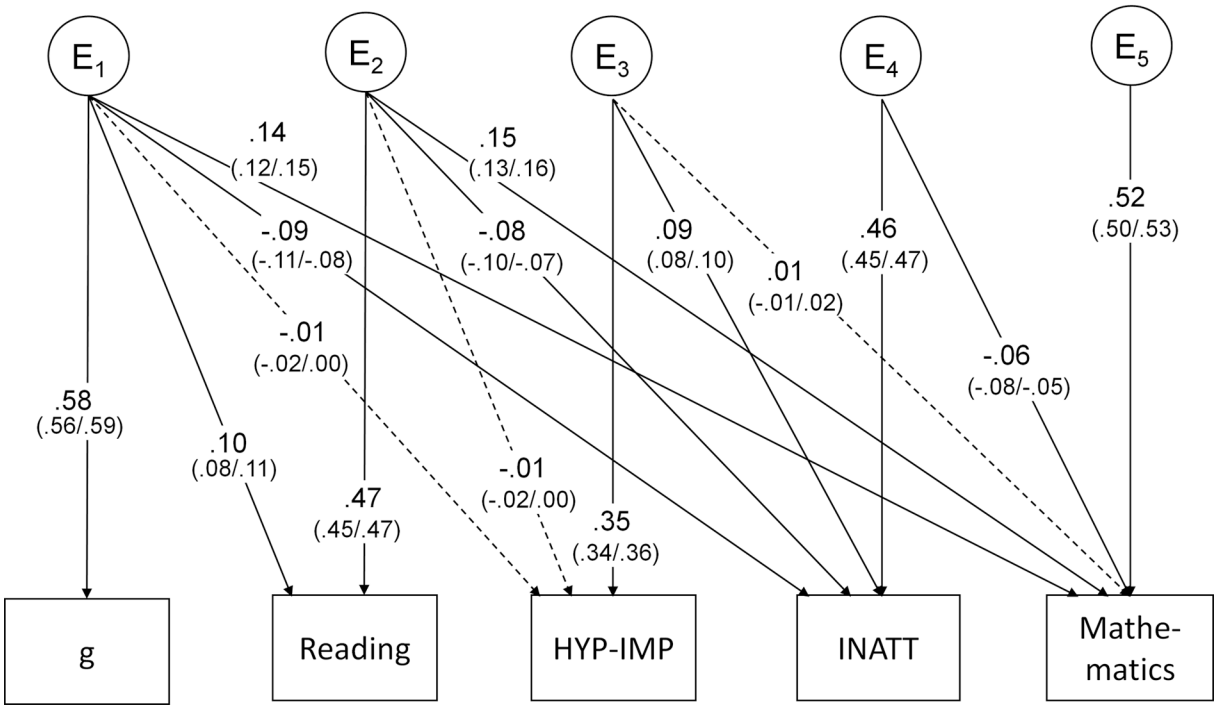


Figure 3.
Cholesky decomposition of general cognitive ability (g), reading, hyperactivity-impulsivity (HYP-IMP), inattentiveness (INATT) and mathematics ability. Path estimates are standardised.

Table 1

Phenotypic correlations

	g	Reading	HYP-IMP	INATT	Mathematics
g	-				
Reading	.57 (.56/.58)	-			
HYP-IMP	−.17 (−.19/−.15)	−.18 (−.20/−.17)	-		
INATT	−.20 (−.22/−.19)	−.27 (−.29/−.26)	.54 (.52/.55)	-	
Mathematics	.64 (.63/.65)	.58 (.57/.59)	−.18 (−.20/−.16)	−.26 (−.28/−.24)	-

g= general cognitive ability; HYP-IMP= hyperactivity-impulsivity; INATT= inattentiveness; MZ= monozygotic, DZ= dizygotic; CTCT= cross-twin cross-trait. 95% confidence intervals are presented in parentheses.

Table 2

Genetic and environmental parameter estimates (on diagonals), genetic and environmental correlations (below diagonals) and genetic and environmental contributions to phenotypic correlations (above diagonals)

	g	Reading	HYP-IMP	INATT	Mathematics
A estimates					
g	**.43** (**.38/.45**)	.34 [59%]	−.08 [48%]	−.13 [64%]	.35 [55%]
Reading	.68 (.62/.72)	**.56** (**.51/.61**)	−.08 [43%]	−.19 [72%]	.29 [51%]
HYP-IMP	−.14 (−.21/−.11)	−.12 (−.18/−.09)	**.73** (**.69/.74**)	.39 [73%]	−.13 [73%]
INATT	−.23 (−.30/−.17)	−.31 (−.32/−.27)	.56 (.53/.58)	**.67**[a] (**.62/.68**)	−.23 [b]
Mathematics	.79 (.73/.85)	.58 (.43/.64)	−.22 (−.28/−.17)	−.41[a] (−.47/−.37)	**.46**[a] (**.40/.48**)
C estimates					
g	**.23** (**.18/.27**)	.18 [31%]	−.08 [49%]	−.02 [10%]	.20 [32%]
Reading	.82 (.70/.89)	**.21** (**.17/.25**)	−.10 [55%]	−.03 [11%]	.20 [35%]
HYP-IMP	−.45 (−.63/−.27)	−.56 (−.72/−.45)	**.15** (**.11/.18**)	.11 [21%]	−.05 [27%]
INATT	−.14 (−.36/.10)	−.21 (−.42/.02)	.93 (.72/.97)	**.10** (**.06/.12**)	.02 [b]
Mathematics	.89 (.79/.90)	.92 (.88/.95)	−.27 (−.44/−.04)	.12 (−.12/.35)	**.23** (**.18/.24**)
E estimates					
g	**.34** (**.32/.35**)	.06 [10%]	.00 [3%]	−.05 [25%]	.08 [13%]
Reading	.20 (.16/.21)	**.23** (**.21/.23**)	.00 [2%]	−.05 [17%]	.09 [15%]
HYP-IMP	−.02 (−.06/.02)	−.02 (−.06/.01)	**.12** (**.11/.13**)	.03 [6%]	.00 [0%]
INATT	−.18 (−.22/−.14)	−.20 (−.24/−.17)	.20 (.16/.22)	**.23** (**.22/.24**)	−.05 [b]
Mathematics	.26 (.22/.27)	.32 (.28/.34)	.00 (−.04/.04)	−.20 (−.23/−.16)	**.31** (**.30/.33**)

g= general cognitive ability; HYP-IMP= hyperactivity-impulsivity; INATT= inattentiveness. Results obtained from a quintivariate correlated factors solution. 95% confidence intervals are presented in parentheses. Genetic (heritability A), shared environmental (C) and non-shared environmental (E) parameter estimates are presented in bold on the diagonals. Genetic and environmental correlations are given below the diagonals. Contributions of the A, C, E parameters to the phenotypic correlations, calculated as the product of the square roots of the A, C, E parameter estimates multiplied by genetic and environmental correlations, are presented above the diagonals. For example, taking the estimates marked with [a], the genetic contribution to the phenotypic correlation between inattentiveness and mathematics ability was √0.67*√0.46*−.0.41 = −.0.23. Genetic and environmental contributions to the phenotypic correlation can be expressed in terms of the proportions of the phenotypic correlation due to genes and environments [shown in brackets].

[b] It was not possible to formally estimate the proportions of the phenotypic correlation between inattentiveness and mathematics ability due to genes and environments as the shared environmental correlation between inattentivenss and mathematics ability was positive (albeit non-significant), whereas the genetic and non-shared environmental correlations were negative. Unfortunately this issue could not be avoided by simply dropping the relevant shared environmental paths. However, examination of the magnitude and significance of A, C, E parameters estimates and genetic and environmental correlations, revealed that the correlation between inattentiveness and mathematics ability was significantly and largely mediated by A, significantly and modestly by E and was not significantly mediated by C.