



Pathways to Health

Charting the Science of Brain, Mind, and Behavior

A Research Strategic Plan for the National Institute of Mental Health Fiscal Years 2000 - 2001

Pathways to Health:
*Charting the Science of Brain,
Mind, and Behavior*

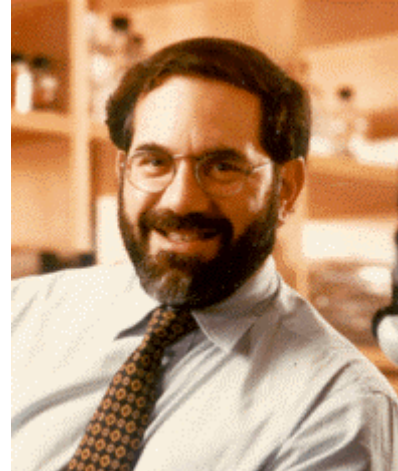
**A Research Strategic Plan for the
National Institute of Mental Health
Fiscal Years 2000 - 2001**

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A MESSAGE FROM THE DIRECTOR

We are pleased to present the Research Strategic Plan for the National Institute of Mental Health (NIMH) for years 2000 and beyond. Many persons and organizations across the United States contributed to the development of this Plan, by means of processes described below. We greatly appreciate their input.



We also acknowledge with thanks and respect the millions of Americans who are increasingly willing to voice their concerns, questions, and insights about the impact of mental illness on individuals and families – and, to voice, as well, their impatience with the gaps in our knowledge about diagnosing, treating, and preventing mental and behavioral disorders.

Fifty years ago, mental illness was poorly understood, often feared, and seldom mentioned. Families with a loved one with a severe mental disorder all too frequently were shamed into silence. Contrast that tragic period of silence and shame with signal events concerning mental illness and health in 1999:

- The White House convened citizens from around the country to call attention to the import and urgency of the Nation's mental health needs. Held at Howard University, in Washington, DC, with the President, the First Lady, the Vice President, and Mrs. Tipper Gore all actively participating, the White House Conference on Mental Health was an important and highly visible means of educating Americans about research and service needs and abolishing the stigma attached to mental disorders.

- U.S. Surgeon General Dr. David Satcher issued the first-ever Surgeon General’s Report on Mental Health.¹ On the strength of conclusions that mental disorders are real illnesses that impose an immense burden of disability on our Nation, and that treatments of well-established efficacy exist, Dr. Satcher urged Americans who are experiencing mental health problems or who have a mental disorder to seek help. The media’s and the public’s response to the Report has been phenomenally positive and has encouraged the Surgeon General to initiate follow-up reports that address the particular mental illness and health concerns of racial and ethnic minorities and youth violence. The Surgeon General also designated the prevention of suicide – a lethal outcome of mental illness – as a public health priority.

- Secretary of Health and Human Services, Dr. Donna Shalala, followed up the White House Conference with an initiative that will focus department-wide resources on national mental health needs, ranging from research on the causes, treatment, and prevention of mental disorders to the provision of essential mental health services that are accessible and affordable to all Americans.

- In another mental health “first,” the Federal government’s *Healthy People 2010* objectives designated mental health as a “leading health indicator” for the Nation. This status ensures that improvements in mental health care will serve as a high-profile benchmark for State, local, and Federal agencies to use in assessing the progress of health initiatives. The *Healthy People 2010* objectives will direct attention at every level of governance to health disparities, particularly as experienced by racial and ethnic minority group members.

¹ U.S. Department of Health and Human Services. Mental Health: A Report of the Surgeon General. Rockville, MD: U.S. Department of Health and Human Services, Substance Abuse and Mental Health Services Administration, Center for Mental Health Services; National Institutes of Health, National Institute of Mental Health, 1999.

This extraordinary public focus on mental illness and mental health adds urgency to this NIMH Research Strategic Plan. We hope to greatly extend the readership of the printed plan through its publication on the world-wide web, at <http://www.nih.nimh.gov>.

We are gaining, on virtually a daily basis, vital information about how the brain works when it is healthy and what can go wrong when mental illnesses occur. Many scientists and advocates are confident that, today, the intersection of neuroscience and behavioral science relevant to understanding mental illness and health marks a point of unparalleled scientific excitement. Indeed, despite strong support for mental illness research in the Congress and the White House, it nonetheless remains a challenge to exploit every scientific opportunity or meet every expectation.

Such difficulties understandably exacerbate the frustration that parents feel as they watch a talented son spiral into schizophrenia, or a daughter waste away from a disorder such as anorexia nervosa; the anger that one might experience when confronted with the unrecognized or untreated symptoms of depression in a spouse; the sorrow in family members that accompanies the onset of Alzheimer's disease.

We at NIMH share the Nation's optimism and impatience. This Research Strategic Plan represents our best effort at this point in time to match remarkable scientific opportunities with "public health need," which we recognize as a statistical representation of one person's experience with mental illness, multiplied many millions of times over.

The overarching goal of NIMH – *to reduce the burden of mental illness through research on mind, brain, and behavior* – challenges us to comprehend the awesome complexity of the brain and its role in every aspect of human behavior. A further challenge is to use the knowledge gained through our research to understand the impact of behavior upon

diseases and help people prevent behaviorally influenced diseases, such as HIV/AIDS. We are confident that progress in responding to the scientific challenges will diminish greatly the lingering stigma that is attached to the illnesses and disorders we study.

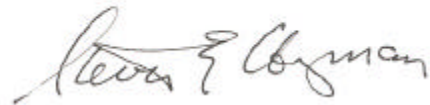
Our Research Strategic Plan opens with a brief listing of *Extraordinary Opportunities* that sketch, in broad-brush strokes, our scientific goals over the next several years. *Setting the Stage* describes priority planning efforts that I have initiated or implemented since being appointed as Director with the aim of strengthening the participation of the broad scientific community and the public in the task of setting an NIMH research agenda. The heart of the Plan is contained in the sections on *Immediate Research Goals*, which identify next, achievable steps that the NIMH will take to achieve its statutory and scientific mission. We close with information about mental illness and mental health in our Nation in the year 2000 and a discussion of our rationale for a Strategic Plan and the process we used to develop it, including a description of efforts we have taken to obtain broad participation in the development of the Plan.

In the months and years ahead, it is likely that scientific breakthroughs in one area will be countered by disproven hypotheses in another, and that the public health agenda will continue to shift with changes in the make-up and age of the Nation's population. Just as research is a dynamic process, the Strategic Plan will continue to be modified and, thus, continue to benefit from the input of the citizenry. Accordingly, this initial Research Strategic Plan considers opportunities that exist across the full breadth of the Institute's scientific portfolio. We intend that future iterations of the Plan will focus more selectively on topics of immediate promise and pressing scientific and public health need. For example, a plan to reduce disparities in mental health among

ethnic minorities is set forth on our web site at

<http://www.nimh.nih.gov/strategic/strategicdisparity.cfm>.

Because we have much yet to learn, we are thankful that we have many dedicated allies in the struggle to conquer mental illness and to develop information needed to promote mental health at every stage of a person's life. In light of the immense challenges that remain, we hope this Plan will stimulate our readers' ideas about the future science of mind, brain, and behavior. We welcome your thoughts.

A handwritten signature in black ink, appearing to read "Steven E. Hyman". The signature is fluid and cursive, with the first name "Steven" and last name "Hyman" clearly legible.

Steven E. Hyman, M.D.

Director

EXTRAORDINARY RESEARCH OPPORTUNITIES

In looking to the future, scientists agree that rapid advances in genetics, neuroscience, and the behavioral sciences have framed extraordinary opportunities for mental health research. The burden of mental illness demands that we exploit these opportunities fully and rapidly. Thus, our research goals and objectives, detailed in subsequent sections, seek to mold these key scientific areas to critical public health needs.

Brain Science

Neuroscientists are gaining the ability to determine just how brain cells and circuits function to enable cognition, emotion, and behavior. This progress further challenges researchers to apply this fundamental knowledge – along with information about how the brain changes as it develops and ages – to reveal precisely what parts of the brain are disturbed in mental illness.

Genetics

The imminent “complete draft” of the Human Genome will provide enormous impetus to ongoing efforts to identify the genes responsible for vulnerability to mental and behavioral disorders; combined with growing knowledge of how these disorders are inherited within families and with information about the environmental triggers needed to activate vulnerability, the genetics revolution permits us to anticipate one day using the word “cure” in the context of mental illness.

Behavior

The explosion in new knowledge about the genetics, structure, and function of the brain challenges behavioral scientists to radically expand the traditional boundaries and methods of their discipline to determine how specific behaviors are directed and influenced by genes, how behavior can modify brain biology, how behavioral

treatments for mental disorders may be strengthened, and how behavioral strategies for the prevention of diseases may be refined.

Treatment

With greater understanding about brain mechanisms involved in memory, decision-making, and emotional responses to traumatic events, there is a growing need to revisit and redesign many of the treatments currently in use for mental disorders. Translation of basic science findings into innovative behavioral and pharmacological strategies that can either correct or compensate for brain dysfunctions will yield more effective treatments. At the same time, understanding and correcting disparities between ethnic minorities in access to and quality of mental health treatment services obtained will present immediate benefits to consumers, family members, and clinicians.

Children

Childhood and adolescence are critical developmental periods that have lifelong ramifications for mental health. Among immediate challenges to researchers are understanding the childhood precursor forms of adult mental illnesses and how and when to intervene preventively in high risk instances; designing the most effective mental health care services for children and adolescents; and recognizing the biological, behavioral, and environmental roots of violence and aggression so as to intervene in a timely and productive way.

Brain Imaging

Advances in the temporal and spatial precision of brain imaging technologies are being matched by reductions in cost and invasiveness of procedures; the net effect is to enhance the practicality of approaches that will image brain function in real time and over periods of development. The monumental challenge today is to link technological prowess to activation models capable of illuminating the complexities and subtleties of brain dysfunction in the onset and course of specific mental disorders.

Disparities in Mental Health

Gender, along with social, cultural, or ethnic factors, is known to increase the susceptibility of some groups of people to certain mental and behavioral disorders. Their response to treatment, their access to and utilization of mental health care, and, importantly, their resiliency, also may be influenced by the same factors. NIMH is dedicated to broadening the diversity of mental health researchers with the expertise and commitment to identify and accommodate for these factors, and to broadening the diversity of populations studied.

NATIONAL INSTITUTE OF MENTAL HEALTH

The National Institute of Mental Health (NIMH) is the largest scientific organization in the world that is dedicated to research focused on the understanding, treatment, and prevention of mental disorders and the promotion of mental health. NIMH is one of 25 components of the National Institutes of Health (NIH), the principal biomedical and behavioral research agency of the United States Government and part of the U.S. Department of Health and Human Services. Authorized in 1946, NIMH is one of the earliest NIH institutes.

Through its extramural research program, NIMH supports more than 2,000 grants and contracts to scientists at universities and other institutions across the country and overseas. The investigators propose most of these projects themselves through grant applications, which undergo extensive scientific review before receiving funding. The scientists then must apply for renewal of the grants at intervals in order to receive continued funding.

NIMH also conducts research within an intramural program, located on the NIH campus in Bethesda, MD. The Mental Health Intramural Research Program consists of approximately 500 scientists in 22 laboratories and branches. Intramural scientists include molecular biologists, geneticists, and behavioral scientists conducting research on fundamental processes and clinical investigators who work with patients at the NIH Clinical Center. The stable funding available through the program makes possible long-term clinical studies that would be difficult for extramural researchers to accomplish. Also, because it involves basic science as well as clinical research, the program is structured to facilitate interdisciplinary studies.

The NIMH budget for fiscal year 1999 was \$859 million. Of the NIMH research budget, 83% is spent on extramural research conducted at facilities across the country, 13% is spent on intramural research, and 4% is spent on research management support.

Mission of NIMH

The mission of the National Institute of Mental Health is to reduce the burden of mental illness and behavioral disorders through research on mind, brain, and behavior.

Vision

NIMH research has opened new windows of opportunity in the national effort to reduce the burden of mental illness through research. Sustained investments in basic brain and behavioral science have positioned the Institute to exploit recent advances in neuroscience, molecular genetics, brain imaging coupled with cognitive research, and information technology; to translate new knowledge about fundamental processes into researchable clinical questions; and to initiate innovative clinical trials of new pharmacologic and behavioral interventions, with emphasis on testing their effectiveness in the diagnostically complex, diverse group of patients typically encountered in front-line service delivery systems.

Mindful of the important contributions of many disciplines to the Institute's broad scientific mission, NIMH supports the development and, where warranted, encourages a refocusing of a wide range of science including, but not limited to, neuroscience, behavioral science, clinical research, epidemiology, prevention research, and mental health services research. AIDS remains a potent threat to health globally and NIMH will continue to work with the NIH Office of AIDS Research in the development of a strategic plan and contribute to the conquest of AIDS through the support of behavioral research that helps to elucidate mechanisms of risk-behavior change and fosters patients' active participation in, and compliance with, often-difficult treatment regimens. An invaluable benefit of the Institute's investment in AIDS prevention is a steadily accelerating appreciation and utilization of knowledge derived from behavioral science throughout the fields of health and medical care.

Ultimately, information gleaned from all research supported and conducted by NIMH will be translated into the design and evaluation of treatment delivery strategies, settings, and systems that are relevant and responsive to the needs of persons with and at risk for mental illness. A thrust of this research will be to eliminate the effects of disparities that impinge on the mental health status of all Americans, including women, children, elderly people, people living in poverty and ethnic/cultural minority groups.

In this era of opportunity, NIMH must direct renewed attention to the education and training of future mental health researchers, including scientists trained in molecular science; cognitive and affective neuroscience; clinical, behavioral, and services research; and other disciplines urgently needed in studies of mental illness and the brain. Such training efforts will strive to ensure that the pool of mental health researchers reflects a multidisciplinary and diverse perspective that is representative of both advancing scientific capabilities and the diversity of our society.

As NIMH develops and refines this and successive Research Strategic Plans to turn this vision into reality, the Institute will rely upon advice from a broad spectrum of sources – researchers, care-givers, people with mental illnesses and their families, policymakers, and others – to help shape the plan.

SETTING THE STAGE FOR STRATEGIC PLANNING

To move research forward, and to hasten the progress from basic knowledge to effective treatment, NIMH must take advantage of broad public participation in planning and setting priorities. Researchers, policymakers, health care providers, and individuals with mental illness and their families recognize that translating research breakthroughs into the procedures and policies of effective clinical practice is an essential and achievable task. Advances in the development of scientific tools must be married to new opportunities and emerging needs and to the contributions made by diverse constituencies who help to identify gaps in knowledge and barriers to progress.

A number of mechanisms are used to enhance the exchange of ideas and information between NIMH and constituencies. Each has direct impact on establishing research priorities. These include:

- **Workgroups of the National Advisory Mental Health Council.** The Council, a statutory advisory body composed of mental health professionals and citizens from outside the mental health field, has completed in-depth reviews of various components of NIMH's extramural research portfolio. These independent assessments of research opportunities and directions in the areas of genetics, mental disorders prevention research, clinical treatment and services research, and behavioral research are available in printed form and on the Institute's world wide web home page (<http://www.nimh.nih.gov>).
- **Review of Intramural Research Program.** In the late 1990s, the National Advisory Mental Health Council organized a Blue Ribbon panel, composed of nationally recognized neuroscientists, behavioral scientists, and mental health clinicians. This group, the NIMH Intramural Research Program Planning Committee, examined the overall structure, operations, and potential of the IRP and made more than 75 recommendations designed to revitalize the program. The majority of these have been implemented. More recent reports

have been issued on intramural clinical research and genetics research; these also are available electronically on the NIMH home page (<http://www.nimh.nih.gov>).

- **The Research Roundtable.** Established in 1997, the NIMH-convened Research Roundtable provides a formal means for representatives of research, health professional, consumer and family advocacy organizations to receive an update of NIMH activities and discuss current and needed directions of research. Communication between and among NIMH and outside organizations culminates annually in a Research Roundtable conference in Washington, DC.

- **The Constituency Outreach and Education Partners Program.** Created as an outgrowth of the NIMH Depression/Awareness, Research, and Treatment education campaign, this group seeks to increase the public's and professional providers' awareness of mental disorders and to decrease associated stigma; to communicate research findings; and to capture and report feedback to the Institute.

- **State and regional mental health forums.** "Town Hall style" meetings are designed to engage large numbers of people across the country in discussions of current NIMH research activities. One aim of the forums is to capitalize on the unique aspects of a given locale in obtaining input from grassroots consumer, provider, and researcher groups, as well as state and local mental health agencies. During 1999 two forums were held: *Mental Health at the Frontier: Alaska*, focused on rural mental health issues, and *Dialogue: Texas*, afforded NIMH staff opportunity to listen to and talk with the people of Texas about mental health issues of importance to the State. Comments received from people at both of these meetings have been integrated into this plan. These forums are an ongoing activity.

- **Draft NIMH Research Strategic Plan on the World Wide Web.** In mid-1999, NIMH posted an outline of the Research Strategic Plan on the NIMH homepage. Thousands of visits to the site resulted in several hundred e-mail and letter responses from interested persons throughout the United States and abroad. NIMH staff drew on this feedback in revising and developing this current version of the Strategic Plan, and we have taken the liberty of publishing as part of the Plan, quoted excerpts from these responses.

NIMH RESEARCH GOALS

The mission of the National Institute of Mental Health is to reduce the burden of mental illness and behavioral disorders through research on mind, brain, and behavior.

In pursuit of the NIMH mission, the Institute has three primary research goals:

GOAL 1: Understand mental illness and mental health

GOAL 2: Understand how to treat and prevent mental illness

GOAL 3: Strengthen the mental health research platform

As the knowledge base in neuroscience and the behavioral sciences grows over time, the Institute's immediate research objectives – which reflect both public health needs and current scientific opportunities – related to each of these goals evolve. In fiscal year 2000, NIMH research priorities for the next 2-5 years include the objectives outlined here.

GOAL I

UNDERSTAND MENTAL ILLNESS AND MENTAL HEALTH

To understand mental illness and mental health, it is necessary to learn how the brain functions and how it is altered in mental illness. Brain functions are affected profoundly by genetic factors, by developmental and aging processes, and by interactions with the environment – a term that, in this context, connotes social factors as well as physical insults to the brain, such as infection and other illnesses. Increased understanding of how brain functions are influenced to cause mental illnesses or maintain mental health will guide the search for ways to repair the altered functions. Accordingly, NIMH research devoted to understanding mental illness and health focuses on the study of brain structure and function; the role of genes in mental illness; interactions of brain and behavior; the effects of other illnesses or disorders upon the course of a person's mental illness; the differential impact that mental illness may exert upon different population groups; and the burden of mental illness for the Nation as a whole. Within these various research areas, specific immediate research objectives are to understand:

- **Normal brain processes;**
- **The contributions of developmental and aging processes to brain and behavior and to mental and behavioral disorders;**
- **Brain organization and function, how these go awry in mental illness, and how they are affected by treatment;**
- **The role of genes in brain and behavior and in vulnerability to and protection against mental illness;**
- **Interactions of the environment with brain and behavior and the role of environment in mental and behavioral disorders;**

- **The interactions of behavior with biological, social, and developmental factors and the effects on adaptive and maladaptive functioning;**
- **Brain and behavioral processes in cognition and emotion;**
- **The interactions when mental illness co-occurs with behavioral, general medical, and other mental disorders;**
- **The disease burden in mental illness and its outcomes in special populations, such as women, children, and ethnic minorities**
- **The extent of mental illness in the Nation and the world.**

For each objective, research initiatives that will be undertaken in FY 2000 and 2001 are described in the Research Plan below.

Research Plan

Brain Function and Structure

In order to understand brain function it is essential to determine the roles that specific brain structures play in integrating information and thus in generating physiological or behavioral actions. These structures can be as small as a single cell, or neuron, or as large as complex networks spanning the brain. While a complete understanding of brain function will require in-depth knowledge about the molecular and cellular details of neural activity, neuroscientists now know that the essence of operations of the human brain – including, for example, its ability to create music or literature or play sports– lies in the collective, integrative actions of large numbers of neurons and neural circuits.

Objectives

Understand normal brain processes and structure.

Our highest cognitive processes – perception, attention, language, memory, and the organization of action, or behavior – along with emotion, all operate to support mental health and are profoundly affected by mental illnesses. Scientists now have greatly improved technologies for studying how these higher functions are organized in the brain and relating the neurobiology of these functions in the brain to human experience.

Immediate research directions for this objective include these examples:

- **Human Brain Imaging Studies.** Brain imaging technologies such as positron emission tomography (PET) scanning and functional magnetic resonance imaging (fMRI) have revolutionized human brain research. With further refinement, these technologies will greatly accelerate understanding of brain function. NIMH imaging studies will discover patterns of connectivity in the human brain and enable imaging of dynamic changes in neurotransmitter systems. NIMH will collaborate in a major NIH-wide initiative, the Neuroimaging Informatics Technology Initiative (NIFTI), that will ensure interoperability of imaging technologies across neuroimaging research projects and, thus, allow researchers to make better use of all imaging data.

- **Non-Invasive Optical Imaging.** Existing brain-imaging techniques do not allow researchers to study short-lived, or transient, changes. Research has shown, however, that the reflectance from a highly directed light beam transmitted through the skull can be used to measure brain activity non-invasively; theoretically, this technology potentially could enable scientists to demonstrate directly, accurately, and simultaneously, the temporal (millisecond resolution) and spatial (millimeter or less resolution) dimensions of brain activity in humans. In addition, optical neuroimaging is far more economical than other modes of imaging. Development of this technique will require research that spans the biology underlying the signals generated, the instrumentation used to detect and characterize these signals, and the manner in which data are acquired, presented and analyzed.

*"I would like to endorse and underline [Objective: Understand normal brain processes that underlie cognition, emotion, and behavior.] I am glad to see that NIMH continues to recognize the need for basic research as the foundation for future clinical advances."
- Physician,
Harvard University*

Understand the contributions of developmental and aging processes to brain and behavior and to mental and behavioral disorders.

Depression – More than 19 million adult Americans age 18 and older suffer from a depressive illness – major depression, bipolar disorder, or dysthymia – each year, with over 2 million people suffering from severe, disabling, and life-threatening forms of depressive illnesses. Nearly twice as many women as men suffer from depressive illness each year. Depending upon the severity, depression may result in reduced productivity, missed workdays, long-term impairment in the quality of life, hospitalization, or all too often suicide.

One form of depression, manic-depressive illness, affects more than 2.3 million Americans 18 and over (about 1 percent of the population) each year and, left undiagnosed, untreated, or treated inadequately, as many as 20 percent of these people die by suicide.

Structural and biochemical changes occur in the brain in association with early neural development throughout childhood, with normal brain functions in adulthood, and, to varying extents, with aging. There is also recent evidence that new brain cells (neurons) are added in response to experiences throughout life. It is important to determine how such fundamental developmental and aging processes influence normal brain function and behavior and how the changes may contribute to mental or behavioral disorders. NIMH will support research that includes:

- **Plasticity in Developing and Adult Brains.** The flexibility of the connections that link neurons within the brain underlies many of the adaptive responses of an individual to the environment. These can include responses to trauma, both at the psychological and physical level, as well as the processes that underlie learning and memory. These processes likely will be determined to have broad clinical relevance since changes in cognitive capacity, including memory loss, are central to most mental disorders. Immediate research challenges include understanding how new neurons establish connections with existing cells; ascertaining what types of information are conveyed by new connections; differentiating the types of behavioral or cognitive change that are mediated by changes in existing neurons from changes due to the incorporation of new neurons; and understanding the “hows and whys” of neural plasticity during normal or abnormal development.

- **Mapping Normal Brain Development.** Brain disorders that begin in early life may progress to serious mental disorders in late adolescence or adulthood. In many cases, it is possible that the adult – and perhaps, lifetime – mental disorders could be averted or lessened if they could be detected and treated during childhood. However, because a child’s brain and behavior changes so rapidly as the child grows and develops, it is very difficult to determine which changes are normal and which abnormal. Noninvasive

Schizophrenia – is the most chronic and disabling of mental disorders. **One in 10 people with schizophrenia eventually commit suicide.** People with this illness suffer terrifying symptoms – hearing voices or believing that other people are reading their minds, controlling their thoughts, or plotting to harm them. Their speech and behavior can be so disorganized that the individuals may become incomprehensible and frightening to others. Even with available treatments, most people with schizophrenia continue to suffer throughout their lives; it has been estimated no more than one in five recovers. However, new treatments recently introduced offer hope that patients may soon be better able to manage their illness and improve their lives.

The symptoms and chronicity of schizophrenia ensure a very high degree of disability. Without treatment, a person is almost totally disabled over a lifetime. Some people are not helped greatly by available treatments or may discontinue treatment because of unpleasant side effects. Even with treatment, persisting consequences of the illness – lost opportunities, stigma, residual symptoms, and medication side effects – may be as troubling as the initial, acute, symptoms.

neuroimaging methods now provide an opportunity for mapping structural and metabolic development in normally developing children and in those afflicted with a variety of disorders and diseases. To exploit this opportunity, NIMH, NINDS and NICHD are initiating a multicenter imaging (magnetic resonance imaging, or MRI) study of normal brain development, in which pediatric study centers across the United States will study a representative sample of approximately 500 healthy, normally-developing children, ages 0 through 18, using several non-invasive imaging methods combined with behavioral and cognitive measures to map brain maturation and relate it to behavioral changes. Findings of this study will be shared widely with other researchers and with the clinical medicine community.

- **Healthy Brain Project.** Significant alterations can occur in the structure and function of the brain in response to many influences during the course of “normal” development and, indeed, in response to emotional stress and other pathological processes that occur throughout life. Disturbances of cognition, mood and emotion afflict millions of people at every stage of the life span. The NIH Healthy Brain Project is a large longitudinal population-based study that will collect the information needed to identify and understand risk factors and to develop plans for interventions to improve the cognitive and emotional health of Americans. NIMH, with the National Institute of Neurological Disease and Stroke (NINDS) and the National Institute of Aging (NIA), will initiate this project; other institutes may also participate.

Understand brain organization and function, how these go awry in mental illness, and how they are affected by treatment.

Scientists now are discovering how the brain organizes itself to process information; how the actions of single neurons relate to the coordinated activity of large numbers of neurons (circuits) in multiple subregions, and how networks of neurons engage in serial and parallel information processing. These studies will provide vital information about how intra-cellular processes, the synapses (or points of connection between neurons), and brain circuits become disturbed

in mental illness and how treatments can reverse or retard these disturbances. Research on brain plasticity in both animals and humans and research involving human brain imaging will accelerate the understanding of brain organization and function and provide insights into new treatments. Other research directions include:

- **Development of Neuroimaging Biomarkers for CNS Disorders.**

Advances in instrumentation and techniques for brain imaging have created wonderful opportunities for researchers to explore the causes and treatments of mental disorders; still, the usefulness of several key techniques – for example, PET and single photon emission computerized tomography or SPECT – is limited because biomarkers (specific radioligands or, more simply, labeled “tags” that a scanner detects) are available for only a few target molecules in the brain. NIMH will encourage research to develop new imaging biomarkers for research on the causes and treatments of mental disorders.

- **Micro-imaging: Novel Probes and Instruments.** Micro-imaging techniques that will enable scientists to study brain structure and function at the molecular and subcellular levels in living cells quantitatively and in real time are urgently needed. NIMH will encourage research to develop these techniques.

Genes and Mental Illness

Identifying the genes that contribute vulnerability for different mental illnesses will offer opportunities to understand the causes of illness and lay a foundation for treatment and prevention. The quest for vulnerability genes must involve the participation of large populations of families affected with a given mental illness. It also requires intensive basic molecular biological research with animals to understand how certain genes influence, and are influenced by, behaviors. In addition, research must examine how environmental risk factors are triggered in order to provide a basis for developing strategies to prevent the onset and exacerbation of mental disorders.

Objectives

Understand the role of genes in brain and behavior and in vulnerability to and protection against mental illness.

"I would like to see more research studies, particularly into the genetic origins of bipolar disorder as well as new treatments, particularly for the often drug resistant rapid cycling forms of this devastating illness.

I'd also like to see more money spent on educating the public (including employers) on mental illnesses and removing some of the stigma associated with these illnesses."
--Michigan Woman

Genetics promises to be a powerful tool for understanding what goes wrong in the brain of individuals with mental disorders. Identification of particular versions of genes (alleles) that create vulnerability to mental disorders will provide critical tools for investigation of the brain and potential new targets for the development of novel treatments. Vulnerability alleles will also provide epidemiologists tools to investigate not only genetic, but also nongenetic factors that contribute to the risk of illness. Examples of research that NIMH will encourage include:

- **Linking Basic Genetic Data to Mental Health.** It is now possible to study the nervous system in mammals at levels of detail previously possible only in model systems. Genetic, cellular, and molecular analysis, in mammals, of important brain molecules identified in simple systems should begin to bridge the gap between findings from model systems and human brain processes that go awry in complex mental health disorders. Research directions could include studies of mammalian brain homologues of important neural genes identified in simple systems and relationships between brain processes mediated by these molecules and a variety of behaviors – ranging from simple behaviors in lower mammals to more complex behaviors in higher mammals, including humans.

- **Genetics of the Brain and Mental Disorders.** The NIMH and NINDS have launched the Brain Molecular Anatomy Project (BMAP), a multidisciplinary effort to catalog the genes expressed in the nervous system and provide a resource to the wider scientific community. A major initial focus of BMAP research is the mouse brain because this is the best-developed mammalian system for genetic analysis. The BMAP initiative will be expanded to permit the comprehensive study of functional gene expression in mammalian systems at multiple levels. Possible research directions could include identification, localization, and characterization of all genes, transcription factors,

Eating Disorders are characterized by a psychological obsession with food and body image. The most common forms of eating disorders are anorexia nervosa (self-starvation) and bulimia nervosa (binge eating and/or purging). Both are serious and possibly fatal if left untreated. Eating disorders are commonly thought of as women's health problems because they affect 8-10 times more women than men; however, the incidence of eating disorders in men is on the rise. Anorexia and bulimia affect 2-4% of adolescent girls and young women.

Anorexia Nervosa is a syndrome in which affected people starve themselves into severe weight loss, a behavior that is associated with a distorted body image and a pathological fear of gaining weight. What may originally appear as a normal concern about weight and dieting can escalate into an obsessive cycle of compulsive dieting and over exercise. An estimated 1% of adolescent girls and young adult women are anorexic.

Bulimia Nervosa is a syndrome in which affected people engage in repeated binge-eating episodes followed by self-induced vomiting, fasting, or use of laxatives or diuretics. Many people with bulimia nervosa experience a sense of lack of control during binge-eating episodes. They are also obsessed with their body shape and weight, both of which are linked to their self-esteem. Bulimia nervosa affects 1-3% of adolescent girls and young women and is often seen in conjunction with obsessive-compulsive behavior.

and transcriptional controllers relevant to brain development; monitoring of RNA expression levels in different cell types; analysis of complex patterns of gene expression data across the genome and in multiple brain regions; development of high-throughput mRNA analysis platforms for large gene expression data sets; and development of rapid screens for all mutations and sequence variations in mouse neural genes.

- **Genetic Mapping of Mental Disorders.** NIMH will encourage research on high-resolution mapping of mental disorders and their biological substrates. The initiative will entail new pedigree collection, assembling of pre-existing data sets for large-scale unified analyses, comprehensive phenotyping, production of large gene expression data sets, and fine-mapping studies in the next generation of molecular genetic studies of mental disorders. Research could map biological traits that co-segregate, or associate, with disease in families of affected individuals; initiate fine-structure linkage disequilibrium mapping in genetically isolated populations; identify genes predisposing to differential treatment responses; identify genes influencing intermediate biological risk factors important in disease susceptibility; and develop a Center for the Genetic Dissection of Complex Traits on the NIH Campus.

- **Clock Genes in Human Mental Health.** Dysfunctional circadian systems are central to emotional and cognitive disturbances. System perturbations also have been shown to affect the performance and behavior of adolescents. A major area of future discovery will involve linking the molecular genetics of the circadian clock system in the mouse with similar genes in humans to understand the impact of altered clock genes and clock gene expression for human health and well being. Research could focus on the expression and functional significance of clock genes in the amygdala, hypothalamus, and other affective circuitry of the brain; how clock gene expression is altered during development and aging; and the impact of circadian mechanisms on the timing of hormonal and other signaling systems and on brain plasticity.

Understand interactions of the environment with brain and behavior and the role of environment in mental and behavioral disorders.

Vulnerability to mental disorders clearly has a significant genetic component, yet in all cases analyzed to date, vulnerability to a given mental disorder is genetically complex, meaning that there is no single gene that causes manic-depressive illness, schizophrenia, or for that matter, any mental disorder or normal cognitive or emotional trait. Rather, it appears that multiple genes found at multiple loci within the genome interact to produce vulnerability to a given mental disorder. In all cases, it also appears that nongenetic factors must interact with the genes to convert vulnerability into illness.

- **Identifying and Modeling Genetic and Environmental Risk Factors for Mental Disorders.** Research in clinical neuroscience and brain imaging has identified certain behavioral, physiological, hormonal, and biochemical changes that appear to be associated with susceptibility to mental disorders or to efficacy of treatment. These observations suggest that it might be possible to develop models of the genetic, molecular and cellular processes responsible for these changes. Two separate aspects of model development are needed: biologically relevant manipulations, representing risk factors for mental illnesses, and specific behavioral measures for assessing the effects of these manipulations. This new research focus on clinically relevant, but simplified, behavioral measures is expected to stimulate the identification of novel genes, signaling molecules, and neurocircuits involved in mental disorders.

- **Genomics of Behavior.** Even at the genetic level, behavior can be modified by interactions with the environment. Research on the functional genomics of mouse behavior and nervous system will expand our understanding of the neurobiological underpinnings of complex behaviors. Using mutant mouse strains, this research will discover gene functions resulting from interactions of the genome and environment and will complement other NIH research on mouse genetics. Research could identify the products of genes influencing nervous system function and complex behaviors; study functions of non-protein-coding sequences in mouse neural genes; develop measures of neural

gene expression; analyze nervous system functional pathways; and construct functional genomic profiles of therapeutic drugs.

Brain and Behavior

All of the conditions for which NIMH has responsibility are manifest at the level of behavior and, ultimately, all interventions that we develop or assess for conditions aimed at the prevention of illness or its treatment must have an impact at the behavioral level. Accordingly, NIMH will continue to support research in both basic and applied behavioral science. Among the goals of such research are to understand, in animal models and in human subjects, the psychological and neural processes underlying cognition, emotion, motivation, psychopathology, and action of psychotropic drugs.

*“Perhaps in several decades we will be able to link every behavior to a brain function, but in the next years we need to understand better normal behavioral development even without the brain links [a] strong basic research component in behavior analysis is critical to the transfer of technology from the laboratory to the field.”
-Psychologist,
New York City*

Objectives

Understand the interactions of behavior with biological, social, and developmental factors and the effects on adaptive and maladaptive functioning.

In the new millennium, a pressing challenge for NIMH will be to marshal the scientists, ideas, and resources needed to support research on the integrative aspects of biology, including behavior. The greatest benefits of the molecular revolution to our understanding of the brain and behavior—and, in turn, of mental disorders— will not be realized without greater attention to anatomy, physiology, pharmacology, and behavior. Examples of research directions include:

- **Mental Health and Violence in Children and Adolescents.** Violent behavior—especially by youth—is commanding increasing attention as a major U.S. public health problem, raising national concern for finding effective approaches to preventing and reducing violence. NIMH will encourage a new generation of studies to clarify relationships between mental disorders and youth violence and suicide, including research to prevent the emergence of syndromes

and disorders, and to interrupt the development, escalation, and/or continuation of serious conduct problems, violent behavior, and other co-occurring disorders.

- **Deficits, Disabilities, and Diagnoses.** Mental illnesses are diagnosed primarily on the basis of symptoms, without a full assessment of the extent of disability caused by the illness. However, a strong emphasis on symptoms that are not predominant contributors to functional disability may impede prevention and rehabilitation research related to schizophrenia and other major mental disorders. NIMH will encourage research to characterize the disability stemming from mental illnesses in systematic or quantifiable ways, and assess functional outcomes related to the reduction of disability; understand protective factors that moderate course and outcome of illness; relate treatment variability to functional outcomes; characterize deficits that stem from specific disabilities, as well as deficits that are more general and shared across a range of disorders; study clinical outcomes, including functional outcomes, in relation to different treatment compounds and modalities thought to affect neurocognitive functioning; and develop standardized measures that relate to functionally significant domains of outcome.

- **Research on Social Cognition and Behavior.** Progress in understanding basic cognitive processes such as memory, attention, and implicit learning have shed little light to date on the neural basis of *social* cognition and behavior; that is, the ways in which people think about themselves and others. Future advances in cognitive neuroscience promise to enrich social psychological research that focuses, for example, on attitude change, stereotyping, and decision-making. Understanding the neural bases and development of social cognition will inform the diagnosis and treatment of disorders such as autism and schizophrenia that are marked by deficits in social-cognitive capacities. Needed still is research to examine common and distinct neural systems that are specialized for processing a variety of social-cognitive inference tasks and behaviors; to clarify and specify the role of conscious and intentional processing, attention, and explicit memory; and to investigate the roots of personality structure. NIMH also will promote cross-disciplinary training and collaborations between neuroscience and behavioral scientists.

"I think that the role of hormones and their effect on mental illness has not been fully explored... My daughter is now in recovery from a very severe case of psychotic depression, and it started when she hit puberty. I have always felt that her hormonal change had a very strong effect on her illness. Recently, she started a course of birth control pills (she is now 18 years old), and within days was feeling really bad again. She has discontinued the pills, and now is back to her usual recovery level... I would strongly urge you to take a look at the role of hormones, especially in adolescent depression and related disorders."

--Health Care Facilitator, California

- **Regulation of the hypothalamic-pituitary-adrenal (HPA) axis.** The hypothalamic-pituitary-adrenal (HPA) axis links the brain's hypothalamus with pituitary and adrenal glucocorticoid hormones, and is a prime example of a biological system that can provide a bridge linking behavior and psychopathology. Behavior, psychopathology, the HPA system, and brain responses to glucocorticoids are each complex issues that have traditionally been studied by investigators in different disciplines. NIMH will encourage research on these elements of biology and behavior through integrated cross-disciplinary research programs that span multiple levels of analysis.

Understand brain and behavioral processes in emotion and cognition.

Throughout history, human emotion was considered to be inextricable from the quasi-philosophical domain of mind and consciousness, and not accessible to neurobiological research. Thus, among the great advances in behavioral neuroscience during the past decade have been initial, successful efforts to delineate the neural circuits with which the brain forms memories about the affective, or emotional, significance of life experiences. Valuable in its own right for elucidating basic mechanisms of brain function, this research has critical implications for understanding the neural substrates of anxiety, affective disorders, and other mental illnesses. The best-understood circuits are, arguably, those involved in fear, which have been identified using tract tracing, physiology, lesions in animal models, and, most recently, neuroimaging in humans. While emotions are transient and often stimulus-bound, mood represents the long-term and predominant emotional state of an organism. An important long-term research goal will be to obtain better empirical data, perhaps in animal models and certainly in humans, of the circuitry that regulates mood and to develop better theoretical models of mood regulation. Examples of research directions include:

- **Research on Cognition and Emotion.** Research in cognitive and affective neuroscience, which is concerned with how we think and experience emotions, has produced advances that can now be integrated with data, methods,

and concepts from other fields to enrich research on mental illnesses. Animal studies that are examining correlates of emotional processes need to be translated into models of human cognition and emotion relevant to clinical populations. Other research will include studies of information processing in emotional and cognitive circuitry; how hormonal modulation affects learning and memory mechanisms; and research seeking to identify specific molecules involved in emotional and cognitive expression associated with mental disorders.

- **Basic Biobehavioral Studies of Anger and Related States.** The study of emotion has progressed markedly over the past two decades. New animal models of emotion have been developed, and the emergence of neuroimaging and related technologies has permitted studies based on animal models that explore brain circuits involved in emotional behavior. This progress has been particularly marked in the understanding of fear and related states. Although much research has focused on violence, aggression, and impulse control, and their pervasively harmful effects, basic research on anger as a fundamental emotion remains understudied. Accordingly, NIMH proposes to fund research projects devoted to anger and related emotional states.

Mental Disorders – Tackling the Complexities of Co-Morbidity

Mental disorders co-occur with notable frequency with diverse other forms of illness. An estimated 15 percent of people with a mental disorder also have a substance use disorder in a given year. Glimpses of the extent of co-occurrence, or comorbidity, of mental and other general medical illnesses are found in the research literature; patients with depression, for example, have been shown to have a high prevalence (between 65- and 71 percent) of any of eight common chronic medical conditions: hypertension, advanced coronary artery disease, gastrointestinal disorder, diabetes, chronic back problems, chronic lung problems, arthritis, and angina. Research that will identify the extent, nature, and causes of comorbidity is urgently needed and will have a dramatic impact on both the quality and cost of health care in the U.S.

Objective

Understand the interactions when mental illness co-occurs with addictive, general medical, and other mental disorders.

*“As the mother of a 36-year-old son who suffers from schizophrenia and alcohol abuse, I would like to see research into why alcohol makes many mentally ill people feel “normal” and makes it so difficult (or impossible) for them to discontinue dependency on it.”
--Florida mother*

Often a person with a mental illness will also have a second mental illness, or a medical illness – such as heart disease or cancer, or a substance abuse disorder. The presence of a second illness or disorder may complicate recovery from the mental illness, or conversely, the mental illness may interfere with recovery from the other disorder(s). There is also evidence that a mental illness, such as major depression, can predispose a person to heart disease or hypertension many years later. Determining the relationships between mental illness and co-occurring mental, medical, and substance abuse disorders is important for public health. NIMH will encourage research on these relationships, including:

- **Comorbidity: Etiology, Prevention, and Treatment.** Mental disorders, substance abuse, and other medical conditions are frequently co-morbid, sometimes occurring simultaneously, while at other times, one disorder is clearly secondary to another – for example, as when depression develops as the result of a life-threatening physical disease. When mental illness occurs along with another disorder, the suffering experienced by individuals and the cost to the nation in lost productivity and health expenditures is much greater than for individual disorders alone. NIMH will encourage research on risk and protective factors that influence the probability of co-morbidity; outcomes of co-morbid mental disorders, substance abuse, and other medical conditions; mechanisms of behavior change that might be applicable to intervention development across a variety of disorders; and interventions based on risk and protective factors and processes that affect the likelihood of co-occurring or secondary disorders. NIMH will also encourage research that aims to improve treatment for patients with co-occurring mental disorders.

Monitoring and Measuring Mental Illness

As the Surgeon General recently has noted, the Nation's present mental health enterprise, like the broader field of health, is rooted in a population-based public health model. The public health model is characterized by concern for the health of a population in its entirety and by awareness of the linkage between health and the physical and psychosocial environment. Public health focuses not only on traditional areas of diagnosis, treatment, and etiology, but also on epidemiologic surveillance of the health of the population at large, health promotion, disease prevention, and access to and evaluation of services. According to current epidemiological estimates, at least one in five people has a diagnosable mental disorder during the course of a year. A confounding factor in such estimates, however, is the difficulty of identifying a severity threshold for mental disorder, particularly in light of how common symptoms of mental distress are and the lack of specific biological indicators of the presence of a disorder. In many cases, symptoms are not of sufficient intensity or duration to meet the criteria for a disorder diagnosis that is based on observable signs and symptoms of illness, the course and duration of illness, response to treatment, and degree of functional impairment. Another limitation of contemporary mental health knowledge is the lack of standard measures of "need for treatment," particularly those that are culturally appropriate. Such measures are at the heart of the public health approach to mental health. Pending the development of valid measures of need, rates of disorder estimated in epidemiological surveys serve as an imperfect proxy for the need for care and treatment.

Public mental health policies must evolve to meet changing mental health problems and demands. It is, therefore, essential to determine these needs. Researchers and mental health care providers have recognized that factors such as gender, cultural background, and ethnicity can markedly affect the diagnosis, treatment success, and etiology of mental disorders.

Objectives

Understand the basis of disparities in mental illness and its outcomes in special populations, such as women, children, and ethnic minorities.

There are important differences in patterns of mental disorders in racial and ethnic minorities vs. the broader U.S. population, and in women vs. men. Racial and ethnic minority populations are affected by cultural bias in the systems devised to classify and measure mental disorders. For example, disparities abound in treatment utilization: some minority groups are underrepresented in the outpatient treatment population while, at the same time, overrepresented in the inpatient population. Substantial sex differences exist in the prevalence of mood and anxiety disorders, and in the clinical course and outcomes of bipolar disorder and schizophrenia. Beyond these gender and ethnic differences, individuals with lower socioeconomic status are over twice as likely to have a mental disorder compared to those in the highest socioeconomic status. Low socioeconomic status is an important risk factor for major depressive disorder in women and for substance abuse and antisocial personality disorders in men. Research directions include this comprehensive initiative:

- **Reducing Disparities in Mental Health among Racial and Ethnic Minorities and Women.** Consistent with the goals of *Healthy People 2010*, NIMH will expand research to untangle the web of causal factors—biological, psychological, social, and cultural—that contribute to disparities in mental health and mental illness among racial and ethnic minorities and women. Research will include epidemiological studies that oversample ethnic groups such as African Americans, Hispanics, and Native Americans to obtain information on disparities in mental health. Additional studies will examine how racial and ethnic minority status influences response to treatments, new interventions designed to overcome such differences, and disparities in access to and quality of mental health care and treatment for different groups.

Measure and monitor the burden of mental illness for the Nation and the world.

During the late 1990s, the U.S. and much of the rest of the world were faced with the sudden realization that mental illness is an immense and heretofore-unsuspected burden on their nations. Greater understanding of the relationships between mental illness and the accompanying disability is needed to aid in understanding and measuring this burden.

“There is a need for more research that demonstrates the cost to society of not treating mental illness. Insurance coverage for mental illness is horribly inadequate, if not virtually non-existent.... [u]nless more research is conducted and the public awareness increased, there can be no headway in increasing insurance coverage for mental illness.”
--Scientist

- **Developing Burden of Disease Assessment.** The Global Burden of Disease (GBD) study emphasized the magnitude of the impact of mental illness on disability in the community. Simultaneously, interest and concern regarding the methodology used in the GBD study, notably Disability-Adjusted Life Years (DALYs), have stimulated examination of various aspects of the methodology, resulting in the development of refined methods to incorporate empirical data as the basis for disability weights, as well as the potential to reflect change in disability level as a consequence of service and treatment interventions. NIMH will expand research to continue to improve the methodology of assessing the burden of mental illness.

GOAL 2

UNDERSTAND HOW TO TREAT AND PREVENT MENTAL ILLNESS

Mental disorders are treatable. During the past 50 years, treatments for mental illnesses have been discovered and demonstrated to be effective. The treatments we now have can reduce, or sometimes alleviate entirely, many disturbing symptoms that accompany these disorders. However, despite this substantial progress in developing treatments, some disorders are more difficult to treat than others and some people do not respond to any of the existing treatments, creating an urgent need for a continued improvement of treatments. Our rapidly expanding knowledge of how the brain works in health and illness, combined with modern technologies of neuroscience and with progress in behavioral and clinical sciences, will lead to new conceptualizations of how to assess symptoms, based on the underlying brain dysfunctions, and then how to tailor treatments to address specific problems.

Knowledge of how the brain develops from before birth through old age – both normally and when mental illness is present – also gives hope that many mental disorders can eventually be prevented. Researchers are studying preventive interventions that might protect against future onsets or exacerbations of illnesses such as schizophrenia, depression, and anxiety disorders. In addition, as with many long term medical conditions such as diabetes, prevention of mental disorders must take the form of long-term maintenance to minimize recurrence of illness and secondary morbidity. Increased understanding of how to prevent mental disorders will help reduce the burden these illnesses impose on individuals, their families, and the Nation.

Suicide is a complex behavior usually caused by a combination of factors. Almost all people who commit suicide have a diagnosable mental illness and/or a substance abuse disorder. Of those with mental illness, the majority suffers from depression, schizophrenia, or personality disorders. On the average day, 86 people actually commit suicide while an estimated 1,900 adults attempt suicide. Suicide rates are the highest among the elderly and continue to rise. In 1995, suicide took the lives of over 30,000 Americans. Suicide was the 8th leading cause of death in the US, and among young adults age 15-34, suicide was the 3rd leading cause of death.

Within the Research Plan outlined below, primary immediate research objectives of NIMH are to:

- **Translate basic biological and behavioral research findings into useful applications in clinical settings;**
- **Determine the best fit and utility of treatment and prevention interventions for diverse populations (children, elderly, minorities, etc.) and settings (community, clinics, schools, etc.);**
- **Identify research innovations in design, methods, and measurement that examine the interplay between treatment, environment, provider and consumer;**
- **Examine the long-term effects of interventions—acute, rehabilitative, and preventive—on the course of mental illness and disability;**
- **Better understand how people learn and change behavior in order to prevent illness, improve treatment outcomes, and prevent disability;**
- **Determine the impact of organization and financing of services on outcomes and how to improve cost-effective service delivery, including early diagnosis and appropriate intervention.**

Research Plan

Improved Treatments for Mental Illness

With advances in our understanding of mechanisms in the brain responsible for cognition, perception, motivation, emotion, and reasoning, the need intensifies to translate these findings into behavioral and pharmacologic treatments targeted to specific mental disorders. Research has established, and will continue to expand, the knowledge base from which better treatments for mental disorders are developed. Attaining the greatest benefit from treatment requires the close participation and cooperation of the individual patient; unfortunately, a wide-

spread stigma against mental illness often deters people from seeking and cooperating with treatment, emphasizing the need for research on how to reduce stigma.

Sometimes the relevance of discrete basic research findings to the treatment of specific problems is not recognized immediately, causing delays in the translation of basic research into clinical practice. It is also true that clinical observations of how different people with mental disorders respond to different treatments can generate questions for basic researchers to address. Thus, a close connection between basic research and the treatment of mental disorders in clinical settings must be maintained.

Objectives

Translate basic biological and behavioral research findings into useful applications in clinical settings.

*"I am the mother of two children with multiple anxiety and mood disorders. One has been hospitalized several times. I would like to see double-blinded, well-controlled studies that show what treatments are effective and whether any of the existing ward practices actually exacerbate a child's illness. Then I would like to see a 'best practices' document."
--Concerned parent, North Carolina*

Basic laboratory research often provides valuable discoveries or insights potentially capable of improving pharmacological and behavioral treatments for mental disorders. However, the clinical significance of the discoveries might not be recognized immediately and additional research typically is required to adapt them for use in treatment – all of which may result in lengthy times between discovery and use in clinical care. NIMH is committed to ensuring that such research discoveries are translated into clinical benefits as rapidly as possible.

- **Mechanisms of Therapeutic Change.** Impressive progress has been made in understanding what type of psychotherapeutic treatment works best for whom, yet underlying questions of how and why these treatments work have not been addressed adequately. NIMH will support research that elucidates the connection between successful behavioral interventions and identification of the underlying mechanisms involved.

- **Innovative Therapeutic Programs.** Through a new initiative NIMH will support research on innovative applications of pharmacotherapeutic and psychotherapeutic interventions. This will include novel applications of psychoactive drugs, augmentation and combination strategies for pharmacotherapies, somatic therapies, and psychotherapies, as well as the development of collaborative relationships (e.g., researchers from intramural, extramural and pharmaceutical organizations) to leverage resources and pursue common goals.

Identify the most effective treatment and prevention interventions for specific populations, including children, the elderly, and ethnic minority groups across a range of settings, including communities, clinics, and schools.

Many persons who could benefit from improved treatments for severe and disabling mental disorders are not receiving treatment. Beliefs about the cause of mental illness, the nature of treatment, motives of clinicians, and fears derived from stigmas, along with physical and financial barriers to obtaining treatment, prevent people from seeking or remaining in treatment. To design user-friendly, effective treatment programs for diverse populations there is a need to examine the interplay of factors that result in obtaining effective treatment for mental disorders.

- **Factors Affecting Use of Treatment.** NIMH will encourage mental health services researchers to collaborate with basic social and behavioral scientists. Incorporating the theory and methods of behavioral science in services research will aid in understanding how characteristics of individuals, families, and social and cultural environments affect individuals' decisions about service use. Among questions to be addressed are whether, how, when, and where care is sought, what types of care are chosen or provided, what happens during the delivery of care, and what outcomes result; how the social, cultural, and psychological characteristics of the provider interact with those of the patient/client; and how the variable economic, social, political, and cultural environments in which services are delivered affect the organization, financing,

*"...[t]he draft strategic plan establishes NIMH's agenda as one that is firmly grounded in brain and genetics research. While it is essential for NIMH to continue cutting edge research in these areas, there is insufficient focus on investigating the social, structural, and contextual factors that influence the development of mental illness."
--American Sociological Association*

management, and delivery of services. Collaborative research also must examine issues regarding access to services and the process, cost, and outcomes of care.

- **Reducing Stigma Associated with Mental Illnesses and Interventions.**

People with mental disorders suffer not only from their illness but also from the added burden of discrimination, prejudice, and occasionally, hate crimes. NIMH will expand research to increase understanding of the variables that underlie the stigmatization of people with mental illness; develop interventions that help individuals cope with stigma and discrimination; and change society's attitudes.

Research Innovations in Design, Methods, and Assessment

Research on mental illness poses particular challenges in terms of behavioral research design and methodology. Challenges stem from the diverse populations under study; the need to examine sensitive behaviors such as violence and substance abuse; the necessity of incorporating the perspectives and approaches of multiple disciplines; and the need to study phenomena in natural settings. The development of both research designs and assessment instruments or methods that capture dynamic interactions is paramount if we are to adequately understand complex human functioning in real-life settings.

For people with mental disorders, both the immediate and long-term success of their treatment is often influenced strongly by the provider and provider's choice of treatment, the clinical setting and other aspects of the environment, as well as an individual's complete participation in treatment. Research that aims to improve treatments must take all of these factors into account and determine how they can be optimized for treatment success. This is a complex and difficult task that calls for the development of innovative methods for clinical research. Researchers are challenged to refine the design of clinical trials and develop better methods of assessing the outcomes of treatments being studied and, particularly, of long-term treatments and interventions used to alleviate the symptoms of mental disorders.

Objectives

Identify research innovations in design, methods, and measurement that examine the interplay between treatment, environment, provider and consumer.

Research has provided an increased understanding of the nature and outcomes of mental disorders that could, in turn, lead to improvements in clinical assessment and measurement methods, the development of new treatments, and the optimization of mental health services. However, the enhancement of existing treatments and services delivery systems calls for innovative research on the design and methodology of clinical trials and diagnostic assessment instruments. NIMH will expand innovative research aimed at increasing the knowledge gained from interventions trials.

- **Clinical Trials.** Clinical trials can often provide valuable information in addition to the effects of the specific treatment being studied. NIMH has initiated large-scale, long-term effectiveness trials in bipolar illness, treatment-resistant depression, and use of atypical antipsychotics in adults and older persons. These trials, as well as ones on treatment of anxiety, major depression in adolescents, and autism, all provide opportunities for new initiatives in experimental therapeutics, patient-oriented research, health services research, and age-specific response research. Studies could include: natural history of complex diseases; genetics and family-based associations; population pharmacokinetics and pharmacogenetics; treatments for varied patterns of coexisting illnesses, particularly substance abuse and chronic disabling physical illnesses; neurobiologic and psychosocial correlates and predictors of variability in treatment response (speed, completeness, durability); extension and adaptation of treatments with established efficacy in adults to children and adolescents; and adaptation of treatments developed for use in psychiatric specialty settings to primary care or community settings.

- **Multi-dimensional Approaches.** NIMH will encourage research on the conceptual and methodological issues in clinical protocol design that rely on different sources of information: these might include, for example, self and

proxy reports; validation studies that use both biological markers and record sources; and studies that compare report data with observational data obtained from different sources such as a patient’s self-ratings and family members’ ratings of a patient’s mood or behavior.

- **Interventions in Real World Settings.** Treatments for mental illnesses are usually shown to work-in short-term trials that involve participants with clearly defined disorders and rigorous treatment levels and schedules (called “efficacy studies”). However, in real life, these treatments may be used for longer periods of time under quite different conditions; for example, by patients whose illnesses may be somewhat different from those in the original efficacy trials, who may have more than one mental disorder simultaneously, or who may not always fully understand or follow treatment directions. Because of factors such as these, a given treatment could be less effective in reducing the burden of mental illness than anticipated; however, an understanding of the reasons could lead to the development of more effective interventions. NIMH will support the development of instruments and the development of design, implementation, and analysis of intervention studies in a range of settings (private – public organizations) with representative samples of patients (minimal exclusion criteria) using broad and multiple outcome measures.

“Please don’t forget the survivors of sexual child abuse, and the mental health issues that plague us. We need for science to find a way to help us be whole again. Don’t just look at the specific diseases, look at the big picture. Why is it that we end up so seriously dysfunctional? We can’t seem to stay in relationships, we can’t keep jobs, we are chronically ill, we cost the country billions of dollars, I am sure. Please look at this subject...”
 --Texas Woman

Examine the long-term effects of interventions—acute, rehabilitative, and preventive—on the course of mental illness and disability.

Severe untreated mental illness may result in significant long-term disability. For the severest forms of mental disorders, some degree of chronic disability may remain even with current treatments, which focus on relief of acute symptoms. Research is needed on the long-term effects of interventions and, especially, on rehabilitative interventions capable of minimizing the disability and improving the quality of life for individuals with serious mental disorders.

Early detection and treatment of disorders may result in improved prognosis and functional outcome in adult life. However, research on early intervention and treatment of these psychiatric disorders in children can be challenging due to

uncertainties about diagnosis in early stages of illness and the limited data on the safety and efficacy of treatment interventions in pediatric subjects.

- **Early Intervention and Treatment for Children and Adolescents with Mental Disorders.** Some mental disorders – such as schizophrenia, schizoaffective disorder, bipolar disorder, obsessive-compulsive disorder and eating disorders – often start in the second decade of life, while others, such as depression and some anxiety disorders, may emerge even earlier. NIMH will solicit research on: malleable and potent risk factors for eating disorders that could serve as targets for early intervention; new interventions to prevent exacerbation of, and functional impairments associated with, depression and anxiety in children; long-term impact of early intervention, especially on disease progression and prognosis; and long-term effectiveness and safety of treatment interventions for patients with chronic or recurrent disorders.

- **Diagnosis and Treatment of Attention Deficit Hyperactivity Disorder (ADHD).** There is a need for improved assessment, diagnosis and treatment of ADHD in such areas as risk factors and mechanisms underlying the development of ADHD; assessment of heterogeneity in ADHD, including brain imaging studies to help understand the course of disorder; most effective treatments and their long-term risks; and extent and effectiveness of services in different service sectors.

- **Prevention and Early Intervention in Psychotic Disorders.** Schizophrenia, a mental disorder marked by periods of psychosis, typically begins in adolescence or early adulthood. There often is a delay of a year or more between onset of full-blown disorder and initiation of antipsychotic treatment. Since complete recovery from schizophrenia is rare once the illness is well established, intervention in the pre-morbid (prodromal) phase may be a crucial strategy to improve course and outcome. Few interventions are available specifically for individuals who are exhibiting the early warning signs of psychotic disorders, and the efficacy of existing pharmacological or behavioral interventions during this phase has not been systematically studied. NIMH will expand its support of 1) diagnostic, clinical, neurocognitive and neurobiological characterization of the pre-morbid phase, including longitudinal studies as this

“As a family member and consumer willingly in treatment for 21 years, [I suggest] research designed to detect the significance of smoking and nicotine on the influence of coping with mental illness [and] research on the supports and treatment needed to aid people with mental illness in smoking cessation. ... Successful smoking cessation was one of the 2 or 3 greatest challenges in managing my illness. I feared greatly the return of symptoms. I feel that people with mental illness who wish to stop smoking need cessation programs that are tailored to their psych. Situation. I must add that having stopped smoking benefited my mental health as my self-esteem grew greatly. The behavioral mechanisms I learned during the process of cessation proved to be template for other learning therapies to aid medication management of my psychiatric disorder.”
 --Mental Health Advocate, Wisconsin

phase evolves into full-blown psychosis; 2) development of methods for identifying individuals who are pre-morbid in clinical and community settings; and 3) development and early testing of new interventions in this phase. Research is expected to lead to clinically useful screens for detection of individuals at high risk for evolution into psychosis, the development and piloting of interventions with these individuals, and clinical trials to test the efficacy of prodromal interventions and feasibility of prevention in this population. In addition to primary prevention, new interventions must be developed to reduce the secondary consequences of serious mental illness including homelessness, incarceration, frequent relapse, and family burden.

Prevention Strategies

For most major mental disorders, the precise causes of the illnesses or how to alter these causes are not known, stymieing the development of interventions that could prevent the onset of illness. However, even for the most serious mental disorders, the severity and frequency of recurrence of illness can be reduced through appropriate preventive strategies, particularly behavioral-change interventions to strengthen adherence to treatment. In addition, for some disorders that are primarily behavioral in nature – such as conduct problems, and risky behaviors leading to HIV infection – research has shown that prevention strategies that encourage behavioral change can be successful in blocking onset of the disorder.

Prevention research includes interventions to reduce the risk of onset, or delay onset, of mental disorders and behavioral dysfunctions; reduce the severity and course of disorders; prevent comorbid conditions and disorders; and prevent relapse, recurrence, excess disability, side effects, and inappropriate service or resource use. Prevention is construed broadly to include not only the prevention of initial cases of mental disorders and related problems, but also the prevention of comorbid conditions, recurrence, relapse, functional impairments, side effects, and inappropriate service or resource use.

Objective

Better understand how people learn and change behavior in order to prevent illness, improve treatment outcomes, and prevent disability.

Prevention of mental disorders and related conditions often requires that individuals with, or at-risk for, these disorders change some aspects of their personal behavior over long periods of time. While controlled research trials have shown that such behavior change can be effective in preventing or reducing the severity of disorders, it is very difficult for people to learn how to change specific behaviors and maintain the changes over time.

- **Adherence in Treatment.** A new initiative encourages research on adherence to treatment and behavior change, building on information achieved through basic behavioral studies. NIMH encourages research that will address innovative approaches to adherence and behavior change; examine why, when, or where people seek or do not seek interventions for mental disorders; formulate and test provider strategies and behaviors to enhance recruitment, retention, and adherence; and promote treatment adherence among racial/ethnic minorities.

- **Suicide Prevention.** Approximately 90% of suicide victims had a mental or substance abuse disorder (or combination) at the time of death. Less than a third of these people were in treatment, and of those that were, few received adequate treatment for their mental and substance abuse disorders. NIMH will encourage research to design and evaluate suicide preventive efforts, determining their safety and effectiveness for particular groups at risk.

- **Prevention of Relapse of Anorexia Nervosa and Bulimia Nervosa.** Current treatments for patients with eating disorders are limited by frequent failure to achieve full recovery and high relapse rates after initial improvement. NIMH will encourage research to develop and test psychosocial and pharmacological interventions and combined treatment modalities and therapeutic strategies aimed at preventing relapse in patients with eating disorders. Because of the difficulties in recruiting and retaining patients with eating disorders in clinical trials, multi-site studies will be encouraged.

“My 16-year-old daughter has a diagnosis of rapid cycling bipolar disorder and/or borderline personality disorder...It’s time to research the existing residential programs throughout the country to assess their effectiveness (both therapeutically and academically). It is also time to establish a model of practices on which to base all new programs for these youngsters. Thank you and please don’t forget the complex and comprehensive needs of our children and adolescents. Perhaps, early intervention will keep some of these kids from getting lost in the adult system. ”
--Mother of Adolescent with Severe Mental Illness

Mental Health Services

The goal of mental health services research is to improve the quality and outcomes of care for individuals with mental disorders. Successful outcomes, or steps toward recovery, depend upon the optimization of interactions between the treatments selected, the care providers, and the participation of the individual patients. A better understanding of these interactions can be gained from collaborative research involving clinical researchers and basic social and behavioral scientists on fundamental questions related to mental health services. NIMH will encourage such multidisciplinary collaborations.

Objective

Determine the impact of organization and financing of services on outcomes and how to improve cost-effective service delivery, including early diagnosis and appropriate intervention.

Depending upon the nature and severity of their disorders, some individuals may require prolonged access to mental health services. There are many ways of organizing and providing mental health care. Economic considerations dictate that mental health care services be assessed both for effectiveness of outcomes – or how much patients are helped – and for costs. This information can guide further research on how to improve services.

- **Improving Mental Health Services for Children and Adolescents.**

Children with mental disorders respond to treatment better if their families are involved in the treatment. However, the vast majority of clinical treatments, services, and preventive models do not involve families in treatment, or give parents or other family members largely passive roles. NIMH will encourage research on the impact of family involvement in treatment planning. NIMH also will collaborate with the Center for Mental Health Services (CMHS), part of the Substance Abuse and Mental Health Services Administration (SAMHSA), on determining the effectiveness of treatments for children and adolescents in

community mental health care through the CMHS Comprehensive Community Mental Health Services Program for Children with Serious Emotional Disturbances.

- **Studying the Effects of Managed Behavioral Health Care.** Managed care has fundamentally changed how mental health services are allocated, thereby altering actual mental health care delivery. Providing mental health insurance parity in benefit packages is possible only through managed behavioral health care. To date, the structural complexity of separate benefits, often managed by separate companies, has not been well studied, especially for people with co-existing conditions – both physical and mental disorders, and mental and substance use disorders. NIMH will encourage research to address these questions.

GOAL 3

STRENGTHEN THE MENTAL HEALTH RESEARCH PLATFORM

For NIMH, more so than for many other components of NIH, mission-oriented research is multifaceted and broad in scope. Mental health researchers must be highly trained and skilled in the technology and knowledge base of fields as varied as the molecular neurobiology of the brain; genetics of mental disorders; behavioral psychology; treatment of mental illnesses; and the prevention of mental disorders. Increasingly, these researchers must be knowledgeable about and able to collaborate with other researchers in more than one field. Because our knowledge base in the neurosciences and behavioral sciences is growing so rapidly, and the methodology and instrumentation of modern neuroscience is of such increasing complexity and sophistication, training mental health researchers is now more challenging than ever before. Research success also requires the necessary resources and supportive infrastructure. In addition, it is essential that the public is knowledgeable about the goals and successes of mental health research, and that these successes are rapidly translated into improved treatment and preventive interventions.

To strengthen the capacity for future research, NIMH will work toward the objectives outlined in the Research Plan below and listed here:

- **Ensure future research capacity through support of research training and career development in those areas that hold the most promise for the next decade;**
- **Increase support for research training and career development where progress has been impeded by a dearth of researchers (for example, child and adolescent mental disorders);**

- **Ensure that adequate support for research training and career development is provided to encourage women to enter mental health research careers, and to remain and succeed in their careers;**
- **Ensure that adequate support for research training and career development is provided to encourage underrepresented minorities to enter mental health research careers, and to remain and succeed in those career tracks;**
- **Educate the public about mental illness risk, treatment, and prevention to reduce stigma and enhance participation in care;**
- **Develop systems for early dissemination of solid research findings that translate into evidence-based clinical practice;**
- **Increase the sharing of knowledge among researchers, providers, and consumers to facilitate the use of research results and best practices and to enhance the study of critical basic and clinical questions;**
- **Ensure the protection of human subjects in research and the maintenance of public trust;**
- **Encourage the development and sharing of research data, and biological materials to improve the speed and efficiency of research;**
- **Expand the availability of shared laboratory facilities, instrumentation, and other research tools and resources to accelerate the pace of scientific discovery and economize on investment.**

Research Plan

Researchers of the Future

Future progress in understanding, treating, and preventing mental illnesses, and in enhancing mental health, depends upon the knowledge and skills of students now in training and those who will be students in the future. It is imperative that good students, who are well trained and well equipped, dedicate themselves to mental health research.

Objectives

Ensure future research capacity through support of research training and career development in those areas that hold the most promise for the next decade.

The training of future mental health researchers must prepare them for the research areas and technologies that hold the greatest promise for the future. It will be equally important to encourage women scientists to develop research careers and attract and retain underrepresented minority groups in mental health.

NIMH supports a full range of National Research Service Award (NRSA) training programs – both institutional and individual – that assist undergraduate and graduate students interested in mental health research. For young scientists just beginning their research careers, the Institute supports a number of Research Career Development programs (K-awards) that provide limited support while the scientists build a record of achievement that will enable them to compete successfully for future grant support. Details of these programs are available on the NIMH web site, <http://www.nimh.nih.gov>. In addition, other training and career development initiatives designed to further the goals and objectives of this plan have recently been developed and are also described on the web site. Several examples of these are mentioned below.

- **Predoctoral Training in the Neurosciences.** NIMH and other NIH institutes have developed an institutional program to support broad training in the neurosciences focused on the early years of training before full-time thesis research is started. Typically, training programs are supported for 3-5 years.

- **Predoctoral Training in Bioinformatics and Computational Biology.** Increasingly sophisticated and complex technologies are generating massive amounts of biological data that require analysis; however, there is a shortage of researchers trained in the handling of such data. NIMH and other NIH institutes are encouraging the training of scientists whose primary professional identification and disciplinary affiliation is bioinformatics or computational biology.

- **Neuroinformatics Institutional Mentored Research Scientist**

Development. To enhance and facilitate research on the brain, NIMH and other NIH institutes will foster the career development of individuals with interdisciplinary expertise that bridges research in neuroscience and behavioral science with research in informatics. These efforts will ensure the development of neuroinformatics techniques in directions necessary for elucidating the major principles of basic and clinical neuroscience that underlie normal health, development, and the origins of mental and neurological disease.

- **Curriculum Development Award in Neuroinformatics Research and Analysis**

Analysis. Neuroinformatics combines neuroscience research with informatics research developed from the computer sciences, mathematics, physics, engineering or related sciences. NIMH and other NIH institutes are encouraging scientists who have the required scientific expertise to develop courses and curricula designed to train interdisciplinary neuroinformatics scientists at U.S. educational institutions.

Increase support for research training and career development where progress has been impeded by a dearth of researchers (for example, child and adolescent psychiatry and related fields).

As research priorities and objectives evolve, or new public health issues come to the fore, research in a new area may be limited by the availability of researchers who are trained in that area. In a timely example, as research evidence accumulated that mental disorders can begin in early childhood and that such early-onset disorders had serious implications for the individuals and for the Nation as a whole, NIMH found that there were very few researchers trained and qualified in child and adolescent psychiatry. In this case and similar situations, the Institute undertakes to correct the imbalance by training and fostering the careers of interested researchers.

- **Research Career Development in Mental Disorders of Children.**

The World Health Organization estimates that mental illnesses in children and adolescents will increase by 50 percent by the year 2020, exceeding other causes

of illness, such as childhood cancers and chronic diseases like asthma and diabetes. Despite these expanding mental health needs, very little research has been done to identify the causes, consequences and effective treatments for these illnesses in children, primarily because there are only a few well-trained investigators committed to research in child and adolescent mental disorders. NIMH is committed to enhancing and sustaining a critical mass of well-trained clinically oriented researchers committed to conducting research on children and adolescents with mental and behavioral disorders.

- **Career Development Awards: Child Abuse and Neglect Research.**

Child abuse and neglect can be extremely damaging to the life and development of a child or adolescent. NIMH and other NIH institutes are supporting career development for investigators who make a commitment to focus their research on child abuse and neglect and to conduct high quality, multi-disciplinary, clinically-relevant research on basic biological, behavioral, and social aspects of child and adolescent abuse and neglect.

- **NIMH Postdoctoral Research Training in Intervention Trials.**

Although effective treatments are available for most mental illnesses, some people with these illnesses are not helped by the treatments or don't stay with a treatment for various reasons. Clinical researchers are needed who are trained in the design and conduct of clinical intervention trials focused on the treatment, rehabilitation and prevention of severe mental disorders. NIMH supports a program of postdoctoral research training that aims to develop a cadre of clinically trained researchers committed to designing and implementing treatment studies for mental illnesses that use a public health model.

Ensure that adequate support for research training and career development is provided to encourage women to enter mental health research careers, and to remain and succeed in their careers.

Researchers, particularly in biology and the neurosciences, are often faced with very demanding work schedules and highly competitive pressures. For many types of experiments, investigators often need to work almost around the clock.

In addition, they must complete experiments and publish the results as quickly as possible, both because of the importance of quickly making research findings available and because of the highly competitive nature of biomedical science. For women researchers, these demands may conflict with childbearing and child rearing to the extent that they feel forced to delay or interrupt their careers. Such interruptions make it very difficult for them to resume their careers later because science is moving so fast; knowledge and skills become outdated within a very few years.

- **Reentry into Biomedical and Behavioral Research Careers.** NIMH, along with other NIH institutes, supports a program to provide administrative supplements to research grants to support individuals with high potential to reenter an active research career after taking time off to care for children or parents or to attend to other family responsibilities. These supplements will encourage fully trained individuals to reenter research careers within the missions of all the program areas of NIH. This program will provide administrative supplements to existing NIH research grants for the purpose of supporting full-time or part-time research by these individuals in a program geared to bringing their existing research skills and knowledge up to date. It is anticipated that at the completion of the supplement, the reentry scientist will be in a position to apply for a career development award or for a research grant award.

Ensure that adequate support for research training and career development is provided to encourage underrepresented minorities to enter mental health research careers, and to remain and succeed in those career tracks.

The NIMH has a long history of supporting nationwide specialized programs to increase the participation of underrepresented minorities in research relevant to the mission of the Institute. Despite these efforts, stretching back decades, racial and ethnic minorities remain underrepresented in the scientific disciplines needed for mental health research. NIMH has recently re-focused some its initiatives designed to encourage minority researchers to careers in mental health research.

- **Underrepresented Minority Fellowship Programs in Mental Health.**

NIMH encourages National Research Service Award (NRSA) institutional training grant (T32) applications designed to support the recruitment into, and training of individuals in doctoral programs in areas relevant to the mission of the NIMH. This program aims to enable minority investigators to undertake active, productive careers in scientific investigations related to mental health and mental illness. Toward that end, it is expected that the program will help train future scientists with state-of-the-art research skills in cutting-edge science, and a commitment to research in their chosen mental health related field. Areas of research interest to the NIMH can be found on the NIMH website at

<http://www.nimh.nih.gov/grants/grantgen2.htm>.

- **Underrepresented Minority Fellowship Program in Psychiatry.**

This initiative aims to increase the numbers of minority scientists trained to conduct patient-oriented mental health research, by supporting a national program of recruitment and training in outstanding research programs across the nation. This institutional fellowship program in psychiatry is designed to support the development and training of underrepresented minority psychiatrists to undertake active, productive careers in scientific research related to mental health and mental illness. Outcomes of successful training should include the mastery of research skills, commitment to future research activity and the promise of future achievement in research endeavors in the mental health field. Areas of research interest to NIMH are indicated in the NIMH Extramural Research Support Programs Announcement, located at:

<http://www.nimh.nih.gov/grants/grantgen.htm>.

- **Underrepresented Minority Dissertation Research Grants in Mental Health.**

A doctoral dissertation represents the most extensive research experience formulated and carried out by doctoral candidates, with the advice and guidance of mentors. Dissertation research involves a major investment of the doctoral student's time, energy, and interest and its substance is often the basis for launching a research career. The usual mechanisms used for the support of doctoral dissertation research have not attracted significant numbers of underrepresented minority students. To correct this situation, NIMH has

developed a program to stimulate and encourage underrepresented minority doctoral candidates to pursue research careers in any area relevant to mental health and/or mental disorders.

- **Scientist Development Award for New Minority Faculty.** NIMH would like to increase the participation of minority scientists as principal investigators in the Institute's research activities. To assist in this effort, the Institute has developed a program to provide new minority faculty members, early in their academic careers, with the time and assistance needed to initiate their own programs of research and to help them become outstanding independent investigators in mental health research. As with any new faculty members, it is expected that they will begin a program of research that will lead to refereed publications, promotion, and perhaps tenure. For new minority faculty members, who are often the first or only members of an underrepresented minority group in a department or program, there are also other expectations. They quickly become focal advisors for ethnic/minority students; they are eagerly solicited for inclusion on departmental, university, community, professional, and governmental committees; and they are expected to carry the usual teaching load, perhaps with the addition of some special cultural-difference seminars. This award, geared for a specific time in career development, will assist in enhancing the research capability and progress of its beneficiaries.

Research Utilization

Reaping the benefits of research requires that the scientific knowledge gained be rapidly translated into treatment or preventive interventions or used to accelerate other research or educate the public. Immediacy in translation of research knowledge into benefits is particularly urgent for mental illnesses. It is also an immensely challenging task, as messages must be tailored for researchers, treatment providers, people with mental illnesses and their families, Congress, insurance providers, and the public.

Objectives

Educate the public about mental illness risk, treatment, and prevention to reduce stigma and enhance participation in care.

Neurobiological research has shown that mental illnesses are disorders of the brain – much as heart diseases are disorders of another organ, the heart – and that these illnesses can be treated effectively. Unfortunately, this knowledge about the nature and treatability of mental illnesses is not widely shared, with the result that stigma harking back to the Middle Ages still surrounds mental illnesses. This stigma is reflected in inequities in insurance coverage for mental illnesses and often causes people with these illnesses not to seek treatment or cooperate fully with their treatments. It is essential that educational efforts both inform the public about mental illnesses and the treatments available, and influence people to act upon this information – to seek treatment and to take an active role in their own treatment.

NIMH considers public education about mental illnesses an important priority and has re-energized the Institute’s educational campaigns. Complete and up-to-date access to educational materials about the range of mental disorders is provided through the Institute’s web site (<http://www.nimh.nih.gov>).

- **Clinical Trials Recruitment.** The translation of research findings into treatment and effective care depends upon the participation in clinical research of people who have mental disorders. All too often, these individuals do not know about clinical research opportunities, or don’t understand the potential importance of a given study for themselves and others with mental disorders. NIMH will intensify efforts to communicate with the public, press, and researchers about ongoing and future NIMH clinical trials. To design more effective recruitment messages and strategies, the Institute will ask for input from individuals with mental disorders, family members, mental health advocacy organizations, and researchers on issues related to clinical trials promotion, participant recruitment, and protocol design.

“Here, in [Alaska], our services tend to lag research findings by ten or 15 years, and in some cases, [Alaska] follows theory-based programs rather than science-based programs. Hence, it would help family advocates if your plan looked at how research findings are being translated into State and local policies and services.”
-- Man from Alaska

- **Constituency Outreach and Education Program.** NIMH has launched a 5-year effort that enlists state mental health organizations as partners in disseminating research-based information on mental health to the public and to health professionals. Each outreach partner will conduct a mental health communications program aimed at public and health professionals within the state through media relations, statewide coalition building, and outreach to minorities and special populations, such as youth and elderly. Partners also will sponsor educational efforts that focus on primary care physicians, nurses, employers, and other groups, and promote recruitment of participants in NIMH-supported clinical studies. This initiative is part of a broader effort by NIMH to speed the translation of science into mental health services.

Develop systems for early dissemination of solid research findings that translate into evidence-based clinical practice.

All too often, years may elapse between the discovery of research results that could significantly improve treatments of mental illnesses and the actual use of this knowledge by mental health treatment providers. NIMH has called for more study of how the translation of research findings into clinical practice can be accelerated.

- **Dissemination Research in Mental Health.** NIMH will encourage studies of factors that influence the dissemination of mental health research knowledge across mental health service settings. Research is needed on the array of influences, and their interactions, that beneficially or adversely affect the adoption of valid mental health research findings into clinical practice, and on the effectiveness of knowledge dissemination interventions.

Increase the sharing of knowledge among researchers, providers, and consumers to facilitate the use of research results and best practices and to enhance the study of critical basic and clinical questions.

*"...[a]s a senior administrator in a large, multi-county, publicly funded mental health agency,... I suggest that consideration be given to making it a priority to strengthen information dissemination to community-based practitioners and programs in the widest possible manner, not only of new research findings but of past research and best practices as well."
--Health Administrator, Florida*

Mental health research, both basic and clinical, often leads to discoveries that could enhance the treatment of mental disorders by mental health care providers or facilitate the research of other mental health researchers, if the providers and researchers were aware of these findings. By the same token, if they knew of the findings, people who have mental illnesses would be better informed about treatment options and prevention strategies. NIMH has undertaken to increase and accelerate the sharing of knowledge among all these groups, using a variety of formats, including workshops, scientific journals, website, and an annual Research Roundtable that brings together representatives of mental health advocacy groups, researchers, and other interested parties. Additional knowledge-sharing initiatives include:

- **Regional Public Mental Health Forums.** As part of the process whereby NIMH sets research priorities, the Institute has initiated a series of regional meetings around the Nation, in which Institute leadership and staff members inform local consumers, mental health organizations, and political leaders of progress in research on mental disorders and mental health and listen to the concerns and issues of most interest to those present. A meeting in Alaska in August 1999, focused on rural mental health research and a meeting in Texas in December 1999 focused on research needs related to serious mental disorders. Similar meetings will be held in 2000 and future years.

Enabling Research of the Future

Neuroscience and other branches of mental health research are, today, on the threshold of a period of unparalleled productivity and rate of progress. To guarantee this prospect, a solid foundation for research of the future will require public trust and research infrastructure, as well as training of researchers. NIMH is dedicated to enabling and enhancing future research capabilities.

Objectives

Ensure the protection of human subjects in research and the maintenance of public trust.

Research on mental health and mental illnesses can only be conducted with the willing cooperation of people with mental illnesses – whether it is “posing” for a brain scan or participating in a clinical trial – because there are no animal models of these most human of illnesses. Although these people play a key role in learning about, and improving treatments for, mental illnesses, they are also uniquely vulnerable in many respects. NIMH is committed to protecting the welfare and well being of people who participate in mental health research.

- **Monitoring the Involvement of Human Subjects in Research.** To provide additional oversight and scrutiny of mental health research in which human subjects participate, NIMH established the Data and Safety Monitoring Board (DSMB). The DSMB is responsible for considering and reviewing all research protocols and consent documents for multi-site clinical trials supported by the Institute and for monitoring safety issues and the quality of the accumulating data. The Board also reviews data on patient outcomes to determine if any study procedures should be altered or stopped because of evidence of benefit or harm to participants. NIMH will strengthen and increase this oversight process. The DSMB will be enlarged by the addition of new members and split into two sections, one of which will focus on newly instituted treatment contracts, while the other section will continue to monitor clinical trials.

- **Human Subject Review Council Workgroup.** At the request of NIMH, the National Advisory Mental Health Council, which reviews and approves all research grants awarded by the Institute, formed a special Human Subject Review Council Workgroup (HSRCW), composed of nine non-NIH voting members – including three ethicists and two consumers – and a Scientific Administrator. This Workgroup meets following each Council session to consider any proposed research that would discontinue medications to which a patient has responded well or use pharmacological or behavioral challenge methods to explore the possible reappearance or worsening of symptoms. In addition, the HSRCW reviews any proposed research studies that would involve delaying treatment or a temporary discontinuation of medications by individuals

“I was pleased to see that you had included a statement in support of protection of human subjects [in research]. I respectfully suggest that you strengthen this statement considerably. ... It would be helpful and reassuring to see ... NIMH take a leading role of reform in these areas.”
--Psychiatric Rehabilitation Practitioner

who might have benefited substantially from the treatments. This Workgroup strives to identify potentially problematic situations, along with appropriate safeguards, and refers these proposals to the full Council for final action. NIMH will continue to support and enhance the work of the HSRCW.

- **Public Participation in the Review of Grants.** NIMH is seeking to broaden the range of perspectives brought to the review of applications for grants involving mental health treatment and services research. For this purpose, persons who have had personal experience with mental disorders – as patients, family members, service providers, policymakers, or educators – have been invited to apply to become members of grant review committees. These individuals provide a unique and valuable perspective on the appropriateness of the informed-consent processes proposed in grant applications. NIMH will continue to include such public participation on grant review committees.

- **Research on Ethical Issues in Human Studies.** NIMH, along with other NIH institutes, will support research on ethical issues that arise with research involving human participants. Because of rapid advances in science and complexity of the research enterprise, more empirical work is needed to guide researchers and Institutional Review Board (IRB) members towards optimal and appropriate protections for research participants. For example, information is needed on how best to provide information about a study's methods and procedures to improve participants' comprehension; the effect of different recruitment strategies on retention of study participants; methods to assess the risk-to-benefit relationship; or the effects investigator characteristics and behavior have on levels of recruitment, retention, and withdrawal.

Encourage the development and sharing of research data, and biological materials to improve the speed and efficiency of research.

Often the fruits of one scientist's research, such as data or biological samples, could also be used by another scientist for a quite different study, thus expanding the knowledge gained, extending the interpretation of results, or accelerating the

pace of research. NIMH will encourage the sharing among researchers of data, biological materials, techniques, and other research resources.

- **Genetics of Neurobehavioral Disorders in Existing Samples.** NIMH will encourage multidisciplinary, collaborative genetic research projects to integrate different pedigree data sets that have already been collected for the study of a given neurobehavioral disorder. Projects will assemble data from multiple research groups for combined analysis, and will focus on one of the following: attention-deficit hyperactivity disorder, bipolar disorder or other related mood disorders, recurrent early-onset depression, eating disorders, obsessive-compulsive disorder or other anxiety disorders, panic disorder, schizophrenia or other psychotic disorders, personality disorders, or Tourette's syndrome. The goal is to assemble a large data set that has adequate statistical power for identifying genomic regions that may harbor loci conferring susceptibility to the neurobehavioral disorder under investigation. Data and biological materials collected and produced in these projects will augment pre-existing resources distributed by the NIMH for genetic analyses by the wider scientific community.

- **Risk Factors for Psychopathology Using Existing Data Sets.** NIMH will encourage extensive and innovative use of existing data sets to study the development of psychopathology or resilience in order to guide the Institute's development of prevention and early intervention strategies. This work will mine the full potential of public-use and other extant data sets to increase knowledge of risk and protective factors for psychopathology or resilience in community-based and clinical populations, and encourage applications from new investigators to examine these research areas using state-of-the-art data analytic procedures. NIMH will also encourage studies to conduct analyses using mental health research data that is in public use format or that is privately held by a principal investigator.

Expand the availability of shared laboratory facilities, instrumentation, and other research tools and resources to accelerate the pace of scientific discovery and economize on investment.

Research can be enhanced and made more efficient and economical through the sharing of research resources, particularly those that require major expenditures to purchase or special expertise to operate. Examples of research sharing encouraged by NIMH include:

- **Development of Neuroimaging Biomarkers for CNS Disorders.** PET and SPECT are abbreviations of two related neuroimaging techniques that have proven valuable in the study of brain disorders. However, the usefulness of these techniques is now limited due to a lack of CNS receptor-specific ligands to serve as biomarkers. As part of a planned research initiative to stimulate the development of new ligands (see Goal 1), NIMH also plans to develop a Center for PET/SPECT Ligand Development on the NIH campus as a cost-effective resource for extramural and intramural scientists from NIMH and other NIH Institutes.
- **Neuroimaging Informatics Technology Initiative.** Neuroimaging studies generate vast amounts of data, much of which is analyzed with unshared tools, and stored in unshared databases. The current lack of interoperability across neuroimaging data processing laboratories has made progress difficult. The *Neuroimaging Informatics Technology Initiative* (NifTI) would allow the biomedical community to make better use of these data. NifTI would serve the extramural and intramural neuroimaging research communities by developing, documenting, and disseminating a range of informatics tools, including tools for simulating, analyzing, segmenting, registering, integrating, visualizing, translating, sharing, and interacting with neuroimaging data.

Anxiety Disorders

Although anxiety is a normal emotion, extreme anxiety can lead to constant feelings of panic, apprehension, or crippling fears. Anxiety disorders are the leading forms of mental illness in the US, affecting more than 20 million Americans each year. There are several major forms of anxiety disorders.

Panic Disorder is marked by “panic attacks” or sudden attacks of terror and irrational fear, feelings of impending doom, and physical symptoms such as palpitations, shortness of breath, sweating, weakness, and feelings of unreality. Individuals with panic disorder are seven times more likely to attempt suicide than those without a history of mental illness. However, medication and behavioral therapy are effective in treating 70-90% of people who suffer from panic disorders. Each year, panic disorder affects 1.3% of the population, or 2.4 million people, and often occurs in combination with other mental disorders.

Obsessive-Compulsive Disorder (OCD) is characterized by recurrent, intrusive and senseless thoughts, images or ideas (obsessions) and unnecessary, ritualized, and repetitive actions (compulsions). Obsessive thoughts often involve contamination, violence, or doubt, and persist even though they are irrational or unwarranted. Compulsions, such as excessive hand washing, repeated checking (e.g., to see if the doors are locked), and counting rituals, are often carried out in an attempt to prevent some unwanted event. OCD can cause much distress, guilt, and disability. **In a 1-year period, 2.1% of the adult US population, nearly 4 million Americans, was diagnosed with OCD.**

Post-Traumatic Stress Disorder (PTSD) is the inability to escape memories and thoughts about horrifying past experiences. PTSD, earlier recognized as “shell shock” or “battle fatigue,” came into public consciousness after Vietnam veterans reported flashbacks of their wartime experiences, but can follow any traumatic event, such as violence, natural disasters, rape, or abuse. Recollections of the event affect everyday functioning and appear in disturbing dreams. PTSD produces several kinds of symptoms, such as avoiding important activities, feeling emotionally numb, or experiencing sleep difficulties or hypervigilance.

Phobias are persistent, irrational fears of an object or situation, coupled with a compelling desire to avoid that fear. In many instances, phobias are seriously disabling, keeping those affected from engaging in normal activities. There are many different types of phobias. Simple phobias are specific fears, like fear of flying, snakes, or heights. Social phobia (a fear of public humiliation or embarrassment) and agoraphobia (the fear of being in open places) are distinguished from simple phobias because they usually prevent people from engaging in routine activities. **Taken together, phobias affect about 10.9% of the population in a given year.**

Generalized Anxiety Disorder (GAD) is a persistent condition marked by exaggerated or unrealistic worries, coupled with physical symptoms of tension, such as trembling, heart palpitations, or difficulty concentrating and sleeping. Generalized anxiety, which often accompanies other illnesses, can be sufficiently severe and prolonged to be diagnosed as a separate disorder. Unlike the structured and specific worries that characterize OCD, those seen in generalized anxiety disorder are diffuse, non-specific, and cover many themes.

ABOUT MENTAL ILLNESS AND MENTAL HEALTH

Mental illness refers collectively to all diagnosable mental disorders. Mental disorders are health conditions that are characterized by alterations in thinking, mood, or behavior (or some combination thereof) associated with distress and/or impaired functioning. During a 1-year period, 22 to 23 percent of the U.S. adult population—or 44 million people—have diagnosable mental disorders, according to reliable, established criteria. In general, 19 percent of the adult U.S. population have a mental disorder alone (in 1 year); 3 percent have both mental and addictive disorders.

Apart from those persons who have diagnosable mental disorders, are those who experience various “mental health problems.” This term refers to signs and symptoms of mental distress that are of insufficient intensity or duration to meet the criteria for any mental disorder. Almost everyone has experienced mental health problems in which the distress one feels matches *some* of the signs and symptoms of mental disorders. Mental health problems may warrant active efforts in health promotion, prevention, and treatment; these interventions, too, should be based on research.

Mental Disorders are Disabling. The burden of mental illness on health and productivity in the United States and throughout the world has long been profoundly underestimated. Data developed by the massive Global Burden of Disease study, conducted by the World Health Organization, the World Bank, and Harvard University, reveal that mental illness, including suicide, ranks second in the burden of disease in established market economies, such as the United States (Table 1).

Mental illness emerged from the Global Burden of Disease study as a surprisingly significant contributor to the burden of disease. The measure of calculating disease burden in this study, called Disability Adjusted Life Years (DALYs), allows comparison of the burden of disease across many different disease conditions. DALYs account for lost years of healthy life regardless of

whether the years were lost to premature death or disability. The disability component of this measure is weighted for severity of the disability. For example, major depression is equivalent in burden to blindness or paraplegia, whereas active psychosis seen in schizophrenia is equal in disability burden to quadriplegia.

By this measure, major depression alone ranked second only to ischemic heart disease in magnitude of disease burden (see Table 2). Schizophrenia, bipolar disorder, obsessive-compulsive disorder, panic disorder, and post-traumatic stress disorder also contributed significantly to the burden represented by mental illness.

Mental disorders impose an enormous emotional and financial burden on ill individuals and their families. These disorders are also costly to the Nation in reduced or lost productivity (indirect costs) and in medical resources used for care, treatment, and rehabilitation (direct costs).

A recently completed NIMH study found that, in 1992, mental disorders cost the U.S. \$94 billion in indirect costs and \$66.8 billion in direct costs (under managed care) for a total of \$160.8 billion.

Table 1. Disease burden by selected illness categories in established market economies, 1990

	<i>Percent of Total DALYs</i>
All cardiovascular conditions	18.6
All mental illness	15.4
All malignant diseases (cancer)	15.0
All respiratory diseases	4.8
All alcohol use	4.7
All infectious and parasitic diseases	2.8
All drug use	1.5

Table 2. Leading sources of disease burden in established market economies, 1990

	Total DALYs (millions)	Percent of Total
All causes	98.7	
Ischemic heart disease	8.9	9.0
Unipolar major depression	6.7	6.8
Cardiovascular disease	5.0	5.0
Alcohol use	4.7	4.7
Road traffic Accidents	4.3	4.4

ABOUT STRATEGIC PLANNING

The principal means by which NIMH supports research is through grants to scientists working at universities and in other research settings throughout the country. This “extramural” research grant system across the National Institutes of Health (NIH) is premised on *independence*, embodied in “investigator–initiated” research; on *self-governance*, evident in peer review of science by scientists as the primary basis for judging the merits of research proposals and awarding funds; and on the powerful incentive of *competition* among highly trained scientists and clinical investigators.

For over half a century, soliciting creative ideas from working scientists has proven to be a more effective approach to science than centrally planned research. The approach has propelled the U.S. to global preeminence in biomedical science.

Strategic planning offers a timely means of strengthening the tried-and-true formula described above. Today, an abundance of scientific capabilities and opportunities exist in the areas of brain and behavioral research and we are increasingly able to perceive how particular research emphases will achieve desired goals or outcomes, whether these are new knowledge about basic processes, the design and development of clinical interventions, or other objectives. As we refine scientific tools and capabilities for treating and preventing mental illness, we also are gaining unprecedented knowledge about the distribution, determinants, and costs of mental disorders, information that underscores the urgency of research. Yet another factor that makes an open strategic planning process timely is the presence of knowledgeable advocates, including patients and families, who can offer valuable information and insights about issues that warrant research.

A research strategic plan constitutes a response to each of these important developments while maintaining those features of our research system – independence, self-governance, and competition – that have made our Nation’s biomedical research programs so successful to date. Development of this

Strategic Plan for Research on Mental Illness and Health has involved a gratifying number of individuals and organizations working in collaboration with staff of the NIMH.

HIGHLIGHTS OF NIMH RESEARCH PROGRESS

NIMH research continuously generates information that enhances the capacities of health care professionals on the front lines of medicine. In the past year, science advances achieved by NIMH-funded scientists have ranged from insights into the fundamental biology of the brain to the development of new therapeutic and preventive strategies. Each advance has a rich history of science behind it, and in many cases, a future of clinical application ahead of it.

Selected Advances in NIMH Science During 1999

Mouse Memory Gene Offers Clue to Human Learning and Memory.

Manipulating a gene that plays a role in the chemical processes involved in memory formation in mice offers insight into the link between genes and “intelligence” in humans. Investigators inserted into a mouse embryo extra copies of a gene normally found in young mice, but not adult animals. Learning abilities decline in many animals as they age, but as these mice matured, they learned faster, remembered more, and were better able to apply what they learned than their littermates who had not received the altered gene. While this is still an early development in the biological study of intelligence, it is encouraging news in the fight against age-related memory loss, senility, and Alzheimer’s disease.

New Brain Cells Formed in Response to Learning. Conventional scientific wisdom long has held that persons are born with a set number of brain cells and that as these cells die off in later adult life, problems such as memory loss and senility are inevitable. Now, NIMH-supported scientists have found that when rats were trained to navigate in spaces that were new to them and to associate disconnected events, there was a dramatic increase in the number of neurons in the hippocampus. Evidently, neurons are generated in response to the

challenge of new learning and live longer when learning is taking place. In other words, learning, practicing, and remembering are all activities that seem to be linked not only to the development of new neurons, but with keeping those new cells healthy, functional, and living longer.

Neural Activity Shapes the Brain's Cells. NIMH-supported researchers have shown that neural activity may play a profound role in shaping dendrites, the branching extensions from neurons, during brain development. The stimulation of one class of neurotransmitter receptors (*N*-methyl-D-aspartate, or NMDA, receptors) enhanced dendrite growth, and these structural changes were long lasting. Such rapid, input-specific changes in the structure of neurons are likely to play important roles in the birth of new connections between neurons and also in more subtle rearrangements of existing connections. These structural changes may also be involved in important changes in brain cell function that occur during development or as an outcome of learning.

The Long-term Impact of Depression in Adolescence. Parents, educators, and even health care providers often attribute the signs of depression in adolescents to “just a phase” and expect the youngster “to grow out of it.” Yet right now, an estimated 4 to 6 percent of all adolescents in the U.S. have a major depression that could lead to suicide, impair development and quality of life, cause conduct problems, and, in some cases, be related to violent behavior, such as recent school shootings. Research shows that depressed adolescents are more likely than their healthy peers to be hospitalized for psychiatric or medical reasons and to be impaired in work, social, and family life. These findings foretell the devastating impact that adolescent depression can have across the lifespan and, in turn, the urgent need for early detection and appropriate treatment.

Exploring Psychosocial Treatments for Depressed Adolescents. Some types of antidepressant medications (tricyclics) do not seem to work for adolescents; other types (serotonin uptake inhibitors) do, if used properly. Now, NIMH-supported research suggests that a form of psychosocial treatment, interpersonal psychotherapy (IPT), can be effective for adolescent depression. In a controlled trial, about twice as many teens receiving IPT remained in treatment

for the entire period, as did matched controls that received clinical monitoring only. By the end of the trial, 75 percent of the group receiving interpersonal therapy had recovered from their depression, compared to only 46 percent of those in the control group. IPT may prove to be an important means of treating depression among adolescents.

An Alternative to Hospitalization for Children with Severe Mental Illness. Multisystemic therapy, or “MST,” relies on teams of providers who take therapy directly to children with severe mental illnesses, offering home-based care and involving families, schools, and neighborhoods in the process. Evaluated in three linked studies funded by NIMH, MST was found to offer an excellent alternative to psychiatric hospitalization or residential treatment, reducing by about 50 percent the need for hospitalization. When hospitalization *was* required, length of stay was reduced by nearly 75 percent. Therapists, families, and the children themselves viewed MST positively. MST demands a different structure for caregiver services from that currently used in most parts of the country, but reorganizing in support of this community-based service promises improved outcomes for children dealing with marked emotional difficulties, while reducing the financial burden of care delivery.

Clues to the Nature of Schizophrenia. A rare, and usually particularly severe, form of schizophrenia begins in childhood. In a continuing study, NIMH intramural researchers are using MRI (magnetic resonance imaging) to examine the brains of children who have childhood-onset schizophrenia, or COS, at 2-year intervals as they mature. Comparing changes in their brain structure with those of healthy children of the same sex and ages, the investigators are detecting clear abnormalities in brain development in the children with COS. They find a pattern of changes in areas of the brain important for memory and planning – a pattern specific to schizophrenia. It is likely that these progressive changes are related to the triggering, or actual onset, of the illness. Further study of these changes may shed light on the cause and progression of the illness and lead to better medications for treating schizophrenia.

Generational Transmission of Psychopathology. In a multi-generational study, NIH-funded investigators found that, in families in which

both grandparents and parents had experienced a clinical depression, a disconcerting 49% of the grandchildren showed signs of psychopathology, with high risk for anxiety. Typically, anxiety in young children is viewed to be a part of normal development, and something that the child will outgrow. In these high-risk families, however, anxiety symptoms are being transmitted across the generations, and, for family members, the onset of an anxiety disorder before puberty is linked to a high risk for the subsequent development of serious, recurring major depression.

It's 9:00 P.M. Have You Tucked Your Teen In? The steady shift toward early morning school openings can contribute to diminished academic performance, memory lapses, and mood changes, as well as behavior problems. Previous research has indicated that optimal alertness in adolescents requires over 9 hours of sleep nightly. This NIMH study shows that early school start times for adolescents are associated with significant sleep deprivation, both because 9 hours of sleep would require unrealistic – if not unattainable – bedtimes and because younger teens, in particular, may have a greater biological need for sleep. In susceptible young people, insufficient sleep may lead to academic, behavioral, and psychological problems, as well as increased risk for accidents and injuries, particularly for teens who drive.

Changing Women's Behavior to Prevent Disease. Women now account for about 20% of new AIDS cases, making the illness a leading cause of premature death for American women and, particularly, for low-income African American and Hispanic women. In response to this trend, NIMH-funded investigators conducted an HIV prevention trial involving almost 700 women living in 18 low-income housing developments in five U.S. cities. The research project taught women how to reduce the risk for HIV infection and involved women who were popular opinion leaders among their peers in other community HIV prevention activities. Twelve months later, the frequency of unprotected intercourse acts within the past 2 months among women participating in the study was lower than when they entered the trial. By contrast, there was essentially no change in risky sexual behaviors among the women in the control groups.

Redefining the Need for Mental Health Care among Older

Americans. Older people visit their primary-care doctors more often than do younger people, but their mental health concerns receive relatively less attention. NIMH-supported researchers screened 224 patients between the ages of 60 and 89 years of age, from a variety of socioeconomic backgrounds. The study confirmed not only that mental health problems are common among older people, but also that the nature of problems differs from those seen in younger individuals. Depression ranks very high as a health problem among the elderly—but so do dementia, alcohol abuse and dependence, and bipolar disorder. Observation and management of these concerns will go far toward controlling costs of care, particularly given the very effective tools (simple but reliable in-office tests, drug therapies) now available to primary-care practitioners.

Stories of NIMH Research Progress

Research progress is cumulative, with newer findings building upon and expanding earlier results. Separate, incremental advances in science, over time, come together in sometimes-unexpected ways to produce giant steps, as in these three chronicles of discoveries.

Research Progress: *Understanding & Preventing Teen Violence: Finding Common Ground*

Antisocial teenagers who commit violent criminal acts are among the Nation's most disturbing burdens. In 1999, more than 80,000 adolescent arrests were reported. Because the precise causes of violence among young people are often unclear, communities and health care agencies urgently need specific information to help them direct resources and money for the most comprehensive results in preventing and reducing violent behavior among teens.

Now, an ambitious series of long-term studies funded by NIMH suggest that aggressive behavior among teens does not result from any single factor; rather, the shaping of a violent adolescent is based on a cluster of related risk factors, including single (or no) parents, abuse and violence at home, early problem behavior during childhood, parents or friends involved in criminal activities, substandard educational opportunities, and poverty. Given these diverse risk factors, where can we best target intervention and treatment programs?

A central research finding is that risk factors for adolescent violence are both learned and cumulative. Violence, in other words, is taught by example as teens "model" the violence seen throughout their childhoods in their homes and communities, accumulating ever-greater risks of an ongoing pattern of aggression and hostility in the process. With a lack of opportunities for education and work thrown into this volatile mix, conditions favor a life based on antisocial behavior, ranging from school failures and emotional withdrawal to acts of extreme violence.

Children-at-risk who receive help in building effective learning skills as early as possible in their lives (beginning with verbal skills and "verbal I.Q.") are better equipped for school success and related developmental advantages. Research involving children as young as age 6 has shown that early, comprehensive programs that cross all areas of a child's life (home and family, school, and self) reduce academic and personal difficulties well before adolescence.

Because early education measures are often missing in the lives of disadvantaged children, approaches are needed for the early teen years, after troubles with violent behavior have often already begun. A form of treatment known as multisystemic therapy ("MST") identifies the natural strengths in a young person and their family as well as resources already in place in a specific community, capitalizing on the combined effect of these positive attributes. An individualized, home-based treatment that joins a young person with family, teachers, school counselors, and therapists in a team approach, MST encourages connections with more successful peers and offers children and families new ways to create support networks and ensure long-term benefits. MST programs have shown a substantial reduction in violence, aggression, and criminal activity.

Researchers are mindful that many antisocial young people also suffer with underlying psychological disorders, including depression and attention deficit hyperactivity disorder. Early, research-based efforts to address these problems clearly confirm that therapeutic programs in high schools can reduce depression among adolescents, reducing the possibility of "self-sabotage" due to personality issues and psychological disorders.

Incorporating the efforts of investigators from across the country, in cities, small towns, and rural areas, research is providing formidable new tools for helping this country's aggressive and violent young people, establishing a vital common ground for treatment and intervention programs.

Research Progress:*Balancing Caring with Self Determination: Community Services for Adults with Severe Mental Disorders*

One of the great achievements seen in mental health care in recent decades has been replacement of long-term inpatient hospitalizations with shorter, acute-care stays and discharge to the community. Many persons with chronic as well as recurrent, episodic mental disorders engage the tasks and challenges of community living fully and independently, yet a substantial proportion require an extra measure of assistance to prevent relapses and increase functioning and stability in the community. People with severe mental disorders may need one or more community-based services, including continued medication, rehabilitation and vocational assistance, substance abuse counseling, and social supports. The system responsible for providing these and other community-based services needs to be flexible to adapt to and meet evolving needs, preferences, and expectations.

For over two decades, clinicians and researchers have been working together to develop and refine models of care that anticipate and respond to an array of needs but, at the same time, do not rob the person with a mental disorder of self-determination. The most successful of these models is the Program for Assertive Community Treatment (PACT or ACT) developed Drs. Leonard Stein and MaryAnn Test, in Wisconsin, with NIMH support. PACT programs have two key components: (1) a mobile, multidisciplinary, continuous care team that actively seeks out and engages clients in programs; thus the term, assertive outreach, and (2) a strong practical help orientation that assures that patients' needs are being met and problems recognized early in their development to prevent patients dropping out of treatment. This model has been tested and adapted for various population and delivery system characteristics in the United States, England, and Australia.

To date over 400 assertive community treatment teams exist in the U.S., which attests to both the endorsement of the program by mental health professionals and advocacy organizations, and the established cost benefits to states – as evidenced by the 1999 authorization by Health Care Financing Administration (HCFA) for State Medicaid directors to use Medicaid funding to support these programs. Since variation in programs is inevitable, SAMHSA established guidelines for programs in 1998 based on the much-researched Wisconsin model. HCFA is also urging State programs to consider recommendations from the Schizophrenia Patient Outcomes Research Team (PORT) landmark study funded by NIMH and the Agency for Health Care Policy Research (AHCPR) to provide more comprehensive care for severely mentally ill persons.

Caring for people with severe mental disorders in community settings will continue to be a challenge for those providing care and for those trying to organize systems that can respond to the needs. But thanks to our investment in research on PACT and other community-based approaches, we have the knowledge necessary to set up programs that can reduce hospitalizations, decrease homelessness, and work toward helping individuals with severe mental illnesses maximize the quality of their lives.

Research Progress: *Depression can be treated!*

Depression is the fourth leading worldwide cause of disability now and is projected to be the second most disabling disorder by 2020. In the 1940s, depression and other mental illnesses were considered virtually untreatable. By the early 1950s, however, with the discovery of brain neurotransmitters, researchers found that not only was depression a biochemical disease, but that the depression-specific biochemical imbalance was correctable. As researchers learned how these neurotransmitters function in the brain, several classes of antidepressant medications – drugs that have helped many people combat depression – were developed. One of the most promising classes of antidepressants, the selective serotonin reuptake inhibitors (SSRIs), of which fluoxetine (Prozac) is the prototype, resulted from four decades of extensive basic research, private-sector R&D and dialogue between basic scientists, clinical researchers, industry, and regulatory agencies. While the progress in treating depression has been monumental, SSRIs are also showing promise in the treatment of other mental disorders such as obsessive-compulsive disorder, bulimia, and panic disorder. Depression is now treatable because our Nation's investment in biomedical research supports a diverse group of scientists who can decipher important breakthroughs from serendipitous discoveries and who can then target their research to develop products that advance health.

NIMH Communications

People confronting mental illness in any form desperately want and need information about the illness. NIMH strives to make information of the highest quality available in a variety of forms.

- The NIMH Office of Communications and Public Liaison answers 60,000 individual requests each year; many requiring highly customized and researched responses to difficult questions; for instance, how to deal with treatment-refractory conditions. Forty percent of people who call ask for information about depression. Anxiety disorders come next, then child and adolescent mental disorders, and 5 percent about schizophrenia. Many people inquire about clinical trials and when new medications will be available.
- NIMH publishes booklets on schizophrenia, depression and other mental disorders.
- Research fact sheets on many areas of mental health research are available, as are briefing papers on many facets of brain research and mental illness, entitled as a series “Science on Our Minds” – a series that was prepared originally for the White House Conference on Mental Health.
- NIMH maintains an internet website, <http://www.nimh.nih.gov>, that averages more than 4 million “hits” per month where much of the communications materials can be obtained. There are presently over 1,000 documents on the website, as well as videos and recorded lectures.
- NIMH reaches out as well through the press to the larger American public, answering about 1800 press calls a year. When traumatic events – such as school shootings – occur, NIMH reaches out to reporters to connect them with advocacy groups, NIMH grantees and specialists who can provide specific information.
- NIMH is initiating a constituency outreach and education program that will develop partnerships with mental health advocacy organizations in each of the 50 states, the District of Columbia, and Puerto Rico. These state organizations will then be able to disseminate science-based information on mental disorders.
- NIMH maintains a ListServ to e-mail out timely information to more than 100 professional and advocacy organizations.
- Copies of NIMH publications may be obtained either through the website mentioned above or by calling 301-443-4513 or writing to:
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