The Fruitless Search for Genes in Psychiatry and Psychology

Time to Reexamine a Paradigm

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THE JUNE 2009 edition of the *Journal of the American Medical Association* reported the results of a meta-analysis by Neil Risch and colleagues.[1] These researchers showed that a 2003 study by Caspi and colleagues, where the investigators believed that they had found a genetic variant associated with depression when it was combined with stressful life events, did not stand up to replication attempts. Caspi and colleagues' original study had been widely reported in the media and elsewhere as constituting a major genetic discovery in psychiatry.[2]

However, to the critical observers of genetic research in psychiatry and psychology, including those who had pointed to several glaring problems in Caspi and colleagues' study, the failure to replicate these results came as no surprise at all.[3] This study merely suffered the same fate as other gene-finding claims in psychiatry over the past forty years, such as the much-publicized but subsequently nonreplicated claims of a generation ago for bipolar disorder and for schizophrenia.[4] Clearly, some type of systematic error is common to these subsequently unsubstantiated findings.

Previously, a group of leading psychiatric genetics researchers had recognized in 2008, "It is no secret that our field has published thousands of candidate gene association studies but few replicated findings."[5] In the same year behavioral geneticist Robert Plomin and colleagues could not cite any substantiated gene findings for personality or IQ (cognitive ability).[6] A pair of personality-trait molecular genetics researchers wrote in 2009 that their field "has evidently not escaped the conundrum of non-replication that continues to plague the genetics of complex human phenotypes."[7] The authors of a 2010 article on cognitive ability and genetics

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noted, "It is difficult to name even one genetic locus that is reliably associated with normal-range intelligence in young, healthy adults."[8] By 2012 the situation remained the same.[9] Risch and colleagues concluded that "few if any of the genes identified in candidate gene association studies of psychiatric disorders have withstood the test of replication." They further concluded:

> Despite progress in risk gene identification for several complex diseases, few disorders have proven as resistant to robust gene finding as psychiatric illnesses. The slow rate of progress in psychiatry and behavioral sciences partly reflects a still-evolving classification system, absence of valid pathognomonic diagnostic markers, and lack of well-defined etiologic pathways. Although these disorders have long been assumed to result from some combination of genetic vulnerability and environmental exposure, direct evidence from a specific example has not been forthcoming.[10]

Thus the fields of behavioral genetics and psychiatric genetics are rapidly approaching a period of crisis and reexamination. In the words of a leading group of psychiatric genetics investigators, writing in 2012 about the decades-long failure to uncover any genes that cause schizophrenia (the most studied psychiatric disorder), these negative results "suggest . . . that many traditional ideas about the genetic basis of SCZ [schizophrenia] may be incorrect."[11]

There are two broad explanations for the ongoing failure to discover genes in psychiatry and psychology. The first, which is favored by genetics researchers and their backers, is that genes for "complex disorders" exist (although each gene may be of small effect size) and will be discovered once researchers improve their methods and increase their sample sizes. The second explanation, rarely considered in mainstream works, is that genes for psychiatric disorders and for normal variation in psychological traits do not exist. The latter explanation is consistent with Latham and Wilson's position that apart from a few exceptions, "genetic predispositions as significant factors in the prevalence of [most] common diseases are refuted," and that the "dearth of disease-causing genes is without question a scientific discovery of tremendous significance."[12]

Over the past two decades both the popular and the scientific literature have been filled with discussions of how improved methods in molecular genetics research will lead to gene discoveries. Although we cannot rule out such possibilities, our purpose here is to suggest that the misreading of previous kinship studies of families, twins, and adoptees has led the scientific community to the premature conclusion that genes for psychiatric disorders and psychological trait variation must exist.

In the past few years molecular genetics researchers have adopted the position of "missing heritability" as an explanation for their failure to discover genes.[13] The missing heritability interpretation of negative results has been developed in the context of the ongoing failure to uncover most of the genes presumed to underlie common medical disorders and virtually all of the genes presumed to underlie psychiatric disorders and psychological trait variation. In 2008 Francis Collins, current director of the U.S. National Institutes of Health and former director of the National Center for Human Genome Research, stated that missing heritability "is the big topic in the genetics of common disease right now."[14] Subsequently, the topic has grown even bigger.[15]

Heritability is "missing," according to one group of prominent researchers, because genomewide association (GWA) studies "have explained relatively little of the heritability of most complex traits, and the [gene] variants identified through these studies have small effects."[16] In 2009 a prominent group of researchers (including Francis Collins) headed by Teri Manolio, director of the U.S. Office of Population Genomics, published an article in *Nature* titled "Finding the Missing Heritability."[17] This article has since served as a reference point for molecular genetics researchers, including those in psychiatry and psychology, who have attempted to come to terms with decades of negative results. Manolio and colleagues recognized that only a few gene variants had been discovered for nonpsychiatric medical conditions, and they pointed to "the lack of variants detected so far for some neuropsychiatric conditions." They had no doubt that the problem is missing heritability, as opposed to nonexistent heritability, because "a substantial proportion of individual differences in disease susceptibility is known to be due to genetic factors." Manolio and colleagues saw missing heritability as the "'dark matter' of genome-wide association in the sense that one is sure it exists, can detect its influence, but simply cannot 'see' it (yet)."[18]

The reason that scientists are certain that "missing" genes exist and await discovery is their belief that previous family, twin, and adoption studies have provided conclusive evidence that genetic factors play a major role. But even if researchers eventually discover specific genes that play a role in intelligence or personality, or that predispose some people to develop psychiatric disorders, society could still choose to focus attention on mitigating psychologically unhealthy family, social, and political arrangements that impede human growth and learning and contribute to emotional problems and psychiatric disorders. Genetic-determinist ideas divert society's attention from these environmental conditions and shift blame onto people's brains and bodies. Even in the case of medical disor-

ders such as type 2 diabetes, where poverty and malnutrition are well-known causes, supporters of genetic determinism continue to press for research dollars to be directed toward genetic research, as opposed to improving social and health conditions.[19]

Kinship studies of families, twins, and adoptees are known collectively as "quantitative genetic research." Although family studies constitute a necessary first step, they are widely seen as being unable to disentangle the potential roles of genetic and environmental factors. Because family members share a common environment as well as common genes, a finding that a trait "runs in the family" can be explained on either genetic *or* environmental grounds. As Plomin and colleagues recognized, "Many behaviors 'run in families,' but family resemblance can be due to either nature or nurture."[20] They concluded, correctly in our view, that "family studies by themselves cannot disentangle genetic and environmental influences."[21]

Twin Studies

Twin studies and adoption studies, which have been carried out since the 1920s, constitute the main quantitative genetic results cited in support of genetics. We will touch on some problem areas in adoption research later, but for now we focus on twin studies, which provide the most frequently cited evidence in support of important genetic influences on psychiatric disorders and variations in "normally distributed" traits such as IQ and personality. There are two main types of research studies of twins: studies of twins reared together and studies of twins reared apart.

Reared-Together Twins. Studies of twins reared together, which use a technique called the "twin method," compare the trait resemblance of reared-together monozygotic (MZ) versus reared-together same-sex dizygotic (DZ) twin pairs. If MZ pairs resemble each other more than DZ pairs (on the basis of correlations or concordance rates), twin researchers conclude that the trait has a genetic component and then go on to calculate heritability estimates based on the magnitude of the difference. They reach this conclusion on the basis of several theoretical assumptions about twins, the most important and controversial of which is the assumption that MZ and same-sex DZ twin pairs experience roughly equal environments. This is known as the "equal-environment assumption" (EEA). The logic appears straightforward, since MZ pairs share a 100 percent genetic similarity, whereas DZ pairs share only 50 percent of their genes on average.

There is, however, a fatal flaw in this logic: The EEA of the twin method is obviously not correct, since most research in this area finds that MZ twin pairs experience much more similar environments than do DZ pairs.[22] In addition, because they are more similar genetically, MZ pairs anatomically resemble each other more than DZ pairs, and this clearly will elicit more similar treatment from the social environment.[23] Therefore, a plausible interpretation of twin method findings is that the greater psychological trait resemblance of MZ versus DZ twin pairs, a result found by most twin researchers, is completely explainable on the basis of nongenetic factors related to MZ pairs' greater environmental and treatment similarity. From the standpoint of environmental confounds, the twin method has precisely the same problem as family studies because in both, the comparison groups experience far different environments. Moreover, new research findings have called into question several long-standing assumptions in the science of genetics, which raise even more questions about the validity of twin research.[24]

Interestingly, most contemporary twin researchers recognize that the environments experienced by MZ pairs are more similar than those experienced by DZ pairs.[25] However, on the basis of two main arguments, they continue to hold that the EEA is valid and that the twin method reliably measures genetic influences.

The first argument is that although MZ and DZ environments are different, these environments must be shown to differ in aspects relevant to the trait in question.[26] Furthermore, twin researchers often implicitly or explicitly suggest that twin method critics bear the burden of proof that these admittedly unequal environments differ on trait-relevant dimensions.[27]

The second argument twin researchers put forward in defense of the EEA and the twin method is that MZ pairs tend to "create" or "elicit" more similar environments for themselves by virtue of their greater genetically caused similarity of behavior.[28] For example, according to one group of behavioral genetics researchers, although MZ twins "may well be treated more similarly" than DZs, "this is far more a consequence of their genetic similarity in behaviour (and of ensuing responses by parents and others) than a cause of such similarity."[29] And in 2009 behavioral geneticists Segal and Johnson wrote, "It is important to note that if MZ twins are treated more alike than DZ twins, it is most likely associated with their genetically based behavioral similarities."[30]

Regarding the first argument, the proponents of a scientific theory or technique, rather than their critics, bear the burden of proof that their theory or technique is correct.[31] Although twin researchers have carried

out a series of tests of the EEA, these studies have done little to uphold the validity of the twin method.[32] Ironically, although EEA test researchers usually conclude that their findings support the EEA, most find that MZ twin pairs experience much more similar environments than do DZ pairs. What they fail to understand is that the differing environments that automatically and without qualification invalidate genetic interpretations of family studies also invalidate genetic interpretations of twin method data.

We have seen that the second argument modern twin researchers put forward in defense of the twin method is that the environments of MZ twin pairs are more similar than those of DZ pairs because MZs "create" more similar environments for themselves on the basis of their greater genetic similarity. However, researchers putting forward this "twins create their own environment" position use circular reasoning because they assume the very thing they need to demonstrate. According to *The Penguin Dictionary of Psychology*, circular reasoning is "empty reasoning in which the conclusion rests on an assumption whose validity is dependent on the conclusion."[33] Twin researchers have used empty reasoning of this type since the 1950s to validate the twin method; they circularly assume that twins' behavioral resemblance is caused by genetics in order to conclude that twins' behavioral resemblance is caused by genetics.[34] Thus the only relevant question in determining the validity of the EEA and the twin method is whether—not why—MZ pairs experience more similar environments than those experienced by DZ pairs.[35]

Buried within the twin research literature on schizophrenia, which is frequently cited in support of a genetic basis for the condition, is a finding that the pooled concordance rate for same-sex DZ twin pairs is two to three times greater than that of opposite-sex DZ pairs (11.3 percent versus 4.7 percent).[36] Because the genetic relationship of same-sex and opposite-sex DZ twin pairs is the same, and because schizophrenia rates among males and females are roughly equal, from the genetic standpoint we should find no significant difference between these pooled rates.[37] Moreover, the pooled schizophrenia concordance rate for DZ twins is almost double that of ordinary (nontwin) siblings, despite the fact that the genetic relationship between DZ twins and ordinary sibling pairs is the same.[38] These findings are consistent with nongenetic explanations of the causes of schizophrenia, since pairs who share the same degree of genetic relatedness, but who experience more similar environments and a closer emotional bond, are consistently more concordant for schizophrenia than are pairs who experience less similar environments and a weaker emotional bond. These results provide additional evidence that—as we

have seen with family studies—the twin method is unable to disentangle potential genetic and environmental causes of schizophrenia and other psychiatric disorders.[39]

Thus there are two main conclusions one can reach on the basis of twin method data:[40]

1. *Contemporary twin researchers' conclusion:* The greater resemblance of MZ versus same-sex DZ twin pairs provides solid evidence that a sizable portion of the population variance for psychiatric disorders and psychological traits can be explained by genetic factors.
2. *Twin method critics' conclusion:* The twin method is a faulty instrument for assessing the role of genetics, given the likelihood that MZ versus same-sex DZ comparisons measure environmental rather than genetic influences. Therefore, all previous interpretations of the twin method's results in support of genetics are potentially wrong.

We argue here that the available evidence calls for the acceptance of conclusion 2, and we agree with three generations of critics who have written that the twin method is no more able than a family study to disentangle the potential roles of nature and nurture. As the Nobel Prize–winning chemist Wilhelm Ostwald wisely lectured his students in the early twentieth century, "Among scientific articles there are to be found not a few wherein the logic and mathematics are faultless but which are for all that worthless, because the assumptions and hypotheses upon which the faultless logic and mathematics rest do not correspond to actuality."[41]

Reared-Apart Twins. Because many scientists and commentators have had doubts about the validity of the twin method, some have pointed to studies of twins reared apart (TRA studies), such as the Minnesota TRA research published by Bouchard and colleagues.[42] These investigations look mainly at psychological traits such as IQ and personality. However, several reviewers have outlined problems with the methodology and underlying logic of these studies.[43] Problem areas include the following: (1) it is doubtful that most reared-apart MZ pairs (known as MZAs) deserve the status of having been "reared apart," since most pairs had significant contact with each other for many years; (2) in several studies there were biases favoring the recruitment of MZA pairs who resembled each other in behavioral traits more than MZA pairs as a population; (3) there is controversy about whether "intelligence" and "personality" are valid and

quantifiable constructs; (4) the Minnesota researchers failed to publish life-history information for the twins under study and then denied independent reviewers access to raw data and other unpublished information; and (5) there was likely researcher bias in favor of genetic explanations of the data.[44]

Perhaps the most important problem is the original TRA researchers' failure to control for several critical environmental influences shared by MZA pairs, including even those extremely rare cases in which studied MZA pairs were reared apart from early life and grew up without knowing that they had a twin sibling.[45] In the study containing the highest percentage of MZA pairs of this type, the author found,

> In all 12 pairs there were marked intra-pair *differences* in that part of the personality governing immediate psychological interaction and ordinary human intercourse. . . . The twins behaved, on the whole, very differently, especially in their cooperation, and in their form of and need for contact. Corresponding with these observations, the twins gave, as a rule, expression to very different attitudes to life, and very divergent views on general culture, religion and social problems. Their fields of interest, too, were very different. . . . Those twins who had children treated, on the whole, their children differently, and their ideas on upbringing were, as often as not, diametrically opposed. Characterologically, the twins presented differences in their ambitions and in their employment of an aggressive behavior. Emotionally, there was a deep-going dissimilarity with regard to the appearance of spontaneous emotional reactions or to the control of affective outbursts. Various traits of personality found their expression in differences in taste, mode of dress, hair style, use of cosmetics, the wearing of a beard or of glasses.[46]

Original descriptions of this type have not prevented the authors of numerous books attempting to popularize genetic research, exemplified by Steven Pinker's *Blank Slate* and Judith Harris's *Nurture Assumption,* from claiming that TRA studies and individual stories reported in the media "suggest that genes can cause striking similarities in personality characteristics, even in the face of substantial differences in rearing environments."[47]

Environmental influences shared even by perfectly separated MZA pairs always include common age, common sex, common ethnicity, common physical appearance, and common prenatal environment, and usually include common socioeconomic class and common culture. Reared-apart twin pairs (as well as genetically unrelated people born at the same time) are subject to the social and historical influences of their birth cohort. As behavioral genetics researcher Richard Rose once observed, "Were one to

capitalize on cohort effects by sampling [genetically] unrelated but age-matched pairs, born, say, over a half-century period, the observed similarities in interests, habits, and attitudes might, indeed, be 'astonishing.' "[48]

Thus, for reasons unrelated to heredity, we should expect to find a much higher correlation in video-game-playing behavior in the United States among pairs of randomly selected 11-year-old middle-class Caucasian boys than we would expect to find among randomly selected pairs drawn from the entire 11- to 100-year-old male and female population of the United States.[49] This hypothetical example illustrates one of the central fallacies of TRA studies. (Bouchard and colleagues were the first TRA researchers to address age and sex confounds, but their adjustments were inadequate to deal with this problem.)[50]

On purely environmental grounds, therefore, we would expect MZA pairs to correlate well above zero for psychological and behavioral traits.[51] This means that the appropriate control group with which to compare MZA correlations would be a group consisting of genetically unrelated pairs of strangers matched on the environmental influences experienced by MZA pairs.[52] Most previous MZA studies, however, mistakenly used reared-together MZs as controls.[53] Thus we see that like the twin method, studies of twins reared apart are subject to their own set of invalidating environmental confounds and other biases.

Adoption Studies

Although twin research has been called the "'Rosetta Stone' of behavior genetics," adoption studies are also used to assess the role of genetic influences on various traits and disorders.[54] Adoption studies investigate people who receive the genes of their birth parents but are reared in the family environment of people with whom they share no genetic relationship. Adoption research originally focused on IQ and was extended to include personality and psychiatric disorders such as schizophrenia, attention-deficit/hyperactivity disorder, and bipolar disorder. In particular, the Danish American adoption studies are widely cited as having established schizophrenia as a genetic disorder.[55] Several commentators, however, have pointed to a number of crucial errors and biases in these studies.[56] In Tienari and colleagues' Finnish schizophrenia adoption studies, the researchers concluded that both genes and family environment play important causative roles.[57]

Like family and twin studies, adoption studies are subject to their own set of environmental confounds and biases that cast doubt on their ability to separate the potential influences of nature and nurture. Included

among these biases are late separation (and accompanying attachment disturbance), range restriction, whether adoptees and family members are representative of their respective populations, and the selective placement of adoptees.[58]

Tienari and colleagues investigated the adoptive families of Finnish adoptees whose biological mothers were diagnosed with schizophrenia (index adoptees) and the adoptive families of control adoptees whose biological mothers were not so diagnosed.[59] Although 7 percent of the index adoptees were diagnosed as psychotic, in contrast to 1 percent of the control adoptees (which can be accounted for by selective placement factors; see below), Tienari and colleagues' analysis of the families of index adoptees diagnosed as psychotic reveals that 6 of 43 adoptees (14 percent) who were reared in "seriously disturbed adoptive families" were diagnosed as psychotic. In striking contrast, none of the 48 index adoptees reared in "healthy or mildly disturbed adoptive families" were diagnosed as psychotic. Moreover, 19 of the 32 adoptees (59 percent; index and control combined) raised in "severe disturbance" Finnish adoptive families developed a major psychological dysfunction (which included "character disorders," "borderline syndrome," and "psychotic"), whereas none of the 15 adoptees reared in Finnish "healthy" adoptive families developed such a dysfunction.[60]

If we look more closely at the "no-selective-placement" assumption of adoption studies, psychiatric adoption researchers must assume that factors relating to the adoption process did not lead agencies to place certain groups of adoptees into environments contributing to a higher rate of the disorder in question. However, the evidence suggests that adoption studies of schizophrenia were confounded by environmental factors on the basis of the perceived genetic undesirability of adoptees with a biological family history of mental disorders placed in early to mid-twentieth-century Europe.[61]

For example, Finland (like Denmark) had a long history of eugenics-inspired legislation aimed at curbing the reproduction of "hereditarily tainted" people.[62] The Finnish government created a commission in 1926 to study the possibility of sterilizing people seen as "mentally retarded," "mentally ill," or epileptic. In 1935 the Finnish parliament passed the Sterilization Act, which allowed the compulsory eugenic sterilization of "idiots," "imbeciles," and the "insane," which included people diagnosed with schizophrenia and manic depression. Compulsory eugenic sterilization was not abolished in Finland until 1970. The Finnish adoptees Tienari and colleagues studied were born between 1927 and 1979 and were therefore placed in an era in which the biological offspring of people diagnosed

with a psychotic disorder were seen as undesirable, "tainted" adoptees. Clearly, few prospective Finnish adoptive parents would have wanted to adopt such a child.

Selective placement has also been identified as a confounding factor in IQ adoption research, since adoption agencies frequently attempt to match adoptees and adoptive families for socioeconomic status, in addition to matching on the basis of the assumed intelligence potential of the adoptee.[63]

Thus, despite adoption studies' theoretical potential to disentangle genetic and environmental influences, most adoption studies published to date have been plagued by methodological problems and potential environmental confounds. However, it is possible that a well-designed adoption study could separate genetic and environmental factors and put the nature-nurture issue to the test. The researchers performing such a study must, at a minimum, (1) choose as participants only those adoptees who were placed into their adoptive homes at or shortly after birth; (2) determine in advance, and publish or submit to a research register before undertaking the study, the specific hypotheses, methods, definitions, and comparison groups that will be used; (3) make a serious attempt to come to grips with problems such as selective placement and range restriction, and be willing to refrain from concluding in favor of genetics if such problems are found; (4) publish or place with a research register raw case-history information and data relating to participants and make this information and data available to qualified reviewers for inspection; (5) ensure that all interviews, tests, diagnoses, and ratings are performed blindly; and (6) study only those traits and disorders whose reliability and validity have been demonstrated by previous research.[64]

Conclusions about the Genetic Paradigm and the Need for an Alternative

We have suggested that the body of quantitative genetic research in psychiatry and psychology is contaminated by environmental factors.[65] In addition, these studies contain many glaring methodological problems and other biases. Although the relatives in these studies frequently manifest traits and disorders in patterns predicted by genetic theories, these patterns usually match the predictions made by theories of nongenetic causation as well.[66] Thus it is likely that family, twin, and adoption studies have been unable to disentangle the potential roles of genetic and environmental influences on traits and disorders, and that the investigators who typically perform this research have greatly underestimated the potential role of environmental confounds. It has been left to critics to focus

on these problems, but their voices have been lost in the vast literature produced in the past few decades by authors claiming major genetic influences on these traits.

We call on behavioral scientists, particularly researchers in psychiatry and psychology, to suspend the current "missing heritability" interpretation of negative molecular genetics findings and to embark on a serious reassessment of the validity of twin and adoption studies. Latham and Wilson concluded that a reasonable interpretation of the failure to identify genes is that "heritability studies of twins are inherently mistaken or misinterpreted," and that the "dark matter" of missing heritability "becomes simply an artifact arising from overinterpretation of twin studies."[67]

In 1994 behavioral geneticists Robert Plomin, Michael Owen, and Peter McGuffin wrote in *Science* about a genetic variant associated with Alzheimer's disease and continued, "We predict that QTL [quantitative trait loci, or genes of various effect sizes] associations will soon be found for other complex human behaviors."[68] However, this prediction turned out to be wrong.[69] Indeed, three genetically oriented Nobel Prize–winning researchers and their colleagues, in a 2010 *Science* "Policy Forum" article, recognized the "frustrating lack of progress" in understanding the genetics of mental disorders.[70]

A final issue to consider is the broader context of genetic research into psychiatric disorders. This context includes not only scientific and social issues that form the assumptions that guide this work but also the scientific and social consequences of this work. This inquiry into the context of research is a branch of philosophy of science known as social studies of science. It is pursued in the Society for Social Studies of Science and in journals such as *Social Epistemology* and *Social Studies of Science*. The social and intellectual context affects the quality of particular research (just as social context affects all behavior). It is also an important avenue for assessing the plausibility and validity of the research.

Research into possible genetic causes of psychiatric disorders partakes of a system of superordinate scientific issues. These include the nature of human psychology and its relation to biochemical mechanisms. If genes cause psychiatric disorders in some specific manner, then they must work through biochemical mechanisms. This raises the broader, superordinate question whether psychiatric disorders are caused by (reducible to) biochemical mechanisms—that is, how can biochemical mechanisms cause someone to experience particular symptoms of, for example, depression, eating disorders, risky behavior, or social phobia? This question about biochemical mechanisms and psychiatric disorders depends on a still-broader,

superordinate question whether psychology in general is determined by biochemical mechanisms. Research into these two superordinate questions strengthens or weakens the genetic hypothesis of psychiatric disorders. If research demonstrates that psychology is not determined by biochemical mechanisms, then psychiatric disorders cannot be determined by genes.[71] Conversely, research into the subordinate issue of whether genes cause psychiatric disorders strengthens or weakens the superordinate issues. Researchers and the authors of authoritative textbooks who claim that genes play a major role in causing psychiatric disorders help strengthen superordinate theories that these disorders have biochemical causes, and that psychology has biochemical causes.

Although pursuing these corollary issues is outside the bounds of this chapter, we recommend that readers do so in order to better understand the question of genetic causes of psychiatric disorders. We believe that research into these issues will support the rejection of the genetic paradigm of psychiatric disorders and will give grounds for an alternative paradigm that emphasizes the role of familial, social, cultural, and political influences.[72]

In a 2000 article titled "Three Laws of Behavioral Genetics and What They Mean," behavioral geneticist Eric Turkheimer concluded, mainly on the basis of twin studies, that "all human behavioral traits are heritable."[73] At that time, behavioral genetics and psychiatric genetics researchers believed that the completion of the Human Genome Project would rapidly lead to gene discoveries.[74] So did Turkheimer, who wrote that "behavior geneticists anticipate vindication" by the discovery of genes causing behavioral variation. On the other hand, wrote Turkheimer, "Critics of behavior genetics expect the opposite, pointing to the repeated failures to replicate associations between genes and behavior as evidence of the shaky theoretical underpinnings of which they have so long complained."[75] A dozen years later the critics indeed appear to have been vindicated, and the real problem may well be, as Turkheimer described it, the "shaky theoretical underpinnings" provided by genetic theories based on family, twin, and adoption studies.

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not violate the equal environment assumption of the twin method, the physical resemblance of monozygotic twin pairs is the result of the splitting of a fertilized egg. Thus, although this physical resemblance is based on the pair's identical genotype, it is not an inherited characteristic because the same physical resemblance will be present regardless of who their biological parents are, or in whose womb they develop. See J. Joseph, "The Equal Environment Assumption of the Classical Twin Method: A Critical Analysis," *Journal of Mind and Behavior* 19 (1998): 325–358.

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K. Hood, C. Tucker Halpern, G. Greenberg, et al. (Malden, MA: Wiley-Blackwell, 2010), 557–625; J. Joseph, "The 'Missing Heritability' of Psychiatric Disorders: Elusive Genes or Non-Existent Genes?," *Applied Developmental Science* (forthcoming). One of the first attempts to use the argument that "twins create their own environment" in support of the twin method was by James Shields in 1954, who wrote, "In so far as binovular [DZ] twins are treated differently from one another and more differently than uniovular [MZ] twins, this is likely to be due, not so much to causes outside the twins as to innate differences in the needs of the binovular twins themselves, manifested by different patterns of behaviour." J. Shields, "Personality Differences and Neurotic Traits in Normal Twin Schoolchildren," *Eugenics Review* 45 (1954): 213–246, at 240. Other examples of researchers invoking this argument since the 1950s include F. J. Kallmann, "The Uses of Genetics in Psychiatry," *Journal of Mental Science* 104 (1958): 542–552; S. V. Vandenberg, "Contributions of Twin Research to Psychology," *Psychological Bulletin* 66 (1966): 327–352; J. C. Loehlin and R. C. Nichols, *Heredity, Environment, and Personality* (Austin: University of Texas Press, 1976); K. S. Kendler, "The Genetics of Schizophrenia: A Current Perspective," in *Psychopharmacology: The Third Generation of Progress,* ed. H. Meltzer (New York: Raven Press, 1987), 705–713; and Rowe, *Limits of Family Influence.*

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