

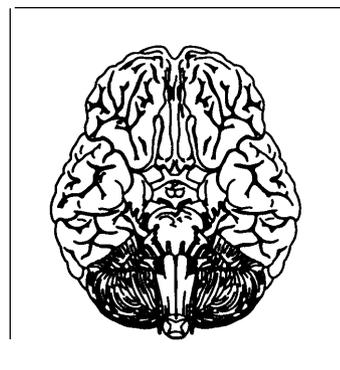
Introduction | 1

In January 1993, the Office of Technology Assessment (OTA) and the National Institute of Mental Health (NIMH) convened a workshop-Understanding the Role of Genetic Factors in Mental Illness: Bridging the Gap Between Research and Society (box 1-1). It reportedly is the first comprehensive discussion focused specifically on the implications of genetics and mental disorders research (5).

All participants acknowledged that the subject of genetics and mental disorders is a complex, consequential, and controversial one. Researchers have long examined the role of inheritance in mental disorders, accumulating evidence over the course of this century. Fast-paced advances in genetics in the 1980s catalyzed more intense interest in the inheritance of mental disorders, and researchers brought to bear new and powerful research tools on these seemingly unfathomable diseases.

The result was exhilarating optimism followed by intense skepticism. The locations of genes linked to bipolar disorder, Alzheimer's disease, and schizophrenia were announced to much fanfare. Media attention and optimism soon plummeted, however, when emerging data proved perplexing, some findings were retracted, and further progress evaded researchers. Naysayers condemned outright the idea that genes contribute to mental disorders at all.

That the genetics of mental disorders would prove difficult to resolve comes as no surprise to long-time experts in the field. "The primarily negative results. . . have led some to become pessimistic. However, I cannot share this pessimism. As a scientist committed to solving this problem, I have always believed that finding genes for schizophrenia would not be easy" (10). What does give cause for alarm is the either-or reduction of this issue:



2 | Mental Disorders and Genetics: Bridging the Gap Between Research and Society

BOX 1-1: Agenda for the OTA-NIMH Workshop

Understanding the Role of Genetic Factors in Mental Illness: Bridging the Gap Between Research and Society

AGENDA

Thursday ~~afternoon~~ January 21, 1993

1:00-1:30 Opening Remarks

Herbert Paroles, M. D., Workshop Chair
Frederick K. Goodwin, M. D., Director, NIMH
Roger Herdman, M. D., Assistant Director, OTAI
Laura Lee Hall, Ph. D., Senior Analyst, OTA
Kate Berg, Ph. D., Schizophrenia Research Branch, NIMH

1:30-1:45 introduction of Workshop Panelists

1:45-3:15 Current Scientific Understanding of Genetic Factors in Mental Disorders

That genetic factors contribute to major mental disorders has been established by various types of studies. However, the extent and nature of the genetic input have not been established and are the subject of intensive research. During the discussion, panelists will consider the following questions:

What is the evidence that severe mental disorders—schizophrenia, major mood and anxiety disorders, and Alzheimer's disease—have a genetic component?

What models exist to explain the genetic contribution? What are the limits of these models?

What is the status of linkage analysis studies of mental disorders?

3:30-5:00 Scientific Findings and Recurrence Risks

Even without complete understanding of the precise role that genetic factors play in major mental disorders, individuals with these conditions and their family members have begun requesting information on recurrence risk. In their discussion, panelists will consider the following questions:

Based on current data, what information about recurrence risks can be given?

What are the limitations of recurrence risk information?

Will genetic tests for major mental disorders be available in the near future?

What concerns surround the relay of information concerning genetic risk for a mental disorder?

5:00-5:15 Comments by Workshop Observers

5:15-5:30 Summary by Dr. Paroles

Friday, January 22, 1993

9:15-9:30 Opening Remarks by Dr. Paroles

9:30-10:45 The Genetic Counseling Milieu

Inevitably, the relay of information on health and genetic status in the clinical setting is laden with challenges. These challenges are amplified in the case of the genetics of mental disorders, in which the con-

¹Dr Herdman was appointed director of OTA in May 1993

BOX 1-1 continued: Agenda for the OTA-NIMH Workshop

tribution of both genetic and nongenetic factors is not yet completely understood. The panelists will address the issues that surround the relay of this information in the clinical setting, including the following questions:

- What is the utility of genetic counseling for mental disorders given the current state of knowledge?
- What benefits and limits do various professions—psychiatry, genetic counseling, social work—bring to genetic counseling for mental disorders?
- What additional training may be needed to help care-providers remain current in their understanding of the genetic factors involved in mental disorders?
- What family planning considerations emerge—e.g., varying perceptions of burden of illness, pregnancy and child-bearing issues?

11:00-12:15 Perceptions of Genetics and Mental Illness

Ignorance of and negative attitudes attached to mental illness abound in our society. Actual information about the genetic components of mental disorders counters many of the erroneous and cruel perceptions about the causes of these conditions. However, the complexity of the genetics of mental illness, and the interplay of nongenetic factors, impedes the easy relay of accurate information. In their discussion, panelists will consider the following questions:

- Given the potency of reports about gene discoveries, how best can research results be disseminated to the scientific and lay press?
- What lessons can be drawn from experience with the stigmatization of other genetic illnesses?
- Are there needs for pro-active efforts to accurately educate the public on these issues?

1:30-3:15 Ethical and Legal Issues

Ethical and legal issues often arise with scientific advances. Genetic research in mental illness is no exception. Questions arise in relation to the actual collection of data, the way in which data are perceived, the context of clinical practice, and the broader social sphere. In discussing relevant ethical and legal concerns, the panelists may consider the following questions:

- What ethical and legal issues surround pedigree studies? What safeguards can be incorporated to protect subject rights without obstructing needed research?
- Are there special informed consent issues involving patients+ children, patients with dementia, actively psychotic patients?
- What issues are raised by subject recruitment?
- Who should have access to information on patients' and family members' current or future health and genetic status that is unveiled in research? Researchers? Institutions funding and supporting research? Other family members? Subjects themselves? Personal clinicians? Insurance companies or employers?

3:30-5:15 An Agenda for Future Research

Given the current state of knowledge and the discussion at the workshop, what kinds of basic, clinical, and social science research are possible? Needed?

5:15-5:30 Comments by Workshop Observers

5:30-5:45 Concluding Comments by Dr. Paroles

schIzoPhrenia and GENETIC RISKS

A GUIDE TO GENETIC COUNSELING

*for patients,
their families,
and
mental health workers*

by

**Irving I. Gottesman, Ph.D.
and
Steven O. Moldin, Ph.D.**



National Alliance for the Mentally Ill

The National Alliance for the Mentally Ill (NAMI) published the second printing of this 11-page pamphlet on schizophrenia and genetic risks in 1992. The NAMI pamphlet represents one of the few, if not the only, source of information for people with mental disorders, their family members, and mental health care providers. The text of this unique resource describes genetic counseling, schizophrenia, and what is known about the inheritance of this condition.

“the mental disorder gene has been found” versus “no genetic contribution exists at all.” Vacillating between jubilant claims of successful gene finds and reactionary doubts impedes the sophisticated and tenacious pursuit needed for a better understanding of the genetic and nongenetic factors involved in mental disorders. As noted by leading geneticists, “the main thrust of modern molecular medicine is towards precisely defining etiology both at the molecular level and at the level of interplay between genes and environment” (6).

The prevailing controversy also obscures the implications of this research for people with mental disorders and their families. Representatives from NIMH and consumer organizations testify to the increasing number of consumer requests for information about the genetics of mental disorders (1,4). Little communication of data from researchers to clinical care-providers and consumers occurs. The ethical and social implications emerging from the conduct of research and research results have received even less notice, in contradistinction to genetic research in general (box 1-2).

The workshop follows up on a 1992 OTA report—*The Biology of Mental Disorders*—requested by several House Committees and endorsed by Senator Edward M. Kennedy, Chairman of the Senate Committee on Labor and Human Resources (11). The report reviewed data concerning the contribution of genetic factors to several severe mental disorders, described methodologies used in the studies, and broached several policy issues relevant to this area of research. NIMH, with its ongoing and substantial support for research into the genetics of mental disorders (table I-1), as well as its interests in related areas of public policy, supported further exploration of the issues raised by genetic research. Building on this base, the OTA-NIMH workshop attended to four major topics:

- the current understanding of genetic factors in mental disorders, including Alzheimer’s disease, schizophrenia, major mood disorders, panic disorder, and obsessive-compulsive disorder;
- ethical issues in research;
- the communication of genetic information in the clinical setting; and
- perceptions and social implications of genetics and mental disorders.

¹Requesters included the House Committees on Appropriations; Energy and Commerce; Science, Space, and Technology; Veteran Affairs; and the Senate Subcommittee on Science, Technology, and Space of the Committee on Commerce, Science, and Transportation.

BOX 1-2: The Ethical, Legal, and Social Issues Programs of NIH and DOE

Since fiscal year 1988, Congress and the executive branch have made a commitment to determine the location of all human genes (e.g., as has been done for sickle cell anemia, cystic fibrosis, and Tay-Sachs disease). The Human Genome Project is estimated to be a 15-year, \$3-billion project. It has been undertaken with the expectation that enhanced knowledge about genetic disorders, increased understanding of gene-environment interactions, and improved genetic diagnoses can advance therapies for the 4,000 or so currently recognized human genetic conditions.

To address the ethical, legal, and social issues of the Human Genome Project, and to define options to address them, the National Institutes of Health (NIH) and the Department of Energy (DOE) each funds an Ethical, Legal, and Social Issues (ELSI) Program. Funds for each agency's ELSI effort derive from a set-aside of 3 to 5 percent of appropriations for the year's genome initiative budget. In fiscal year 1991, DOE's ELSI spending was \$1.44 million (3 percent); in fiscal year 1992, \$1.77 million (3 percent). Its fiscal year 1993 spending was targeted at \$1.87 million. NIH's ELSI spending for fiscal years 1990 and 1991 has been \$1.56 million (2.6 percent) and \$4.04 million (4.9 percent) respectively. NIH's ELSI spent \$5.11 million (5 percent) for fiscal year 1992 and aimed to spend \$5.30 million in fiscal year 1993 (5 percent).

ELSI funds bioethics research related to the Human Genome Project to expand the knowledge base in this area. The program operates in the model of peer review competition for grant funds. The ELSI Working Group, which advises both programs, initially framed the agenda and established priority research areas. Nevertheless, the nature of grant programs means the ultimate direction evolves from the bottom up—i.e., from the individual perspectives of researchers pursuing independent investigations—rather than from the top down—i.e., through policy makers or an overarching federal body. Furthermore, no formal mechanism exists for ELSI-funded research findings to directly make their way back into the policy process. And although the ELSI programs have a large funding base for grants, they lack resources for in-house policy analysis. The ELSI Working Group, however, has played a role in policy analyses related to genetics and the Americans With Disabilities Act, cystic fibrosis carrier screening, and genetic research involving several family members.

SOURCE U.S. Congress, Office of Technology Assessment, Biomedical Ethics U.S. *Public Policy—Background Paper*, OTA-BP-BBS-105 (Washington, DC: U.S. Government Printing Office, June 1993).

The text of this background paper recounts the workshop discussion, supplementing it with information from the previous OTA report and new research data and sources.

We can conclude that genetic factors contribute to many of the major mental disorders discussed in this report. Indeed, researchers have located and in some cases identified specific genes involved in Alzheimer's disease. The consistent evidence for a genetic contribution to schizophrenia and major mood disorders, together with the rapid advances in molecular genetics, makes continued research in this area a promising endeavor. But progress is likely to be slow, given the complexity of these conditions.

Workshop panelists agreed that what we currently know about the genetics of mental disorders has implications for our society. Genetic research into mental disorders raises ethical issues for people with these conditions and their family members who participate in such studies; these issues warrant ongoing consideration. Individuals with mental disorders and their family members seek information about the risk of mental disorders that their other family members or offspring may face. Available data can shed light on this risk. But such information is generally not specific or detailed. Furthermore, most mental health care-providers and genetic counselors are not equipped to offer genetic counseling services for

TABLE 1-1: NIMH Genetic Research Investment for Fiscal Year 1991^a

	Total costs of genetic research	Number of grants	Percentage of total budget
Division of Clinical Research	\$25,629,833 ^b	88	15.0
Division of Basic Brain and Behavioral Sciences	13,351,201	55	10.9
NIMH total	38,981,034	143	8.7

^aThese figures represent funding for research where the primary focus is human genetics of mental disorders. ^bOf this figure, \$2,060,812, or 8.14 percent, of the Division of Clinical Research's genetic budget is devoted to Diagnostic Centers Cooperative Agreements.

SOURCE: National Institute of Mental Health, 1992.

mental disorders. Finally, many individuals with mental disorders and their family members find comfort in the ongoing pursuit of genes involved in mental disorders. These genetic advances as well as society's perception of them could present problems, however, if used in a discriminatory fashion.

EMERGENT WORKSHOP THEMES

While the workshop discussion considered a variety of topics, a few themes emerged that imbued nearly each subject brought up by the workshop participants:

- the transitional stage of research;
- the specious but persistent nature-versus-nurture debate;
- family as a key focus of concern;
- negative attitudes attached to mental disorders; and
- the information gap.

The transitional stage of research. Several workshop participants acknowledged that research of the genetics of mental disorders has entered a transitional stage, characterized by rapid technological developments, complex research issues, and unpredictable course. Difficulties presented by the research stubbornly persist. Although several experts have adeptly described the problems that originally beset linkage analysis of mental disorders, no one can fully explain the nonreplication and reversal of results character-

istic of the field to date (3,8,9). Also, scientists grapple with fundamental issues—diagnostic categories, subtypes of disorders, and the best-fitting genetic models—as they fashion more sophisticated hypotheses. These questions juxtapose continued efforts and advances. Research tools are evolving rapidly. Scientists can more promptly confirm or disclaim data implicating a link between a genetic location and mental disorder. Researchers resolutely trudge forward with linkage studies, collecting data and specimens from large, extended families and other pedigree types.

This transitional stage does not negate the accrued evidence from family, twin, and adoption studies strongly supporting a genetic contribution to some mental disorders. Rather, this stage implicates the complexity of these conditions and their underlying causes. It also complicates decisions about research support, educational efforts, and speculation about social implications.

The specious nature-versus-nurture debate. As already noted, this debate persists. Scientists, commentators, and analysts often frame data from research in all-or-nothing terms: a single gene completely explains a disorder or genes have no impact whatsoever on these conditions. Rebutting such simplistic conclusions, data point to heterogeneous causes, including genetic and nongenetic factors, at play in mental disorders. Nonetheless, nature-versus-nurture sloganeering too frequently holds sway in media presentations and analyses.

This false polarization fuels continued controversy, fear, and ignorance, thus compelling the dissemination of factually correct information.

Family as a key focus of concern. When talking about genetics, one is necessarily talking about families. Research studies involve not just a single participant; whole families may participate. Family members and prospective spouses may seek information about the risk of mental disorder in offspring. Public policies about insurance coverage and employment impact on people with mental disorders and family members alike. Unfortunately, policies that guide the way in which research is performed, clinical information is relayed, and legislation is fashioned have yet to grapple fully with family involvement.

Negative attitudes attached to mental disorders. No discussion of mental disorders can ignore the stigma and discrimination attached to these conditions. Although attitudes are apparently improving (2), often people with mental disorders are feared, avoided, and disparaged (for review of data, see 11,12). Their family members have long stood accused of poor parenting or neglect. This reality of mental disorders colored every issue discussed at the workshop, including family support for research, concerns about privacy of research and clinical information, and skepticism among consumers and other analysts about the application of genetic technology.

The information gap. Complex data, controversy, and negative attitudes result all too often in ignorance and misinformation about mental disorders and genetics. Workshop panelists pointed out the many faces of this information gap. People with mental disorders and their family members hunger for information on genetic research to help them make sense of their condition and the confusing reports that appear in the media. In order to provide this information to consumers, mental health care-providers need a better understanding of genetic data as well as the principles of genetic counseling; genetic counselors require information on mental disorders. Researchers and panels reviewing research ethics require information on the risks and unique issues presented by genetics and mental disorders. Members of the press also

need accurate and understandable information to assist them in gaining perspective on newly reported findings (7). Finally, accurate information directed at society at large—about genetics and mental disorders—may help prevent or at least diminish injurious social perceptions and policies.

CHAPTER 1 REFERENCES

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