BEHAVIOURAL GENOMICS OF MATHEMATICS

Maria G.Tosto, 1, 3, Claire M. A. Haworth2, &, Yulia Kovas1, 2, 3\*

1 Department of Psychology, Goldsmiths, University of London

2 Social, Genetic and Developmental Psychiatry Centre, King’s College London

3 Department of Psychology, Tomsk State University

\*Corresponding author: y.kovas@gold.ac.uk

The first complete DNA sequence of the human genome was outlined in 2001. This significant breakthrough occurred less than fifty years after James Watson and Francis Crick first proposed a model of the molecular structure of DNA. Since then, our understanding of human genetics has leapt forward exponentially, leading to the application of genetic knowledge and methodologies to unravelling the aetiology of psychopathologies and of individual differences in cognition, abilities, and personality.

In this chapter we address the contribution of behavioural genetic approaches, which include both quantitative methods (e.g. twin, adoption, and other family studies) and molecular genetic methods (e.g. association studies) to the investigation of mathematical development. We start with providing a brief overview of the quantitative genetic methodologies. The chapter then reviews the growing body of research into the relative contribution of genes and environments to the variation in mathematical ability at different ages and in different populations, including the examination of the aetiology of any observed sex differences in mathematics. This review also includes a relatively small body of multivariate twin research into the aetiological links between mathematics and other areas of cognition and achievement, as well as the links between mathematical ability and disability. In the multivariate section, we review the latest results examining the genetic and environmental relationships between mathematical achievement and mathematical motivation. In the molecular genetic section, we present the few molecular genetic studies that have specifically explored mathematical abilities. We conclude the chapter with outlining the future directions of the behavioural genetic research into mathematical learning and the potential implications of this research.

*Quantitative genetic methodologies*

Recent behavioural genetic research leaves no doubt that individual differences in behaviour and cognition are a product of both genetic and environmental factors (e.g. Plomin et al. 2012). This research also suggests that the path leading from genes to behaviour is intertwined with the environment. While molecular genetic research (reviewed in the next section) aims to detect and identify the genes implicated in the variation in different aspects of behaviour and cognition, quantitative genetics aims to quantify the relative contribution of genes and environment to the variation in traits and co-variation among traits.

Genetic influences refer to the influence of multiple alleles – genetic markers that can differ in the population (rather than evolutionarily conserved invariant markers). Mostly, genetic influences are of the additive type, meaning that the variance of a trait that is attributed to genetic factors can be derived by adding the independent effects of all alleles at all loci that affect the trait. Some genetic influences may derive from interactions between genes at different loci. These epistatic processes, by which the effects of a gene on a specific trait depend on the influences of one or more other genes remain very poorly understood (e.g. Cordell 2002).

From the behavioural genetic perspective, environmental influences are very broadly defined as effects on a trait produced by anything other than heritable DNA sequence variation. In twin and other family designs, any environmental influences that contribute to differences between family members are referred to as "non-shared"; whereas any environmental influences that contribute to the similarity between family members are referred to as "shared" (see Plomin and Daniels 1987; Rijsdijk and Sham 2002; Plomin et al. 2012).

Non-shared environments are defined as any event that is experienced or perceived differently by family members and contributing to dissimilarities between them. These may include perinatal events, accidents, surgical procedures, and different peers. Intuitively, environments that are objectively shared among individuals within a family seem more likely to increase their similarities. We can think of nutrition, parenting practices, or socio-economic status as shared experiences that may make family members more similar in a specific trait, if these factors affect the trait in question. For example, it is reasonable to think that family members would share similar eating habits that could increase similarity in weight among them. However, research shows that adult family members do not resemble each other in weight beyond genetically influenced similarity (e.g. Grilo and Pogue-Geile 1991). Often, objectively shared environments lead to differences rather than similarities, through differential perceptions and other poorly understood mechanisms (e.g. Plomin and Daniels 1987; Dunn and Plomin 1990). Parental divorce, for instance, is a family event and as such is shared by siblings, but research shows that divorce often impacts siblings’ behaviour in different ways (Hetherington and Clingempeel 1992; Amato 2000). The estimate of non-shared environment in quantitative genetic methodology also includes any measurement and procedural errors, as non-systematic error can only contribute to dissimilarity in assessed traits between twins or other family members.

One of the most prevalent methods used in quantitative genetic research is the twin design. As with any approach, the twin method has some limitations and relies on several assumptions (see Plomin et al. 2012 for additional details). One of these assumptions is that the same shared environmental influences will equally affect monozygotic or identical twins (MZ) and dizygotic or fraternal twins (DZ), that is to say that shared environment is the same for both MZ and DZ twins (e.g. Rijsdijk and Sham 2002). Violation of the equal environments assumption would incorrectly include the environment together with genetic influences as causes for the observed MZ twins’ similarity. Although MZ twins are more likely to be treated alike, research that has investigated the equal environments assumption has shown that this similar treatment is a reflection of their increased genetic similarities (e.g. Evans and Martin 2000). Because twins are not a random sample, their representativeness has been questioned. For example, newborn twins on average weigh less than singletons; however, by middle childhood the weight differences disappear (MacGillivray et al. 1988). Similarly, twins’ achievement in adolescence has been shown to be the same as singletons’ (Christensen et al. 2006), despite the slightly lower average IQ displayed by twins in early childhood (Ronalds et al. 2005). Many studies tested the twin method and concluded that findings from twin studies are valid and are applicable to the general population (e.g. Kovas et al. 2007a; Plomin et al. 2012; Hart et al. 2010a).

The twin method relies on the comparison of intraclass correlations between identical and fraternal twins. In the univariate genetic analysis, this comparison allows estimating the proportion of variance in a trait that can be attributed to genetic, shared and non shared environmental influences (Plomin et al. 2012). MZ twins result from the division of one single zygote - one fertilised egg. It is generally assumed that MZ twins are genetically identical, although recent research suggests some genetic differences (e.g. Bruder et al. 2008). DZ twins occur when two eggs are fertilised at the same time. DZ twins, like any other pair of siblings share on average 50 percent of the segregating genes. Twins brought up in the same family may be similar to each other because of the influence of their common environment as well as because of their shared genes. If genes play an important role in a trait, identical (MZ) twins must be more similar on that trait, compared to fraternal (DZ) twins. The influence of genetic factors (heritability) is calculated as twice the difference between MZ and DZ twin correlations. Shared environmental factors are implicated if the DZ twin correlation is greater than half of the MZ twin correlation, and can be calculated as the difference between the MZ twin correlation and the heritability. Non-shared environmental influences are indicated by the extent to which the correlation between MZ twins is not 100 percent. In a practical example, if the MZ twins correlation for a trait is 0.8 and the DZ correlation is 0.5, heritability for that trait would be 60% [2 \* (0.8 - 0.5) = 0.6], shared environment would be 20% (0.8 – 0.6 = 0.2) and non-shared environment would be 20% (1 – 0.8 = 0.2). The effects of genetic, shared and non-shared environmental influences are more accurately estimated using structural equation modelling, as the latent variables that are more likely to reproduce the observed MZ and DZ variance and covariance. The analysis also calculates confidence intervals around the estimates, which give an indication of their significance (see Plomin et al. 2012).

Multivariate genetic analysis allows the estimation of genetic and environmental sources of covariation among different traits (see Martin and Eaves 1977). Comparison between MZ and DZ twins is conducted on the cross-trait twin correlations. For example, in the investigation of the aetiology of the covariation between mathematics and reading the analyses would be conducted on the correlation between one of the twins in the pair in mathematics and the co-twin in reading. An MZ twin cross-trait correlation greater than the DZ twin cross-trait correlation indicates that common genetic factors contribute to the covariation between the two traits. DZ twin correlations exceeding half the MZ twin correlation indicate shared environmental influences. The absence of a significant cross-trait twin correlation implies that the common aetiological influences are due to non-shared environmental factors. From multivariate genetic analysis it is also possible to determine the bivariate heritability, which indexes the extent to which the phenotypic correlation between two traits is genetically mediated. The remaining phenotypic correlation is explained by bivariate shared and bivariate non-shared environment. Another important statistic derived from multivariate analyses is the genetic correlation: the extent to which genetic influences on one trait correlate with the genetic influences on another trait - independently from univariate heritability of both traits. For example, it is possible that two traits have low heritability (genetic influences are very small), but have a high genetic correlation (the same genetic factors influence both traits) (for details see Neale and Maes 2003; Kovas et al. 2007a).

The multivariate method can be extended to longitudinal data, as an alternative to univariate analysis on cross-sectional data (see Loehlin 1996). Longitudinal genetic analyses provide estimates of genetic (and environmental) stability and change. The analyses are conducted on the same trait (e.g. mathematical performance) assessed at different ages. For example, it is possible that mathematics is influenced by similar genetic (or environmental) factors at different ages, but these influences vary their strength with time (quantitative differences). If different genetic (or environmental) factors affect mathematics across ages, qualitative changes take place.

Genetic methodologies are also well suited to unravel the aetiology of the links between ability and disability. Low/high mathematical abilities may be qualitatively different from normal variation if different factors influence variation at the extremes and in the normal range of mathematical performance. Alternatively, the same factors may drive individual differences in high/low and normal abilities, but to different extents (quantitative differences). One of the methods used to investigate the relationship between abilities and disabilities is the DeFries-Fulker extremes analysis (DeFries and Fulker 1985).This method relies on identifying low or high ability groups by way of cut-offs, after which probandwise concordances are calculated. Probandwise concordances index the probability of both twins in a pair manifesting the same disorder/talent. The comparison of MZ and DZ concordances allows the calculation of the group heritability. This indexes the extent to which the mean differences between the proband group and the rest of the population are due to genetic or environmental factors. A concordance higher for MZ than DZ twins suggests that the mean differences between the proband group and the population (the unselected sample) are driven by genetic influences, to some extent. If identical and fraternal twins had the same concordance, the group heritability would be zero (no genetic influences). However, in absence of genetic influences, the proband deficit could be due non-shared environmental factors (an injury or illness not shared by the co-twin) or shared environmental factors (family nutrition for example) - or a combination of both. Group heritability helps to understand whether the proband group is "special" or different from the rest of the population. If the aetiology of individual differences in the proband sample is the same as in the whole distribution, the group heritability should not be significantly different from the heritability of the unselected sample (for details see Kovas et al. 2007a; Haworth et al. 2009a).

Finally, sex-limitation models can address whether the same genetic and environmental factors influence variation in males and females. Quantitative sex differences exist if the same genetic and environmental factors affect males and females but with different strength. If different environmental and/or genetic factors explain individual differences in males and females the differences are qualitative. It is also possible that there are no differences in the aetiology of individual differences between males and females. In this case the factors that drive individual differences in males are the same factors that drive individual differences in females (for details see Neale and Maes 2003). It is important to note that the aetiological sex differences related to variance do not necessarily translate into mean sex differences.

*Genetic and environmental aetiology of individual differences in mathematics*

Over the last few decades, the social desirability of good mathematic skills has increased due to the wide range of advantages associated with them. A recent survey reports a relationship between improvement in the numeracy skills of a population and the increase in productivity for that Nation (OECD 2010). Similarly, social and economic disadvantages have been related to low numeracy (Gross et al. 2009). The quest for understanding how different people acquire and can improve mathematical skills is therefore more important than ever. This importance is reflected in the increased number of quantitative genetic studies into the aetiology of individual variation in mathematically-relevant traits.

One of the first twin studies that examined mathematical ability used 146 MZ and 132 DZ pairs of 6 to 12 year old twins from the Western Reserve Twin Project. The study found that mathematics, measured by standardised tests of school achievement, was modestly heritable (.20), with shared and non-shared environment explaining most of the variation (.71 and .10, respectively) (Thompson et al. 1991). Another study used a sample of twins with age ranging between 8 and 20 years (Alarcόn et al. 2000). 570 twin pairs of this sample were controls, in 555 pairs one of the twins manifested reading or mathematical problems or both. The results showed an average heritability of .90 in both groups with virtually non-significant environmental influences. The wide range of univariate estimates illustrated in these studies deserves some methodological consideration. Twin correlations for a trait may be overestimated because of common factors unrelated to the trait. Twins in a pair are of the same age; MZ twins and around half of the DZ twins are of the same sex. In twin analyses it is common practice to correct for age and sex in order to avoid inflating correlations because of these factors (McGue and Bouchard 1984). The estimates reported from Thompson et al. (1991) were in fact affected as the measures were not corrected. When the correction for age and sex was applied, the estimates revealed moderate genetic and shared environmental influences (~.40 for both) (in Kovas et al. 2007a).

Other factors also need to be considered. Quantitative genetic investigations of complex traits suggest somewhat different patterns of genetic and environmental influences on different traits. Reading abilities, for example, have shown consistently substantial genetic and shared environmental influences across ages and populations (e.g. Light et al. 1998; Stromswold 2001; Byrne et al. 2005, 2006). Conversely, the heritability of *g* has been shown to increase consistently from early to middle childhood (Davis et al. 2009a; Haworth et al. 2010). Although it is unclear whether the inconsistencies in the estimates of mathematical heritability can be explained by differences in participants’ age, the findings suggest that age-homogeneous twin samples should be used in behavioural genetic investigations for at least two reasons. First, the trait itself changes across the school years - what we call “mathematics” may involve very different cognitive and motivational processes at different ages, reflected in the changes in how mathematics is measured. Second, new genes and environments may become active or relevant during development, for example reflecting changes in pubertal processes or in socialising. Estimates of genetic and environmental contributions are population-based as they explain the sources of individual differences within a particular population; these estimates may differ not only for different ages, but also for different countries or cultures. If a particular environment is uniform within a culture (e.g. a national curriculum or educational standards), this environment is unlikely to explain much of the inter-individual variation. In such a population, heritability of a trait may be higher. Much more research is needed in order to clarify the sources of inconsistencies among different studies, including careful examination of cultural norms and provisions. Further, although Thompson et al. (1991) and Alarcόn et al. (2000) used samples with a respectable number of twins, power calculations indicate that twin studies need samples as large as 600 twin pairs (Martin et al. 1978) to many thousand pairs (Martin et al. 1994) in order to provide accurate estimates.

Much recent research into the aetiology of variation in mathematical ability and achievement comes from the Twins’ Early Development Study (TEDS), a large-scale longitudinal study comprising of three cohorts of twins recruited at birth in 1994, 1995 and 1996 in the United Kingdom. TEDS twins have been regularly assessed from birth on multiple measures of behaviour, cognition, and achievement - by different means: in person; with child, parent and teacher questionnaires; by telephone; and more recently with web-based test batteries. About 12,000 pairs are currently active in the study (Oliver and Plomin 2007; Haworth et al. in press). The large representative sample and the longitudinal nature of TEDS, have allowed researchers to address many of the methodological issues raised by previous studies.

The first large-scale assessment of mathematical achievement was conducted in over two thousand TEDS twin pairs when they were 7 years of age (Oliver et al. 2004). Teacher-rated mathematics was found to be moderately heritable (.66), with negligible shared environmental influences, and modest non-shared environmental influence (.25). As the mathematical domain is multifaceted (e.g. Dowker 2005), it is important to examine the relative contributions of genes and environments to the different aspects of mathematical ability and achievement. Oliver et al (2004) estimated genetic and environmental influences on three different mathematical components, which are part of the UK National Curriculum for mathematics: “Using and Applying Mathematics”, “Numbers”, and “Shapes, Space and Measures”. The heritability and environmental estimates were similar for the three components.

A very similar pattern of results emerged in the assessment of 5,421 TEDS twins (individuals) at 9 years (Kovas et al. 2007a). Mathematics, rated by teachers, showed genetic influences of .72, almost non-existent shared environmental influences, and very modest (.23) non-shared environment. The three mathematical components again yielded highly similar estimates: genetic influences ranged between .63 (Shapes, Space and Measures) and .73 (Using and Applying Mathematics); shared environment was negligible for all three components; and estimates for non-shared environment ranged from .26 (Using and Applying Mathematics) to .28 (Shapes, Space and Measures). At 10 years, 2,674 twin pairs were assessed using an online battery of three mathematical sub-tests: “Understanding Number”, “Non-Numerical Processes”, and “Computation and Knowledge” (Kovas et al. 2007b). Similarly to previous estimates, shared environment had very small effects on all three measures and the non-shared environmental influences were between .42 and .48. Although “Non-Numerical processes” showed a lower heritability (.32) compared to the other two components (.42 and .45 respectively), the differences in heritability among the three measures were not significant. Assessment of over 5,000 TEDS twin pairs at 12 years showed strong genetic influences on mathematical achievement (.61), and small shared (.18) and non-shared (.21) environmental influences (Davis et al. 2009b). The latest assessment of the TEDS twins at age 16, carried out on over 3,000 twin pairs, again showed high genetic influences on web-tests of mathematical achievement (.57), with small shared (.21) and non-shared environmental influences (.22) (Tosto, Plomin, Petrill et al. in preparation). Overall, these results demonstrate consistent genetic and non-shared environmental influences effects on different aspects of mathematical ability across the school years.

Several other recent studies have addressed the aetiology of different aspects of mathematical skills using different twin samples. The US-based Western Reserve Reading Project for Math (WRRPM) assessed 228 ten year-old twin pairs on four different mathematical components: “Calculation”, “Fluency”, “Applied Problems”, and “Quantitative Concepts” (Hart et al. 2010b), reporting univariate heritability estimates of .35 and .34 for “Calculation“ and “Fluency“, and a slightly higher heritability for “Applied Problems“ and “Quantitative Concepts“ (.41 and .49 respectively). Interestingly, the shared environmental influences estimated in this study (.32-.46) were higher compared to the TEDS estimates for mathematical sub-components at the same age (.07-.23); whereas the non-shared influences (.19-.25) were lower than in TEDS (.42-.48).The discrepancy observed in the strength of environmental influences between the two samples could be due to different curricula or school environments in the two countries. It is possible that the UK educational system, with its standardised programmes across schools, ensures a homogeneous mathematical environment, which in turn reduces the proportion of variance in mathematics explained by shared environment. Alternatively, different estimates may reflect differences in the aetiology of different facets of the mathematical domain assessed in the studies. Cross-cultural research using identical measures of mathematical ability and performance in large samples of the same age are needed in order to make meaningful comparisons and to establish the true sources of differences in estimates from different studies.

In summary, analyses of school-aged twins reveals substantial genetic influences on individual differences across the range of mathematical components, with environmental factors being primarily of the non-shared type, at least in the UK population. What specific environments could account for these influences? Teacher and school quality have been hypothesised as important in explaining differences in mathematical achievement (e.g. Eide and Showalter 1998; Darling-Hammond 2000; Saxe et al. 2001). If schools and teachers had equal effect on all the children within a class and school, children with the same genes (MZ twins) who have the same mathematics teacher should be more similar in mathematical skills than those taught by different teachers. However, this does not appear to be the case. At 10 years, twin pairs of the TEDS sample who were taught by the same teacher were compared to twins who had different teachers (Kovas et al. 2007a, 2007c).The results showed no significant differences in similarity in mathematical performance between twins taught by the same teacher vs different teachers, leading to the same estimates of heritability and environmental influences in both groups (Kovas et al. 2007a, 2007c). If being in the same class does not contribute to similarity among children in mathematics, the influence of a teacher and classroom may be hypothesised to have a non-shared effect, influencing mathematical abilities of different children in different ways. The absence of differences in twin similarity across classrooms may reflect the uniform National Curriculum and standardised teacher training applicable in the UK: the curriculum and schools contribute to invariance across the populations, whereas genetic and non-shared environmental effects explain individual differences.

*The aetiology of the relationships between mathematics and other cognitive and motivational traits*

In recent years, behavioural genetic research has moved beyond simple evaluation of the relative contributions of genetic and environmental factors to a single phenotype (e.g. mathematical variation). Multivariate methodology examines the aetiology of the relationships between mathematics and other cognitive and motivational traits. For example, it has been suggested that motivational factors, such as self-perceived ability and enjoyment of mathematics may make unique contributions to mathematical development. The relationship between liking mathematics and achievement was investigated in the TEDS sample at age 9 (Spinath et al. 2008). Liking mathematics was moderately influenced by genetic factors (.40) and the rest of its variation came from non-shared environment (.60). Moreover, the relationship between liking mathematics and mathematical achievement was very small. In a regression analysis, liking mathematics explained .5% of the total variance in mathematical scores, and only in the female sample.

Reciprocal relationships between academic achievement and self-evaluation have been previously reported (Marsh et al. 1999; Marsh and Yeung 1997), but the aetiology of these relationships can only be examined in genetically sensitive studies. Self-evaluation of mathematical abilities has been assessed in TEDS at 9 and 12 years. At both ages this measure showed moderate genetic (~ .40) and non-shared environmental influences (~ .59), without any shared environmental influences (Spinath et al. 2008; Luo et al. 2011). A study that employed a cross-lagged design reported that self-evaluation at 9 predicted mathematical achievement at 12, and that achievement at 9 predicted self-evaluation at 12, although the effect size of these relationships was very small (r = ~.10). These reciprocal relationships were found to be largely genetically mediated (Luo et al. 2011). Genetic influences on self-evaluation at 9 years were also associated with the genetic influences on later mathematics at 12 years, independent of the genetic influences on mathematics at 9 years. This interesting phenomenon, requiring further investigation, suggests that the new genetic influences on mathematics that emerge at age 12, may be partially driven by the same genetic factors influencing self-evaluation in previous years.

The insight that self-perception of abilities and enjoyment of mathematics depend to a large extent on genetic and non-shared environmental factors, rather than shared (family-wide or school-wide) influences requires reconceptualisation of many hypothesized motivational mechanisms. It is possible that a better understanding of these mechanisms and their link will mathematics will lead to changes in the way we teach mathematics and perhaps other academic subjects. It is likely that the biggest progress in education will come when environments are individualized to fit the unique genetic profiles and unique needs of each individual (Haworth et al. 2011; Haworth and Plomin 2011; Kovas and Plomin 2012).

Self-evaluation is only one of the many domains that have been explored in terms of genetic and environmental sources of covariation with mathematics. One of the first studies for normal variation investigated the relationships between mathematics and English, and mathematics and vocabulary, in a sample of over 2,000 twin pairs in U.S. High Schools (Martin et al. 1984). The study reported genetic correlations of .52 and .39 respectively, suggesting that when genes associated with mathematical abilities are identified, many of the same genes will be associated with English and, to a lesser extent, with vocabulary. A later study (Thompson et al. 1991) reported strong genetic correlations between mathematics and reading (.98), and mathematics and language (.98), suggesting that largely the same genes contributed to variation in all of the examined traits. The same study showed that shared environments were also largely the same for the three traits (the shared environmental correlation was .93 on average). Non-shared environmental factors explained most of the differences among the traits (correlations ranged from .28 to .54). Multivariate analyses in 314 10-year old twin pairs of the WRRPM study investigated the relationship between different components of mathematics, reading and general cognitive ability (*g*) (Hart et al. 2009). It was found that there was no significant genetic overlap between “Reading Fluency”, *g* and the mathematical subcomponent of “Calculation”. Conversely, the overlap in shared environmental influences on “Reading Fluency” with those on “Calculation” and *g* was significant, suggesting that the within-families environments that are important for “Reading Fluency” and *g*, also influence the learning of “Calculation”. “Mathematical Fluency” shared genetic influences with “Reading Fluency” (.43) and *g* (.20). However, some genetic influences on “Mathematical Fluency” (.59) were independent from reading and *g*. Further, “Mathematical Fluency” showed no significant environmental overlap with “Reading Fluency” and *g,* indicating a degree of independence from these two abilities.

The assessment in TEDS at 7 years found a genetic correlation between mathematics and *g* of .67 and between mathematics and reading of .74 (Kovas et al. 2005). In the same sample at 10 years, the genetic correlation between mathematics and *g* was .68, while the genetic correlation between mathematics and reading was .73 (Davis et al. 2008). Overall, the results of several TEDS studies suggest that, to a large extent, the same genes and the same shared environments contribute to mathematics and aspects of reading and general intelligence – explaining most of the observed correlations among these traits. On the contrary, non-shared environmental overlap was very small across the measures, indicating the contribution of non- shared environments to differences among the measures (Kovas, et al. 2005; Davis et al. 2008; Haworth et al. 2008).

The aetiology of the relationship between mathematics and spatial abilities (e.g. Webb et al. 2007; [Wai et al. 2009](#_ENREF_30)) has been also examined using data collected in TEDS at 12 years. The study investigated the relationship between three components of mathematics (Understanding Numbers, Non-Numerical Processes and Computation and Knowledge) and spatial abilities measured with two tests (Hanscombe et al. submitted). Overall, spatial abilities showed modest (.26) heritability, with no sex differences in the aetiology of individual differences. The phenotypic correlation between spatial abilities and the three mathematical components was on average .43. Common genetic factors explained ~ 60% of the correlation between the three components of mathematics and spatial ability; shared and non-shared environmental factors explained 26% and 14% of the phenotypic correlation respectively. The computational components of mathematics showed less genetic influence in common with spatial abilities (genetic correlation .66) compared to processes such as symmetry or rotation (genetic correlation of .91 between spatial ability and “Non-Numerical Processes”). These results suggest that although mostly the same genes contribute to spatial and mathematical skills (genetic correlation between the composite of the three mathematical components and spatial ability was .75), individual differences in spatial abilities are largely driven by environmental influences, of the non-shared type. The extent to which mathematics and spatial abilities co-vary was explained by shared and non shared environmental factors, as well as genetic factors.

In the TEDS sample multivariate genetic analyses have also been applied to investigate the aetiology of the links among different aspects of mathematics. At age 10, phenotypic correlations among five different aspects of mathematics (“Mathematical Application”, “Understanding Number”, “Computation and Knowledge”, “Mathematical Interpretation”, “Non-Numerical Processes”) ranged from .45 (“Computation and Knowledge” and “Non-Numerical Processes”) to .68 (“Mathematical Application” and “Understanding Number”) (Kovas et al. 2007c). On average, the genetic correlation among the five sub-tests was .91, indicating that the same genetic influences affect these different aspects of mathematics. For example, the genetic correlation between “Understanding Number” and “Mathematical Application” was .94, meaning that the genetic influences involved in these two mathematical components were almost the same. The examination of the bivariate heritability and enviromentalities suggested that the observed covariation among different aspects of mathematics is largely explained by genetic factors. For example, the bivariate heritability of “Understanding Number” and “Mathematical Application” was .49 indicating that half of the phenotypic correlation of .68 is genetically mediated. The bivariate shared environment explained 29% of the phenotypic correlation, while 22% was explained by non-shared environment. Overall, these results suggest that observed correlations among different components of the mathematical domain are largely explained by the same genetic factors affecting them. The dissociation in performance across the different components largely stems from component-specific influences of non-shared environments.

To summarise, multivariate results suggest that genetic influences on individual differences in mathematics are largely the same as those on a wide range of other cognitive and learning abilities, achievement, and motivation, supporting the Generalist Genes Hypothesis (Plomin and Kovas 2005). According to this hypothesis, if a gene is involved in one domain (e.g. mathematics), the same gene is also likely to be associated with other abilities, such spatial skills, language, *g*, and reading. On the contrary, most of the environmental effects on mathematics are not shared with other domains, suggesting that discrepancies in abilities largely stem from the influence of different environments (e.g. Davis et al. 2008).

Despite the large amount of genetic overlap, some genetic effects seem specific to mathematics, indicating that some genes are uniquely involved with mathematics (Kovas et al. 2005; Hart et al. 2009). It is possible that this genetic specificity is related to some specific aspect of mathematically-relevant cognition. One cognitive ability, assumed to be aetiologically and behaviourally associated with mathematical skills, is estimation (e.g. Halberda et al. 2008; Siegler and Opfer 2003). It is thought that estimation abilities may be evolutionarily conserved, as they are present in many animal species and in infants (e.g., Agrillo et al. 2010; Xu and Arriaga 2007; Feigenson et al. 2002). In other words, something in the genetic code of humans and other animals enables the appreciation of approximate numerical information. For this reason, it has been hypothesised that individual differences in estimation abilities may also be largely driven by genetic factors. Moreover, it has been hypothesised that these genetic factors may be uniquely associated with mathematical variation, explaining the portion of genetic effects in mathematics that is not shared with other abilities (Tosto, Plomin, Halberda et al. submitted). In order to test this hypothesis, over 3,400 twin pairs from TEDS were assessed on a large battery of mathematics-related tests at 16 years of age. The battery included measures categorised as *Number Sense:* estimation of numerical magnitude and estimation of numerosities (Tosto, Plomin, Petrill et al. in preparation). Contrary to the predictions, these estimation measures (e.g. number line, comparison of large numerosities) revealed modest genetic influences, indicating that most of the individual differences in estimation skills (~70%) are influenced by non-shared environmental factors.

It may seem puzzling that such skills, considered to be hardwired in the human biology, show such low heritability estimates. However, entirely different factors may explain the species-universal behaviour (e.g. humans are capable of quantity discrimination) and individual differences in behaviour (humans differ in precision of their quantity discrimination). From this first large scale study examining genetic and environmental aetiology of the individual variation in estimation, it appears that genes have only a modest effect on it. However, the multivariate genetic analysis showed that the phenotypic correlation between mathematics at 16 and two Number Sense measures (.40 for number line and .29 for estimation of large numerosities) was largely explained by genetic factors (average bivariate heritability .73). This suggested that the modest genetic influences on Number Sense abilities were to a large extent the same as those on mathematical ability at this age (Tosto, Plomin, Petrill et al. in preparation). The results also showed that there were no genetic influences shared between Number Sense and mathematics independently from *g*, suggesting that the relationship between Number Sense and mathematics is mediated by *g*. This first genetically sensitive investigation into the relationship between Number Sense and mathematics suggests that the mathematic-specific genetic influences do not refer to Number Sense, therefore the question on the aetiology of these mathematics specific influences is still open. More research is needed in order to examine whether these common Number Sense-mathematics genetic factor genes have more general effects on other cognitive traits.

*Genetic and environmental influences on stability and change*

Multivariate analyses have also been applied to the examination of the sources of phenotypic stability and change in mathematical ability and performance. As these analyses rely on large longitudinal samples, only a handful of studies to date have addressed the extent to which the same genetic and environmental factors drive variation across different ages (e.g. whether genetic and environmental influences on mathematics at one age are the same that influence mathematics at a different age). It is reasonable to expect that largely the same genes and environments will be contributing to mathematical learning across development. On the other hand, it is also reasonable to hypothesize that new genetic and environmental influences contribute to mathematical learning across development – reflecting the growing complexity of material, conceptual shifts, and maturational factors. For example, between the ages of 7 and 9, children in U.K. schools progress to a different stage in their formal mathematical education, leading to greater focus on children’s ability to understand and manipulate mathematical concepts. In addition, genetic and environmental factors influencing individual variation in biological maturation, such as the onset of puberty, may also contribute to variation in cognition at different ages.

In order to investigate the extent of aetiological change and continuity, one study examined mathematical performance in the same children at age 7 and 9, as part of the TEDS study (Haworth et al. 2007a).The results showed that genetic influences on mathematical variation at the two ages were largely the same, accounting for 80% of the .60 phenotypic correlation between mathematics at 7 and 9. In other words, genetic influences contributed to the stability of mathematical abilities at the two ages, although some genetic effects were specific to each age. Shared environmental influences were almost overlapping (.87), but contributed very little (22%) to the total phenotypic correlation between mathematics at 7 and 9 years. The non-shared environments at 7 and 9 years were different and contributed to the changes in mathematical performance between the two ages. The extent to which children carried on in their mathematical learning from 7 to 9 was mostly due to genetic influences, as is the case for many other cognitive abilities (e.g. Bartels et al. 2002; Kovas et al. 2007a). A second investigation into the aetiology of the stability and change in mathematical performance in TEDS looked at school ages of 7, 9 and 10 together (Kovas et al. 2007a).This study showed that almost half of the genetic variance at 10 years was shared with the genetic variance at 7 years, indicating that almost half of the genetic influences active at 7 were still influencing mathematics at 10. Some of the genetic influences were, however, time specific, meaning that some new genetic influences emerged respectively at 9 and 10 years. Some of this new genetic variance at 9 was shared with the genetic variance at 10, contributing to mathematics stability. Shared environment also contributed to continuity of mathematical performance across the three time points (shared environments influencing one age also influenced the other two ages to a large extent, although the overall influence of shared environment on all traits was very modest). Again, non-shared environments contributed mostly to change, meaning that they were specific to each age.

To summarise, longitudinal multivariate studies suggest that phenotypic stability in mathematical ability and other cognitive traits can largely be explained by the contribution of the same genes (e.g. Plomin et al. 1994a; Bartels et al. 2002; Petrill et al. 2004).The continuity of genetic effects on mathematics at different ages implies that the same genetic factors are needed to support the complex cognitive functions required for mathematical reasoning across development. Many of these genetic influences also affect other cognitive and learning domains. At the same time, discontinuity of genetic effects may reflect changes in the phenotype (what we call mathematics and measure at different ages), as well as developmental changes in genetic expression – associated with hormonal and environmental changes.

*The nature of the relationship between mathematical ability and disability*

So far in this chapter we have only dealt with normal variation in mathematical ability. Another question to be addressed is whether mathematical disabilities and high abilities are influenced by the same genetic and environmental factors responsible for the normal variation in mathematics, or whether disabilities and exceptionally high performance are aetiologically different from normal ability (qualitative differences). If the latter hypothesis is true, twin model fitting analyses should show qualitative differences in genetic and environmental factors that drive normal variation and extremely low or high performance.

Indeed, some mathematical impairment may stem from a particular genetic mutation or a particular case of severe environmental deprivation. For example, several single genetic abnormalities, such as Prader Willi Syndrome, Turner Syndrome, and others, are associated with disproportionate mathematical problems (e.g. Mazzocco 1998; Bertella 2005; Murphy and Mazzocco 2008).The extent to which the normal variation in the genetic regions associated with these syndromes is also associated with normal variation in mathematics is currently unknown. However, quantitative genetic research, described in this section, suggests that most mathematical disability (and high performance) seem to lie on the same aetiological continuum as the rest of the variation (Plomin et al. 2009).

Only a handful of studies have examined the aetiology of low mathematical performance. One early study (Alarcón et al. 1997) investigated the aetiology of low mathematical ability, finding a probandwise concordance of .73 for MZ, and .56 for DZ twins, suggesting moderate genetic influences for the low mathematical performance group. Similarly, in the TEDS sample at 7 years, low mathematical ability was found to be as heritable as normal mathematical ability; in fact, the heritability of normal and low ability was almost identical (group heritability for the low group was .65, and heritability was .66 in the unselected sample) (Oliver et al. 2004). In TEDS at 9 years, the low ability children, selected with a 15% cut-off criteria, showed a group heritability very similar to the heritability of the whole distribution (.75 low; .68 normal variation), again suggesting the same aetiology for low and normal ability (Haworth et al. 2007a). In TEDS, low and normal ability groups at age 10 also showed similar heritability estimates in the three sub-components of mathematics “Understanding Number”, Non-Numerical Processes”, “Computation and Knowledge” (with moderate genetic influences and modest shared environment) (Kovas et al. 2007b). However, all three measures suggested stronger genetic influences for low performance than for the normal range (normal ~ .40 vs low ~ .62), suggesting that the low end of the distribution may be more affected by genetic influences. It is possible that some genetic effects only operate in the low end, rather than contributing to the normal variation across all levels of ability.

Low mathematical performance, like mathematical performance in the normal range, has been shown to be affected by similarly stable genetic factors. In a longitudinal investigation of low mathematical ability in TEDS, low ability children were identified with scores below the 15th percentile (Haworth et al. 2007a).The low group heritability was .65 at the age of 7 and .75 at age 9. These estimates were very similar to the heritability in the whole sample (.66 at age 7 and .68 at the age of 9). The genetic correlation of the low groups at the two ages was very high suggesting that the same genetic influences are involved in low abilities at the ages of 7 and 9.

The aetiology of high mathematical ability also seems to be strongly related to the aetiology of normal performance. At 10 years, high ability children in the TEDS sample were identified as scoring above the 85th percentile in web-administered mathematical tests (Petrill et al. 2009). Group heritability (.53) in the high ability sample was similar to that in the normal distribution (.49). Further, no sex differences were found in the aetiology of high mathematical abilities at this age. In other words, the genetic and environmental factors that contribute to individual differences in boys in the high ability group, also contribute to individual differences among high-mathematically achieving girls. The aetiology of high mathematical abilities was again investigated in TEDS at age 12 (Haworth et al. 2009b). The results confirmed again that largely the same genetic influences affect high and normal performance, although some genetic influences are specific for high abilities only.

To summarise, research suggests that mathematical achievement in different ranges of ability is largely influenced by the same genetic factors (Plomin and Kovas 2005; Kovas et al. 2007d; Haworth et al. 2009a, b; Petrill et al. 2009). More genetically sensitive research is needed into the aetiology of mathematical giftedness, including measures that allow high levels of sensitivity - to detect and examine variation at the top end.

Several twin studies examined the relationship between mathematical disabilities and other cognitive disabilities.This research suggests that to some extent mathematics and other learning disabilities are driven by the same genetic and shared environmental factors. For example, the relationship between reading and mathematical disability was addressed in a study of 148 MZ and 111 DZ school-age twins, specifically selected for at least one of the twins in the pair displaying reading problems (Light and DeFries 1995).The probandwise concordance for reading was 68% for MZ and 40% for DZ. Moreover, although the sample was not specifically selected for mathematical disability, it was found that 49% of the MZ and 32% of DZ co-twins displayed mathematical disability. Further analyses suggested that the observed cross-trait concordance was explained by both common genetic and common shared environmental influences on reading and mathematics. The authors concluded that approximately 26% of the proband reading deficits in this sample were due to genetic factors that also influence mathematics performance. Approximately 25% of the proband reading deficit was due to environmental factors also affecting mathematics.

Another study examined the nature of the covariation between reading and mathematical disability in a sample of 8- to 20-year-old twins, and found that the observed relationship between the two traits was substantially explained by genetic factors (Knopik et al. 1997). In a study of over 1,500 17-18 year-old twin pairs, unselected for disability, children with low reading and low mathematics were identified (Markowitz et al. 2005). Both mathematical and reading problems were highly heritable (~.90), with a large degree of genetic overlap between the two traits: 64% of the genetic factors influencing mathematical disability also influenced reading disability. Moreover, the observed concordance between mathematical and reading disability in this sample was almost entirely explained by common genes.

In the TEDS sample, at 10 years, low achieving children in reading and mathematics were selected in the lowest 15% of the distribution (Kovas et al. 2007d). Reading and mathematical disability were moderately heritable and most of the covariation (63%) between reading and mathematics was genetically mediated. The shared environmental influences almost completely overlapped (.96), although shared environment only contributed a very small amount to the observed covariation of the two disabilities as the influence of the shared environment on each trait was very small.

Very few studies examined the relationship between mathematical disabilities and other traits, such as low language and low general cognitive abilities (*g*). In the TEDS sample, over 4,000 twin pairs were assessed at 12 years, with the bottom 15% of the sample selected for low performance in mathematics, language, reading and *g* (Haworth et al. 2009a). As expected, there was a significant amount of overlap among the measures (average observed comorbidity .58). The genetic correlations for the low performance groups in all measures were also high (.67 average genetic correlation for mathematics, language, reading and *g*). This genetic correlation was similar in magnitude to the average genetic correlation among the measures for the entire unselected sample (.68) indicating similar aetiology for disabilities and abilities in mathematics, language, reading and *g*. The comorbidity between disabilities was largely mediated by genetic factors.

The relationship between high mathematical abilities and other cognitive abilities was investigated in TEDS at 12 years (Haworth et al. 2009b). High ability twins were identified as performing in the top 15% in mathematics, reading, language and *g*. The observed overlap among the traits was high (.59 on average) Similar to low ability, there was substantial genetic and shared environmental overlap across all high abilities. As is the case for low abilities, the non-shared environment contributed to discrepancies in performance across abilities. A substantial portion of the phenotypic correlation among the high ability scores was explained by genetic and shared environmental influences. However, the contribution of the genetic effects to the phenotypic correlation in the high abilities was lower compared to low abilities (.42 on average). For example, common genetic factors explained only 34% of the observed overlap between high mathematics and high *g*, as compared to explaining 58% of the observed overlap between low mathematics and *g*.

These studies suggest that the comorbidity between mathematics and other low and high abilities is mediated by genetic and shared environmental factors, with some inconsistencies across the studies in the degree to which genes and shared environment contribute to this covariation. These inconsistencies may stem from the differences in samples, such as age or cultural differences, and need to be investigated further.

Overall the research so far suggests that cognitive traits, such as mathematics, are polygenic - influenced by many genes of small effects (Plomin et al. 2012).These genes are called *Quantitative Trait Loci* (QTL; Plomin et al. 2012). For complex or quantitative traits, it appears that a disorder is also the result of the effect of many genes - each having only a small effect on the trait (Plomin and Kovas 2005).This implies that genetic variants (the QTLs) contribute to the disorder or disability in a cumulative/quantitative way, producing a continuum of ability, rather than discrete ability groups. Therefore, for complex traits, disability can be defined as driven by an accumulation of risk factors, both genetic and environmental. In other words high ability and disability can be seen as the high and low end of the same distribution (Plomin et al. 1994b; Plomin and Kovas 2005; Kovas and Plomin 2006). Moreover, it is likely that a unique combination of polygenic and environmental effects leads to a particular observed performance profile in each person.

*The aetiology of sex differences in mathematics*

Many psychological and educational studies have investigated sex differences in mathematical ability across development and across different aspects of mathematics (e.g. Lord and Clausen-May 2003; Benbow and Stanley, 1980). In line with these studies, in the school years males in the TEDS sample tend to have higher mathematical scores than females, although the effect size of these average differences is very small (e.g. Kovas et al. 2007a). Several reasons have been proposed for any observed average sex differences (Kovas et al 2007a, b).

However, the sources of average group differences may differ from those driving individual variation within the groups. Quantitative genetic sex-limitation models examine the extent to which the same genetic and environmental factors contribute to variation within the sex groups (testing for qualitative differences); and whether these factors have the same effect on variation in each group (testing for quantitative differences). Because the genetic relatedness of DZ twins is .5 on average, if different genes influence males and females, the genetic correlation of DZ opposite sex pairs should be less than .5. If the genes influencing variation in males and females are the same, but the extent to which the genes influence variation is different, the estimates of genetic, shared and non shared environment will be different for male and female pairs. Applying sex-limitation models to TEDS data at the age of 10, revealed no qualitative or quantitative sex differences in the aetiology of mathematical abilities or disabilities (Kovas et al. 2007b). Furthermore, no sex differences were found in the three components of mathematics (Understanding Number, Non-Numerical Processes, Computation and Knowledge), both in the low ability group and in the unselected sample (Kovas et al. 2007b). At age 16, when the TEDS twins were assessed on a large battery of numerical tests, again no qualitative or quantitative sex differences emerged for mathematical performance (Tosto, Plomin, Petrill et al. in preparation). Similarly, no aetiological sex differences were found for parent-rated normal mathematical variation or low mathematical performance in a sample of 17-18 year-old Dutch twins (Markowitz et al. 2005). These findings suggest that genetic factors that make males better or worse at mathematics are the same genetic factors that make females better or worse at mathematics; and they exert the same amount of influence on males and females. The same studies also indicate equality of environmental effects on male and female variation.

*Molecular genetic investigations into mathematical variation*

Quantitative genetic investigations into the aetiology of mathematical variation suggest that mathematics is highly heritable. Molecular genetic studies have begun to search for specific genes associated with mathematical abilities and disabilities. Approximately 99% of human DNA is invariant, meaning that out of the 3 billion base-pairs that form our DNA chain, only a small proportion differs across people. However, in a stretch of invariant DNA sequence, there may be a particular locus where some individuals may have the nucleotide Adenine, while others have Guanine. These variants are called Single Nucleotide Polymorphisms (SNPs) and are the most common type of DNA variability. More than 3 million common SNPs have been discovered in human DNA, providing the basis for the Quantitative Trait Locus (QTL) model described previously. Mapping phenotypic variation in complex traits, such as mathematical ability and disability, to QTLs is complicated by the fact that many DNA loci of very small effect are likely to be contributing to the variation.

In recent years, molecular genetic methods and technologies have advanced dramatically (Plomin and Davis 2009; Plomin et al. 2012).The advent of microarray (“gene-chip”) technology has revolutionised molecular genetic research, by way of tagging almost all of the segregating polymorphic DNA sequence at the same time. Moreover, genetic variance not directly tagged by these chips can be reliably estimated through bioinformatic methods, such as imputation that considers the correlation between SNPs. Genome Wide Association Studies (GWAS) use this technology to comprehensively genotype large numbers of individuals for a large number of SNPs and to look for associations between these genetic markers and variation in complex traits.

While a number of molecular genetic studies have been conducted on cognitive abilities, only one has focused on mathematics. This Genome Wide Association Study set out to identify genes associated with mathematical performance and achievement, comparing 10 year-old children selected from the TEDS sample for high and low mathematical performance (Docherty et al. 2010a). The study adopted a cost-efficient method known as DNA pooling (Butcher et al. 2004; Davis et al. 2009c) to select the top-ranking 3000 SNPs with the highest probability of genetic association with mathematical performance. As a second stage, the top 43 SNPs were validated in an individual genotyped sample (2,356 TEDS individuals) and carried forward for association testing. Out of these 43 SNPs, 10 were found to be significantly associated with the phenotypic variance in this sample. The study revealed a number of functionally plausible candidate genes associated with mathematical performance. These include the *NRCAM* gene, which encodes a neuronal cell adhesion molecule and is implicated in memory processes (Hoffman 1998). Taken individually, each of the 10 SNPs accounted for a very small amount of the variance in mathematics (.13% to .58%); however, the 10 SNPs were found to work in an additive way, collectively explaining 2.9% of the total variance in individual differences in mathematics. These results are consistent with the QTL hypothesis, which suggests that the trait is influenced by many genes of small effect, leading to the observed continua of ability/performance. For a single molecular study, finding this amount of variance explained is very encouraging, considering that for cognitive traits, GWAS studies typically report considerably less variance explained. For example, a study (Davies et al. 2011) revealed that the SNPs found so far to be associated with intelligence explained only approximately 1% of individual variance in crystallised and fluid intelligence.

According to the Generalist Genes Hypothesis, genes implicated in one cognitive trait are likely to be implicated in other cognitive traits. Some support for this hypothesis has already been found. One study screened 100,000 SNPs in 4,258 TEDS and found that 10 SNPs were associated with early reading ability at age 7 (Haworth et al. 2007b). The same SNPs were also found to be associated with language, *g* and 3 aspects of mathematical performance at the same age. The correlations between the genes found for reading and other cognitive abilities were very small (between .08 and .11), but statistically significant. To further test the generalist genes hypothesis, the 43 SNPs found to be associated with mathematics and the subset of 10 SNPs significantly associated with mathematics at 10 years were used in a follow-up behavioural genomic analysis and tested for association with three different components of mathematics, reading and *g* at age 10 (Docherty et al. 2010b). Both SNP-sets significantly correlated with all three mathematical components, with different degrees of magnitude. For example the web-test assessing “Non-Numerical Processes” had the lowest correlation with both SNP-sets (.11 with the 10 SNPs and .11 with 43 SNPs).The highest correlation was between the 10-SNP set and the web-test “Understanding Number” (.15). As predicted by the Generalist Genes Hypothesis (Kovas and Plomin 2005), the sets also correlated with reading and *g* measured at the same age, with similar magnitude of effects (e.g. .11 correlation between 10-SNP set and reading). The same study found that the mathematics SNP sets identified at age 10 also explained variation in mathematics at ages 7, 9 and 12 years (correlations between .03 and .10). This last finding further supports the continuity of mathematical abilities throughout development, but also highlights some specificity of genetic influences at different ages, as predicted by the findings from quantitative genetic studies.

As described earlier, quantitative genetic findings are characterised by some degree of variability in heritability estimates, with differences in methods, measures, and samples potentially explaining the discrepancies in the literature. It is also possible that heritability estimates may change as a result of different environmental influences. In other words, the impact of genetic variation on a particular trait is dependent on the environmental background in which the genes operate. Heritability estimates may differ for mathematical abilities in populations exposed to different schooling, parenting and socio-economic factors. For example, where the relevant environmental influences are more variable, heritability estimates may be lower. Once the mechanisms through which genes contribute to variation in complex traits are better understood, we will be able to use environmental interventions to modulate genetic propensities. To date, only one study examined gene-environment interactions in their effect on mathematical ability, testing the association between mathematics and the previously identified 10 SNPs, as a function of 10 environmental measures (Docherty et al. 2011). The study used a sub-set of 1,888 TEDS children with complete genotype data for all 10 SNPs. Each SNP was assigned a value of 0 for the homozygote genotype (when the two genetic variants in the locus are of the same form) associated with low mathematical ability, a value of 1 was assigned for the heterozygote genotype and 2 for the homozygote genotype associated with higher mathematical ability. The values of the 10 SNPs were summed to obtain a global value for the entire 10 SNP set (ranging from 0 to 20). A SNP set with a low value indicated that the majority of the alleles across the 10 SNPs were associated with poorer mathematical performance. Environmental measures, assessed at the ages of 9 and 12 years, included socio-economic status, parental negativity, parental discipline, mathematical environment (mathematical relevant activities carried out in schools), home and classroom chaos (the level of environmental noise, confusion and disruption of routines), and children’s perceptions of their teacher. Overall, the association between mathematics and the 10 SNPs was stronger in the condition of a greater home chaos and when the parents’ negativity rate was high. However, the effect size of these interactions was small: after correcting for multiple testing, the interactions of the 10 SNP set with home chaos and parent negativity at the age of 12 explained only .49% each of the variance in mathematical scores. These results suggest that at the age of 12, the greatest genetic effects of the low SNP sets occurred when the parents' negativity and home chaos were high. In other words, the negative environments made the effects of the “bad” genotype worse. In line with the diathesis-stress model (e.g. Asbury et al. 2005), these results indicate the presence of a gene-environment interaction. Simply, taken in isolation, genetic risk factors may not be sufficient to fully account for poor mathematics. Genes are expressed in response to the environment. Chaos in home environment and parents' negativity appear to trigger mathematical genetic risk response. Other types of gene-environment interplay, yet to be investigated, may also be important for mathematical learning.

These first genetic polymorphisms represent a promising beginning in the search for DNA influences on mathematics. The finding of several SNPs of additive small effect is in line with the predictions made by quantitative genetic studies of mathematical variation. The first 10 SNPs identified for mathematical ability need to be replicated in other samples, and further research is required in order to find many other SNPs and other types of DNA variation involved in the development of individual differences in mathematics.

*Conclusions*

The field of quantitative genetics has made important contributions to our understanding of the aetiology of mathematical variation, its stability, and its relationship with other cognitive traits. Consistent with the QTL model, individual variation in mathematical ability depends on the influence of many genes, each of small effect. Genetic factors contributing to mathematical performance across the range of the distribution are mostly the same, suggesting that common mathematical disability is not a product of some abnormal genetic mutation, but rather stems from the accumulation of many ability-decreasing genetic variants that also operate throughout the ability range. The implication of these findings is that there are no genes for “bad” mathematics or low abilities. From a genetic perspective, abilities and disabilities are not qualitatively different as they emerge from the additive effects of the same set of genes. Moreover, genetic variation is the foundation for the ability of humans to adapt to new environmental demands. Genetic variants that, under certain environmental conditions, today contribute to lower mathematical ability may become important for adaptation in other environments or with new societal demands. This means that molecular genetic research into complex traits does not aim to reduce genetic variance among people. On the contrary, the ultimate aim of genetic and genomic investigations is to optimise the current environments and to create new environments (e.g. individualised educational programmes) in order to capitalise on existing genetic variation.

Genes do not act in isolation, and although mathematics is a highly heritable trait, around 40% of individual differences in mathematics are due to the environment. Moreover, new evidence suggests that the effects of genes can be modulated by environments. The challenging task of molecular genetics will be to identify all the genes contributing to mathematical heritability at different ages. Quantitative genetic studies will continue to guide the molecular search for these genes. For example, the absence of sex differences in the aetiology of individual differences in mathematics justifies combining the data from males and females in the search for genetic associations. New advances in molecular technologies, such as the ability to conduct complete genome sequencing on each individual, will lead to new discoveries, including the investigation of the role of rare genetic variants in mathematical variation. Better understanding of genetic effects on mathematical variation may help in the search for the relevant environments. Genetically-sensitive cross-cultural comparisons will also aid our understanding of the complex ways in which genetic and environmental effects interact. The exact applications of this future knowledge are currently difficult to predict. However, we believe that the way we conceptualise and influence mathematical development will be affected by continuous advances from the field of behavioural genetics.

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