The Genetics of Cognitive Abilities and Disabilities

Investigations of specific cognitive skills can help clarify how genes shape the components of intellect

by Robert Plomin and John C. DeFries

People differ greatly in all aspects of what is casually known as intelligence. The differences are apparent not only in school, from kindergarten to college, but also in the most ordinary circumstances: in the words people use and comprehend, in their differing abilities to read a map or follow directions, or in their capacities for remembering telephone numbers or figuring change. The variations in these specific skills are so common that they are often taken for granted. Yet what makes people so different?

It would be reasonable to think that the environment is the source of differ-

ences in cognitive skills—that we are what we learn. It is clear, for example, that human beings are not born with a full vocabulary; they have to learn words. Hence, learning must be the mechanism by which differences in vocabulary arise among individuals. And differences in experience—say, in the extent to which parents model and encourage vocabulary skills or in the quality of language training provided by schools—must be responsible for individual differences in learning.

Earlier in this century psychology was in fact dominated by environmental explanations for variance in cognitive abilities. More recently, however, most psychologists have begun to embrace a more balanced view: one in which nature and nurture interact in cognitive development. During the past few decades, studies in genetics have pointed to a substantial role for heredity in molding the components of intellect, and researchers have even begun to track down the genes involved in cognitive function. These findings do not refute the notion that environmental factors shape the learning process. Instead they suggest that differences in people's genes affect how easily they learn.

Just how much do genes and envi-



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ronment matter for specific cognitive abilities such as vocabulary? That is the question we have set out to answer. Our tool of study is quantitative genetics, a statistical approach that explores the causes of variations in traits among individuals. Studies comparing the performance of twins and adopted children on certain tests of cognitive skills, for example, can assess the relative contributions of nature and nurture.

In reviewing several decades of such studies and conducting our own, we have begun to clarify the relations among specialized aspects of intellect, such as verbal and spatial reasoning, as well as the relations between normal cognitive function and disabilities, such as dyslexia. With the help of molecular genetics, we and other investigators have also begun to identify the genes that affect these specific abilities and disabilities. Eventually, we believe, knowledge of these genes will help reveal the biochemical mechanisms involved in human intelligence. And with the insight gained from genetics, researchers may someday develop environmental interventions that will lessen or prevent the effects of cognitive disorders.

Some people find the idea of a genetic role in intelligence alarming or, at the very least, confusing. It is important to understand from the outset, then, what exactly geneticists mean when they talk about genetic influence. The term typically used is "heritability": a statistical measure of the genetic contribution to differences among individuals.

Verbal and Spatial Abilities

Heritability tells us what proportion of individual differences in a population—known as variance—can be ascribed to genes. If we say, for example, that a trait is 50 percent heritable, we are in effect saying that half of the variance in that trait is linked to heredity. Heritability, then, is a way of explaining what makes people different, not what constitutes a given individual's intelligence. In general, however, if heritability for a trait is high, the influence of genes on the trait in individuals would be strong as well.

Attempts to estimate the heritability of specific cognitive abilities began with family studies. Analyses of similarities between parents and their children and between siblings have shown that cognitive abilities run in families. Results of the largest family study done on specific cognitive abilities, which was conducted in Hawaii in the 1970s, helped to quantify this resemblance.

The Hawaii Family Study of Cognition was a collaborative project between researchers at the University of Colorado at Boulder and the University of Hawaii and involved more than 1,000 families and sibling pairs. The study determined correlations (a statistical measure of resemblance) between relatives on tests of verbal and spatial ability. A correlation of 1.0 would mean that the scores of family members were identical; a correlation of zero would indicate that the scores were no more similar than those of two people picked at random. Because children on average share half their genes with each parent and with siblings, the highest correlation in test scores that could be expected on genetic grounds alone would be 0.5.

The Hawaii study showed that fami-

TWINS ARE COMMON RESEARCH SUBJECTS in studies of specific cognitive abilities. The identical (*opposite page*) and fraternal (*below*) pairs depicted here are participants in the authors' research. They are performing a task in a test of spatial ability, trying to reconstruct a block model with their own toy building blocks. On such tests, which are given to each child individually, the scores of identical twins (who have all the same genes) are more similar than the scores of fraternal twins (who share about half their genes)—a sign that genetic inheritance exerts an influence on spatial ability.



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ly members are in fact more alike than unrelated individuals on measures of specific cognitive skills. The actual correlations for both verbal and spatial tests were, on average, about 0.25. These correlations alone, however, do not disclose whether cognitive abilities run in families because of genetics or because of environmental effects. To explore this distinction, geneticists rely on two "experiments": twinning (an experiment of nature) and adoption (a social experiment).

Twin studies are the workhorse of behavioral genetics. They compare the resemblance of identical twins, who have the same genetic makeup, with the resemblance of fraternal twins, who share only about half their genes. If cognitive abilities are influenced by genes, identical twins ought to be more alike than fraternal twins on tests of cognitive skills. From correlations found in these kinds of studies, investigators can estimate the extent to which genes account for variances in the general population. Indeed, a rough estimate of heritability

TESTS OF VERBAL ABILITY	
1. VOCABULARY: In each row, circle the we nearly the same as the underlined word. The neach line. a. arid coarse clever b. piquant fruity pungent 2. VERBAL FLUENCY: For the next three you can that start with F and end with W 3. CATEGORIES: For the next three minut think of that are FLAT.	ord that means the same of here is only one correct choice modest dry harmful upright minutes, write as many words as

can be made by doubling the difference between identical-twin and fraternaltwin correlations.

Adoption provides the most direct way to disentangle nature and nurture in family resemblance, by creating pairs of genetically related individuals who do not share a common family environment. Correlations among these pairs enable investigators to estimate the contribution of genetics to family resemblance. Adoption also produces pairs of genetically unrelated individuals who share a family environment, and their correlations make it possible to estimate the contribution of shared environment to resemblance.

Twin studies of specific cognitive abilities over three decades and in four countries have yielded remarkably consistent results [*see illustration on page 66*]. Correlations for identical twins greatly exceed those for fraternal twins on tests of both verbal and spatial abilities in children, adolescents and adults. Results of the first twin study in the elder-

How Do Cognitive Abilities Relate to General Intelligence?

by Karen Wright

Since the dawn of psychology, experts have disagreed about the fundamental nature of intelligence. Some have claimed that intelligence is an inherent faculty prescribed by heredity, whereas others have emphasized the effects of education and upbringing. Some have portrayed intelligence as a global quality that permeates all facets of cognition; others believe the intellect consists of discrete, specialized abilities—such as artistic talent or a flair for mathematics—that share no common principle.

In the past few decades, genetic studies have convinced most psychologists that heredity exerts considerable influence on intelligence. In fact, research suggests that as much as half of the variation in intelligence among individuals may be attributed to genetic factors.

And most psychologists have also come to accept a global conceptualization of intelligence. Termed general cognitive ability, or "g," this global quality is reflected in the apparent overlap among specific cognitive skills. As Robert Plomin and John C. De-Fries point out, people who do well on tests of one type of cognitive skill also tend to do well on tests of other cognitive abilities. Indeed, this intercorrelation has provided the rationale for IQ (intelligence quotient) tests, which yield a single score from combined assessments of specific cognitive skills. Because specific and general cognitive abilities are related in this manner, it is not surprising that many of the findings regarding specific abilities echo what is already known about general ability. The heritabilities found in studies of specific cognitive abilities, for example, are comparable with the heritability determined for g. The developmental trend described by the authors—in which genetic influence on specific cognitive abilities seems to increase throughout childhood, reaching adult levels by the mid-teens—is also familiar to researchers of general cognitive ability.

And because measures of g are derived from intercorrelations of verbal and spatial abilities, a gene that is linked with both those traits is almost guaranteed to have some role in general cognitive ability as well—and vice versa. This month in the journal *Psychological Science*, Plomin and various collaborators report the discovery of the first gene associated with general cognitive ability. Although the finding should further understanding of the nature of cognition, it is also likely to reignite debate. Indeed, intelligence research may be one realm where understanding does little to quell disagreement.

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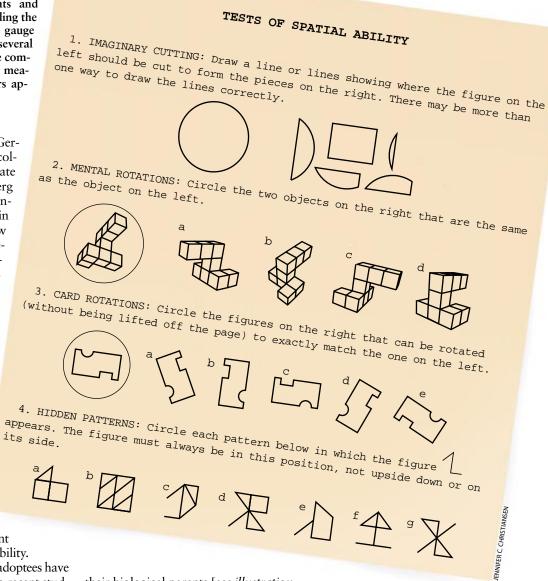
TESTS OF SPECIFIC ABILITIES administered to adolescents and adults include tasks resembling the ones listed here. The tests gauge each cognitive ability in several ways, and multiple tests are combined to provide a reliable measure of each skill. (Answers appear on page 69.)

ly-reported last year by Gerald E. McClearn and his colleagues at Pennsylvania State University and by Stig Berg and his associates at the Institute for Gerontology in Jönköping, Sweden-show that the resemblances between identical and fraternal twins persist even into old age. Although gerontologists have assumed that genetic differences become less important as experiences accumulate over a lifetime, research on cognitive abilities has so far demonstrated otherwise. Calculations based on the combined findings in these studies imply that in the general population, genetics accounts for about 60 percent of the variance in verbal

ability and about 50 percent of the variance in spatial ability.

Investigations involving adoptees have yielded similar results. Two recent studies of twins reared apart—one by Thomas J. Bouchard, Jr., Matthew McGue and their colleagues at the University of Minnesota, the other an international collaboration headed by Nancy L. Pedersen at the Karolinska Institute in Stockholm—have implied heritabilities of about 50 percent for both verbal and spatial abilities.

In our own Colorado Adoption Project, which we launched in 1975, we have used the power of adoption studies to further characterize the roles of genes and environment, to assess developmental trends in cognitive abilities and to explore the extent to which specific cognitive skills are related to one another. The ongoing project compares the correlations between more than 200 adopted children and their birth and adoptive parents with the correlations for a control group of children raised by



their biological parents [*see illustration* on page 67].

These data provide some surprising insights. By middle childhood, for example, birth mothers and their children who were adopted by others are just as similar as control parents and their children on measures of both verbal and spatial ability. In contrast, the scores of adopted children do not resemble those of their adoptive parents at all. These results join a growing body of evidence suggesting that the common family environment generally does not contribute to similarities in family members. Rather family resemblance on such measures seems to be controlled almost entirely by genetics, and environmental factors often end up making family members different, not the same.

The Colorado data also reveal an interesting developmental trend. It appears that genetic influence increases during childhood, so that by the mid-teens, heritability reaches a level comparable with that seen in adults. In correlations of verbal ability, for example, resemblance between birth parents and their children who were adopted by others increases from about 0.1 at age three to about 0.3 at age 16. A similar pattern is evident in tests of spatial ability. Some genetically driven transformation in cognitive function seems to take place in the early school years, around age seven. The results indicate that by the time people reach age 16, genetic factors account for 50 percent of the variance for verbal ability and 40 percent for spatial ability-numbers not unlike those derived from twin studies of specific cognitive abilities.

The Colorado Adoption Project and other investigations have also helped

clarify the differences and similarities among cognitive abilities. Current cognitive neuroscience assumes a modular model of intelligence, in which different cognitive processes are isolated anatomically in discrete modules in the brain. The modular model implies that specific cognitive abilities are also genetically distinct—that genetic effects on verbal ability, say, should not overlap substantially with genetic effects on spatial ability.

Psychologists, however, have long recognized that most specialized cognitive skills, including verbal and spatial abilities, intercorrelate moderately. That is, people who perform well on one type of test also tend to do well on other types. Correlations between verbal and spatial abilities, for example, are usually about 0.5. Such intercorrelation implies a potential genetic link.

From Abilities to Achievement

Genetic studies of specific cognitive abilities also fail to support the modular model. Instead it seems that genes are responsible for most of the overlap between cognitive skills. Analysis of the Colorado project data, for example, indicates that genetics governs 70 percent of the correlation between verbal and spatial ability. Similar results have been found in twin studies in childhood, young adulthood and middle age. Thus, there is a good chance that when genes associated with a particular cognitive ability are identified, the same genes will be associated with other cognitive abilities.

Research into school achievement has hinted that the genes associated with cognitive abilities may also be relevant to academic performance. Studies of more than 2,000 pairs of high schoolage twins were done in the 1970s by John C. Loehlin of the University of Texas at Austin and Robert C. Nichols, then at the National

Merit Scholarship Corporation in Evanston, Ill. In these studies the scores of identical twins were consistently and substantially more similar than those of fraternal twins on all four domains of the National Merit Scholarship Qualifying Test: English usage, mathematics, social studies and natural sciences. These results suggest that genetic factors account for about 40 percent of the variation on such achievement tests.

Genetic influence on school achievement has also been found in twin studies of elementary school–age children as

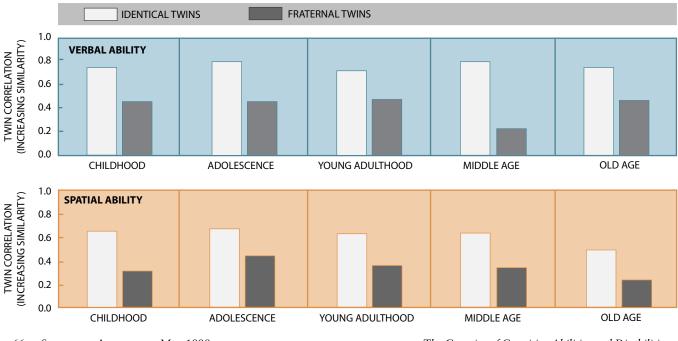
What Heritability Means

'L'he implications of heritability data are commonly misunderstood. As the main text indicates, heritability is a statistical measure, expressed as a percentage, describing the extent to which genetic factors contribute to variations on a given trait among the members of a population.

The fact that genes influence a trait does not mean, however, that "biology is destiny." Indeed, genetics research has helped confirm the significance of environmental factors, which generally account for as much variance in human behavior as genes do. If intelligence is 50 percent heritable, then environmental factors must be just as important as genes in generating differences among people.

> well as in our work with the Colorado Adoption Project. It appears that genes may have almost as much effect on school achievement as they do on cognitive abilities. These results are surprising in and of themselves, as educators have long believed that achievement is more a product of effort than of ability. Even more interesting, then, is the finding from twin studies and our adoption project that genetic effects overlap between different categories of achievement and that these overlapping genes are probably the very same genetic fac-

TWIN STUDIES have examined correlations in verbal (*top*) and in spatial (*bottom*) skills of identical twins and of fraternal twins. When the results of the separate studies are put side by side, they demonstrate a substantial genetic influence on specific cognitive abilities from childhood to old age; for all age groups, the scores of identical twins are more alike than those of fraternal twins. These data seem to counter the long-standing notion that the influence of genes wanes with time.



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Moreover, even when genetic factors have an especially powerful effect, as in some kinds of mental retardation, environmental interventions can often fully or partly overcome the genetic "determinants." For example, the devastating effects of phenylketonuria, a genetic disease that can cause mental retardation, can often be nullified by dietary intervention.

Finally, the degree of heritability for a given trait is not set in stone. The relative influence of genes and environment can change. If, for instance, environmental factors were made almost identical for all the members of a hypothetical population, any differences in cognitive ability in that population would then have to be attributed to genetics, and heritability would be closer to 100 percent than to 50 percent. Heritability describes what is, rather than what can (or should) be. —*R.P. and J.C.D.*

tors that can influence cognitive abilities.

This evidence supports a decidedly nonmodular view of intelligence as a pervasive or global quality of the mind and underscores the relevance of cognitive abilities in real-world performance. It also implies that genes for cognitive abilities are likely to be genes involved in school achievement, and vice versa.

Given the evidence for genetic influence on cognitive abilities and achievement, one might suppose that cognitive disabilities and poor academic achievement must also show genetic influence. But even if genes are involved in cognitive disorders, they may not be the same genes that influence normal cognitive function. The example of mental retardation illustrates this point. Mild mental retardation runs in families, but severe retardation does not. Instead severe mental retardation is caused by genetic and environmental factors-novel mutations, birth complications and head injuries, to name a few-that do not come into play in the normal range of intelligence.

Researchers need to assess, rather than assume, genetic

links between the normal and the abnormal, between the traits that are part of a continuum and true disorders of human cognition. Yet genetic studies of verbal and spatial disabilities have been few and far between.

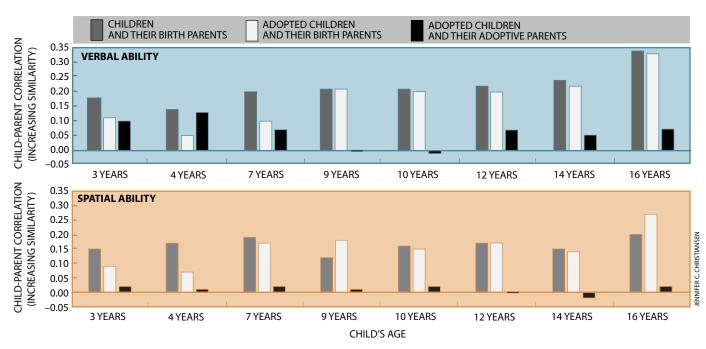
Genetics and Disability

Most such research has focused on reading disability, which afflicts 80 percent of children diagnosed with a learning disorder. Children with reading disability, also known as dyslexia, read slowly, show poor comprehension and have trouble reading aloud [see "Dyslexia," by Sally E. Shaywitz, SCI-ENTIFIC AMERICAN, November 1996]. Studies by one of us (DeFries) have shown that reading disability runs in families and that genetic factors do indeed contribute to the resemblance among family members. The identical twin of a person diagnosed with reading disability, for example, has a 68 percent risk of being similarly diagnosed, whereas a fraternal twin has only a 38 percent chance.

Is this genetic effect related in any way to the genes associated with normal variation in reading ability? That question presents some methodological challenges. The concept of a cognitive disorder is inherently problematic, because it treats disability qualitatively you either have it or you don't—rather than describing the degree of disability in a quantitative fashion. This focus creates an analytical gap between disorders and traits that are dimensional (varying along a continuum), which are by definition quantitative.

During the past decade, a new genetic technique has been developed that bridges the gap between dimensions and disorders by collecting quantitative information about the relatives of subjects diagnosed qualitatively with a dis-

COLORADO ADOPTION PROJECT, which followed subjects over time, finds that for both verbal (*top*) and spatial (*bottom*) abilities, adopted children come to resemble their birth parents (*white bars*) as much as children raised by their birth parents do (gray bars). In contrast, adopted children do not end up resembling their adoptive parents (*black bars*). The results imply that most of the family resemblance in cognitive skills is caused by genetic factors, not environment.



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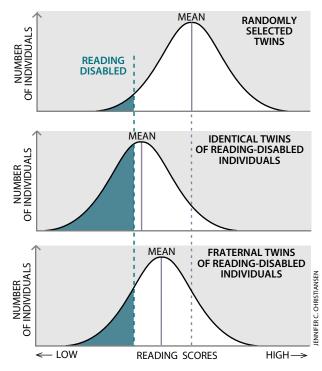
ability. The method is called DF extremes analysis, after its creators, DeFries and David W. Fulker, a colleague at the University of Colorado's Institute for Behavioral Genetics.

For reading disability, the analysis works by testing the identical and fraternal twins of reading-disabled subjects on quantitative measures of reading, rather than looking for a shared diagnosis of dyslexia [see illustration at right]. If reading disability is influenced by genes that also affect variation within the normal range of reading performance, then the reading scores of the identical twins of dyslexic children should be closer to those of the reading-disabled group than the scores of fraternal twins are. (A single gene can exert different effects if it occurs in more than one form in a population, so that two people may inherit somewhat different versions. The genes controlling eye color and height are examples of such variable genes.)

It turns out that, as a group, identical twins of reading-disabled subjects do perform almost as poorly as dyslexic sub-

jects on these quantitative tests, whereas fraternal twins do much better than the reading-disabled group (though still significantly worse than the rest of the population). Hence, the genes involved in reading disability may in fact be the same as those that contribute to the quantitative dimension of reading ability measured in this study. DF extremes analysis of these data further suggests that about half the difference in reading scores between dyslexics and the general population can be explained by genetics.

For reading disability, then, there could well be a genetic link between the normal and the abnormal, even though such links may not be found universally for other disabilities. It is possible that reading disability represents the extreme end of a continuum of reading ability, rather than a distinct disorder—that dyslexia might be quantitatively rather than qualitatively different from the normal range of reading ability. All this suggests that if a gene is found for reading disability, the same gene is likely to be associated with the normal range of variation in reading ability. The defini-



READING SCORES of twins suggest a possible genetic link between normal and abnormal reading skills. In a group of randomly selected members of twin pairs (*top*), a small fraction of children were reading disabled (*blue*). Identical (*middle*) and fraternal (*bottom*) twins of the reading-disabled children scored lower than the randomly selected group, with the identical twins performing worse than the fraternal ones. Genetic factors, then, are involved in reading disability. The same genes that influence reading disability may underlie differences in normal reading ability.

tive test will come when a specific gene is identified that is associated with either reading ability or disability. In fact, we and other investigators are already very close to finding such a gene.

The Hunt for Genes

Until now, we have confined our discussion to quantitative genetics, a discipline that measures the heritability of traits without regard to the kind and number of genes involved. For information about the genes themselves, researchers must turn to molecular genetics—and increasingly, they do. If scientists can identify the genes involved in behavior and characterize the proteins that the genes code for, new interventions for disabilities become possible.

Research in mice and fruit flies has succeeded in identifying single genes related to learning and spatial perception, and investigations of naturally occurring variations in human populations have found mutations in single genes that result in general mental retardation. These include the genes for phenylketonuria and fragile X syndrome, both causes of mental retardation. Single-gene defects that are associated with Duchenne's muscular dystrophy, Lesch-Nyhan syndrome, neurofibromatosis type 1 and Williams syndrome may also be linked to the specific cognitive disabilities seen in these disorders [see "Williams Syndrome and the Brain," by Howard M. Lenhoff, Paul P. Wang, Frank Greenberg and Ursula Bellugi; SCIENTIFIC AMERICAN, December 1997].

In fact, more than 100 single-gene mutations are known to impair cognitive development. Normal cognitive functioning, on the other hand, is almost certainly orchestrated by many subtly acting genes working together, rather than by single genes operating in isolation. These collaborative genes are thought to affect cognition in a probabilistic rather than a deterministic manner and are called quantitative trait loci, or OTLs. The name, which applies to genes involved in a complex dimension such as cognition, emphasizes the quantitative nature of certain physical and

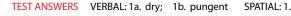
behavioral traits. QTLs have already been identified for diseases such as diabetes, obesity and hypertension as well as for behavioral problems involving drug sensitivity and dependence.

But finding QTLs is much more difficult than identifying the single-gene mutations responsible for some cognitive disorders. Fulker addressed this problem by developing a method, similar to DF extremes analysis, in which certain known variations in DNA are correlated with sibling differences in quantitative traits. Because genetic effects are easier to detect at the extremes of a dimension, the method works best when at least one member of each sibling pair is known to be extreme for a trait. Investigators affiliated with the Colorado Learning Disabilities Research Center at the University of Colorado first used this technique, called QTL linkage, to try to locate a QTL for reading disability-and succeeded. The discovery was reported in 1994 by collaborators at Boulder, the University of Denver and Boys Town National Research Hospital in Omaha.

Like many techniques in molecular genetics, QTL linkage works by identifying differences in DNA markers: stretches of DNA that are known to occupy particular sites on chromosomes and that can vary somewhat from person to person. The different versions of a marker, like the different versions of a gene, are called alleles. Because people have two copies of all chromosomes (except for the genderdetermining X and Y chromosomes in males), they have two alleles for any given DNA marker. Hence, siblings can share one, two or no alleles of a marker. In other words, for each marker, siblings can either be like identical twins (sharing both alleles), like fraternal twins (sharing half their alleles) or like adoptive siblings (sharing no alleles).

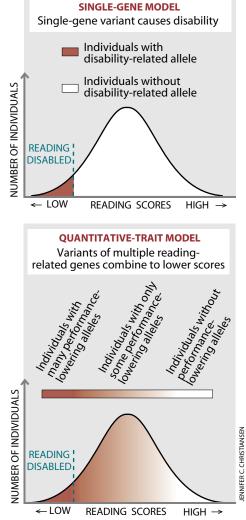
The investigators who found the QTL for reading disability identified a reading-disabled member of a twin pair and then obtained reading scores for the other twin-the "co-twin." If the reading scores of the co-twins were worse when they shared alleles of a particular marker with their readingdisabled twins, then that marker was likely to lie near a OTL for reading disability in the same chromosomal region. The researchers found such a marker on the short arm of chromosome 6 in two independent samples, one of fraternal twins and one of nontwin siblings. The findings have since been replicated by others.

It is important to note that whereas these studies have helped point to the location of a gene (or genes) implicated in reading disability, the gene (or genes) has not yet been characterized. This distinction gives a sense of where the genetics of cognition stand today: poised



The Authors

ROBERT PLOMIN and JOHN C. DEFRIES have collaborated for more than 20 years. Plomin, who worked with DeFries at the University of Colorado at Boulder from 1974 to 1986, is now at the Institute of Psychiatry in London. There he is research professor of behavioral genetics and deputy director of the Social, Genetic and Developmental Psychiatry Research Center. DeFries directs the University of Colorado's Institute for Behavioral Genetics and the university's Colorado Learning Disabilities Research Center. The ongoing Colorado Adoption Project, launched by the authors in 1975, has so far produced three books and more than 100 research papers. Plomin and DeFries are also the lead authors of the textbook *Behavioral Genetics*, now in its third edition.



on the brink of a new level of discovery. The identification of genes that influence specific cognitive abilities will revolutionize researchers' understanding of the mind. Indeed, molecular genetics will have far-ranging consequences for the study of all human behavior. Researchers will soon be able to investi-

2. b, c; 3. a, c, d; 4. a, b, f

TWO MODELS illustrate how genetics may affect reading disability. In the classic view (top), a single variant, or allele, of a gene is able to cause the disorder; everyone who has that allele becomes reading disabled (graph). But evidence points to a different model (bottom), in which a single allele cannot produce the disability on its own. Instead variants of multiple genes each act subtly but can combine to lower scores and increase the risk of disability.

gate the genetic connections between different traits and between behaviors and biological mechanisms. They will be able to better track the developmental course of genetic effects and to define more precisely the interactions between genes and the environment.

The discovery of genes for disorders and disabilities will also help clinicians design more effective therapies and to identify people at risk long before the appearance of symptoms. In fact, this scenario is already being enacted with an allele called Apo-E4, which is associated with dementia and cognitive decline in the elderly. Of course, new knowledge of specific genes could turn up new problems as well: among them, prejudicial labeling and discrimination. And genetics research always raises fears that DNA markers will be used by parents prenatally to select "designer babies."

We cannot emphasize too much that genetic effects do not imply genetic determinism, nor do they constrain environmental interventions. Although some readers may find our views to be controversial, we believe the benefits of identifying genes for cognitive dimensions and disorders will far outweigh the potential abuses.

Further Reading

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