

Chapter-by-Chapter Summary of

THE MISSING GENE:
PSYCHIATRY, HEREDITY, and the FRUITLESS
SEARCH FOR GENES

By Jay Joseph, Psy.D.

Algora Publishing, 2006. 332 pp.

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CHAPTER ONE | Introduction. The Twin Method: Science or Pseudoscience?

In *The Missing Gene: Psychiatry, Heredity, and the Fruitless Search for Genes*, Psychologist Jay Joseph examines the claim that the major psychiatric disorders have an important underlying genetic basis. The main pillar supporting this view is a research technique called the *twin method*, which is utilized mainly by the fields of behavior genetics¹ and psychiatric genetics.² The twin method compares the trait resemblance of reared-together identical twin pairs (also known as monozygotic, or MZ), who share 100% genetic similarity, versus the resemblance of reared-together same-sex fraternal twin pairs (also known as

¹ *Behavior genetics* is a discipline, rooted in the field of psychology, which uses family, twin, and adoption studies to assess possible genetic influences on “continuously distributed” psychological traits such as personality and I.Q, and also on psychiatric disorders. In other areas of behavior genetics, researchers work primarily with non-human animals.

² *Psychiatric genetics* is a discipline founded by Ernst Rüdin and his German colleagues in the early part of the 20th century. German psychiatric geneticists used family and twin studies in an attempt to establish the genetic basis of psychiatric disorders. Their primary goal was to promote the eugenic program (called “racial hygiene” in Germany) of curbing the reproduction of people they viewed as carrying the “hereditary taint of mental illness,” by sterilization or other means. After the Nazi seizure of power in 1933, the leaders of Rüdin’s “Munich School” of psychiatric genetics supported and helped popularize Hitler’s program of forcibly sterilizing “eugenically undesirable” people. Contemporary psychiatric geneticists investigate the causes of mental disorders in order to better treat and prevent them. Unlike the previous era, they usually avoid discussions of eugenics in relation to their findings. The implications of their theories, however, are obvious, and they often promote the use of genetic counseling.

dizygotic, or DZ), who average a 50% genetic similarity. (Twin resemblance is usually measured with concordance³ rates or correlations.) Based on the assumption that the childhood and adult environments of both types of twins are comparable, known as the “equal environment assumption” or “EEA,”⁴ twin researchers attribute to genetic factors the usual finding of a significantly greater trait resemblance among identical versus same-sex fraternal twin pairs.

In his previous book, *The Gene Illusion: Genetic Research in Psychiatry and Psychology Under the Microscope*,⁵ Joseph showed that, regardless of how it has been defined, the equal environment assumption of the twin method is not supported by the evidence. Thus, it is likely that the twin method has recorded nothing more than the greater environmental similarity, more similar treatment, and greater level of identity confusion experienced by identical versus fraternal twin pairs. In Chapter 1 of *The Missing Gene*, Joseph elaborates on his previous critique of the twin method and shows that the arguments presented by psychiatric geneticist Kenneth Kendler, a leading contemporary defender of the twin method, do not hold up to critical examination.

Joseph then suggests that, because it rests on at least one clearly false theoretical assumption, the twin method can be understood within the framework others have created to separate science from pseudoscience.⁶ For example, it is common for defenders of the twin method to state or imply that *critics* of the twin method bear the burden of proof for demonstrating that the greater environmental similarity experienced by identical pairs versus fraternal pairs invalidates the twin method.⁷ As others who have attempted to distinguish science from pseudoscience have pointed out, however, “a basic tenet of science is that the burden of proof always falls squarely on the claimant, not the critic...Consequently, it is up to the

³ When both members of a twin pair are diagnosed with the same trait or disorder, they are said to be *concordant*. When one twin is diagnosed with the trait or disorder but the other is not, they are said to be *discordant*.

⁴ The *Equal Environment Assumption (EEA)* is the most important, and most controversial, assumption of the twin method. It holds that reared-together identical and same-sex fraternal twin pairs experience the same environments. All conclusions in favor of genetics derived from twin method data depend on the validity of this assumption. The *traditional* equal environment assumption states, without qualification, that identical and same-sex fraternal twin pair environments are equal. After belatedly recognizing that identical pairs do indeed experience more similar environments than fraternal pairs, several twin researchers added the qualification that these environments need only be equal regarding *trait relevant* features of the environment. Going further, they placed the burden of proof on critics of the twin method for showing that identical and fraternal twin pair environments are unequal as they relate to trait-relevant aspects of the environment.

⁵ Joseph, J. (2004). *The Gene Illusion: Genetic Research in Psychiatry and Psychology Under the Microscope*. New York: Algora. (2003 United Kingdom Edition by PCCS Books)

⁶ A *pseudoscience* is a set of ideas or claims based on theories purporting to be scientific, but are not scientific. According to psychologist Scott Lilienfeld and his colleagues, the ten “warning signs” of pseudoscience are “an overuse of ad hoc hypotheses designed to immunize claims from falsification,” “absence of self-correction,” “evasion of peer review,” “emphasis on confirmation rather than refutation,” “reversed burden of proof,” “absence of connectivity,” “overreliance on testimonial and anecdotal evidence,” “use of obscurantist language,” “absence of boundary conditions,” and “the mantra of holism.” See Lilienfeld, S. O., Lynn, S. J., & Lohr, J. M. (2003, p. 7). Science and pseudoscience in clinical psychology: Initial thoughts, reflections, and considerations. In S. Lilienfeld, S. Lynn, & J. Lohr (Eds.), *Science and Pseudoscience in Clinical Psychology* (pp. 1-14). New York: Guilford.

⁷ Examples of twin researchers reversing the burden of proof onto critics include Lyons, M. J., Kendler, K. S., Provet, A., & Tsuang, M. T. (1991). The genetics of schizophrenia. In M. Tsuang, K. Kendler, & M. Lyons (Eds.), *Genetic Issues in Psychosocial Epidemiology* (pp. 119-152). New Brunswick, NJ: Rutgers University Press; Bouchard, T. J., Jr. (1997). IQ similarity in twins reared apart: Findings and responses to critics. In R. Sternberg & E. Grigorenko (Eds.), *Intelligence, Heredity, and Environment* (pp. 126-160). New York: Cambridge University Press; Faraone, S. V., & Biederman, J. (2000). Nature, nurture, and attention deficit hyperactivity disorder. *Developmental Review*, 20, 568-581.

proponents of these techniques to demonstrate that they work, not up to the critics of these techniques to demonstrate the converse.”⁸

Research has confirmed the obvious fact that identical twin pairs experience much more similar environments than do fraternal twin pairs. Therefore, regardless of how twin researchers have attempted to validate the twin method (see the discussion of Chapter 10), the simple fact that identical twin pair environments are more similar is sufficient for us to conclude that the twin method, like a family study (see below), is unable to disentangle potential genetic and environmental influences on psychiatric disorders.

CHAPTER TWO | ADHD Genetic Research: Activity Deserving of Attention, or Studies Disordered by Deficits?

Chapter 2 examines the argument that attention-deficit hyperactivity disorder (ADHD) has an underlying genetic basis. Here, Joseph highlights the invalidating flaws of family, twin, and adoption research in this area, and argues that, contrary to the widely disseminated view in psychiatry, there is little scientifically acceptable evidence supporting a genetic basis for the condition. ADHD molecular genetic research, which has failed to identify any “ADHD genes,”⁹ is discussed in Chapter 11.

Research suggests that ADHD, like most psychiatric disorders, tends to aggregate in families. However, although many behavioral tendencies may be *familial* in the sense that they “run” or cluster in families, we cannot determine whether this clustering is caused by the greater *genetic* resemblance of family members, since they are also exposed to more similar environmental factors. As schizophrenia genetic researchers Gottesman and Shields have written, “that a disease is familial does not necessarily imply that it is genetic. Familial clustering can also be transmitted through culture, infectious sources, or learning.”¹⁰ Indeed, most contemporary behavioral genetic researchers recognize that a family study cannot disentangle genetic and environmental influences.¹¹ However, they continue to assert, albeit as Joseph argues, that the twin method *is* able to disentangle these potential influences. Joseph shows that family studies and the twin method contain similar obvious environmental confounds.

Researchers’ understanding that the familial clustering of ADHD can be explained on environmental grounds led them to seek other methods to determine whether genetic factors play

⁸ Lilienfeld et al. (2003, p. 3).

⁹ Akil, H., Brenner, S., Kandel, E., Kendler, K. S., King, M., Scolnick, E., Watson, J. D., Zoghbi, H. Y. (2010). The future of psychiatric research: Genomes and neural circuits. *Science*, 327, 1580-1581; Faraone, S. V., Doyle, A. E., Lasky-Su, J., Sklar, P. B., D’Angelo, E., Gonzalez-Heydrich, J., Kratochvil, C., Mick, E., Klein, K., Rezac, A. J., & Biederman, J. (2008). Linkage analysis of attention deficit hyperactivity disorder. *American Journal of Medical Genetics Part B (Neuropsychiatric Genetics)*, 147B, 1387-1391; Hudziak, J. J., & Faraone, S. V. (2010). New genetics in child psychiatry. *Journal of the American Academy of Child and Adolescent Psychiatry*, 49, 729-735

¹⁰ Gottesman, I. I., & Shields, J. (1982, p. 69). *Schizophrenia: The Epigenetic Puzzle*. New York: Cambridge University Press.

¹¹ Joseph, J. (2010). Genetic research in psychiatry and psychology: A critical overview. In K. Hood, C. Tucker Halpern, G. Greenberg, & R. Lerner (Eds.), *Handbook of Developmental Science, Behavior, and Genetics* (pp. 557-625). Malden, MA: Wiley-Blackwell; Plomin, R., DeFries, J. C., McClearn, G. E., & McGuffin, P. (2008). *Behavioral Genetics* (4th ed.). New York: Worth Publishers.

a role. Most have turned to the twin method to answer this question. However, since the evidence overwhelmingly suggests that identical twin pairs are treated more alike, spend considerably more time together, and experience greater levels of identity confusion and closeness than fraternal pairs, we would expect identical twins—on purely environmental grounds—to correlate higher than same-sex fraternal twins on ADHD-related measures. Thus, as we have seen, the twin method is unable to disentangle the potential influences of genes and environment, and therefore supplies no evidence supporting a genetic basis for ADHD. It is also noteworthy that most ADHD twin researchers (more than 25 ADHD twin studies have been published) did not discuss the merits of the equal environment assumption in their research publications.

Another method used to assess for genetic influences on ADHD and other conditions is the study of adopted individuals. In theory, an adoption study is able to disentangle potential genetic and environmental influences on psychiatric disorders because adoptees receive their genes from one family, but are raised in the environment of another family. Six ADHD adoption studies have been published by to date. The results of these studies are frequently cited in textbooks, review articles, and scientific papers as supporting genetic theories of ADHD. However, these studies contain several invalidating flaws. Problems in ADHD adoption research include:

- In striking contrast to schizophrenia adoption research, ADHD adoption researchers were unable to study adoptees' biological relatives
- The researchers used non-blinded diagnoses in most studies, which they sometimes made on the basis of relatives' hazy recollections
- ADHD was not adequately defined in most studies
- The researchers were often unable to control for environmental confounds
- The researchers did not control for the status of adoptive parents as a population screened for psychiatric disorders
- There was potential researcher bias
- The researchers used late-separated adoptees

Unfortunately, ADHD genetic researchers and the authors of review articles usually fail to discuss the severe limitations of ADHD adoption models unless compelled to do so by critics.¹² As Joseph documents, they sometimes obscure the fact that—unlike the schizophrenia adoption studies before them—ADHD adoption researchers were unable to study adoptees' biological relatives. This by itself calls into question any conclusions in favor of genetics.

In subsequent chapters Joseph shows that the problem of secondary sources' potentially misleading accounts of psychiatric genetic research is by no means limited to ADHD. In fact, the misrepresentation and uncritical acceptance of psychiatric genetic research is a running theme throughout the entire book.

Joseph assesses of the total weight of the evidence put forward in favor of a genetic basis or predisposition for ADHD, and concludes that a role for genetic factors is not supported. Thus, future research should be directed towards psychosocial causes.¹³ Of course, this conclusion

¹² For example, see Faraone & Biederman (2000).

¹³ Timimi, S., & Leo, J. (Eds.). (2009). *Rethinking ADHD*. New York: Palgrave Macmillan.

lends support to the increasing number of people who question the validity of the ADHD concept itself.

CHAPTER THREE | A Critique of the Spectrum Concept as Used in the Danish-American Schizophrenia Adoption Studies

The leaders of psychiatry defend their field's basic principles by citing research. A major principle is that most psychiatric disorders have an important genetic basis. However, psychiatry usually does not subject its core positions to in-depth critical analysis. This is particularly true of genetic research in the field.

Yet, conclusions in favor of genetics frequently depend on the investigators' decision-making process during the course of their studies. Whom should they count as cases? How should they define the disorder in question? What statistical procedures should they use? Which comparisons should they emphasize? Too often, studies have been published in which the methods, results, and conclusions appear together for the first time, allowing researchers to present the study as a neat package.

This can occur because there is no procedure in psychiatry (and most other fields) requiring researchers to submit and/or publish their methods *before* they collect data. Thus, even highly ethical investigators might be tempted to pick and choose results enabling them to find statistically significant results, which are often a prerequisite for having their study published.¹⁴ These problems could be reduced through the establishment of a system requiring researchers to submit a description of their methods prior to the collection and analysis of data, and by requiring journals to agree to publish the results regardless of whether statistical significance is achieved.¹⁵ Although it is understood that there "is a cardinal rule in experimental design that any decision regarding the treatment of data must be made *prior* to an inspection of the data,"¹⁶ accountability in psychiatric research, as well as research in other fields, is inadequate.

The Danish-American adoption studies of the 1960s and 70s played a crucial role in establishing schizophrenia as psychiatry's paradigmatic genetic disorder. Yet, although the results depended on greatly expanding the definition of schizophrenia, there is no evidence that Seymour Kety, David Rosenthal, Paul Wender, and their Danish associates agreed on this expanded definition before they collected and analyzed their data. Furthermore, Joseph shows that these investigators made faulty calculations of their *published* data, which led them, mistakenly, to conclude in favor of genetic influences on schizophrenia.

Having provided a detailed critical review of the Danish-American adoption studies in Chapter 7 of *The Gene Illusion*, Joseph zeroes in on a crucial aspect of schizophrenia adoption research: the "schizophrenia spectrum" concept. In doing so, he shows that the spectrum concept does not hold up to critical examination, and that the researchers should have limited their

¹⁴ Hubbard, R., & Armstrong, J. C. (1997). Publication bias against null results. *Psychological Reports*, 80, 337-338.

¹⁵ Joseph, J., & Baldwin, S. (2000). Four editorial proposals to improve social sciences research and publication. *International Journal of Risk and Safety in Medicine*, 13, 117-127.

¹⁶ Walster, G. W., & Cleary, T. A. (1970, p. 18). A proposal for a new editorial policy in the social sciences. *The American Statistician*, 26, 16-19.

definition of schizophrenia to the chronic form as it was understood at the time they performed their research. His analysis is relevant today (1) because these adoption studies remain the most frequently cited evidence in support of the genetic theory of schizophrenia, and (2) as an example of how a close examination of one aspect of genetic research can uncover serious and invalidating flaws—even in studies that form the basis of existing scientific paradigms.

Interestingly, Eugen Bleuler, the founder of the schizophrenia concept, argued against diagnosing people manifesting milder symptoms with schizophrenia. “Only a few isolated psychotic symptoms can be utilized in recognizing the disease,” wrote Bleuler, “and these too, have a very high diagnostic threshold value.”¹⁷ Moreover, it was improper for the Danish-American investigators to count as schizophrenia “uncertain” cases in general, and “uncertain borderline schizophrenia” cases in particular.

Joseph suggests that the Danish-American schizophrenia spectrum was created not on the basis of theoretical or empirical soundness, but rather to enable the researchers (1) to have enough subject to study, and (2) to be able to find statistically significant results in the genetic direction. He concludes that the “schizophrenia spectrum” concept, as the Danish-American researchers defined it, is invalid on several grounds. Thus, “chronic schizophrenia” is the only diagnosis they should have used in their studies, implying that the Danish-American schizophrenia adoption studies, and their authors’ conclusions in favor of genetics, should be reevaluated on this basis.

CHAPTER FOUR | Pellagra and Genetic Research

In Chapter 4 Joseph engages in a bit of historical speculation by predicting the results of twin and adoption studies of pellagra, an early 20th century often fatal disease characterized by severe skin rash, gastrointestinal problems, and mental disturbance. Pellagra was ultimately discovered to be caused by a vitamin deficiency linked to malnutrition.

Joseph discusses pellagra as the subject of genetic research, both real and hypothetical, in order to illustrate how psychiatric genetic research methods are potentially confounded by environmental factors, and how the “genetic predisposition” concept is often irrelevant and, in some cases, is potentially harmful. Joseph evaluates a published pellagra family pedigree study, and then imagines what pellagra twin and adoption studies (which were never performed) might have found. Although there is currently a widespread consensus in psychiatry that individuals diagnosed with mental disorders are genetically predisposed to develop them, many of the environmental factors thought to trigger these disorders are controversial. However, the cause of pellagra is known, and, as Joseph argues, psychiatric genetic methods would be expected to mistakenly point to the operation of genetic factors in a condition known to be caused not by genes, but by a dietary deficiency.

Early 20th century proponents of eugenics¹⁸ and genetic determinism, such as Charles Davenport, mistakenly interpreted pellagra family histories as showing that the condition had a

¹⁷ Bleuler, E. (1950, p. 294). *Dementia Praecox or the Group of Schizophrenias*. New York: International Universities Press. It is beyond the scope of this analysis to challenge Bleuler’s characterization of schizophrenia as a “disease.” For a critique of the disease model of schizophrenia, see Chapters 1 and 3 of Thomas Szasz’s 1976 work, *Schizophrenia: The Sacred Symbol of Psychiatry*.

¹⁸ *Eugenics* is a doctrine holding that humans can be “improved” by selective breeding to eradicate “undesirable” traits in society. Eugenists argue that many social problems and psychiatric disorders are caused by inherited genetic traits, which can be bred

strong genetic basis.¹⁹ Joseph goes on to argue that, had researchers then decided to perform studies using (1) the twin method, (2) reared-apart twins, and (3) adoptees, the “converging evidence” from these studies would likely have confirmed the “finding” from family research that pellagra has an important genetic basis.

But suppose it had been shown that some people *are* genetically more vulnerable to develop pellagra. That is, despite the clear cause of pellagra being a vitamin deficiency linked to malnutrition, suppose it had been shown that some individuals, because of their genetic predisposition, were more likely to develop pellagra following malnutrition. In this case, Joseph argues, the discovery of a genetic predisposition for pellagra would not have been of major importance. Pellagra was wiped out in the United States by the relief programs of the 1930s, and, more importantly, by a federally-mandated World War II-era program requiring the enrichment of flour and corn meal with the vitamins needed to prevent pellagra. In other words, once the environmental factor was identified and eliminated, any possible genetic predisposition had been rendered unimportant. Perhaps this explains why no one ever bothered to perform a pellagra twin or adoption study, or for that matter, a pellagra molecular genetic study.

As Joseph concludes, “For psychiatric conditions believed to carry a genetic predisposition requiring an unknown environmental trigger, the importance researchers give to the genetic predisposition represents little more than a recognition that they have not identified the environmental cause or trigger.”

The example of pellagra shows that an emphasis on genetics, and a misunderstanding of the genetic predisposition concept, can delay discovery of the true causes of a condition at the cost of unnecessary suffering, and can promote the unwarranted stigmatization of diagnosed individuals. For psychiatric disorders, the claim of a hereditary component—even if true—can have similar consequences.

CHAPTER FIVE | A Generation Misinformed: Psychiatry and Psychology Textbooks’ Inaccurate Accounts of Schizophrenia Adoption Research

Textbooks are valuable tools for transmitting the knowledge and history of various academic fields to students and professionals. Unfortunately, they can also help perpetuate myths. Modern psychiatry is dominated by the biological/psychopharmacology paradigm, which must show that its diagnoses are biologically/genetically based. Furthermore, the prevailing views in psychiatry influence psychology and other related fields.

Chapter 5 examines textbooks’ reporting of a specific area of psychiatric research: the study of adoptees as a means of testing the hypothesis that genetic factors influence schizophrenia. Joseph surveys 43 psychiatry and psychology textbooks’ discussions of schizophrenia adoption research. These include fifteen psychiatry textbooks, eleven abnormal psychology textbooks, six books devoted entirely to schizophrenia, six books whose authors argue that genes play an important role in determining human behavioral differences, two chapters from annual psychiatry reviews, two neuroscience textbooks, and the American

out of the population for the benefit of future generations. Many German eugenicists of the first half of the 20th century preferred the term *racial hygiene* to eugenics.

¹⁹ Chase, A. (1980). *The Legacy of Malthus: The Social Costs of the New Scientific Racism*. Urbana, IL/Chicago: University of Illinois Press (Originally published in 1977)

Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders* (IV-Text Revision). Simply put, these sources constitute the authoritative texts of psychiatry and abnormal psychology. Unfortunately, textbook descriptions of schizophrenia adoption research are sometimes inaccurate, and critical analysis is largely absent.

Problem areas in the surveyed textbooks include:

- They emphasize the original researchers' conclusions at the expense of independent critical analysis
- They often rely on secondary sources
- They typically do not discuss, or mention only briefly, the views and publications of critics
- They often misreport studies' methods and results
- While some surveyed textbooks discuss possible environmental confounds²⁰ in schizophrenia twin research, few discuss the likelihood that genetic inferences from adoption data are confounded by the selective placement of adoptees with a family history of mental disorders
- Few discuss problems with the reliability and validity of a schizophrenia diagnosis in the context of genetic research
- Few discuss adoption study problems such as late placement and attachment disturbance
- Some authors cite studies failing to find statistically significant results in the genetic direction as evidence in favor of genetic factors
- Most authors accept the original researchers' definition of schizophrenia (or "schizophrenia related disorders") without question. In particular, they typically present the Danish-American investigators' results as supporting a "schizophrenia spectrum of disorders," but rarely question the validity of this concept, which was usually necessary in order to find statistically significant results (discussed in Chapter 3)

After carefully documenting these problems, Joseph concludes that, in general, the surveyed textbooks have rubber stamped the original investigators' and contemporary psychiatry's conclusions about the results of schizophrenia adoption research. It is clear that many textbook authors did not carefully review the original studies, and sometimes did not even read them. Moreover, a major bias in favor of genetics is evident. In fact, only about 10% of the textbooks cited a publication critical of a schizophrenia adoption study's methods and conclusions, and even fewer attempted to provide a limited critical analysis. While the textbooks occasionally discussed the controversial assumptions of the twin method, only two mentioned the crucial "no selective placement assumption" of adoption studies. A violation of this assumption could lead to a higher experimental versus control group schizophrenia rate for reasons having nothing to do with genetics.²¹

²⁰ A *Confound* is an unforeseen or uncontrolled-for factor that threatens the validity of conclusions researchers draw from their studies. Although twin and adoption researchers usually interpret their findings as supporting genetic factors, uncontrolled-for environmental influences might lead others to interpret their findings solely in terms of environmental influences.

²¹ *Selective Placement* is a potentially confounding aspect of adoption studies whereby children are systematically placed into adoptive homes sharing some characteristics (e.g., socioeconomic status, psychiatric diagnostic status) of their biological

Psychologist Mary Boyle has written that psychiatry textbooks teach “large numbers of people...not to think critically.”²² Clearly, those studying the causes of schizophrenia must be exposed to a wider variety of viewpoints than they currently receive, and inaccurate reporting and bias in favor of genetics must be documented further.

CHAPTER SIX | Irving Gottesman’s 1991 *Schizophrenia Genesis: A Primary Source for Misunderstanding the Genetics of Schizophrenia.*

Any review of textbook discussions of the “genetics of schizophrenia” topic would be incomplete if it failed to discuss what is perhaps the most influential and widely relied upon secondary source on the topic: Irving I. Gottesman’s 1991 *Schizophrenia Genesis: The Origins of Madness*. Since the early 1990s, this work has served as a major source of information for professionals and students interested in the causes of schizophrenia, and many textbooks include Gottesman’s figures (often in tabled form) on the “morbidity risks” of various relatives classified in terms of their degree of genetic relatedness to a person diagnosed with schizophrenia.

Schizophrenia Genesis, winner of the American Psychological Association’s 1992 William James Book Award, was put forward as a relatively accessible, balanced account of the manifestation and causes of schizophrenia. While every aspect of this book is ripe for critical analysis, Joseph concentrates on the chapters reviewing the evidence supporting the “diathesis-stress” (genetic predisposition) view of schizophrenia.²³ In Gottesman’s view, schizophrenia is “the same kind of common genetic disorder as coronary heart disease, mental retardation, or diabetes....”²⁴

Gottesman calculated pooled schizophrenia risks among different groups of relatives, distinguished by their varying degrees of genetic relatedness, and argued that these risks show that schizophrenia is strongly influenced by heredity factors. In doing so he developed his famous Figure 10, which illustrates that, according to Gottesman’s calculations, the more closely a person is genetically related to a person diagnosed with schizophrenia, the greater risk that person has of being diagnosed with schizophrenia as well. Joseph attempts to show, however, through a careful analysis of the data, that the risk factors Gottesman presented in his Figure 10, (1) include methodologically unsound and biased research, (2) are not reflective of more recent findings, (3) are inflated by Gottesman’s use of the probandwise concordance rate calculation in twin studies, and, most importantly, (4) are consistent with a completely environmental etiology of schizophrenia. Following this analysis, Joseph takes issue with several aspects of Gottesman’s description of published twin and adoption studies.

families. Researchers must assume that factors relating to the adoption process, including the policies of adoption agencies, did not lead to the placement of experimental group adoptees into environments contributing to a higher rate of the disorder in question. If this “no selective placement assumption” is false, a higher rate of the disorder among experimental group adoptees could be entirely the result of environmental factors.

²² Boyle, M. (2004, p. 81). “Schizophrenia” and genetics: Does critical thinking stop here? *Journal of Critical Psychology, Counselling and Psychotherapy*, 4, 78-85.

²³ The *Diathesis-Stress Theory* holds that a given disorder is caused by an inherited biological (genetic) predisposition in combination with environmental conditions or events. It is also known as the genetic predisposition theory.

²⁴ Gottesman, I. I. (1991, p. 84). *Schizophrenia Genesis*. New York: W. H. Freeman & Company.

After covering other problem areas in *Schizophrenia Genesis*, Joseph turns to Gottesman's attempt to dismiss several critics of psychiatric genetics on the grounds that they are "ideological." For his part, Gottesman wrote favorably of the German founding fathers of psychiatric genetics, such as Ernst Rüdin, Hans Luxenberger, Franz Kallmann, and Bruno Schulz. As Joseph shows, however, these founders were enthusiastic ideologues of eugenics, racial hygiene, and compulsory eugenic sterilization. According to the American psychiatric genetic researcher Myron Baron, who in 1998 wrote of the "past crimes of our discipline," Rüdin "played a central role in inspiring, condoning and promoting forcible sterilization and castration of schizophrenics...[whose] sterilization program was a precursor to the notorious 'euthanasia' program, which the Nazis implemented with characteristic efficiency and brutality."²⁵

As a whole, we could ask what positive contributions to the human condition the field of psychiatric genetics has made in its roughly 100 years of existence? Joseph argues that its influence has been overwhelmingly negative. According to the British psychologist Richard Bentall, the "fundamental error" of psychiatry is that "psychiatric disorders are genetic diseases." Bentall concluded,

No patient, not a single one, has ever benefited from genetic research into mental illness, although many have been indirectly harmed by it (because it has discouraged the development of adequate services for patients and, during one shameful period, was used to justify their slaughter). No effective treatments have so far been devised on the basis of genetic information and, given what we now know, it seems very unlikely that further research into the genetics of psychosis will lead to important therapeutic advances in the future. Indeed, from the point of view of patients, there can be few other areas of medical research that have yielded such a dismal return for effort expended.²⁶

CHAPTER SEVEN | Autism and Genetics: Much Ado About Very Little.

In Chapter 7, Joseph examines the evidence supporting autism as a genetically influenced disorder. Indeed, autism is often regarded as the psychiatric disorder most strongly influenced by genetics. Strikingly, however, the evidence is plausibly explained on non-genetic grounds. Behind the claims of autism as a "highly heritable strongly genetic" disorder lie a handful of small sample-size twin studies. There are no studies of twins reared apart. There are no adoption studies. There are no gene discoveries.²⁷ And, as is usually the case, the results of psychiatric twin studies are explainable on non-genetic grounds. Even Kendler, a staunch supporter of the idea that the major psychiatric disorders have an important genetic basis, recognized in 2010,

²⁵ Baron, M. (1998, p. 96). Psychiatric genetics and prejudice: Can the science be separated from the scientist? *Molecular Psychiatry*, 3, 96-100.

²⁶ Bentall, R. P. (2009, p. 145). *Doctoring the Mind: Is Our Current Treatment of Mental Illness Really Any Good?* New York: New York University Press.

²⁷ Akil et al. (2010); Plomin et al. (2008); Smoller, J. W., Sheidley, B. R., & Tsuang, M. T. (Eds.). (2008). *Psychiatric Genetics: Applications in Clinical Practice*. Washington, DC: American Psychiatric Publishing.

“It is common knowledge in our field that autism is among the most heritable of psychiatric disorders. Yet the empirical basis for this claim is slender as we have no adoption studies of autism and only a handful of classical twin studies, with small sample sizes, have been conducted.”²⁸

In contrast to other psychiatric disorders, there is evidence suggesting that autism is caused by biological factors. However, “biological” is not the same as “genetic,” and the current emphasis on alleged genetic factors drains away resources from research on potentially relevant biological causes, such as prenatal and postnatal exposure to mercury and other harmful substances. Autism molecular genetic research is covered in Chapter 11.

Genetically-oriented researchers and authors frequently cite autism as an example of what they see as the fallacy of purely environmental explanations of psychiatric disorders, often citing discredited decades-old “refrigerator mother” theories of autism. But even if autism were found to be caused by faulty genes, this would do little to strengthen genetic arguments about behavior in general. That true genetic disorders exist, such as Huntington’s Disease, does not mean that variations in human psychological traits in general have a genetic component, just as the fact that brain tumors exist does not mean that behavioral disorders in general are caused by brain diseases. And yet, as Joseph documents, there is little scientifically acceptable evidence supporting autism as a genetic disorder.

Finally, Joseph draws a comparison between current genetic theories of autism, and the mid-20th century genetic theory of polio (poliomyelitis). He shows that both theories were based on genetic interpretations of the results of family and twin studies, and suggests that contemporary autism researchers have made the same mistaken interpretation of these studies as did the polio genetic researchers before them.

CHAPTER EIGHT | The 1942 “Euthanasia” Debate in the *American Journal of Psychiatry*

In Chapter 8, Joseph describes and analyzes an astonishing 1942 debate in the *American Journal of Psychiatry*. There, neurologist Foster Kennedy argued in favor of “euthanizing” (that is, killing) “defective” and “feebleminded” people. According to Kennedy, “I am in favor of euthanasia for those hopeless ones who should never have been born — Nature’s mistakes.”²⁹ This had already occurred in Nazi Germany, where, even before the Holocaust, tens of thousands of “hereditarily defective” people were exterminated with the active participation of psychiatrists.³⁰

²⁸ Kendler, K. S. (2010, p. 1291). Advances in our understanding of genetic risk factors for autism spectrum disorders. *American Journal of Psychiatry*, 167, 1291-1293.

²⁹ Kennedy, F. (1942). The problem of social control of the congenital defective: Education, sterilization, euthanasia. *American Journal of Psychiatry*, 99, 13-16.

³⁰ Lifton, R. J. (1986). *The Nazi Doctors*. New York: Basic Books; Müller-Hill, B. (1998). *Murderous Science*. Plainview, NY: Cold Spring Harbor Laboratory Press. (Original English version published in 1988); Proctor, R. N. (1988). *Racial Hygiene: Medicine Under the Nazis*. Cambridge, MA: Harvard University Press.

In response, child psychiatrist Leo Kanner argued against killing because, in addition to being immoral, there would remain fewer people to perform society's dirty work. "Do we really wish to deprive ourselves," Kanner asked, "of people whom we desperately need for a variety of essential occupations?" He urged his fellow psychiatrists to "leave the cotton pickers, oyster shuckers and bundle wrappers alone, regardless of their IQ, so long as they are industrious and good natured!"³¹ Kennedy and Kanner were followed by an anonymous editorial leaning towards Kennedy's position in favor of killing. The editorial called on psychiatrists to focus their attention on the "morbid" attachment of parents opposed to the "disposal by euthanasia of their idiot offspring."³²

Joseph concludes by drawing parallels between the current popularity of genetic explanations of human behavioral differences, and the popularity of genetic theories that led to the unspeakable crimes of the Nazis, and to proposals such as those put forward by Kennedy. He warns that the current ascendancy of genetic theories, albeit on the basis of extremely unsound research, could lead to a rebirth of the eugenics movement and to new proposals similar to Kennedy's.

CHAPTER NINE | The Twin Method's Achilles Heel: A Critical Review of the Equal Environment Assumption Test Literature

Chapter 9 surveys a large body of literature that twin researchers cite in support of the equal environment assumption (EEA) of the twin method. Although Joseph argues in Chapter 1 (and argued previously in *The Gene Illusion*) that the EEA is untenable regardless of how twin researchers have defined it, twin method results are accepted without question in mainstream psychiatry publications. A major reason is that leading twin researchers argue that the EEA is supported by a number of empirical studies. Joseph performs a detailed critical review of these studies, and concludes that they do nothing to uphold the validity of the EEA.

Regardless of what "EEA test" studies find, however, the widely recognized greater environmental similarity of identical versus fraternal twin pairs *invalidates the twin method on its face*. Thus, the twin method is confounded by environmental factors regardless of what EEA-test researchers claim. What they actually must demonstrate — without qualification — is that identical and fraternal twin pairs experience roughly equal environments.

³¹ Kanner, L. (1942). Exoneration of the feeble-minded. *American Journal of Psychiatry*, 99, 17-22.

³² Anonymous. (1942). Euthanasia. *American Journal of Psychiatry*, 99, 141-143.

CHAPTER TEN | Bipolar Disorder and Genetics

In Chapter 10, Joseph challenges psychiatry's consensus position that bipolar disorder (BPD) is strongly influenced by genetic factors. Like schizophrenia, ADHD, and autism, he shows that the available evidence from kinship research lends little support to genetic theories of causation. As usual, the evidence consists mainly of family and twin studies, which cannot disentangle possible genetic and environmental influences. In addition, there have been a few adoption studies of affective disorders (of which BPD is one component). As Joseph clearly shows, no adoption study published to date has come close to providing evidence that genetic factors underlie bipolar disorder. In fact, the authors of one of the two most frequently cited adoption studies of bipolar disorder, while claiming to have found "a significant genetic contribution to unipolar depression and suicide," recognized their "failure to find such a differential for bipolar illness..."³³

Continuing a major theme of *The Missing Gene*, Joseph provides quotes from over two dozen publications whose influential authors claimed—falsely—that adoption studies provide evidence in favor of genetics for BPD as a component of the "affective disorder" umbrella, or that adoption studies discovered genetic influences on BPD as a distinct diagnosis. As Joseph shows, this simply is not the case.³⁴

One of many examples of secondary sources' faulty reporting of BPD genetic research Joseph cites is taken from the 1999 *Report of the U.S. Surgeon General*. According to this Report, "In studies of monozygotic twins reared separately ('adopted away'), the results also revealed an increased risk of depression and bipolar disorder compared with controls (Mendlewicz & Rainer 1977; Wender et al., 1986)."³⁵ However, neither Mendlewicz and Rainer, nor Wender et al., studied "monozygotic twins reared separately," or any other type of twins.³⁶

Authoritative secondary sources have played an important role in creating myths about psychiatric genetic research, leading professionals and students alike to believe that there is overwhelming evidence that the major psychiatric disorders have an important underlying genetic basis.

Joseph shows that, in fact, no such evidence exists.

³³ Wender, P. H., Kety, S. S., Rosenthal, D., Schulsinger, F., Ortmann, J., & Lunde, I. (1986, p. 923, 928). Psychiatric disorders in the biological and adoptive families of adopted individuals with affective disorders. *Archives of General Psychiatry*, 43, 923-929.

³⁴ One influential bipolar genetic researcher who recognized that BPD adoption studies are inconclusive was Elliot Gershon, who wrote in 1990, "We would conclude that the adoption data do not provide a broad base of supportive data on the hypothesis that [bipolar] disorders are transmitted before the age of adoption." See Gershon, E. S. (1990, p. 378). Genetics. In F. Goodwin & K. Jamison, *Manic-Depressive Illness* (pp. 373-401). New York: Oxford University Press.

³⁵ Surgeon General. (1999, Chapter 4, p. 256). *Mental Health: A Report of the Surgeon General*. Retrieved online 10/22/2004 from <http://www.surgeongeneral.gov/library/mentalhealth/pdfs/c4.pdf>

³⁶ Mendlewicz, J., & Rainer, J. D. (1977). Adoption study supporting genetic transmission in manic-depressive illness. *Nature*, 268, 327-329; Wender et al., 1986.

CHAPTER ELEVEN | Genotype or Genohype? The Fruitless Search for Genes in Psychiatry

Chapter 11 provides a detailed critical assessment of psychiatric molecular genetic research. The most remarkable result of this research is that, despite decades of sustained work, genes for the major psychiatric disorder have not been discovered.³⁷ Virtually all previous claims in favor of gene findings in psychiatry have failed replication attempts in subsequent studies.³⁸

Unfortunately, it is widely believed that such genes *have* been discovered. A major reason is that the media tends to report “gene discoveries” for abnormal behavior and psychiatric disorders (including those discussed in this chapter), but pays little attention to, or fails to report entirely, the inevitable replication failures and retractions.

Buried in the avalanche of sensational claims by researchers and reporters, we find more realistic evaluations by some prominent molecular genetic researchers. For example, by 2005 Kendler would write,

“The strong, clear, and direct causal relationship implied by the concept of ‘a gene for ...’ does not exist for psychiatric disorders. Although we may wish it to be true, we do not have and are not likely to ever discover ‘genes for’ psychiatric illness.”³⁹

Molecular genetic research in psychiatry is reaching the crisis stage as negative results continue to pile up. Indeed, veteran German psychiatric genetic researcher Peter Propping wrote the following sobering assessment in 2005: “Whereas genetically complex traits are being successfully pinned down to the molecular level in other fields of medicine, psychiatric genetics still awaits a major breakthrough.”⁴⁰ (In 2011, psychiatric geneticists are still awaiting a “breakthrough.”)

Three years later, psychiatric genetic researcher Stephen Faraone his colleagues observed, “It is no secret that our field has published thousands of candidate gene association studies but few replicated findings”⁴¹

³⁷ Akil et al. (2010); Latham, J., & Wilson, A. (2010). The great DNA data deficit: Are genes for disease a mirage? *The Bioscience Research Project* (retrieved online 12/18/10 from <http://www.biosciencesource.org/commentaries/article.php?id=46>); Risch, N., Herrell, R., Lehner, T., Liang, K., Eaves, L., Hoh, J., Griem, A., Kovacs, M., Ott, J., & Merikangas, K. R. (2009, p. 2463). Interaction between the serotonin transporter gene (5-HTTLPR), stressful life events, and risk of depression. *Journal of the American Medical Association*, 301, 2462-2471.

³⁸ Joseph, J. & Ratner, C. (2010). The fruitless search for genes in psychiatry and psychology: Time to re-examine a paradigm? *Council for Responsible Genetics: “Gene Myths Project.”* Available online at <http://www.councilforresponsiblegenetics.org/pageDocuments/1NX6VC0254.pdf>

³⁹ Kendler, K. S. (2005, p. 1250). “A gene for ...”: The nature of gene actions in psychiatric disorders. *American Journal of Psychiatry*, 162, 1243-1252.

⁴⁰ Propping, P. (2005, p. 2). The biography of psychiatric genetics: From early achievements to historical burden, from an anxious society to critical geneticists. *American Journal of Medical Genetics Part B (Neuropsychiatric Genetics)*, 136B (1), 2-7.

⁴¹ Faraone, S. V., Smoller, J. W., Pato, C. N., Sullivan, P., & Tsuang, M. T. (2008, p. 1). The new neuropsychiatric genetics. *American Journal of Medical Genetics Part B (Neuropsychiatric Genetics)* 147B, 1-2.

In a 2009 article published in the *Journal of the American Medical Association*, molecular genetic researcher Neil Risch and his colleagues recognized the failure of gene finding efforts in psychiatry and psychology, and that “few if any” findings have been substantiated:

“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. Few if any of the genes identified in candidate gene association studies of psychiatric disorders have withstood the test of replication.”⁴²

In a 2010 “Policy Forum” article published in the prestigious journal *Science*, three Nobel Prize winning researchers and their colleagues recognized the “frustrating lack of progress” in understanding the genetics of mental disorders.⁴³

Although most researchers continue to believe that genes both exist and await discovery, commentators Jonathan Latham and Allison Wilson concluded in late 2010 that the “dearth of disease-causing genes is without question a scientific discovery of tremendous significance,” and that, on the basis of this discovery, “most disease, most of the time, is essentially environmental in origin.” It must follow, according to these authors, that “heritability studies of twins are inherently mistaken or misinterpreted.”⁴⁴ Indeed, they are.

Instead of recognizing the possibility that decades of failed gene finding efforts may indicate that genes do not exist, which would necessitate a thorough re-examination of family, twin, and adoption studies, most researchers choose instead to emphasize *optimism* and de-emphasize *failure*. As Latham and Wilson observed, “The history of scientific refutation... is that adherents of established theories construct ever more elaborate or unlikely explanations to fend off their critics.”

A recent example of the use of optimistic rhetoric in place of drawing the balance sheet on the unexpected, decades-long failure to discover genes, is psychiatric geneticists James Hudziak and Stephen Faraone’s 2010 assessment of the status of molecular genetic research in child psychiatry:

“Only 10 years ago, the first draft of the human genome was reported. In the intervening period, genetic research on developmental psychopathology has grown exponentially, as reflected not only in the number of published papers but also in the power of molecular genetic and statistical technologies. Although we are only in the infancy of our field, the

⁴² Risch et al. (2009, p. 2463).

⁴³ Akil et al. (2010, p. 1580).

⁴⁴ Latham, J., & Wilson, A. (2010). The great DNA data deficit: Are genes for disease a mirage? *The Bioscience Research Project* (retrieved online 12/18/10 from <http://www.bioscienceresource.org/commentaries/article.php?id=46>).

pathway to discovery is clear. One can only imagine the incredible progress that will be made in the next decades.”⁴⁵

Rather than emphasize the failures to uncover the genes they believe underlie childhood psychiatric disorders such as ADHD and autism, and to recognize the possibility that they were wrong in believing that these genes exist, Hudziak and Faraone instead speak of the “exponential” growth of genetic research and the “power” of their technologies. They imply that the “number of published papers” constitutes scientific progress, instead of emphasizing that the findings of these published papers—literally thousands of them as Faraone had written in 2008—were not replicated. Hudziak and Faraone also implied that failures are to be expected because the field is only in its “infancy.” A full decade earlier, Faraone, in a reply to Joseph’s 2000 article on genetics and ADHD, also characterized ADHD molecular genetic research as being in its “infancy,” while claiming that “molecular genetic studies have already implicated several genes as mediating the susceptibility to ADHD.”⁴⁶

Finally Hudziak and Faraone, again choosing to de-emphasize decades of failure, claimed that the “pathway to discovery is clear,” and that “incredible progress... will be made in the next decades.” However, psychiatric geneticists have been saying this for 30 years. Rather than being in its infancy, two decades of molecular genetic studies of childhood psychiatric disorders have produced an important finding: The genetic basis of these disorders appears to have been refuted.⁴⁷ Thus, the main finding of the molecular genetic research they speak of is that *genes for childhood psychiatric disorders do not appear to exist.*

The standard explanation researchers give for failed gene finding efforts is that many genes of small effect cause these disorders, and that genes are difficult to find. Having shown in previous chapters that studies of families, twins, and adoptees are faulty, Joseph analyzes molecular genetic research in schizophrenia, ADHD, autism, and bipolar disorder. He concludes that the fruitless search for genes may be the result of psychiatry’s misplaced faith in the results of these previous kinship studies.

The following is a partial list of major problem areas in psychological and psychiatric molecular genetic research:⁴⁸

⁴⁵ Hudziak, J. J., & Faraone, S. V. (2010, p. 734). New genetics in child psychiatry. *Journal of the American Academy of Child and Adolescent Psychiatry*, 49, 729-735.

⁴⁶ Faraone & Biederman (2000, p. 572); see also Joseph, J. (2000). Not in their genes: A critical view of the genetics of attention-deficit hyperactivity disorder. *Developmental Review*, 20, 539-567, and Joseph, J. (2000). Problems in psychiatric genetic research: A reply to Faraone and Biederman. *Developmental Review*, 20, 582-593.

⁴⁷ Latham & Wilson (2010) made a similar point about the failure of molecular genetic studies to uncover genes causing common diseases. If we take the results “at face value,” they wrote, “genetic predispositions as significant factors in the prevalence of common diseases are refuted.”

⁴⁸ See Joseph, J. (2010). Genetic research in psychiatry and psychology: A critical overview. In K. Hood, C. Tucker Halpern, G. Greenberg, & R. Lerner (Eds.), *Handbook of Developmental Science, Behavior, and Genetics* (pp. 557-625). Malden, MA: Wiley-Blackwell.

- The field is massively plagued by false positive results. Clearly, some type of systematic error is common to many or most of these studies
- Researchers (usually mistakenly) assume that previous family, twin, and adoption studies have definitively established the genetic basis of the trait or disorder under study. Few have subjected this body of research to critical analysis
- Researchers frequently interpret negative results as evidence that the trait is more complex than they originally believed. Proponents of genetic theories have rhetorically transformed decades of fruitless gene finding efforts into evidence of the “complex genetic nature” of psychiatric disorders and psychological trait variation. It seems the more failures that are recorded, the more “genetically complex” these traits and disorders become
- The validity and reliability of psychiatric disorders, the establishment of which is a prerequisite for performing genetic research in psychiatry, is questionable⁴⁹
- Some methods and accompanying statistical calculations assume that some type of genetic transmission is occurring, although it is possible that, in reality, no genetic transmission is occurring
- The association (correlation) of a gene and a trait does not mean that the gene causes the trait, and a basic principle of statistics is that “correlation does not imply cause.” There are, in fact, several non-causal explanations for gene-trait correlations
- Even if a gene is a “necessary component” of a trait, it does not necessarily mean that the gene *causes* the trait⁵⁰
- Researchers rarely consider the possibility that the genes they are searching for do not exist
- It is often assumed that the discovery of genes would be an important achievement. However, focusing research and money on environmental interventions might be a far better choice, even if genes actually are involved

In 2005 Kendler attempted to reconcile the accumulating fruitless gene finding efforts with his interpretation of the results of family, twin, and adoption studies.⁵¹ He identified “four major research paradigms,” consisting of (1) “Basic genetic epidemiology” and (2) “Advanced genetic epidemiology,” which are based on family, twin and adoption studies, and the (3) “Gene finding” and (4) “Molecular genetics” paradigms, which respectively determine the genomic location of susceptibility genes, and the pathways from DNA variants to disorder. While recognizing that “a substantial portion” of psychiatric gene finding claims “do not survive the test of replication,” Kendler argued that family, twin, and adoption studies have found “genetic risk factors...for nearly all psychiatric and drug abuse disorders examined to date...” Moreover,

⁴⁹ Kirk, S. A., & Kutchins, H. (1992). *The Selling of DSM: The Rhetoric of Science in Psychiatry*. New York: Aldine De Gruyter.

⁵⁰ Ratner, C. (2004). Genes and psychology in the news. *New Ideas in Psychology*, 22, 29-47.

⁵¹ Kendler, K. S. (2005). Psychiatric genetics: A methodologic critique. *American Journal of Psychiatry*, 162, 3-11. An exchange between Joseph and Kendler can be found in the October, 2005 edition of *The American Journal of Psychiatry*
http://jayjoseph.net/yahoo_site_admin/assets/docs/Joseph_Kendler_2005_AJP_Letter_Exchange.15582343.pdf

“Unless there are strong and consistent methodologic biases operating across study designs, this body of work indicates that genetic risk factors are of substantial etiologic importance for all major psychiatric and drug disorders.”

However, Joseph argues that family, twin, and adoption studies do indeed suffer from “strong and consistent methodologic biases operating across study designs.”

Kendler then noted that the “low” replication level for linkage findings “contrasts strikingly with the high level of consistency seen in the results of genetic epidemiologic studies — for example, the results of family and twin studies of schizophrenia.” In fact, there is no striking contrast between these results *if they are viewed as evidence supporting a purely environmental etiology for psychiatric disorders*. With respect to a particular disorder, environmental theories of causation predict (a) familial clustering, (b) higher concordance of identical versus fraternal twins, and (c) the failure to find genes. And this is precisely what we find.

Rather than consider a purely environmental explanation as a competing paradigm, Kendler argued that molecular genetic studies cannot be used to test “whether a twin or adoption study was correct in its conclusion that disorder x is heritable...” This may have been true in the past, but enough negative data has come in to allow us to conclude, as did Latham and Wilson, that decades of fruitless gene finding efforts in psychiatry constitute “a scientific discovery of tremendous significance.”

Although Kendler viewed the four strategies he outlined as “competing paradigms,” Joseph argues that all four are components of the *same* biological/genetic paradigm, in contrast to what we might call the “environment/treatment/stress” paradigm.

Finally, Kendler called for integrating the four “paradigms” he identified, which would “require an appreciation of the complementary sources of information obtained by genetic epidemiologic and gene identification approaches.” Kendler called this “explanatory pluralism,” but what this means in practice is falling back on family, twin, and adoption results to explain the unexpected failure to find genes. It would be far better, in Joseph’s view, to re-examine the assumptions, methods, and biases of these studies in the context of considering the possibility—merely the possibility—that genes for the major psychiatric disorders do not exist.

* * *

The psychiatric genetics field is now suffering the consequences of the enormously flawed and biased research it has produced. As Joseph describes and documents in detail in *The Missing Gene*, and previously in *The Gene Illusion*, 100 years of psychiatric genetic research has been plagued by factors such as (1) the frequent denial of, or failure to mention, the fact that the origins of psychiatric genetics lie in eugenics and racial hygiene; (2) the reliance on highly questionable theoretical assumptions; (3) changing the definition of particular mental disorders to ensure results in favor of genetics; (4) non-blinded diagnoses and zygosity determination⁵²; (5) unwarranted assumptions about the reliability and validity of psychiatric diagnoses; (6) arbitrary and biased methods of counting relatives; (7) putting forward statistically non-significant results as evidence in favor of genetics; (8) the failure to take potential environmental confounds seriously; (9) ignoring, distorting, and dismissing important observations by critics; (10) overlooking critical methodological flaws; (11) ignoring, attempting to discredit, or twisting the results of studies whose results do not fit genetic predictions; (12) conclusions drawn more from

⁵² *Zygosity Determination* refers to the method used to determine whether a given twin pair is identical or fraternal.

researchers' beliefs than from the data itself; (13) the interpretation of family data as evidence in support of genetics; (14) textbooks' creation of myths about "landmark" psychiatric genetic studies and the existence of "overwhelming" evidence in support of genetic influences on mental disorders; (15) the rhetorical conversion of hypotheses into "facts"; (16) a reliance on secondary sources' interpretation of previous research; (17) the premature conclusion that previous kinship research proves that genes for mental disorders must exist; (18) basing linkage results on models assuming a genetic transmission of the condition under study; (19) the use of rhetoric as a means covering up the unexpected and disappointing failure to find genes; and, finally (20) the transformation decades of fruitless gene finding efforts into evidence of the "complex genetic nature" of psychiatric disorders.

Joseph ends by writing that the sum total of these items leads to the following conclusion: *Genes for the major mental disorders are unlikely to exist.*

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