simulations shown in Fig. 1 and by the general predictions embodied in Table 1. Significant departures from these expectations would indicate that there are new populations of astronomical objects or that previously identified populations have evolved in unexpected ways. In particular, the presence or absence of large numbers of brown dwarfs (Eq. 1) should be obvious from an analysis of the first deep scientific exposures with the WFC.

The HST project is developing the capability for operating instruments in a "parallel" mode, a mode in which one could, for example, take an exposure with the WFC in whatever direction it is oriented while another instrument is taking data on a specific object or field in a pointed mode. The typical length of time that the HST will be pointed at a particular target is about 20 minutes. The calculations presented in this article suggest that at high Galactic latitudes one may expect to detect in 20 minutes, with the WFC and a broad band visual filter, of order 100 galaxies and 20 stars over the entire WFC field. In the ultraviolet, a smaller number of objects are expected to be detected because galaxies, and particularly faint stars, have spectral energy distributions that decrease toward shorter wavelengths and the sensitivity of the WFC is much less in the ultraviolet than in the visual. The number of detected objects expected for different exposure times can be estimated from Table 1 and the fact that the limiting brightness that can be observed depends (for longer exposures) on approximately the square root of the observing time. The number of objects to a given magnitude that will be detected by the FOC is reduced by a factor of 50 compared to the WFC because of the smaller observing area; the FOC quantum efficiency peaks in the ultraviolet (but is never as large as the visual band efficiency of the WFC).

REFERENCES AND NOTES

1. D. N. B. Hall, Ed., *The Space Telescope Observatory* (NASA Scientific and Technical Information Branch, Washington, DC, 1982); L. Spitzer, *Science* **161**, 225 (1968).
2. M. S. Longair and J. W. Warner, Eds., *Scientific Research with the Space Telescope*, IAU Colloquium 54, NASA CP-2111 (U.S. Government Printing Office, Washington, DC, 1980).
3. J. A. Tyson, *Astron. J.* **96**, 1 (1988).
4. J. Westphal, in (*1*), p. 28.
5. F. Machetto, in (*1*), p. 40.
6. J. N. Bahcall and R. M. Soniera, *Astrophys. J. Suppl.* **47**, 357 (1981).
7. J. N. Bahcall, *Annu. Rev. Astron. Astrophys.* **24**, 577 (1986); ——— and R. M. Soneira, *Astrophys. J. Suppl.* **44**, 73 (1980).
8. F. D'Antona and I. Mazziteli, *Astrophys. J.* **296**, 502 (1985); F. D'Antona, *ibid.* **320**, 653 (1987); J. Liebert, *Stellar Evolution, 50th Anniversary Symposium of McDonald Observatory*, D. L. Lambert, Ed. (Astronomical Society of the Pacific, in press).
9. A. Burrows, W. B. Hubbard, J. L. Lunine, *Astrophys. J.* **345**, 939 (1989).
10. B. J. Boyle *et al.*, *Mon. Not. R. Astron. Soc.* **235**, 935 (1988).
11. J. N. Bahcall and D. P. Schneider, in *IAU Symposium 126*, J. E. Grindlay and A. G. K. Phillip, Eds. (Reidel, Boston, 1988), p. 455.
12. J. F. Jarvis and J. A. Tyson, *Astron. J.* **86**, 476 (1981).
13. R. G. Kron, thesis, University of California, Berkeley (1978).
14. H. L. Johnson, *Ann. Rev. Astron. Astrophys.* **4**, 193 (1966).
15. P. Guhathakurta, in preparation.
16. C. A. Gullixson, P. C. Boeshaar, J. A. Tyson, P. Seitzer, in preparation.
17. J. A. Tyson and R. A. Wenk, in preparation; J. A. Tyson, *Astronomical Society of the Pacific Hubble Symposium*, R. G. Kron, Ed., in press.
18. O. Lahav, private communication.

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The Role of Inheritance in Behavior

ROBERT PLOMIN

Inheritance plays a major role in behavior as shown by selection and strain studies for animal behavior and by twin and adoption studies for human behavior. Unlike simple Mendelian characteristics, genetic variance for behavioral dimensions and disorders rarely accounts for more than half of the phenotypic variance, and multiple genes with small effects appear to be involved rather than one or two major genes. Genetic research on behavior will be transformed by techniques of molecular biology that can be used to identify DNA sequences responsible for behavioral variation. However, the importance of nongenetic factors and the multigenetic control of behavior require new strategies to detect DNA markers that account for small amounts of behavioral variation.

BEHAVIOR IS A NEW FRONTIER FOR MOLECULAR BIOLOGY. IT is the most complex phenotype that can be studied because behavior reflects the functioning of the whole organism and because it is dynamic and changes in response to the environment. Indeed, behavior is in the vanguard of evolution for these very reasons. Genetic analysis of behavioral dimensions and disorders is especially difficult for three additional reasons. First, unlike characteristics that Mendel studied in the edible pea such as smooth versus wrinkled seeds, most behaviors and behavioral problems are not distributed in "either/or" dichotomies—we are not either smooth or wrinkled, psychologically. Second, unlike classic Mendelian disorders such as Huntington's disease that are caused by a single gene with little effect from other genes or environmental background, most behavioral traits appear to be influenced by many genes, each

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with small effects. Finally, behavior is substantially influenced by nongenetic factors.

In this article, I will provide an overview of the results of quantitative genetic research on behavior with a focus on the multigenetic control of behavior and the magnitude of genetic influence and, second, will consider the implications of these findings for the application of molecular biology techniques to the investigation of behavior. But the question must be asked at the outset, why should scientists bother with behavior if it is so complex? The answer lies in the importance of behavior per se rather than in its usefulness for revealing how genes work. Some of society's most pressing problems, such as drug abuse, mental illness, and mental retardation, are behavioral problems. Behavior is also key in health as well as illness, in abilities as well as disabilities, and in the personal pluses of life, such as sense of well-being and the ability to love and work.

Although the effects of major genes and chromosomal abnormalities on behavior are sometimes studied, most genetic research on behavior employs the theory and methods of quantitative genetics. Quantitative genetics identifies genetic influence even when many genes and substantial environmental variation are involved. This theory emerged in the early 1900s as a resolution to the problem of how Mendelian laws of inheritance could be applied to quantitatively distributed complex characteristics, such as behavior. The essence of quantitative genetic theory is that Mendel's laws of discrete inheritance also apply to such complex characteristics if we assume that many genes, each with small effect, combine to produce observable differences among individuals in a population. Quantitative genetics also applies to behavioral differences among individuals dichotomized into affected and unaffected categories, as is typical in research on behavioral disorders.

Quantitative genetic research determines the sum of heritable genetic influence on behavior, regardless of the complexity of genetic modes of action or the number of genes involved. However, quantitative genetics does not tell us which genes are responsible for genetic influence. An exciting direction for genetic research on behavior is the identification of genes responsible for genetic variance on behavior, the theme of the second half of this article. In the first half of the article, I review results of quantitative genetic research on animal and human behavior. I hope to provide an overview that will be useful for researchers outside the field who might be interested in the role of inheritance in behavior. For details concerning the methods and results of animal and human behavioral genetic research, see (*1*).

Animal Behavior

Applied behavioral genetics began thousands of years ago when animals were bred for their behavior as much as for their morphology. The results of such artificial selection can be seen most dramatically in differences in behavior as well as physique among dog breeds, differences that testify to the great range of genetic variability within a species and its effect on behavior. Selection studies in the laboratory still provide the most convincing demonstrations of genetic influence on behavior. The results of two selection studies in mice, the favorite mammalian organism of behavioral geneticists, are depicted in Fig. 1. In one of the longest mammalian selection studies of behavior, replicated high and low lines were selected for activity in a brightly lit open field, an aversive situation thought to assess emotional reactivity (*2*). After 30 generations of selection, a 30-fold difference exists between the activity of the high and low lines, and there is no overlap between them. Similar results have been found for most mouse behaviors subjected to selection in the laboratory, such as alcohol sensitivity (*3*), preference, and withdrawal; various types of learning; exploratory behavior; nest building; and aggressiveness. Many behaviors of rats and *Drosophila* have also responded to selective breeding (*1*).

In addition to providing dramatic evidence of the existence of genetic influence on behavior, two other implications can be drawn from the results of these selection studies. The first concerns the magnitude of the genetic effect as measured by statistical tests. Heritability is a descriptive statistic that estimates the extent to which observed variability is due to genetic variability. In selection studies, heritability estimates derived from the magnitude of the response to selection are nearly always less than 50%. Even though genetic influence of this magnitude can result in major differences between selected lines after just a few generations of selection, most behavioral variability is not genetic in origin.

The second implication of these results is that many genes appear to affect behavior. Despite intense selection pressure, the response to selection continues unabated during the course of most selection studies of behavior. For example, in the study of open-field activity in Fig. 1, although the low-active lines have reached the bottom limit of zero activity scores, the high lines show no sign of reaching a selection limit, even after 30 generations of selection. If only one or two major genes were responsible for genetic effects on these behaviors, the relevant alleles would be sorted into the high and low lines in a few generations. The steady divergence of selected lines provides the best available evidence that many genes affect behavior.

Other genetic methods used to investigate animal behavior are family studies and studies of inbred strains. Family studies assess the sine qua non of transmissible genetic influence, the resemblance between genetically related individuals. They also provide test

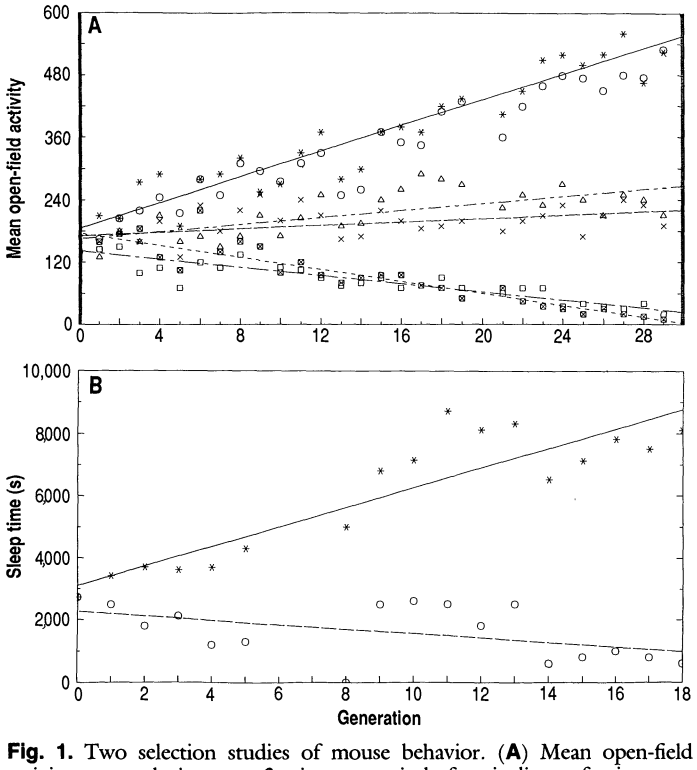

Fig. 1. Two selection studies of mouse behavior. (**A**) Mean open-field activity scores during two 3-min test periods for six lines of mice: two selected for high open-field activity [H1 (*) and H2 (○)], two selected for low open-field activity [L1 (☒) and L2 (□)], and two randomly mated within line to serve as controls [C1 (X) and C2 (△)]. Data reported by (*2*). (**B**) Sleep time (loss of righting response after ethanol injection) for two lines of mice: one selected for long sleep times (*) and one selected for short sleep times (○). Data reported in (*3*).

crosses that can be used to explore hypotheses of single-locus transmission. Hundreds of single-locus mutations have been found that result in neurological defects. For example, there is a gene responsible for head shaking and rapid circling in "waltzer" mice. However, normal behavioral variability has not shown the effects of one major gene.

Inbred strains are created by mating brother to sister for at least 20 generations. This severe inbreeding eliminates heterozygosity and results in animals that are virtually identical genetically. Behavioral differences between inbred strains reared under the same laboratory conditions can be ascribed to genetic differences. Similar to the results of selection studies, comparisons among inbred strains point to significant genetic influence on most behaviors that have been examined (*1*). Also in line with selection studies, estimates of the magnitude of genetic influence from comparisons among inbred strains indicate that, although substantial, genetic factors do not explain the majority of the variance in behavioral characteristics. Crosses and backcrosses between inbred strains and their progeny have been used to find patterns of inheritance consistent with single-gene transmission, but this approach in fact has little power to discriminate single-gene from multiple-gene transmission.

A powerful strategy to uncover major-gene effects in animal behavior is the recombinant inbred (RI) strain method (*4*). RI strains are different inbred strains that were derived from separate brother-sister pairs from the same genetically segregating F_2 generation (crosses among hybrid offspring of two inbred strains). They are called RI strains because parts of chromosomes from the parental strains have recombined in the F_2 generation from which the RI strains were derived. If a single gene is responsible for a behavior that differs between the two parental strains, half of the RI strains should be like one parent and half like the other. In other words, there should be no intermediate phenotypes if just one locus is involved, because each RI strain will be homozygous for the allele of either one or the other parental strain. Behaviors studied in RI strains show no single-gene effects; a few, but only a few, major-gene effects have been suggested (*1*).

Human Behavior

For human behavior, no quantitative genetic methods as powerful as selection or inbred strain studies exist. Human behavioral genetic research relies on family, adoption, and twin designs. As in studies of nonhuman animals, family studies assess the extent of resemblance for genetically related individuals, although they cannot disentangle possible environmental sources of resemblance. That is the point of adoption studies. Genetically related individuals adopted apart give evidence of the extent to which familial resemblance is due to hereditary resemblance. Twin studies are like natural experiments in which the resemblance of identical twins, whose genetic identity can be expressed as genetic relatedness of 1.0, is compared to the resemblance of fraternal twins, first-degree relatives whose coefficient of genetic relatedness is 0.50. If heredity affects a behavior, identical twins should be more similar for the behavior than fraternal twins. As in studies of nonhuman animals, family, adoption, and twin studies can be used to estimate the magnitude of genetic influence as well as its statistical significance. For example, for height, an exemplar of a complex quantitative trait, correlations for first-degree relatives are 0.45, where reared together or adopted apart, and identical and fraternal twin correlations are 0.90 and 0.45, respectively. These results suggest that heritability, the proportion of phenotypic variance that can be accounted for by genetic factors, is 90% for height.

Below I review results of family, twin, and adoption research on the role of inheritance in human behavior, emphasizing the focal areas of cognitive abilities and disabilities, personality, and psychopathology.

Cognitive abilities and disabilities. One of the most studied traits in human behavioral genetics is general cognitive ability (IQ). In more than 30 twin studies involving more than 10,000 pairs of twins, identical and fraternal twin correlations averaged 0.85 and 0.60, respectively (*5*). The IQ correlation for first-degree relatives living together is about 0.40; for adopted-apart first-degree relatives, the correlation is about 0.20; and for adoptive parents and their adopted children, the correlation is about 0.20. These results, and model-fitting analyses that incorporate all of the data on IQ, are consistent with heritabilities of about 50% (*6*). The error surrounding this estimate may be as high as 20%, so we can only say with confidence that the heritability of IQ scores is between 30 and 70%. Nonetheless, even if the heritability of IQ scores is at the bottom of this range, it is a remarkable finding. To account for 30% of the variance of anything as complex as IQ scores is a remarkable achievement.

One direction for research on IQ is to trace the unfolding of genetic influence during development (*7*). For example, for 15 years, my colleagues and I have been engaged in a prospective longitudinal adoption study of over 200 adoptive and 200 matched nonadoptive families in which adopted and nonadopted children are studied yearly (*8*). For IQ, model-fitting analyses indicate that heritability increases steadily from infancy to the early school years (*9*) and also suggest that genetic effects on IQ during childhood are highly correlated with genetic effects on IQ in adulthood (*10*).

Specific cognitive abilities such as verbal ability and spatial ability show as much genetic influence as IQ; some types of memory ability appear to be less influenced by heredity than other specific cognitive abilities (*11*). Measures of academic achievement also show genetic influence, and recent multivariate research suggests that genetic effects on academic achievement tests correlate highly with genetic effects on cognitive abilities (*12*). Surprisingly, there are no twin or adoption studies of mental retardation.

There is no evidence for major-gene effects on normal variation in general or specific cognitive abilities. For example, earlier reports of sex linkage for spatial ability have not been confirmed (*13*). Common cognitive problems such as reading disability have yielded no clear major-gene effects. For example, a 1983 report of chromosome 15 linkage for reading disability (*14*) is in doubt—only 1 in 21 families now shows a near significant lod score (logarithm of the likelihood ratio for linkage) (*15*). However, as in mouse research, many rare genes have been identified that drastically disrupt normal cognitive development. Of the more than 4000 single-gene effects cataloged for human beings, more than a hundred include lowered IQ scores as a clinical symptom (*16*). Although these recessive alleles may have devasting effects for homozygous individuals, they are rare and thus can account for only a minuscule portion of IQ variance in the population. For example, the fragile X marker, which appears to be a source of the excess of mild mental retardation in males (*17*), cannot account for much IQ variance in the population because its incidence is less than 1 in 1000 and many males with the fragile X marker do not show lowered IQ (*18*).

Personality. Twin and adoption studies that use personality questionnaires typically yield heritability estimates in the range of 20 to 50%. For example, identical and fraternal twin correlations are on average about 0.50 and 0.30, respectively. Activity level, emotional reactivity (neuroticism), and sociability-shyness (extraversion) have accumulated the best evidence for significant genetic influence (*19*). For example, four twin studies in four countries involving over 30,000 pairs of twins yield heritability estimates of about 50% for neuroticism and extraversion (*20*). Adoption studies of first-degree

relatives suggest lower estimates of heritability for these traits than do twin studies—about 30% rather than 50%. This may be due to nonadditive genetic variance (especially higher order interaction among loci, called epistasis), which covaries completely for identical twins but contributes little to the resemblance of first-degree relatives (*21*).

For the past decade, my colleagues and I have conducted a large-scale behavioral genetic study in the last half of the life-span: a Swedish study of hundreds of pairs of identical and fraternal twins reared apart and matched twins reared together. The results of this study support the hypothesis of nonadditive genetic variance for personality and also suggest that heritability of these traits may be somewhat lower, about 30%, later in life (*22*). As in the case of cognitive abilities, there is no evidence for major-gene effects on personality.

Psychopathology. A third major domain of behavioral genetic research is psychopathology. In the past, most research focused on schizophrenia; attention has now turned to the affective disorders, which include major depressive disorder and manic-depressive disorder.

In 14 studies involving over 18,000 first-degree relatives of schizophrenics, their risk was 8%, eight times greater than the base rate in the population (*23*). Twin and adoption studies suggest that familial resemblance for schizophrenia is due to heredity rather than to shared family environment. For example, the most recent twin study involves all male twins who were veterans of World War II (*24*). Twin concordances were 30.9% for 164 pairs of identical twins and 6.5% for 268 pairs of fraternal twins. Adoption studies of schizophrenia support the twin findings of genetic influence (*23*). Although these data suggest that inheritance plays a major role in schizophrenia, the same data also indicate that nongenetic factors are of critical importance as well. A risk of 30% for an identical co-twin of a schizophrenic far exceeds the population risk of 1%, but it is a long way from the 100% concordance expected if schizophrenia were entirely a transmissible genetic disorder. There is no way to explain such substantial discordance for identical twins for schizophrenia as currently diagnosed other than by nongenetic factors.

Genetic effects on schizophrenia appear to be independent of genetic effects on the affective disorders. Furthermore, unipolar depression may be distinct genetically from bipolar manic-depressive disorder (*25*). The most recent family study of unipolar depression involved 235 probands with major depressive disorder and their 826 first-degree relatives (*26*). Major depression was diagnosed for 13% of the male relatives and for 30% of the female relatives, which exceeds the base rate in the population. The familial risk for bipolar illness is lower, 6% in eight studies of 3000 first-degree relatives of bipolar probands, with no gender differences in risk, as compared with a risk of 1% in a control sample (*27*). Twin results for affective disorders suggest greater genetic influence than for schizophrenia, but adoption studies indicate less genetic influence (*28*). In the most recent adoption study, affective disorders were diagnosed in only 5.2% of biological relatives of affectively ill adoptees, although this risk was greater than the risk of 2.3% found in the biological relatives of unaffected adoptees (*29*).

Psychopathology was the first behavioral domain for which major-gene linkages were reported with restriction fragment length polymorphisms (RFLP) markers. In 1987, bipolar manic-depressive disorder was reported to be linked to a dominant gene on the short arm of chromosome 11 in an Amish pedigree of 81 individuals, 19 of whom were affected (*30*). However, the Amish results have essentially been withdrawn (*31*): Follow-up work on the original Amish pedigree yielded two new diagnoses of manic-depressive disorder, which reduced the evidence for linkage to nonsignificance, and an extension of the original pedigree also failed to replicate the original result. Manic-depression may be linked to the X chromosome in some families, despite the frequent occurrence of father-son transmission, which rules out a major X-linked gene for manic-depressive illness in the population (*32*).

For schizophrenia, linkage to a dominant gene on chromosome 5 was reported in 1988 for five Icelandic and two English families with a high incidence of schizophrenia (*33*). Several failures to replicate the linkage have been reported (*34*), and as yet no positive replication has appeared.

Molecular Biology and Behavior

This overview of behavioral genetic research suggests that genetic influence is nearly ubiquitous for both animal and human behavior. However, these same data lead to two additional conclusions with important implications for the application of molecular biology techniques to the investigation of behavior: Genetic influence on behavior appears to involve multiple genes rather than one or two major genes, and nongenetic sources of variance are at least as important as genetic factors. This suggests the need for molecular biology strategies that can detect DNA markers that account for small amounts of behavioral variation.

If this view is correct, current linkage studies—including the large-pedigree approach as well as the affected-sib-pair method (*35*)—will not succeed in identifying linkage because they can only detect major-gene effects in which one gene is largely responsible for a behavioral disorder. Linkage is a powerful strategy for identifying the chromosomal location of a disorder caused by a single gene that has its effect regardless of environmental or genetic background, as in Huntington's disease (*36*). However, replicated linkages have not been demonstrated for human behavior, despite claims for linkages in manic depression and schizophrenia. Attention has shifted to the possibility that certain families may have their own unique major gene responsible for a disorder (genetic heterogeneity). In this view, multiple-gene influence is seen in the population because of the concatenation of different major genes in different families. Failure to find major-gene effects on complex characteristics in plants and animals and the absence of major-gene linkages to date for human behavioral variation does not prove that linkages will not be found. Only a small portion of the genome and only a few families have been examined for such linkages. Linkages may be found during the coming decades because closely spaced markers are available for nearly all human chromosomes; however, this will also make it possible to exclude linkage for behavior. I predict that such exclusions will eventually provide the best evidence that human behavior and behavioral disorders are not due to major genes. This should not be interpreted to mean that genes do not affect human behavior; it only demonstrates that genetic influence on behavior is not due to major-gene effects.

An alternative hypothesis is that genetic influence on behavior is not due to a major gene in the population or in a family. That is, for each individual, many genes make small contributions toward behavioral variability and vulnerability. Nonetheless, some rare major-gene effects may be found in some families, just as hundreds of rare single-gene mutations have been found that cause neurological defects in mice and more than a hundred rare alleles are known for human beings that drastically lower IQ scores in affected individuals. This suggests an important principle: Although any one of many genes can disrupt behavioral development, the normal range of behavioral variation is orchestrated by a system of many genes, each with small effects.

Rare alleles that disrupt behavioral development are probably just the most easily noticed tip of the iceberg of genetic variability. It

seems reasonable to expect that many more alleles nudge development up or down and do not show such striking single-gene effects on a few individuals. It is not the case that we are identical genetically with the exception of major mutational flaws: Many loci are polymorphic and many of these are likely to contribute to variability in behaviors as complex as cognitive abilities and in behavioral disorders as complex as schizophrenia.

Applications of molecular biology techniques to the study of behavior are unlikely to succeed if they need to assume that a major gene is largely responsible for genetic variation. Behavior is not too complex for molecular biology; strategies are needed to identify genes that account for a small amount of variance.

If this quantitative genetic view of behavior is correct, we need to find many tiny needles in the haystack. Research in plant genetics suggests that a very large number of genes with very small effects are responsible for genetic influence on complex characteristics. For example, the results of a study of associations between 20 electrophoretic genetic markers and 82 quantitative traits in maize (*37*) can be summarized as follows: (i) Significant associations were found for each of the 82 quantitative traits; (ii) the maximum variance of any quantitative trait explained by a single marker was 16%; (iii) more than half of the significant associations accounted for less than 1% of the trait variance; (iv) only 5% of the marker loci accounted for more than 5% of the variance; and (v) in concert, the genetic markers predicted between 8 and 37% of the variance of a subset of 25 relatively independent traits, which is most of the genetic variance for these traits.

Such association studies may be useful in finding the needles in the haystack because sample sizes can be increased to provide sufficient power to detect associations that account for small amounts of variance. Association, usually called *linkage disequilibrium*, refers to covariation between allelic variation in a marker and phenotypic variation among individuals in a population. The use of genetic markers to study associations with complex traits is not new (*38*); the first association between genetic markers and quantitative traits was found more than 60 years ago (*39*). Many associations were reported even before the widespread use of RFLP markers (*40*). However, this approach is greatly enhanced by the increase in available markers that permits quantitative trait loci (QTL) interval mapping—appraisal of associations with many closely spaced RFLPs simultaneously by the use of the interval between markers rather than the markers themselves (*41*). With this method, six QTL were identified that together accounted for 58% of the variance of fruit mass in a backcross between a domestic tomato and a wild green-fruited tomato.

Research of this type uses crosses between inbred strains because their chromosomes have segregated as units broken up only slightly by recombination. As a result, a genetic marker indexes a region of millions of base pairs. In contrast, in outbred populations including humans, many generations of recombination have eliminated linkages between alleles on the same chromosome so that the range of a marker is limited to a very small stretch of DNA not broken up by recombination, probably no more than a few hundred thousand base pairs. For this reason, trying to find associations between markers and human behavior is very much like trying to find needles in a haystack. Nonetheless, a blood marker (HLA A9) has been found that appears to be associated with paranoid schizophrenia (*42*). Perhaps because the marker accounts for only a small portion of variance, linkage studies have not yet found evidence for linkage between the marker and schizophrenia.

Instead of using random RFLPs to look painstakingly through the human genome, a more efficient initial strategy may be to screen candidate genes with known function, especially genes suspected to be involved in neurological processes, for their individual and joint contributions to behavior (*43*). For example, an association has recently been found between alcoholism and alleles of the aldehyde dehydrogenase locus (*44*). However, association studies of common disorders such as heart disease and diabetes indicate that this approach is not a panacea.

Although association studies using very large samples might begin to uncover some QTL, success in identifying all of the many genes responsible for genetic variance for a particular behavior is likely to depend on the development of new techniques. It may not be overly optimistic to expect such developments given the pace of advances in molecular biology (*45*). For example, it may be possible to use new modifications of subtractive hybridization (*46*) to identify genes that differ between groups or even between individuals, yielding a set of trait-relevant DNA sequences that could be used as markers in association studies. The human genome project is another example. One of the many benefits of the project will be the identification of more markers and genes that might play a role in genetic variation in behavior. In addition, the human genome project will no doubt foster technological spin-offs such as sequence-tagged sites which, with new developments in polymerase chain reaction techniques and automated sequencing equipment, make it possible to produce genetic markers from published sequence data without obtaining the DNA itself (*47*).

Conclusions

Just 15 years ago, the idea of genetic influence on complex human behavior was anathema to many behavioral scientists. Now, however, the role of inheritance in behavior has become widely accepted, even for sensitive domains such as IQ (*48*). Indeed, acceptance of genetic influence has begun to outstrip the data in some cases, such as alcoholism (*49*). For most domains of behavior, too few twin and adoption studies have been conducted to answer the basic question of whether genetic influence is significant. Only for a handful of behaviors is it possible to estimate effect size with reasonable certainty, estimates that one might expect to be prerequisite to exploring the relative importance of individual genes. More quantitative genetic research is needed, too, because such research can go well beyond the basic question of the relative importance of nature and nurture. For example, new developments include multivariate analyses of the genetic covariance among behaviors or between biology and behavior, consideration of age-to-age change as well as continuity of genetic effects as they unfold during development, and exploration of the interface with the environment (*1*).

An equally important conclusion from behavioral genetic research must be emphasized: Nongenetic sources of variance are important because genetic variance rarely accounts for as much as half of the variance of behavioral traits. That is, evidence for significant genetic influence is often implicitly interpreted as if heritability were 100%, whereas heritabilities for behavior seldom exceed 50%. Another conclusion with far-reaching implications for molecular biology is the absence of evidence that genetic influence on behavior is primarily due to one or two major genes. It seems more reasonable to hypothesize that many genes each with small effect are involved.

If it is the case that behavioral variation involves many genes and much environmental influence, linkage analyses are unlikely to succeed in the population or even in a single family if they can only detect major-gene effects. New strategies are required that can isolate DNA markers associated with small amounts of variance. Quantitative genetic research will be important in this endeavor in order to assess the extent to which genetic variance accounts for phenotypic variance and the extent to which individual genes account for genetic variance.

In conclusion, the use of molecular biology techniques will revolutionize behavioral genetics, and the quantitative genetic perspective of behavioral genetics will transform our use of these techniques as we continue to explore the role of inheritance in the most complex of phenotypes, behavior.

REFERENCES AND NOTES

1. R. Plomin, J. C. DeFries, G. E. McClearn, *Behavioral Genetics* (Freeman, New York, 1990).
2. J. C. DeFries, J. C. Gervais, E. A. Thomas, *Behav. Genet.* **8**, 3 (1978).
3. G. E. McClearn, in *Aspects of Genetics in Paediatrics*, D. Barltrop, Ed. (Fellowship of Postdoctorate Medicine, London, 1976), pp. 31–39.
4. D. W. Bailey, *Transplantation* **11**, 325 (1971).
5. T. J. Bouchard, Jr., and M. McGue, *Science* **212**, 1055 (1981).
6. H. M. Chipuer, M. Rovine, R. Plomin, *Intelligence*, in press.
7. R. Plomin, *Development, Genetics, and Psychology* (Erlbaum, Hillsdale, NJ, 1986).
8. ———, J. C. DeFries, D. W. Fulker, *Nature and Nurture During Infancy and Early Childhood* (Cambridge Univ. Press, New York, 1988).
9. D. W. Fulker, J. C. DeFries, R. Plomin, *Nature* **336**, 767 (1988).
10. J. C. DeFries, R. Plomin, M. C. LaBuda, *Dev. Psychol.* **23**, 4 (1987).
11. R. Plomin, in *Advances in the Psychology of Human Intelligence*, R. Sternberg, Ed. (Erlbaum, Hillsdale, NJ, 1988), pp. 1–33.
12. L. A. Thompson, D. K. Detterman, R. Plomin, *J. Ed. Psychol.*, in press.
13. J. C. DeFries *et al.*, *Behav. Genet.* **9**, 23 (1979).
14. S. D. Smith, W. J. Kimberling, B. F. Pennington, H. A. Lubs, *Science* **219**, 1345 (1983).
15. S. D. Smith, W. J. Kimberling, Y. Y. Shugart, P. S. Ing, B. F. Pennington, *Am. J. Hum. Genet.* **45**, A65 (1989).
16. V. A. McKusick, *Mendelian Inheritance in Man* (Johns Hopkins Univ. Press, Baltimore, MD, 8th ed., 1988).
17. R. L. Nussbaum and D. H. Ledbetter, *Annu. Rev. Genet.* **20**, 109 (1986).
18. D. M. Barnes, *Science* **243**, 171 (1989).
19. A. H. Buss and R. Plomin, *Temperament: Early Developing Personality Traits* (Erlbaum, Hillsdale, NJ, 1984); L. J. Eaves, H. J. Eysenck, N. G. Martin, *Genes, Culture and Personality* (Academic Press, New York, 1989).
20. J. C. Loehlin, *Am. Psychol.* **44**, 1285 (1989).
21. R. Plomin, H. M. Chipuer, J. C. Loehlin, in *Handbook of Personality Theory and Research*, L. A. Pervin, Ed. (Guilford, New York, in press).
22. N. L. Pedersen, R. Plomin, G. E. McClearn, L. Friberg, *J. Pers. Soc. Psychol.* **55**, 950 (1988); R. Plomin, N. L. Pedersen, G. E. McClearn, J. R. Nesselroade, C. S. Bergeman, *Psychol. Aging* **3**, 43 (1988).
23. I. I. Gottesman and J. Shields, *Schizophrenia: The Epigenetic Puzzle* (Cambridge Univ. Press, Cambridge, 1982).
24. K. Kendler and C. D. Robinette, *Am. J. Psychiatry* **140**, 1551 (1983).
25. S. G. Vandenberg, S. M. Singer, D. L. Pauls, *The Heredity of Behavioral Disorders in Adults and Children* (Plenum, New York, 1986).
26. T. Reich *et al.*, *J. Psychiatry Res.* **21**, 613 (1987).
27. J. P. Rice *et al.*, *Arch. Gen. Psychiatry* **44**, 441 (1987).
28. J. C. Loehlin, L. Willerman, J. M. Horn, *Annu. Rev. Psychol.* **39**, 101 (1988).
29. P. H. Wender *et al.*, *Arch. Gen. Psychiatry* **43**, 923 (1986).
30. J. A. Egeland, D. S. Gerhard, D. L. Pauls, J. N. Sussex, K. K. Kidd, *Nature* **325**, 783 (1987).
31. J. R. Kelsoe *et al.*, *ibid.* **342**, 238 (1989).
32. M. Baron, N. Risch, R. Hamburger, B. Mandel, S. Kushner, *ibid.* **326**, 289 (1987).
33. R. Sherrington *et al.*, *ibid.* **336**, 164 (1988).
34. J. L. Kennedy *et al.*, *ibid.*, p. 167; D. St. Clair *et al.*, *ibid.* **339**, 305 (1989); S. D. Detera-Wadleigh *et al.*, *ibid.* **340**, 391 (1989); compare W. F. Byerley, *ibid.*, p. 340.
35. D. E. Weeks and K. Lange, *Am. J. Hum. Genet.* **42**, 315 (1988).
36. J. F. Gusella *et al.*, *Nature* **306**, 234 (1983).
37. M. D. Edwards, C. W. Stuber, J. F. Wendel, *Geneticae* **116**, 113 (1987).
38. H. W. Kloepfer, *Ann. Eugenics* **13**, 35 (1946).
39. K. Sax, *Genetics* **8**, 552 (1923).
40. J. N. Thompson, Jr., and J. M. Thoday, *Quantitative Genetic Variation* (Academic Press, New York, 1979).
41. A. H. Paterson *et al.*, *Nature* **335**, 721 (1988).
42. P. McGuffin and E. Sturt, *Hum. Hered.* **36**, 65 (1986).
43. E. Boerwinkle, R. Chakraborty, C. F. Sing, *Ann. Hum. Genet.* **50**, 181 (1986).
44. D. W. Crabb, H. J. Edenberg, W. F. Bosron, T-K. Li, *J. Clin. Invest.* **83**, 314 (1989).
45. U. Landegren, R. Kaiser, C. T. Caskey, L. Hood, *Science* **242**, 229 (1988).
46. G. H. Travis and J. G. Sutcliffe, *Proc. Natl. Acad. Sci. U.S.A.* **85**, 1696 (1988).
47. M. Olson, L. Hood, C. Cantor, D. Botstein, *Science* **245**, 1434 (1989).
48. M. Snyderman and S. Rothman, *The IQ Controversy, the Media and Public Policy* (Transaction Books, New Brunswick, NJ, 1988).
49. J. S. Searles, *J. Abnormal Psychol.* **97**, 153 (1988).

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"Don't worry about it. It's probably just another one of those sociological experiments."