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Annual review

Genetics and educational psychology

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Background. Molecular genetics, one of the most energetic and exciting areas of science, is slowly but surely coming to educational psychology.

Aims. We review recent molecular genetic research on learning disabilities as a sign of things to come in educational psychology. We also consider some misconceptions about genetics that have slowed the acceptance of genetics in educational psychology.

Samples. Diverse samples of children with learning disabilities have been studied, primarily in the UK and the USA.

Methods. Linkage analysis can detect genes that have large effects on learning disabilities. Association analysis can detect genes of much smaller effect size, which is important because common disorders such as learning disabilities are likely to be influenced by many genes as well as by many environmental factors.

Results. For reading disability, replicated linkages have been identified on chromosomes 6, 15 and 18. A gene responsible for a rare type of language impairment has recently been identified. For common language impairment, linkages on chromosomes 16 and 19 have recently been reported. More than 200 genetic disorders, most extremely rare, include mental retardation among their symptoms, and chromosomal abnormalities are a major cause of mental retardation.

Conclusions. Although finding specific genes associated with learning disabilities is unlikely to have much of a direct application for teachers in the classroom, such findings will have far-reaching implications for diagnosis, treatment and prevention of learning disabilities and for research in educational psychology. Educational psychology has been slower to accept evidence for the importance of genetics than other areas of psychology in part because of misconceptions about what it means to say that genetics is important for common complex disorders such as learning disabilities.

During the past century, genetics has been one of the most exciting areas of science. The word *gene* was first coined in 1903. Fifty years later, the double helix structure of

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DNA was discovered, in which four nucleotide bases (G, A, T, C) are the steps in a spiral staircase. The genetic code was cracked in 1966: the 4-letter alphabet of DNA is read as 3-letter words that code for the 20 amino acids, which create proteins, the building blocks of life. The crowning glory of the century was the Human Genome Project, which provided a working draft of the sequence of 3 billion nucleotide bases of DNA in the human genome. There is no single human genome – about one in every thousand nucleotide bases differs among us. The goal now is to identify these 3 million DNA differences (polymorphisms), called single-nucleotide polymorphisms (SNPs, pronounced 'snips'), because they are responsible for the hereditary differences among us. An immediate goal is to identify SNPs in genes, the basic unit of inheritance that codes for a unique sequence of amino acids, which accounts for only about 2% of all DNA.

The goal of this paper is to describe examples of recent genetic research relevant to educational psychology. Molecular genetic research has begun to harness the power of the Human Genome Project to identify SNPs that are associated with educationally relevant problems such as reading disability and other learning disabilities. In part, molecular geneticists are turning to educationally relevant disorders because, despite their complexity, these disorders are highly heritable. The vast majority of what we know about the genetics of these disorders comes from quantitative genetic research (family, twin and adoption studies that attempt to decompose phenotypic variance into genetic and environmental components) rather than molecular genetic (DNA) research which has only recently made its debut. We focus on molecular genetic research in part because it is new and represents the future of genetic research, and in part because quantitative genetic research demonstrating substantial genetic influence on educationally relevant disorders and dimensions has often been reviewed (e.g., Plomin, DeFries, McClearn, & McGuffin, 2001). Our focus on molecular genetics is not meant to denigrate the importance of quantitative genetic research, which has become even more valuable because it charts the course for molecular genetic research (Plomin, DeFries, Craig, & McGuffin, 2003). Quantitative genetic research is also valuable in terms of helping us to understand the role of the environment – indeed, some of the most important findings from quantitative genetic research involves nurture rather than nature (Plomin, 2001). Nonetheless, finding a specific sequence of DNA that is associated with behaviour is more appealing than the abstract decomposition of components of variance which involves greater complexities concerning interactions and correlations between genes and environments (Plomin *et al.*, 2001). Another preliminary issue that should at least be mentioned is that our focus is on the 0.1% of DNA that makes us different from each other – the source of all hereditary differences – rather than the 99.9% of DNA that is the same for all of us, most of which is also surprisingly similar to other organisms such as mice and even fruitflies (Plomin *et al.*, 2001).

Although the history of genetics in the behavioural sciences has been tumultuous, genetic contributions to behavioural traits are becoming widely accepted in most areas of the behavioural sciences (Plomin *et al.*, 2001). Acceptance of nature as well as nurture has been slower in educational psychology but there are signs that this is changing. For example, we reviewed recent editions of major educational psychology textbooks and found that, although some textbooks still do not include *genes*, *genetics*, or *heredity* in their subject index, coverage of genetic research is generally increasing in terms of developmental disorders such as reading disability and hyperactivity. Nonetheless, no text we reviewed has more than three pages devoted to genetics.

We also used PsycINFO to search for journal articles and dissertations on genetics during the last 40 years in educational psychology journals. We used PsycINFO code number 3500 which includes journals broadly relevant to educational psychology and the keywords 'genetics, genes, heritability, heredity and behavioural genetics'. As shown in Figure 1, 78 journal articles were found but 51 of these were in the period 1968–1972 and were written in reaction to the *Harvard Educational Review* monograph by Arthur Jensen on genetics and intelligence (Jensen, 1969). The number of journal articles during 5-year intervals since 1978 has been four (1978-82), three (1983-87), four (1988-92), three (1993-97), and, remarkably, only one article was found during the past five years (1998-2002). A more positive sign is that the number of relevant dissertations has increased during these five 5-year intervals: nought (1978-82), nought (1983-87), two (1998-92), six (1993-97), and 10 (1998-2002). We recognise the limitations of such computer searches; by way of contrast, a comparable search for the keywords *nurture, environment,* and *school environment* yielded 1,245 journal articles using the same PsycINFO code number 3500 for educational psychology journals. Our goal is merely to document the assertion that genetic research has been slow to come to educational psychology but there are signs (textbook coverage and dissertations) that this is changing.

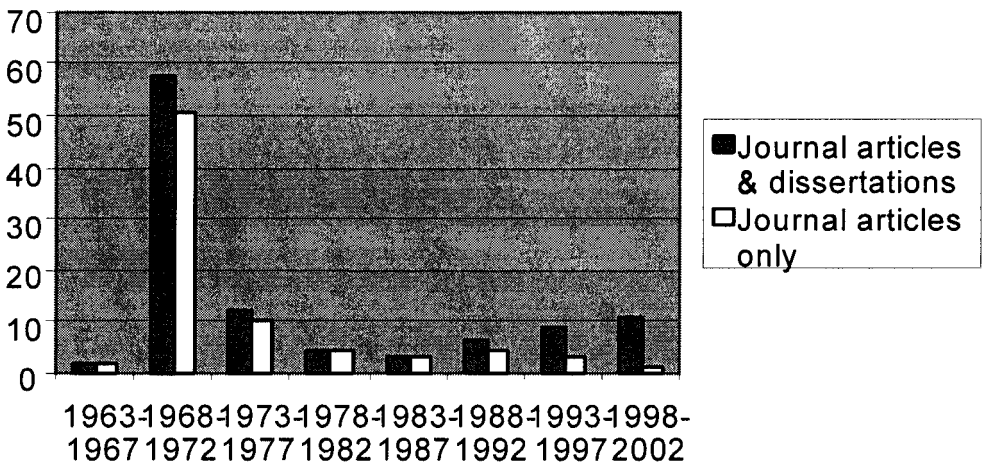

Figure 1. Journal articles and dissertations obtained through a PsycINFO search of educational psychology journals (as defined by PsycINFO code number 3500) for the keywords genes, genetics, heritability, heredity, and behavioural genetics

Later we consider some of the factors that might contribute to the late arrival of genetics in educational psychology. We begin with some new findings from molecular genetics as a sign of things to come. Rather than attempting to review all areas of relevance to educational psychology – which would encompass all cognitive abilities and disabilities, childhood psychopathology, and personality (Plomin *et al.*, 2001) – we will focus on learning disabilities. Although it has been more difficult than expected to identify replicable DNA associations for complex disorders, greater progress is likely given new techniques from the Human Genome Project and the realisation that greater power is needed to be able to detect genes of small effect size, as explained below. Few behavioural researchers will join the hunt for genes because it is expensive and

difficult, but when replicable DNA associations are found they will soon be used in research relevant to educational psychology, eventually in clinics for diagnosis and treatment, and ultimately in early interventions that prevent problems before they develop. These issues are discussed later.

Finding genes for common complex disorders

Although a detailed description of methods used to identify genes associated with behaviour is not appropriate in this context, the two major methods, linkage and association, need to be mentioned (Plomin *et al.*, 2001). Linkage traces the co-transmission within families between a disorder and a DNA marker such as a SNP. If the gene for the disorder and the SNP are close together on the same chromosome (one of 23 pairs of structures in the nucleus of each human cell that contains DNA), they will be inherited together within a family. Linkage points to the general neighbourhood of a gene on chromosome and a house-to-house search is then needed to find the culprit gene that is directly associated with a disorder. Linkage is most powerful for finding single-gene disorders in which a single gene is necessary and sufficient for the emergence of the disorder. Linkage has been used to localise several thousand single-gene disorders (Online Mendelian Inheritance in Man, 2000).

The second method, association, involves a correlation between a particular allele (form of a gene) and a trait in a population. For example, a gene called apolipoprotein E (*APOE*) has an allele (called *APOE-4*) that has a frequency of about 40% in individuals with late-onset Alzheimer's disease and about 15% in controls. Association methods are able to detect genes of much smaller effect size than linkage, although newer linkage designs are able to detect genes when a disorder is influenced by more than one gene. Power to detect genes of small effect size is important because common disorders such as reading disability and hyperactivity are caused by multiple genes as well as by multiple environmental factors. Genes in such multiple-gene systems are called quantitative trait loci (QTLs) because, if many genes are involved, they are likely to result in dimensions (quantitative continua) rather than disorders (qualitative dichotomies).

The QTL perspective is the molecular genetic extension of quantitative genetics in which genetic variation is viewed as normal and distributed quantitatively (Plomin, Owen, & McGuffin, 1994). A general rule emerging from genetic research is that single-gene disorders are rare and severe, whereas common, less severe disorders are caused by multiple genes as well as multiple environmental influences. This QTL hypothesis is by no means proven but it is entirely an empirical issue. It predicts that, when genes are found that are associated with common disorders such as learning disabilities, the genes will be associated with variation throughout the distribution. The goal of QTL research is not to find *the* gene for a complex trait, but rather to find the *multiple* genes that make contributions of varying effect sizes to the variance of the trait. Perhaps one gene will be found that accounts for 5% of the trait variance, 5 other genes might each account for 2% of the variance, and 10 other genes might each account for 1% of the variance. If the effects of these QTLs are independent, the QTLs would in total account for 25% of the trait's variance.

It is unlikely that all of the genes that contribute to the heritability of a complex trait will ever be identified because some of their effects may be too small to detect or their effects may be non-additive (called epistasis) in the sense that the genes interact rather

than add up in their effects on a trait. The problem is that we do not know the distribution of effect sizes of QTLs for any complex trait in plant, animal or human species. If effect sizes are 1% or smaller, this would explain the slow progress to date in identifying genes associated with behaviour because research so far has been woefully underpowered to detect and replicate QTLs of such small effect size . A new direction for molecular genetics research is to use designs and large samples that are up to the job of breaking the 1% barrier of QTL effect sizes (Plomin *et al.*, 2003).

Learning disabilities

Although most molecular genetic research has focused on single-gene disorders for which it is much easier to find genes, research during the last few years has begun to investigate complex disorders presumed to be influenced by multiple genes (Plomin & McGuffin, in press). Some of the most exciting research involves learning disabilities, especially reading disability, language impairment and mental retardation. Other areas not reviewed below that have been targets of intense molecular genetic research during the past few years include autism (Pericak-Vance, 2003), hyperactivity (Thapar, 2003) and dementia (Williams, 2003).

Reading disability

Reading disability was the first success story for educationally relevant QTL research. In 1994, reading disability was found to be linked to a region of chromosome 6 (Cardon, Smith, Fulker, Kimberling, Pennington, & DeFries, 1994), a finding that has been replicated in three independent studies (Willcutt *et al.*, 2002). Another linkage has also been found for chromosome 15 in three studies (Williams, 2003). The first systematic screen of all chromosomes for linkage with reading disability points to another linkage with chromosome 18 in three samples (Fisher, 2003). These linkages involve diverse reading processes – they are not specific to a single process. Association studies have begun to narrow down the linkage regions (Fisher, 2003; Morris *et al.*, 2000; Turic *et al.*, in press), although the culprit genes have not yet been identified.

Language impairment

A specific gene associated with learning disabilities has recently been identified that is responsible for a unique type of language impairment found in a well-studied family known as the KE family (Vargha-Khadem, Watkins, Alcock, Fletcher, & Passingham, 1995; Vargha-Khadem *et al.*, 1998). In this three-generational family, transmission of the disorder was consistent with a single-gene dominant pattern of inheritance. The gene was tracked to the long arm of chromosome 7 (Fisher, Vargha-Khadem, Watkins, Monaco, & Pembrey, 1998) and has been shown to be due to a single nucleotide substitution in a coding region of a gene called *FOXP2* (Lai, Fisher, Hurst, Vargha-Khadem, & Monaco, 2001).

Despite the authors' caution in noting that the KE family's unusual type of speech and language impairment with a single-gene autosomal inheritance pattern has not been found in any other family, the *FOXP2* finding has been hailed in the media as 'the language gene'. In order to investigate the extent to which the *FOXP2* mutation responsible for the genetic defect in the KE family also contributes to common language impairment, we genotyped the *FOXP2* mutation for 270 language-impaired

children (Meaburn, Dale, Craig, & Plomin, 2002). Not a single low-language child had the *FOXP2* mutation, a finding replicated in another study (Newbury *et al.*, 2002). In other words, although the *FOXP2* mutation appears to be responsible for the unusual speech and language disorder of the KE family, the mutation is not found among children with common language impairment.

For common language impairment, molecular genetic research from a QTL perspective has also begun. The first genome-wide scan for QTL linkage with language impairment has recently reported linkages on chromosome 16 and chromosome 19. We are conducting an association analysis of language impairment designed to detect QTLs of small effect size by studying a sample of 300 language-impaired children and 1000 representative controls (Plomin, Colledge, & Dale, 2002).

Mental retardation

We use the term 'mental retardation' merely to refer to the *International Classification of Diseases–10* syndrome of low intellectual functioning and poor adaptive skills. More than 200 genetic disorders, most extremely rare, include mental retardation among their symptoms (Zechner *et al.*, 2001). For example, phenylketonuria (PKU) is a single-gene recessive disorder with occurs in about 1 in 10,000 births and, left untreated by dietary intervention, causes severe mental retardation. An important genetic discovery a decade ago was fragile X, the second most common cause of mental retardation after Down syndrome (Kaufmann & Reiss, 1999). The retardation is caused by a gene (*FMR1*) on the X chromosome that regulates the expression of other genes (Weiler *et al.*, 1997). Three of the most common single-gene disorders that include mental retardation among their symptoms whose primary problem is something other than retardation are Duchenne muscular dystrophy, Lesch-Nyhan syndrome, and neurofibromatosis.

Much more common than such single-gene causes of mental retardation are chromosomal abnormalities that lead to mental retardation. Most common are abnormalities that involve an entire extra chromosome, such as Down syndrome caused by a trisomy of chromosome 21, which is the single most important cause of mental retardation, occurring in 1 in 1,000 births. As the resolution of chromosomal analysis becomes finer, more minor deletions are being found. A study of children with unexplained moderate to severe retardation found that 7% of them had subtle chromosomal abnormalities as compared to only 0.5% of children with mild retardation (Knight *et al.*, 1999).

Although severe mental retardation has drastic consequences for the affected individual, mild mental retardation has a tremendously larger cumulative effect on the educational system because many more individuals are affected. Despite its importance, there has never been a major twin or adoption study of mild mental retardation and perhaps as a result there have been no QTL studies (Plomin, 1999).

Using genes

How will the identification of specific genes associated with learning disabilities benefit teachers confronted with a particular student with learning difficulties? We suggest that the answer is 'not much' although, as explained later, it is our view that such research will have a major impact on research and policy at the level of the population rather

than the particular child. In terms of a teacher confronted with a particular child, the impact will be much less for two reasons. First, for complex disorders, many genes are involved which means that each gene is likely to have only modest predictive power. As mentioned earlier, whilst for rare single-gene disorders a single gene is necessary and sufficient to cause the disorder, common disorders are influenced by many genes in which genetic effects are probabilistic, not preprogrammed. Second, the heritabilities of most common disorders including learning disabilities are about 50%. That is, unlike rare single-gene disorders, common disorders are not due entirely to genes but also to multiple environmental factors. Thus, even if we could identify all of the genes that affect a common disorder – which is highly unlikely because some of the effects may be so small that they will be extremely difficult to detect – we would not be able to make a good prediction about a particular child's risk.

Nonetheless, one way in which finding specific genes associated with learning disabilities might affect teachers is at the level of increasing awareness of the influence of genetic factors in children's development. Identifying specific genes provides much more direct evidence of genetic influence than quantitative genetic research using twin and adoption studies. Moreover, DNA has a unique causal status in that the association between DNA differences such as SNPs and behavioural differences can only be explained causally in one direction: DNA differences cause behavioural differences. This causal status is unique in the sense that associations between behavioural traits and other biological variables such as brain neurotransmitter levels and neuroimaging are just correlations that can be explained in either causal direction – behavioural differences can cause brain differences. For these reasons, finding specific genes might encourage the textbooks that teach teachers to recognise the contribution of nature as well as nurture in children's development. Our review of educational psychology textbooks makes it clear that teachers are not taught much about genetic research but we are not aware of any surveys about experienced teachers' views about nature and nurture or the impact of their views on their teaching.

Although finding specific genes associated with learning disabilities is unlikely to have much direct effect on teachers in the classroom when confronted with a particular child with learning disabilities, we suggest that such findings will have a major impact on educational psychology in terms of research and policy at the level of the population rather than the particular child. Genetics will have far-reaching implications for diagnosis, treatment and prevention of childhood disorders. In terms of diagnosis, finding genes for disorders will lead to new diagnostic classifications that are based on aetiology rather than symptomatology. For example, as mentioned earlier, QTL linkages with reading disability are general to all reading-related processes rather than specific to a single process, suggesting a genetic basis for general reading disability. Moreover, the best documented linkage for reading disability on chromosome 6 also shows linkage with hyperactivity (Willcutt *et al.*, 2003) which suggests that there may be an even more general type of disorder with co-morbid reading disability and hyperactivity.

In terms of treatment, QTLs will become widely used clinically if QTLs are found that indicate that different treatments should be prescribed. For example, 11 of 15 published studies have found evidence of an association between hyperactivity and a dopamine receptor gene called *DRD4* with an overall significant odds ratio of about 2 (Faraone, Doyle, Mick, & Biederman, 2001). Two of three studies have found a stronger *DRD4* association for children who respond well to methylphenidate (Thapar, 2003). Much more research is needed to document this association, but if *DRD4* predicts which hyperactive children will respond to methylphenidate, children will be

genotyped for *DRD4* in order to avoid administering the drug to children who are less likely to profit from it (Masellis *et al.*, 2002).

The most important benefit of identifying genes that put children at risk for disorders is that genes can serve as an early-warning system which will facilitate research on interventions that can prevent these problems before they occur. Interventions for learning disabilities will involve not genetic but environmental engineering. For example, phenylketonuria (PKU) is a metabolic disorder mentioned earlier that can cause severe mental retardation. This form of mental retardation has been largely prevented, not by high-tech solutions such as correcting the mutant DNA or by eugenic programmes or by drugs, but rather by a change in diet that prevents the mutant DNA from having its damaging effects. Because it is possible to prevent the disorder by changing children's diets early in life, newborns throughout the world are screened for PKU. The example of PKU serves as an antidote to the mistaken notion that genetics implies immutability, as discussed later. Moreover, the teacher is the key source of information for parents about their children's progress. Early identification of problems by knowledgeable teachers can help parents, particularly those in economically disadvantaged situations with little access to such information, to have a better understanding of their children and perhaps proactively modify the home learning environment.

In terms of research, educational psychologists are unlikely to become involved in the quest to find QTLs of learning disabilities because such research is expensive and difficult. However, QTLs will be used in research in educational psychology once well-replicated associations are found. What has happened in the field of gerontology will happen eventually in educational psychology as well. As mentioned earlier, the *APOE* gene is associated with dementia. In a meta-analysis of more than 40 studies including 15,000 older adults, individuals with dementia were consistently more likely to have an *APOE-4* allele than individuals without the risk allele – the odds ratio is about 3 in Caucasian populations (Farrer *et al.*, 1997). Although this QTL association was identified only a decade ago (Corder *et al.*, 1993), epidemiological and drug research on dementia now routinely involves *APOE* genotyping in order to assess the extent to which risk factors and treatments differ for individuals with this genetic risk factor. Incorporating *APOE* risk into epidemiological studies has led to other discoveries such as finding that smoking and serious head injury increase the risk for dementia especially for individuals with *APOE-4* vulnerability (Farrer *et al.*, 1997). On the basis of this development in the field of gerontology once an important gene was identified, we predict that researchers in educational psychology will also eventually obtain genotype information as risk indicators on a routine basis. Although it used to be necessary to collect blood samples, DNA can now be obtained painlessly and inexpensively from cheek swabs. Cheek swabs yield enough DNA to genotype hundreds of genes, and the cost of genotyping is surprisingly inexpensive. Departments of educational psychology will not need to have molecular genetics laboratories because companies already exist that can extract DNA and genotype specified DNA markers, capitalising on economies of scale that make genotyping much less expensive than much of the diagnostic testing that is routinely conducted in educational psychology. We are not suggesting that educational psychologists will become molecular geneticists but rather than educational psychologists will use DNA risk indicators in much the same way as they use demographic risk indicators.

When genes associated with learning disabilities are found, the next step in research is to understand how genes have their effect, called functional genomics. Functional

genomics represents the future of genetic research in the postgenomic era in which all DNA sequences and variations in the DNA sequence are known. Functional genomics is usually considered in terms of the bottom-up agenda of molecular biology which focuses on the cellular level of analysis. However, the behavioural level of analysis may be even more valuable in understanding how genes work in relation to the functioning of the whole organism, for example, in understanding interactions and correlations between genes and environment and in leading to new treatments and interventions (Plomin *et al.*, 2003). The phrase *behavioural genomics* has been proposed to emphasise the importance of such top-down levels of analysis for understanding how genes work (Plomin & Crabbe, 2000). Bottom-up and top-down levels of analysis of gene-behaviour pathways will eventually meet in the brain. For this reason, the grandest implication for science is that DNA will serve as an integrating force across diverse disciplines including educational psychology.

Why so slow?

We noted earlier that educational psychology has been slower to accept the evidence for the importance of genetics than other areas of psychology. Some issues may be specific to the history and epistemology of education and educational psychology (Wooldridge, 1994). However, we suspect that much of the reluctance involves general issues that have been faced in other disciplines. For example, misconceptions about what it means to say that genetics is important need to be overcome (Rutter & Plomin, 1997). One set of misconceptions is fuelled by the way we learn about genetics. Mendel discovered the laws of inheritance by working with single-gene 'disorders' in pea plants such as wrinkled seeds. Such single-gene mutations are necessary and sufficient for the development of the disorder. It is for this reason that the word *genetic* has come to be associated with hard-wired defects. This deterministic view fuels a feeling of environmental nihilism, that is, if a disorder is heritable, then there is nothing that we can do about it environmentally (Sternberg & Grigorenko, 1999). To the contrary, it is sometimes possible to do something about a disorder even if it is caused by a single mutation, as mentioned earlier in relation to PKU.

In contrast to single-gene disorders, common disorders such as learning disabilities are not hard-wired by a single-gene mutation. In the 1980s, geneticists thought that common disorders were heterogeneous concatenations of single-gene disorders, a view facetiously called the *one-gene-one-disorder* (OGOD) hypothesis (Plomin *et al.*, 1994). Most geneticists now accept that common disorders are influenced by multiple genes. If many genes are involved, genetic effects on complex traits involve probabilistic propensities rather than predetermined programming. Genes merely *influence* (whose etymology means *to flow in*) rather than determine behaviour. In short, genes in multiple-gene systems are not destiny, and heritability does not imply immutability. More specifically in relation to educational psychology, finding genetic influence on learning disabilities does not imply that children with these disorders are not educable, regardless of whether these genetic influences are specific or general (Adey, 1997). As the example of PKU shows, even a disorder caused by a single gene can be circumvented by environmental intervention.

The myth of environmental nihilism feeds into a related myth lurking in the shadows of such discussions: finding genetic influence will serve to justify social inequality. We do not accept this view. Knowledge alone does not account for societal and political

decisions – values are just as important in the decision-making process. We are aware that the relationship between knowledge and value is a complicated area of philosophy but we are making the simple point that decisions, both good and bad, can be made with or without knowledge. For example, finding specific genes associated with reading disability does not mean that we ought to put all of our resources into educating the best readers and forgetting the rest. Depending on our values, genetics could be used to argue for devoting more resources to help disadvantaged children. We firmly believe, however, that better decisions can be made with knowledge than without. There is nothing to be gained by sticking our heads in the sand and pretending that genetic differences do not exist.

Even further back in the shadows is a general uneasiness with genetics in terms of our view of the essence of humanity. Are we not all created equal? The authors of the American Bill of Rights did not mean that we are all created identical – we obviously differ in height, for example. They clearly meant that in a democracy we should all be treated equally before the law and, more optimistically, that we should all have equal opportunity (Husen, 1978). Indeed, if we are all identical there would be no need for a Bill of Rights because its purpose is to ensure equality of treatment *despite* our differences. Such issues are addressed in detail in a recent book called *The Blank Slate* (Pinker, 2002).

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