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Recent Developments in Human Behavioral Genetics: Past Accomplishments and Future Directions

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Summary

The field of behavioral genetics has enormous potential to uncover both genetic and environmental influences on normal and deviant behavior. Behavioral-genetic methods are based on a solid foundation of theories and methods that successfully have delineated components of complex traits in plants and animals. New resources are now available to dissect the genetic component of these complex traits. As specific genes are identified, we can begin to explore how these interact with environmental factors in development. How we interpret such findings, how we ask new questions, how we celebrate the knowledge, and how we use or misuse this knowledge are all important considerations. These issues are pervasive in all areas of human research, and they are especially salient in human behavioral genetics.

Introduction

Human behavioral genetics has been characterized by both excitement and controversy. Both historical and contemporary findings suggest that human behavioral characteristics may be shaped by genetic as well as environmental influences. These findings have aroused concerns about the implications for social, political, and public policy.

Only a few decades ago, psychologists believed that characteristics of human behavior were almost entirely the result of environmental influences. These characteristics now are known to be genetically influenced, in many cases to a substantial degree. Intelligence and memory, novelty seeking and activity level, and shyness and sociability all show some degree of genetic influence. Contributions from behavioral-genetic studies have required developmental psychologists to revise two major tenets of their theories. Traditional dogma asserted that genetic influences were important in infancy and early childhood, only to be superseded by environmental influences as the child matured. Recent behavioral-genetic findings have shown convincingly that, for many traits, genetic effects increase throughout early childhood and adolescence, rather than diminish (McCartney et al. 1990). Traditional dogma also asserted that salient environmental influences on behavioral development were shared by family members, rather than experienced uniquely by individuals. In contrast, it appears that, for many traits, environmental influences make family members different, rather than making them more similar to one another (Plomin and Daniels 1987).

The preceding findings are largely a product of traditional methods of behavioral-genetic analysis: twin, family, and adoption studies. In recent years these have been greatly enhanced by the use of model-fitting techniques. In addition, new possibilities from molecular genetics have emerged to complement and extend the traditional methods.

The acknowledgment that genetic as well as environmental influences underlie human behavior is consistent with Darwinian natural selection and hence places human behavior within a broad evolutionary framework. Behavioral genetics is distinct from fields such as sociobiology and evolutionary psychology because it focuses on the role of genetic influences as contributors to individual differences, rather than on their role in accounting for shared species characteristics. Nevertheless, all of these fields share an emphasis on the continuities between animal and human behavior. This emphasis has important conceptual and methodological benefits for behavioral genetics, the latter including studies of homologous regions of the genome conserved across the evolution of species.

The potential social implications of behavioral-genetic findings often have contributed both to excitement and controversy. Recommendations for new social policies or for political change are not dictated by novel scientific findings. In contrast, policy development results from interpreting these findings within the context of a culture and set of values. As these differ, so will the perceived social implications of scientific findings.

We present an overview of human behavioral-genetic research, with this distinction between science and values in mind. Although later we discuss some ethical and social issues that may be raised by such research, the main purposes of this paper are to describe behavioral-genetic methods, to highlight recent findings, to discuss new research avenues resulting from burgeoning molecular-genetic techniques, and to suggest potentially fruitful directions.

Throughout the paper, we will use two complex traits to illustrate the application of behavioral-genetic methods and possible results and interpretations. Emotional stability will provide an example of a trait based on normal variation, and schizophrenia will provide an example of a trait falling within the pathological range. Both have been studied extensively by traditional behavioral-genetic methods and now have become the focus of the newer molecular-genetic methods as well. For both traits, research advances have depended on the genetic-linkage maps developed from the localization of thousands of polymorphic genetic markers in humans as well as in other animals. Prior to this extraordinary resource, only genes that played a major role in the development of a trait could be identified; now identification of genes that play only a minor role is technically feasible.

Traditional Methods of Behavioral-Genetic Analysis: Family, Twin, and Adoption Studies

Methods used in behavioral genetics are built on the theories of quantitative genetics developed more than half a century ago by geneticists concerned with the practical problems of improving economically important characteristics of domestic plants and animals (Lush 1937; Mather 1949). These methods have been applied to a wide variety of traits, including intelligence and other cognitive abilities, facets of personality such as extraversion and emotionality, and disorders such as schizophrenia and bipolar illness. Using the methods described below, behavioral geneticists have explained why individuals differ in these characteristics, in terms of both genetic and environmental factors. For convenience, we will separate methods into "traditional" and "new" approaches, although each will continue to complement the other in behavioral-genetic research.

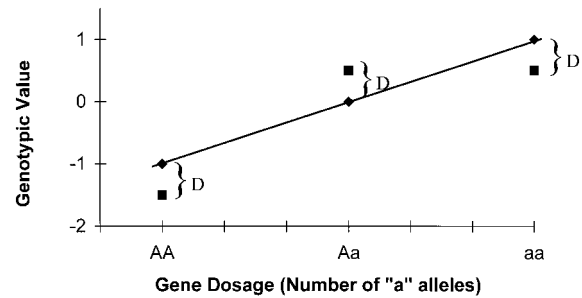For behavioral traits, as for any human trait, we are

Figure 1 Example of genotypic values under an additive model (*diamonds*) and in the presence of nonadditive variance (*squares*). For an additive model, an increase in the number of "a" alleles leads to a regular increase in genotypic value. Differences between the additive genetic values and genotypic values indicate nonadditive effects, or dominance (D).

interested in understanding differences among individuals. Such differences may be caused by environmental factors and/or by one or many genes. Environmental factors may be prenatal or postnatal, biochemical or social. Some genetic factors may cause small differences, and others may cause large differences (i.e., they have varying effect sizes). The effects of some genes may be independent of other genes and may have "additive" effects. Alternatively, the effects of some genes may be "nonadditive" and depend on other genes, either at the same locus (dominance) or at other loci (epistasis). Moreover, alleles can have both additive and nonadditive effects (fig. 1).

The aggregate importance of genes for a trait can be assessed from their contribution to the observed phenotypic variation in a population. The concept of heritability refers to the ratio of the genetic variance to the overall phenotypic variance. It is based on a specific situation involving a particular phenotype in a population with some array of genetic and environmental factors at a given time. It can differ from population to population and from time to time. It can change with age during development. It is important to keep in mind that heritability is a descriptive statistic of a trait in a particular population, not of a trait in an individual.

Because individual differences in most behavioral characteristics are defined on a continuous scale, traditional approaches in human behavioral genetics primarily use the methodology of quantitative genetics. In this framework, a categorical phenotype, such as schizophrenia, may indicate individuals who lie above some threshold on an underlying liability continuum to which both genetic and environmental influences contribute (fig. 2).

Three traditional methods have been employed to assess genetic and environmental influences on complex human behavioral characteristics: family, twin, and adoption studies. Each of these methods has been used to analyze the cause of individual differences within the
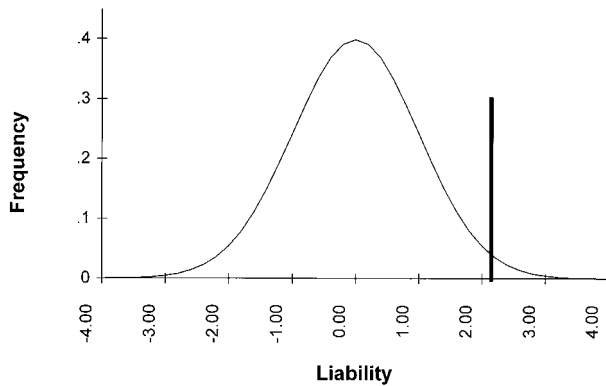
Figure 2 Single-threshold model for categorical traits. Affected individuals lie above the threshold (i.e., to the right of the line) on the underlying liability scale; liability is based on contributions from both genetic and environmental influences.

normal range of variation, as well as the etiology of various psychopathologies. As will be discussed later, a currently popular approach is to fit models jointly to data gathered by all three methods.

Family Studies

Resemblance among family members is a function of both genes and common (shared or family) environmental influences. Thus, it is necessary, but not sufficient, evidence for the presence of heritable variation. For emotional stability, correlations between first-degree relatives tend to be low but positive, averaging ~.15 (Loehlin 1992). Thus there is evidence of some familial resemblance for this trait, although such resemblance is modest.

For schizophrenia, most family studies focus on relative risk. For example, although there is variability in breadth of diagnosis, the lifetime risk of schizophrenia in the general population is typically reported as ~1%. However, siblings of schizophrenics are ~10 times more likely to suffer from schizophrenia. The average risk for children of schizophrenics is ~13%. As expected, the risks for second- and third-degree relatives are lower, ~3% and ~2%, respectively (Gottesman 1991). Thus, schizophrenia is clearly a familial trait.

Twin and Adoption Studies

Twin and adoption studies can tell us the extent to which family resemblance is due to shared genes and the extent to which it is due to shared environments. For more than a century, behavioral scientists have been using twin studies to assess hereditary and environmental influences on behavioral development. Adoption studies of behavioral traits date back ≥70 years.

Design issues in twin and adoption studies.—The correlation between identical twins reflects all of the genetic variance, both additive and nonadditive, whereas that between fraternal twins reflects only one-half of the additive genetic variance plus smaller fractions of nonadditive components. If nonadditive effects are minimal, simply doubling the difference between identical and fraternal-twin correlations provides an approximate estimate of heritability. If nonadditive effects are substantial, this comparison overestimates genetic influence. Additional assumptions of the traditional twin method include little or no assortative mating and equal shared-environmental influences for identical and fraternal-twin pairs. If the parents of twins mated assortatively for the characteristic under investigation, doubling the difference between the identical and fraternal-twin correlations would underestimate genetic influence. Conversely, if identical twins are treated more similarly than fraternal twins, and if this treatment has influenced the characteristic under study, the genetic effect would be overestimated. In cases in which the equal-environments assumption has been tested empirically, the results suggest that the assumption was not seriously violated (Plomin et al. 1990). Many estimates of assortative mating have been made. For most behavioral traits it tends to be slight, although for a few, such as intelligence and social attitudes, assortative mating is substantial.

If one member of a twin pair has been ascertained because of extreme scores for a continuous measure, a multiple-regression analysis of twin data facilitates an alternative test of genetic etiology. It also provides an analysis of individual differences within the selected sample (DeFries and Fulker 1985, 1988). In samples of twin pairs selected in this manner, cotwins of identical and fraternal probands are both expected to regress toward the mean of the unselected population. However, regression to the mean should be greater for fraternal cotwins to the extent that the extreme scores of the probands are due to heritable influences. Multiple-regression analysis of such data provides a general, statistically powerful, and versatile test.

For categorical traits, a comparison of concordance rates in identical and fraternal-twin pairs can be used as a test of genetic etiology. A pair is concordant if both members are affected, but it is discordant if only one member is affected. Again, members of identical-twin pairs are genetically identical (although there are exceptions that result from such processes as somatic mutations), whereas fraternal twins share, on average, only one-half of their segregating genes; thus, identical-twin pairs should more often be concordant than fraternal twins if the condition is due, at least in part, to heritable influences.

Several types of adoption designs have been used to study behavioral characteristics. To assess genetic influences, adopted-apart relatives are studied. These individuals include biological parents and their adopted-away offspring, or twins separated early in life. To assess envi-

ronmental influences, genetically unrelated individuals living together are compared. These relations include adoptive parents and their adopted children, or genetically unrelated children reared in the same family. Measures of several different family relationships, including spouse correlations, biological and adoptive parent-offspring correlations, and sibling correlations, also can be analyzed. For example, simultaneous analysis of these measures by use of the statistical method of structural equation model fitting can test various models of genetic and environmental transmission.

Thus, the adoption design, like the twin design, yields estimates of various genetic and environmental components of variance. In addition, the adoption design facilitates (1) identification of specific environmental influences unconfounded by heredity (e.g., the effects of life stressors), (2) analyses of the role of heredity in ostensibly environmental relationships, and (3) assessment of genotype-environment interactions and correlations (Plomin et al. 1988).

Example: twin studies of emotional stability.—Several recent studies have included moderate to large size populations (300–12,000 pairs) and have obtained data on measures of emotional stability (or its opposite, emotional instability or neuroticism), using valid and reliable questionnaires. In table 1, we present data from selected studies. Although differing in the measures used and in the populations sampled, these studies have used common analytic methods. In each study, state-of-the-art model-fitting approaches, discussed in more detail below, were used to estimate phenotypic-variance components and to test alternative hypotheses regarding the nature of individual differences. Heritability estimates given in table 1 are derived under the best-fitting model in each case. None of the best-fitting models suggested shared environmental influences; thus, the environmental effects, although substantial, are unique to individuals.

The heritability estimates were in the range of .27–.61 over the studies, suggesting a moderate role of genetic influences in explaining individual differences in emotional stability. Some general trends emerge across studies when results are considered by age and gender. For example, taken together, the studies of Loehlin and Nichols (1976), Floderus-Myrhed et al. (1980), Pedersen et al. (1988), and Viken et al. (1994) suggest that emotional stability is more heritable in younger than in older adults: genetic differences explain ≥50% of individual differences in the late teens to mid 20s but only 30%–45% of the variance in middle adulthood and older age. When the two genders have been examined separately, emotional stability also appears to be more heritable in women than in men, particularly in middle and older adulthood (Martin and Jardine 1986; Eaves et al. 1989; Viken et al. 1994). In a later section we discuss the interpretation of such differences among population subgroups.

Example: twin and adoption studies of schizophrenia.—Five twin studies of schizophrenia that were initiated before World War II (Gottesman and Shields 1982) yielded results that are strikingly similar to those of six recent studies (Gottesman 1993): concordance rates for identical twins are four or more times greater than those for fraternal twins. Table 2 shows the probandwise rates, without age correction, for the six studies using varied but judicious definitions of schizophrenia. Overall, the median identical-twin rate was 46%, whereas the same-sex fraternal-twin rate was 14%. The consistency over all studies indicates substantial evidence for a genetic component influencing the susceptibility to develop schizophrenia.

Several adoption studies focus on schizophrenia. Studies from Finland (Tienari 1991), Denmark (Kety et al. 1994), and Oregon (Heston 1966) report results similar to those published by Kendler et al. (1994). In the study by Kendler and colleagues, Kety et al.'s (1994) Danish national sample of adoptees who grew up to be schizophrenic and of their biological and adoptive relatives were reanalyzed. DSM-III criteria were applied to the proband and control adoptees, to their biological relatives (to whom the adoptees had no exposure), and to the adoptive relatives who had reared or were reared with the adoptees. Neither group of adoptive relatives had a rate of schizophrenia greater than that of the general population (1%–2%). The prevalence of schizophrenia and other schizophrenia-spectrum disorders among first-degree relatives was 23.5%, compared with only 4.7% among those of normal control adoptees. This study confirms the results of the smaller studies listed above and excludes the hypothesis that only environmental factors are involved in the transmission of schizophrenia.

New Approaches and Future Directions: Quantitative-Trait Loci (QTL) Analysis and Biometric Model Fitting

In this section we discuss examples of recent approaches and some promising future directions in behavioral-genetic research. First we discuss the identification of specific loci involved in the development of behavioral traits—QTL analysis—both in humans and in model systems. Then we discuss methods in model fitting that can foster the integration of behavioral-and molecular-genetic methods. In addition, these methods enhance the ability to specify and generalize findings regarding genetic and environmental influences on traits and their development over time.

QTL Analysis

The development of genetic linkage maps during the past decade has permitted the mapping of single-locus

Table 1

Large Twin Studies of Emotional Stability/Neuroticism

Investigators and Sample[a]	Country	Age	Measure[b]	Heritability
Langinvainio et al. (1984):[c] 30 MZ apart 95 DZ apart 47 MZ together 135 DZ together	Finland	Adults	EPI	.27
Tellegen et al. (1988):[c] 44 MZ apart 27 DZ apart 217 MZ together 114 DZ together	United States	40.7 years (SD 12.0 years) MZ apart 41.1 years (SD 11.3 years) DZ apart 23.5 years (SD 11.1 years) MZ together 19.8 years (SD 4.3 years) DZ together	MPQ (negative emotionally)	.55
Pedersen et al. (1988):[c] 99 MZ apart 229 DZ apart 160 MZ together 212 DZ together	Sweden	58.6 years (SD 13.6 years)	EPI	.31
Loehlin and Nichols (1976):[d] 217 MZ males 137 DZ males 297 MZ females 199 DZ females	United States	17–18 year olds	CPI (items with a priori loading on Eysenck's N)	.52 (males and females)
Floderus-Myrhed et al. (1980):[e] 12,898 same-sex pairs from three birth cohorts	Sweden	16–48 years olds	EPI	.53 males 16–28 years old, .39 males 29–38 years old, .38 males 39–48 years old, .61 females 16–28 years old, .51 females 29–38 years old, .40 females 39–48 years old
Martin and Jardine (1986): 567 MZ males 1,233 MZ females 352 DZ males 751 DZ females 907 DZ opposite sex	Australia	18–88 years olds	EPQ	.45 males, .51 females; male-female genetic correlation .58
Viken et al. (1994): 7,467 same-sex twin pairs from six birth cohorts	Finland	18–53 year olds with 6-year follow-up	EPI	.54 males 18–23 years old, .31 males in all other 5-year birth cohorts, .53 females 18–23 years old, .42 females in all other 5-year birth cohorts
DiLalla et al. (1996): 65 MZ apart 54 DZ apart	United States	40.4 years (SD 12.6 years) MZ apart 45.1 years (SD 13.5 years) DZ apart	MMPI (scales: clinical—psychasthenia; content—depression, poor morale)	Psychasthenia .60, depression .44, poor morale .39

[a] MZ = identical twins; and DZ = fraternal twins.

[b] EPI = Eysnck Personality Inventory (Eysenck 1970; Floderus 1974); MPQ = Multidimensional Personality Questionnaire (A. Tellgen, personal communication); CPI = California Psychological Inventory (Megargee 1972); EPQ = Eysenck Personality Questionnaire (Eysenck and Eysenck 1975); and MMPI = Minnesota Multiphasic Personality Inventory (Hathaway and McKinley 1983).

[c] Gender-specific heritability estimates were not computed.

[d] Twins were ascertained as a result of their participation in the 1962 administration of the National Merit Scholarship Qualifying Test. Heritability estimates are derived from analyses presented by Eaves et al. (1989). Tests of heterogeneity indicated nonsignificant gender differences in phenotypic-variance components.

[e] Heritability estimates are derived from analyses presented by Eaves et al. (1989).

Mendelian disorders to proceed at an extremely rapid pace. Much attention now is focused on the identification of susceptibility genes for common, complex disorders, by use of the so-called QTL approach. Family, twin, and adoption studies have indicated a substantial genetic component for many behavioral traits and disorders. In addition to psychiatric disorders such as schizophrenia and bipolar illness, other complex medical disorders, including non–insulin-dependent diabetes

mellitus (NIDDM), are under intense study to identify susceptibility genes. Thus, large-scale QTL linkage studies are now underway for a variety of complex disorders.

Examples: schizophrenia and emotional stability.—In 1995, for the first time and after several earlier failures, several reports replicated findings for a genetic region linked to one or more genes involved in the susceptibility to develop schizophrenia (Antonarakis et al. 1995; Gurling et al. 1995; Moises et al. 1995; Mowry et al. 1995;

Table 2

Probandwise Concordance Rates for Schizophrenia in Recent Identical and Fraternal Twin Studies

STUDY	CONCORDANCE RATE/ NO. OF PAIRS	
	Identical Twins	Fraternal Twins
Finland 1963, 1971	.35/ 17	.13/ 20
Norway 1967	.45/ 55	.15/ 90
Denmark 1973	.56/ 21	.27/ 41
United Kingdom 1968, 1987	.58/ 22	.15/ 33
Norway 1991	.48/ 31	.04/ 28
United States 1969, 1983	.31/164	.06/268
Overall	.46/310	.14/480

NOTE.—Data are adapted from Gottesman (1991).

Schwab et al. 1995; Straub et al. 1995). The work was characterized by international collaboration, careful psychiatric diagnosis using standardized techniques, and the use of hundreds of genetic markers to conduct linkage studies in families with schizophrenia. Four research groups implicated the same region on the short arm of chromosome 6, whereas two groups did not find positive results. Some initial, and probably appropriate, skepticism has greeted these new findings, partly because of the checkered history of molecular studies in schizophrenia. Nevertheless, additional linkage studies are continuing, and association and physical-mapping efforts are underway to identify candidate genes. The eventual goal of this work is identification of neurodevelopmental pathways and interactions of the susceptibility genes with their internal and external environments.

Recently, Flint et al. (1995) used a novel approach to identify specific genes that may influence emotional stability. They used the mouse as a model system and defined emotionality by the covariance of a set of four measures. Using these measures, they conducted a genomewide linkage search and identified three candidate regions that influence emotionality. Several lines of evidence suggest that the genetic basis of emotionality in mice is similar to that in other species and that it may underlie the psychological trait of emotional instability in humans. The discovery of QTL in the mouse would provide the first step toward molecular characterization and may lead to the identification of genes influencing human emotional instability.

Methodological improvements.—Methods used to locate genes involved in complex traits are not straightforward, and many times findings are difficult to replicate. In early studies, reports of linkage for schizophrenia on chromosome 5, as well as linkage for bipolar illness on chromosome 11, were not replicated by other investigators. Moreover, for both disorders, evidence in the origi-

nal sample became negative as additional family members and/or marker information were obtained. This suggests that the lack of confirming reports was due to the initial results being false positives, rather than to population or clinical heterogeneity or to other systematic differences in study design. This nonreplication has led to confusion in the literature and to a general distrust of results reported in psychiatric genetics.

Early analyses of complex traits used parametric methods in which a single-locus mode of inheritance was assumed and in which standard LOD-score analysis was performed. The interpretation of evidence from this approach has been controversial, especially in the context of a genome screen. Setting a significance criterion that is too stringent will reduce the power to detect a true linkage, whereas setting one that is too low may produce many false-positive reports.

For genome scans of complex traits, false-positive reports of linkage are likely to result from an individual study, and scientific principles of replication and extension are necessary. The fact that the early claims of linkage for behavioral phenotypes subsequently were rejected indicates that the scientific process works as it should. Unfortunately, both the attention to initial reports and the lack of cautious interpretation by the media, lay public, and some scientists led to serious misperceptions of the scientific process and research results.

Over the past few years, methods to identify candidate loci for complex traits have undergone major improvements. For example, nonparametric approaches based on haplotype sharing in affected sib pairs have proved to be successful and are widely available. These methods do not require the assumption of single-locus inheritance. Multipoint affected-sib-pair analyses are now available (e.g., see Kruglyak and Lander 1995) and permit both localization of disease genes and exclusion mapping for a complex trait. Such methods have been used successfully to identify a susceptibility gene for Crohn disease (Hugot et al. 1996) and susceptibility genes for NIDDM (Hanis et al. 1996).

These methods necessarily have less resolution when applied to complex disorders as opposed to simple genetic disorders. For many behavioral traits, measurement of the phenotype is more complicated than it is for other complex disorders such as NIDDM (Pennington 1997). However, behavioral-genetic methods can be used to improve diagnoses and to increase the ability to detect true linkage. Large sample sizes will be necessary to achieve adequate sensitivity. Even so, the predictive value of such reports may be low, so that replication studies are essential, even when the evidence appears to be strong by standards of simple Mendelian disorders. With appropriate interpretation of the results and implications of linkage studies for complex traits, genes will be identified. The APO-E findings for late-onset Alzhei-

mer disease is an example of such a susceptibility gene. The initial reports of linkage gave modest evidence, but subsequent studies have provided consistent evidence for an elevated risk to those carrying an e4 allele (Li et al. 1996; Roses 1996).

Overall, the improvement of analytical methods, the refinement of the genetic and physical maps, and results from QTL analyses in model systems have led to the possibility of dissecting the genetic component of complex traits. Large-scale national and international collaborations have been established to study behavioral traits including schizophrenia, bipolar illness, alcoholism, and autism. Such collaborations will assemble large, uniformly collected samples that will increase the probability of identifying true linkages to susceptibility genes.

Biometric Model Fitting

Another avenue that will improve the ability to delineate the genetic and environmental aspects of complex behavioral traits is based on advances known as "biometric model fitting." These techniques were developed mainly in the 1970s by a number of quantitative geneticists who relied heavily on the statistical methods of path analysis and structural equation modeling (e.g., see Jinks and Fulker 1970; Martin and Eaves 1977). Biometric-model-fitting analyses have a number of advantages over the simple inspection of familial and twin correlations or regressions. Data from different familial relationships can be combined in a comprehensive model that includes both genetic and environmental influences and, in more complex versions, genotype-environment correlation and interaction. In addition, a greater variety of models of genetic and environmental transmission can be formally contrasted, and more accurate parameter estimates can be obtained, than is the case with the more conventional methods, which are based on piecemeal examination of familial correlations. Results from studies of emotional stability, which are shown in table 1, are based on such model fitting.

Analysis of consistency over populations.—Critics of findings from behavioral-genetic studies sometimes have argued that estimates of heritability are useless because they vary greatly across populations, whereas advocates of behavioral-genetic methods have argued for the validity and consistency of their findings across disparate groups. Biometric-model-fitting methods can be used to determine whether genetic and environmental influences can be generalized across different populations. For example, Loehlin (1992) has used such methods to analyze correlations for extraversion from different familial relationships compiled from many primary studies. Estimates of heritability and of environmental influences were consistent across samples from Australia, Sweden, the United Kingdom, and the United States, differing only for a sample from Finland—and not greatly there.

The advantage of such methods is that they simultaneously allow the examination of the consistency of genetic and environmental influences across populations while testing competing models.

Analysis of traits over time.—Biometric-model-fitting analyses have been extended to investigate the effects of genes and environment on the development of traits over time (e.g., see McArdle 1986; Boomsma and Molenaar 1987). In one such example, analyses of longitudinal twin-study data on cognitive ability measured repeatedly from 3 mo to 15 years suggested that the same genetic influences are involved in cognitive ability across this broad age span (Eaves et al. 1986). Specifically, these genetic influences appeared to underlie both continuities in cognitive ability and increases in heritability with age.

Incorporation of specific genetic loci and environmental factors in model fitting.—A recent trend in behavioral-genetic studies is to incorporate specific genetic markers and environmental measures in biometric-model-fitting analyses. The results of traditional behavioral-genetic analyses typically are broad, abstract genetic and environmental variance components, rather than specific genetic and environmental causal mechanisms. In studies of emotional stability, for example, it would be useful to know how much of the overall genetic variance—heritability—is accounted for by some small set of candidate loci. For a trait for which shared environmental influences appear to be important, such as adolescent-conduct problems, it would be informative to determine how much of the overall shared environmental influence is due to specific factors such as inconsistent parental supervision, antisocial peers, or high neighborhood crime rates. For schizophrenia, specific environmental factors, both pre- and postnatal, that result in discordance among identical twins are already the subject of extensive investigation (Gottesman and Bertelsen 1989; Torrey et al. 1994).

Analysis of multiple phenotypes.—One final direction being explored involves the use of behavioral-genetic analyses to examine common genetic and environmental influences among multiple phenotypes. Multivariate behavioral-genetic models can be used to investigate the relations and boundaries among different traits or disorders, as well as to elucidate the complex causal pathways between genotype and phenotype. For example, common genetic influences appear to underlie a substantial part of the overlap between depression and anxiety disorders. Future applications of this sort that include physiological and biochemical phenotypes will help bridge the gap between distal causes and traits of interest. Multivariate behavioral-genetic analyses of psychiatric disorders can be enhanced further by the inclusion of particular genetic markers and specific environmental measures, as described above. Demonstrating that two or more disorders are influenced by the same candidate

genes will bring a new type of evidence to bear on many problems in psychiatric classification.

Ethical and Social Issues

Significant historical events in human genetics include the idealistic and elitist tenets of the early Eugenics movement in Great Britain and the United States and the infamous Nazi attempts to achieve racial purity in Germany. Behavioral geneticists conducting their research into the nature and diversity of human behaviors have an acute awareness of these historical events (Gottesman and Bertelsen 1996). In this section, we discuss two areas in which the study of genetic influences on human behaviors is especially likely to arouse social and ethical concerns—namely, genetic counseling and the study of group differences in behavioral traits. We end the section with a brief comment on professional responsibility of the scientific community.

Genetic Counseling

Dilemmas for geneticists become especially acute in the myriad scenarios in genetic counseling. As we learn more about the genetic components of complex human traits, both behavioral and nonbehavioral, we can expect more frequent inquiries from parents about the possibilities for manipulating the genotypes of their offspring to ensure a desired outcome. The issues for counseling become correspondingly more complex, largely because of the perception that ethical issues concerning complex behavioral traits are more controversial than those for single-gene "medical" disorders. Even if one or more individual genes that contribute to a complex trait are identified, the geneticist is obligated to convey the idea that knowledge of the genotype for a single gene has limited predictive value, if any, with respect to the ultimate phenotype. Furthermore, the geneticist acquires the obligation to explain enough elementary statistics to help the parents or family appreciate both the concept of the size of the effect of a particular single gene on a complex trait and the possible futility of testing for individual genes in some cases. For persons who are seeking firm answers to inquiries about quantitative traits, the geneticist must explain that no such answers exist.

On the other hand, the geneticist has an obligation, based on the fiduciary nature of the professional-patient relationship, first to provide information that is as complete as possible and, second, to respect the choice of patients who exercise their right of personal autonomy in making their own decisions about their own families (Pelias 1991). At a time when knowledge is changing, there is also a need to warn families to anticipate new information and perspectives during their lifetime. These quandaries are far from settled, because each genetic-

counseling scenario creates a new set of questions derived from a unique family with unique values. Perhaps the prudent path for the geneticist is to provide complete, forthright information, with deference to the personal, even if sometimes questionable, decisions of persons who seek genetic information.

Studies of Group Differences

Differences among individual members within populations are a sine qua non of Darwinian evolution and are often of intense social interest. These differences include variations in body characteristics, physical skills, intellectual and artistic abilities, personality, attitudes, and motivation. Average differences of such traits also often are found between groups defined by sex, ethnicity, age, interests, occupation, and many other criteria.

Group differences often have been a source of ideological distortion, because people tend to exaggerate their significance. A modest average difference between two groups on some characteristic is taken to mean that all or nearly all the members of one group exceed all or nearly all the members of the other. This is rarely the case for measured human traits.

The tendency of people to exaggerate group differences—and the injustices that this tendency can cause—often has led well-intentioned members of the public, the press, and, sometimes, even the scientific community to the opposite extreme of denying that such differences exist at all—a posture of recent "political correctness." A preferable strategy is to accurately assess both the magnitude of group differences and the predictive power of such differences—usually small—and to educate the public and press about these facts.

Example: Emotional stability in men and women.—How predictive for individuals are group differences? For example, men and women tend to differ, on average, in their scores on typical measures of emotional stability, with women having lower average scores. But, within either group, individuals range widely. It is a mere stereotype that all men are emotionally stable and that all women are emotionally unstable. For this trait—and for nearly all behavioral traits—within-group variation vastly exceeds average between-group variation.

As a practical example, suppose that, in emotional stability, men and women differ, on average, by one-third of an SD, a representative empirical finding (fig. 3). This is a difference that falls somewhere between small (.20) and medium (.50) in Cohen's (1977) classification of effect sizes. The correlation, between sex and emotional stability, implied by this average difference is ~.16. Squaring this value tells us that we can reduce our uncertainty about people's emotional stability by only ~3% by knowing what sex they are. In short, even for a trait with an appreciable and dependable average
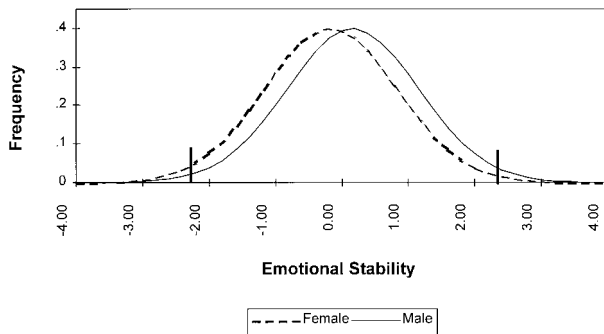
Figure 3 Illustration of group differences of emotional stability, by sex. Note that at the ends of the curve (the ~1% tails of the overall distribution are marked by lines) the ratio of males to females is the most extreme; this is the basis of many stereotypes (see text).

group difference, the group difference predicts almost nothing about individuals; people are nearly as different from each other within each group as they are within the total population. Only when variation within groups is small relative to the average difference between the groups does knowledge of group membership help predict what an individual will be like; but, for the most part, this happens only in the realm of stereotypes, not for actual measured traits. Why do people overestimate the power of prediction based on average group differences? One reason is the fact that moderate differences between group averages can lead to considerable disproportions at extreme values of a trait—and stereotypes are greatly influenced by extreme cases (fig. 3).

Genetic and environmental contributions to group differences.—Even though group differences tend to have limited predictive value at the level of individuals, there still may be interest in their origins. This is reasonable whether the desire is to celebrate existing group differences or to change some aspect of them. Family, twin, and adoption studies have confirmed that individual differences for many behavioral traits have a substantial genetic component. However, demonstration of a substantial genetic component in individual differences does not permit the conclusion that group differences in such traits are due primarily to genes. Different variables may contribute to differences among individuals and to differences between groups, or the same variables may contribute to both but to different degrees. Indeed, individual variation within groups might be largely genetic in origin, whereas the difference between groups may be due wholly to environment. Speculating that this is possible is not the same, of course, as proving that it is so. Once more, the actual facts for any particular groups and any particular trait are empirical questions to be tested rather than decided by fiat (see Rowe et al. 1994).

Determination of genetic and environmental contributions to group differences would be made more straightforward if particular genes and environmental factors could be identified and measured. Identification of specific QTL influences on quantitative traits will begin to resolve these questions. If the causes of some group differences are in part genetic, it will be important to be aware that average group differences tend to be weak predictors for individuals. And we also must remember that genetic influences on the development of traits are usually just that—influences—and not blind and irrevocable determiners.

Responsibilities of the Scientist

With so many potential sources of confusion and misinterpretation of information about complex traits, the geneticist is hard pressed to define the scope of professional responsibilities. At the very least, the professional must acknowledge both the issues and the obligation to address the issues. In genetic counseling, the fundamental approach is a commitment to provide thorough information to clients, in understandable language. In the case of research on group differences and in the broader range of human behavioral-genetic research, there is an important obligation to participate in educating the public, in nontechnical language, about the complexity of human traits, as well as about the simple facts of human variation. This obligation entails participation in public education programs, whether through the media, through classroom instruction, or through personal presentations to public or private interest groups. The fact that such activities can be both time-consuming and burdensome does not diminish the social importance or the serious nature of the obligation.

There are many ethical dilemmas inherent in human genetics; some are clearly unique to behavioral genetics. Some professionals have suggested slowing the pace of research, specifically in the field of behavioral genetics, until the ethical issues are resolved. This proposal fails to acknowledge the fact that ethical issues continually are evolving in response to innovations in genetic knowledge and technologies. Not only would such an approach ignore the immediacy of present ethical questions, but it would compound the problems that will unfold in the future: answers to present ethical dilemmas do not necessarily solve or avoid any future questions. The dynamism in research and ethics must be appreciated, as well as the basic nature of the relationship between professionals in genetics and the people who rely on geneticists for information and help. The ongoing responsibility of geneticists is to confront the issues privately, professionally, and publicly.

A second challenge is, Why study behavioral-genetic traits at all, since resulting findings are socially and politically sensitive and may be used to rationalize discrimination or to dismantle social programs? One common argument for studying behavioral traits is that under-

standing the basis for normal variation may help us to understand better the extremes (i.e., pathology). Thus, as with blood pressure and hypertension or with glucose metabolism and diabetes, studies of normal variation in personality and cognitive abilities may inform us about personality disorders and mental retardation. Perhaps an even more compelling argument is that individual differences in behavioral traits, including personality and abilities, are of wide public interest and of considerable social importance even when differences fall within the nonpathological range. Public knowledge, program design, and policy development should rest not on popular myths but on findings from the best available science.

Acknowledgments

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