National Institute of Mental Health

NATIONAL INSTITUTES OF HEALTH

DEPARTMENT OF HEALTH AND HUMAN SERVICES

FY 2004 Budget

6001 Executive Blvd., Bethesda, Maryland 20892

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
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NIMH
National Institute of Mental Health

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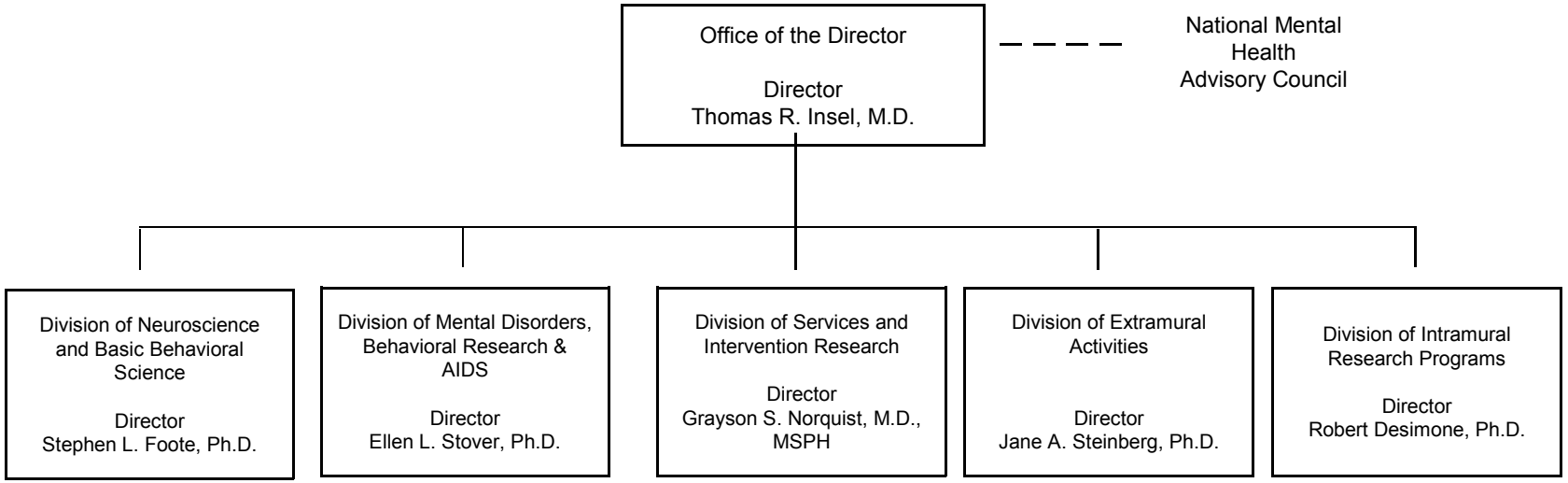


NATIONAL INSTITUTES OF HEALTH

National Institute of Mental Health

For carrying out section 301 and title IV of the Public Health Service Act with respect to mental health, $1,382,114,000

National Institutes of Health
National Institute of Mental Health

Amounts Available for Obligation 1/

Source of Funding	FY 2002 Actual	FY 2003 Amended President's Budget	FY 2004 Estimate
Appropriation	$1,248,626,000	$1,343,728,000	$1,382,114,000
Enacted Rescissions	(1,986,000)	(0)	---
Subtotal, Adjusted Appropriation	1,246,640,000	1,343,728,000	1,382,114,000
Real transfer to:			
Other HHS Agencies through Secretary's one-percent transfer authority	(1,348,000)	(0)	(0)
Comparative transfer from:			
Fogarty International Center for International Services Branch	47,000	47,000	0
Comparative transfer to:			
Office of the Director for program changes	(1,181,000)	(1,275,000)	(0)
National Institute of Biomedical Imaging and Bioengineering	(10,000,000)	(10,000,000)	(0)
Subtotal, adjusted budget authority	1,234,158,000	1,332,500,000	1,382,114,000
Unobligated Balance, start of year	0	0	0
Unobligated Balance, end of year	0	0	0
Subtotal, adjusted budget authority	1,234,158,000	1,332,500,000	1,382,114,000
Unobligated balance lapsing	(0)	---	---
Total obligations	1,234,158,000	1,332,500,000	1,382,114,000

1/ Excludes the following amounts for reimbursable activities carried out by this account:
FY 2002 - $5,128,000; FY 2003 - $5,128,000; FY 2004 - $5,128,000
Excludes $153,428 in FY 2002 and $159,565 in FY 2003 for royalties.

Justification

National Institute of Mental Health

Authorizing Legislation: Section 301 of the Public Health Service Act, as amended. Reauthorizing legislation will be submitted.

Budget Authority:

FY 2002 Actual		FY 2003 Amended President's Budget		FY 2004 Estimate		Increase or Decrease	
FTEs	BA	FTEs	BA	FTEs	BA	FTEs	BA
759	$1,234,158,000	763	$1,332,500,000	750	$1,382,114,000	(13)	$49,614,000

This document provides justification for the Fiscal Year 2004 activities of the National Institute of Mental Health (NIMH), including HIV/AIDS activities. A more detailed description of NIH-wide Fiscal Year 2004 HIV/AIDS activities can be found in the NIH section entitled "Office of AIDS Research (OAR)."

Introduction

Implicit in the National Institute of Mental Health's (NIMH) mission – to reduce the burden of mental illness and behavioral disorders through research on mind, brain, and behavior – is the challenge of ensuring that new information finds its way into the hands of the end users of research. These include individuals with mental disorders, health care providers, mental health service delivery systems, and policymakers at all levels of governance. Today, with the decoding of the human genome accelerating the pace of discovery in all areas of basic and pre-clinical medical science, there is increased urgency at multiple downstream points to move new information forward. This task will assume added importance with release of the final report of The President's New Freedom Commission on Mental Health later this year. The Commission's charge is to identify specific examples of community-based care models that are demonstrably successful in achieving desired outcomes.

Given these emphases on public health applications of NIMH-funded research, it is timely to review steps the Institute is taking to ensure that new scientific information is transmitted systematically and continuously into the clinical and public health domains. Following this brief introductory discussion, subsequent sections of the narrative will highlight scientific advances realized under NIMH support in the past year, and describe new research initiatives NIMH will undertake in FY 2004 that build on recent progress in genetics, epidemiology, neurobiology, and other areas of research.

The Path of Knowledge: From Discovery to Application

Among the nodal points in the clinical information pipeline are those at which investigators translate basic knowledge into clinically relevant questions and protocols. Once questions are so framed, the process continues with controlled clinical efficacy trials, clinical effectiveness trials to ascertain that interventions shown to be efficacious in rigorously controlled settings also are practical in the "real world," and a range of efforts to disseminate proven interventions and facilitate their incorporation into community-based mental health care.

Translational Research: An early and critical point for facilitating appropriate public health use of new scientific information occurs at the divide where essentially raw data about the workings of basic brain and behavioral processes accumulate and are examined in a clinically relevant framework. Investigators who can bridge this divide are particularly important in behavioral science, where pressing questions include (1) how basic behavioral processes are altered in mental illnesses and how these processes are critical for improving diagnosis, treatment, rehabilitation, and prevention; (2) how mental illnesses and various treatments affect people's ability to function within their families, school, and the workplace; (3) how social, cultural, and other environmental contexts affect the origins, treatment, and prevention of mental illnesses; and (4) how to interpret and understand information derived from molecular genetics and basic neuroscience in a broader environmental and behavioral context.

To better position the field to conduct translational research across disciplinary boundaries, NIMH encourages collaborations between basic and clinical researchers, using funding initiatives designed to support teamwork at various levels of scale and effort. These include research networks for the development of new collaborations; infrastructure grants for the development of resources and pilot projects; research grants supporting focused collaborations between basic and clinical scientists; and research centers for comprehensive, large-scale translational programs. At all levels of collaboration, NIMH seeks the inclusion of relevant integrative neuroscience research.

The Institute recently has issued two program announcements (PAs) to expand support for the development of translational research. In addition, NIMH has developed mechanisms for collaboration between basic and clinical researchers that have served as the basis for several disorder-specific initiatives, including issuance of requests for applications (RFAs) for the study of specific components of impairment or dysfunction in major mental disorders; pilot projects in social neuroscience; interdisciplinary research networks in child and adolescent mental disorders; and research on borderline personality disorder.

Clinical Research and Human Subject Protections: Successful navigation of the translational research terrain often leads to the design of new interventions or refinement of existing therapeutic approaches and, in turn, the need for randomized, controlled clinical trials to demonstrate the efficacy of new treatment modalities. To help ensure the success of this research, NIMH assigns high priority to the scientific investigation of research ethics, including the ongoing process of informed consent in studies involving research participants with mental

disorders, the use of surrogate decision-makers (legally authorized representatives), and factors that influence Institutional Review Board decisions regarding additional safeguards for participants in research on mental disorders, symptoms, and related disability. A workshop convened by NIMH in December 2002 identified under-studied areas relevant to research ethics and additional ways to further stimulate research on these topics.

Clinical Effectiveness Trials: While rigorously controlled clinical efficacy trials will remain an essential step in bringing new treatments to the public health sphere, the need for information more relevant to the real world is underscored by the policies of managed care organizations and by the perceptions and experiences of employers who pay the insurance bills for many American employees, including those who seek treatment for mental disorders. NIMH has launched a series of community-based effectiveness trials of interventions for adolescent depression, treatment-resistant depression in adults, bipolar disorder, and the effectiveness of newer atypical antipsychotic medications in Alzheimer's disease and schizophrenia. In mid-FY 2003, all of these trials will be on their way to attaining the targeted number of research participants, a process that typically requires up to 36 months of active recruitment efforts in industry- and government-sponsored trials.

Combating Stigma: The most innovative and effective treatments for mental disorders that achieve a place in the therapeutic repertoire of community-based mental health care providers will be of no use if the stigma attached to mental disorders deters individuals from acknowledging their illness, and from seeking help and remaining in treatment. Since issuance of the landmark Surgeon General's Report on Mental Health (1999), NIMH has taken numerous steps to develop a program of research to reduce mental illness stigma and discrimination. Over the course of recent years, an NIMH Stigma Working Group assessed existing knowledge, identified pressing research questions, and developed strategies to overcome barriers to research in this area. In July 2002, NIMH convened a conference on "Stigma, Mental Illness, and the Media"; the conference was part of a larger effort to examine how the media portrays mental illness and the effects these portrayals have, and the use of mass media to change attitudes toward mental illness. Television and broadcast news are the primary source of information about mental illness for many Americans and thus can strongly influence beliefs and attitudes. In addition, members of NIMH are participating in the development of a curriculum on Mental Illness and the Brain for middle school (grades 6-8) children. The goals of the curriculum are to help students understand that mental illness is a brain disease and to address the social stigma associated with such an illness. This effort is sponsored by the NIH Office of Science Education as part of the response to the National Science Education Standards, released by the National Academy of Sciences in 1995. Field testing of the curriculum began in January 2003.

NIH/SAMHSA Science-to-Service Initiative: An ambitious effort to transmit solidly documented, research-based interventions to the field and incorporate them in clinical service systems is underway now in a collaboration between NIH and the Substance Abuse and Mental Health Services Administration (SAMHSA). In this initiative, each of three institutes—NIMH, the National Institute on Drug Abuse, and the National Institute on Alcohol Abuse and

Alcoholism—have identified a dozen psychosocial treatment and preventative interventions that have a strong scientific evidence base. The Institutes provided SAMHSA officials an overview of each intervention, a description of the target population toward whom the intervention is directed, a summary of supporting research evidence, references, and contact information for a knowledgeable investigator who can be helpful to SAMHSA in creating or reviewing dissemination materials and plans for implementing the intervention. SAMHSA's efforts to facilitate the incorporation of these interventions into States-administered public mental health programs will be an essential step in establishing a feedback loop that will draw on real world experiences with evidence-based practices to inform and guide future interventions research.

SCIENCE ADVANCES AND STORY OF DISCOVERY

Discovering the Function of Brain Structures

As noted in the Surgeon General's landmark report on mental health, the human brain is the most complex structure ever investigated by science. The complexity of the organ is seen in its structure and neurochemical properties as well as in its capacity – called plasticity – to change, to remold itself as a function of learning, stress, and a variety of other experiences. The advent of increasingly high resolution-capable brain imaging technologies, computational power, and molecular biological techniques continues to encourage new questions about the workings of the brain and novel approaches to answering them.

Cortical Cartography Takes on New Latitude. At the center of this mapping effort is the use of animal systems to identify molecules and signals that direct development of the various functional divisions of the brain's cortex. Previous characterization of expression patterns of growth factor FGF8 and its receptors in the anterior portion of the developing brain suggested that this secreted protein is a crucial signal in specifying the boundaries between discrete areas of the cortex. NIH-funded researchers successfully modified the expression and function of this protein by direct transfer of the FGF8 gene into specific regions of embryonic mouse brain. This elegant procedure allowed specific manipulation of gene expression during early, critical developmental periods. The results indicate that alterations in the expression and function of a single signaling molecule during development may have profound effects on development of the mammalian cortex, including those responsible for cognition and sensory function in humans. This landmark study provided the first direct demonstration that a secreted molecule regulates and specifies the formation of the neocortical map. Since FGF8 and other signaling molecules are expressed in the developing human brain, alterations in the expression of or response to secreted factors may be at the basis of a spectrum of mental disorders. This crucial technological advance will hasten the identification of additional signals that mediate development of complex cortical structure and function, and allow scientists to create a more complete map of the human mind.

Novel Brain Mapping Strategy Reveals How Genes Affect Human Brain Structure. Despite large-scale efforts to map genetic and brain variations in human populations, there were no technologies available to link these two types of information until an international team of scientists designed a brain mapping strategy to create the first maps of genetic influences on human brain structure. Using a database of magnetic resonance imaging (MRI) scans from the Finnish twin registry, researchers developed a novel supercomputing approach to encode how brain structure varied between identical and fraternal pairs of twins. Qualities under genetic control showed a characteristic pattern of varying hardly at all between identical twins, who have the same genes; quite a lot between fraternal twins, who share about half their genes; and a great deal between unrelated individuals. The study found that the more closely related two people were, the more likely they shared similar brain structure in regions heavily controlled by genetics, such as the frontal cortex and language regions. They were also more likely to share vulnerabilities to specific diseases affecting these areas. This is the first study to create maps showing how strongly brain structure is determined by genes and inheritance, and it provided a technology to examine how genes affect brain structure in thousands of individuals. The mapping strategy is now being used to attempt to identify genetic and non-genetic triggers in diseases such as schizophrenia and dementia. The scientists are applying the new brain mapping method in several international projects to screen individuals at genetic risk for schizophrenia and Alzheimer's disease for early brain changes.

Story of Discovery: Closing in on Schizophrenia's Vulnerability Genes

Last October, an international group of investigators identified a gene, called *G72*, that plays a role in regulating the activity of the neurotransmitter glutamate at the NMDA receptor. Because scientists hypothesize that decreased activity of glutamate along the NMDA receptor pathway is associated with certain core symptoms of schizophrenia, the *G72* finding is a remarkable accomplishment, one that has been described as a "watershed" in research on the genetic basis of mental disorders. The finding is a milepost in an increasingly exciting and urgent scientific quest to identify genes that can be shown to be responsible for susceptibility to a major mental disorder or can account for core symptoms of such a disorder. To those familiar with what often has appeared to be a seemingly impenetrable wall around the complex genetics of major mental illness, the recent progress offers an exhilarating incentive for redoubled efforts.

This story of discovery begins nearly 100 years ago, with the German scientist Emil Kraepelin. He first proposed a conceptual framework for the illness known today as schizophrenia, a debilitating, often devastating, brain disorder that most often tends to appear in late adolescence or early adulthood and, with rare exception, to persist over the course of a person's lifetime. Schizophrenia affects about 1% of the population worldwide, striking women and men with equal frequency. In the United States, this prevalence rate translates into more than 2 million persons with the illness, who account for an estimated 2.5% of the Nation's health care costs. [1]

Schizophrenia is marked by simultaneously occurring sets of symptoms: "positive" symptoms such as delusions, hallucinations, and thought disorder, and "negative," or deficit, symptoms including social withdrawal, a lack of motivation and expressiveness, and an apparent inability to experience pleasure. Negative symptoms are those believed to be associated with decreased glutamate activity.

[1]/Bromet EJ, Fenning S. Epidemiology and natural history of schizophrenia. Biol Psychiatry 46:871-881, 1999

Early on, it was clear to Kraepelin that schizophrenia was, in large part, a product of heredity. Over the past century, however, theories about the origins of schizophrenia have veered sharply between attributing its cause to "nature," connoting genetics and biology, or to "nurture," a term that refers to diverse environmental influences, including, unfortunately, the wrongly speculated role of family dynamics. Carried to either extreme, these theories and speculations were equally damaging to patients with schizophrenia, their families, and to science.

The introduction of the first antipsychotic medications in the 1950s and the clear, albeit inadequate response of schiozphrenia to a biological intervention strengthened arguments that the illness was, indeed, a biologically based brain disorder. Then, in the 1960s and 1970s, NIMH-funded investigators and others conducted a series of landmark twin and adoption studies. This research traced the health outcomes of twins, both concordant and discordant for schizophrenia, who were reared in various circumstances – alone and together, and with their biological families as well as in adoptive families who lacked a history of schizophrenia. Findings pointed quite definitively to a strong genetic component in the illness, but also made a compelling case for the role of environmental influences in the onset of illness. Although the interaction of biology and environment in the etiology of schizophrenia fast became incontrovertible, the search for a causative gene, or genes, has been frustrating to scientists and families alike, with early promising findings repeatedly failing to replicate.

Still, scientists gained increasing ability in recent decades to identify specific brain regions implicated in schizophrenia and to delineate the neural circuits, or signaling pathways in the brain, that seem to be disrupted in the illness. More recently, this progress has been matched by the rapid maturation of molecular genetics. On this front, researchers came to realize that a "schizophrenia gene" likely would not be found; rather, the illness appeared to be a complex genetic disorder, in which multiple genes are involved, no single one of which is sufficient or necessary to cause the disease. To result in illness, moreover, it is presumed necessary for a number of genes to interact and for an environmental influence to trigger, or activate, the genetic susceptibility.

To date, some 20 genome-wide linkage scans in more than 1,200 families claiming a member with schizophrenia support the hypothesis concerning schizophrenia's genetic complexity, but until recently, specific vulnerability genes have eluded investigators. Nonetheless, the finding last year of *G72* came hard on the heels of other research that has taken unprecedented steps toward identifying genes associated with schizophrenia. In recent years, for example, through several lines of research in both animals and humans, investigators have zeroed in on the prefrontal cortex (PFC) – which provides the "executive" functions of the brain – as critical in the development of schizophrenia. To that point, in addition to *G72*, three recently discovered genes putatively linked to susceptibility for schizophrenia may function by interfering with neurotransmitters in the PFC and related brain regions.

One of the newly identified genes encodes catechol-O-methyltransferase (COMT), an enzyme that terminates the activity of dopamine in the PFC. In work led by an NIMH intramural scientist who also participated on the *G72* discovery team, this research has identified two alleles, or variants, of the COMT gene; one of these alleles has been shown in clinical studies to be associated with deficits in information processing and memory. Others of the newly identified genes appear to affect the principal cortical neurotransmitters, glutamate and the inhibitory transmitter, gamma amino butyric acid, or GABA. As noted above, reducing glutamate activity leads to activation of primary neurons in several brain regions that produce schizophrenic symptoms. Release of glutamate and GABA seems to be regulated in part by the action of dopamine. This could explain in part how antipsychotic medications that target dopamine receptors can reduce psychotic symptoms like hallucinations.

A hundred years after Emil Kraepelin speculated about the role of genetic mechanisms in schizophrenia, the discovery of susceptibility genes for the illness opens the door to improved understanding of its pathogenesis and, in turn, to further refining treatments and reducing or preventing the terrible toll of disability associated with schizophrenia.

New Method Targets Complex Trait Analysis of Transcriptional Networks. Genes are regions of DNA that contain codes for proteins. Proteins are not synthesized directly from the DNA that encodes them, however, but in two sequential steps: the *transcription* of DNA into mRNA, followed by *translation* of mRNA into protein. Understanding the control and modulation of transcriptional networks in the central nervous system (CNS) is now regarded as one of the most critical problems in basic and clinical neuroscience. A group of investigators supported by NIH's multi-institute Human Brain Project has developed a powerful new bioinformatic method to analyze complex transcriptional infrastructure. The method exploits isogenic lines of mice that can be studied using a battery of tests. Databases on variation in gene expression are coupled to imaging and brain behavioral databases, thus permitting a researcher interested in a particular behavioral phenotype in mice (e.g., anxiety) to search for transcriptional regulators that may influence that trait. A key component of the overall bioinformatic approach is transcriptome-QTL mapping. Using statistical gene mapping methods, this procedure can identify upstream genes (also known as quantitative trait loci or QTLs) that modulate the transcriptional activity of many more downstream gene products. In work with animals, investigators have discovered that variation in expression level of several hundred downstream transcripts maps to the precise chromosomal location as the transcript itself. Under study are both so-called *cis*-QTLs, (*cis* indicates that transcription factors are contained on the same stretch of DNA as the genes they regulate) and trans-acting QTLs (meaning the transcript and its controlling QTL do not share a common chromosomal location). Investigators now have successfully mapped over 300 trans-acting QTLs that group into 20 major "master" control QTLs. A single important upstream control QTL appears to be capable of influencing the expression of dozens or even hundreds of downstream targets. In some cases, families of several hundred genes have been shown to be controlled by single polymorphic regions of the mouse genome that likely correspond to master control factors. The main challenge now is to extract the common denominator of these families--what is the specific factor and cascade that coregulates these sets of downstream targets? The transcriptome-QTL method and the results of its first application to the mouse forebrain represent a major step forward in the genetic dissection of transcriptional networks. The integration of these data with pre-existing behavioral and anatomical data will permit more rapid progress in understanding brain disorders and behavioral abnormalities, and identifying novel therapeutic targets.

Disease and Its Biological Correlates

Efforts to understand disease processes, particularly diseases and disorders affecting and mediated by the brain, long have been stymied by the inaccessibility of brain to observation and manipulation. The following advances illustrate a variety of innovative approaches being utilized by NIMH-supported investigators to develop models for and to explain the pathophysiology of brain disorders. Understanding the biological correlates of brain disease opens the way to the development of increasingly safe and targeted therapeutic interventions.

Face Processing in Autism Engages Unusual Neural Circuitry. A major feature of autism is the lack of social interaction. Studies of face processing, using functional magnetic resonance imaging (fMRI), have consistently demonstrated that a specific region of the fusiform gyrus ("the

fusiform face area") is active when healthy individuals view faces. Most people become experts at recognizing familiar faces in the course of normal development, but people with autism do not. Young children with autism make little eye contact and fail to recognize others based on facial features, instead relying on nonessential and changeable details such as hair style, glasses, or hats that can lead to failures of recognition. People with autism also appear to process faces in a manner that differs qualitatively from those of their healthy peers. NIMH-sponsored researchers investigated the neural correlates of face processing in autism by having seven high-functioning adults with autism and eight normal controls perform a face perception task (pressing a button in response to female faces) and a control task (shape perception, pressing a button in response to circles), while changes in cerebral blood flow and volume (an indirect indication of neuronal activity) were measured with fMRI. Both groups were able to perform the tasks well, showing no significant differences in accuracy or speed. Consistent with earlier research, healthy control subjects activated the fusiform face area, particularly on the right side of the brain. In contrast, patients with autism showed greatly reduced activation of this region (averaging 25% of that seen in controls). In addition, only controls activated the amygdala, a limbic structure thought to be involved in assigning social-emotional significance to objects, including faces. The fusiform face area showed the greatest activation in every control subject. In contrast, participants with autism maximally activated other brain regions, which differed from person to person, suggesting that individuals with autism see faces using uniquely programmed neural circuitry.

The Role of the Amygdala in Evaluating Threats in Social Situations. The amygdala is an important brain area that may be centrally involved in emotions. To understand its precise role, NIH-sponsored investigators developed a technique to functionally eliminate the amygdala without damaging neural fibers that pass through that area. When the amygdala was eliminated in adult monkeys, they were capable of interpreting and generating social gestures from other monkeys and could solicit affiliative social interactions more than normal animals. But is the amygdala involved in learning appropriate social behaviors? To answer this question, the research team compared monkeys from which the amygdala was removed at two weeks of age to normal infant animals. At two weeks, infant monkeys typically cling to their mother's sides, and there is virtually no social interaction with other monkeys. Interactions between infants and their mothers were similar in animals with lesioned amygdalas compared to normal animals. Infants with lesioned amygdalas showed little fear of objects like rubber snakes that normally provoked fearful behavior in infants. In novel interactions with other monkeys, however, lesioned animals showed increased fear and less interaction, although social behavior such as grooming, play, and facial expressions seemed normal for their age. Perhaps a primary role of the amygdala is to evaluate the environment for potential threat and that without a functioning amygdala, macaques do not evaluate monkeys unknown to them as potential adversaries. The amygdala does not appear to be essential for learning social behavior at an early age or for adult social behavior. Instead, the amygdala may modulate the amount of social behavior based on an evaluation of the safety of the social context. This could also mean that some social anxiety disorders in humans involve problems in the amygdala's evaluative process.

Brain Circuitry Underlying Obsessive-Compulsive Disorder. During any task, we continually compare our current status against our expectation for reaching a goal, with expectation increasing over the course of the activity. Presumably, there are neurons in the brain that signal this rising expectation for completion. One obvious place to look for such signals is the anterior cingulate cortex, a region deep in the front of the brain that has been shown to contribute to generation of emotions, and the influence of emotions on behavior selection. Researchers at NIH looked for such signals in single neurons of the brains of non-human primates. They trained the monkeys to perform a repetitive task and if the monkey completed enough repetitions correctly, it received its favorite fruit juice as a reward. As the reward neared, the monkeys worked more accurately, as though driven to complete the task. The investigators found a group of neurons in the anterior cingulate cortex whose activity increased in parallel with the reward expectancy, and the activity abated when the goal was achieved and the state of anticipation resolved. Abnormalities of the anterior cingulate cortex have been implicated in a variety of behavioral disorders including obsessive-compulsive disorder, post-traumatic stress disorder, depression, and mania. Understanding the brain circuitry underlying the role of emotions in behavior will allow development of more effective behavioral therapies for these disorders.

Research Links the Interaction of Childhood Abuse and a Specific Gene to Adverse Behavioral Outcomes. Although children who are subject to physical, sexual, or emotional abuse are known to be at elevated risk for later adjustment problems, including antisocial behavior and criminality, most maltreated children do not grow up to become violent offenders. What might explain this variability in outcome among maltreated children and youth who appear to share most demographic characteristics? Last year, an NIMH-funded longitudinal study that is tracking the development into adulthood of a large cohort of boys born in Dunedin, New Zealand shed light on this question. Over the course of their childhood, adolescence, and early adulthood, youth in the study completed a comprehensive battery of physical and mental health assessments that tracked behavioral symptoms, neuropsychological functioning, motor development, and cognitive development. At age 26, study participants provided DNA samples for genetic analysis. Examining a genetically homogenous subset of the full cohort, the researchers linked multiple forms of the gene that encode the enzyme monoamine oxidase A (MAOA) that regulates many neurotransmitters in the brain to the effects of maltreatment. Specifically, a form of the gene that conferred *low* levels of MAOA expression was found in 85% of the young men who had been severely maltreated during childhood and subsequently were convicted of violent crimes or had other antisocial behavioral outcomes. Individuals with a history of maltreatment but whose genotype conferred *high* levels of MAOA expression were strikingly less likely to develop antisocial behavior problems later in life. Although only 12% of the entire sample of children had the combination of a history of maltreatment and low MAOA activity level, this subset accounted for 44% of the entire study cohort's convictions for violent offenses. If replication of the finding verifies that a genetic variant has a protective effect against the trauma of maltreatment and subsequent behavioral problems, the research may lead to a means of identifying children who are most vulnerable to adverse outcomes stemming from abusive experiences and, in turn, providing them with early preventive interventions.

Transcriptomics: Patterns of Serotonin 2C Receptor Editing as a Marker of Suicide? The 5-HT2C serotonin receptor is widely distributed in the brain and is implicated in the regulation of mood and affective behavior. This receptor is unique not only among serotonin receptors but among the larger superfamily of G-protein coupled receptors, in that the pre-mRNA, which encodes the 5-HT2C receptor protein, can be edited by enzymes that alter the genetic sequence at five different sites (referred to as A, B, C', C, and D). Editing of the pre-mRNA at any combination of these five sites produces a receptor protein with altered signaling properties. The edited 5-HT2C receptors, referred to as isoforms, typically have a decreased ability to couple to messenger signaling molecules in the cell resulting in a decrease in receptor function. There is emerging evidence that RNA transcripts are altered in psychiatric disorders. Researchers reported that the pattern of 5-HT2C receptor editing is altered in the prefrontal cortex of people who have committed suicide. In the normal human brain, the most common pattern of editing occurs at the A site. In contrast, the pattern in suicide victims was increased editing at the C' and C sites, decreased editing at the D site, and very low levels of non-edited 5-HT2C mRNA in comparison with controls. These findings suggest there is an overall decrease in 5-HT2C receptor activity in the prefrontal cortex of suicide victims with a history of major depression. In parallel studies conducted in mice treated chronically with fluoxetine, the patterns of 5-HT2C receptor editing were opposite to those seen in suicide victims, i.e., less editing at the C' and D sites and increased conconcentrations of the A-edited isoforms. These results suggest that a serotonin-mediated mechanism may regulate editing of 5-HT2C receptor pre-mRNA.

Olfactory Neurons Act as a "Window" on the Etiology of Schizophrenia. Schizophrenia is a severe mental illness characterized by disordered thinking and mood, impaired social interactions, delusions, hallucinations and psychosis that affects about 2 million people nationwide. Research suggests that schizophrenia is caused by biological abnormalities in multiple brain systems and that these abnormalities may start when the brain is developing. Olfactory neurons are a specialized population of neural cells that continues to develop throughout life. Patients with schizophrenia, as well as their relatives without schizophrenia, have numerous characteristic defects in their olfactory systems, which made this a likely place to look for abnormalities. NIH-supported researchers used antibody stains specific for three different stages of maturation in olfactory neurons (basal or "stem" cells, immature neurons, and mature neurons), and examined autopsied brains from patients with schizophrenia and from unaffected control subjects. The number of mature cells did not differ between the patients and the controls. However, the number of olfactory stem cells was lower and the number of immature neurons was higher in the patients, even when smoking and medication history were taken into consideration. Apparently, the development of these neurons is first accelerated, thereby depleting the olfactory stem cell population, and then arrested at an immature stage in the brains of patients with schizophrenia. The inability of the arrested cells to make proper connections leads to a testable hypothesis that schizophrenia is a neurodevelopmental disorder.

Narrowing the Window of Fetal Vulnerability for Adult Schizophrenia. Recent findings from psychiatric epidemiological studies suggest that some forms of schizophrenia may result from disruption of normal brain development during the sixth month of gestation. NIH researchers

assessed schizophrenia-related features in 2,309 young men who were and 2,065 who were not exposed in utero to an influenza epidemic. Schizotypal personality characteristics, such as phobias, obsessions, compulsions, or excessive anxiety, were measured using the Minnesota Multiphasic Personality Inventory Schizophrenia and Psychasthenia scales at age 20, and were compared for the exposed and non-exposed (control) subjects. The study was designed to identify discrete periods of neural development associated with the onset of the disorder in adulthood. A significantly higher proportion of persons exposed in utero to an influenza epidemic during the sixth month of pregnancy (39%) had elevated schizotypal personality scale scores compared to the non-exposed control group (26%). These differences were traced to exposure during gestation week 23. Those exposed during week 23 were more likely to achieve elevated schizotypal personality scale scores (51%) than controls (24%). Exploratory analyses for the other months revealed no significant differences between the exposed and control groups in vulnerability to schizotypal personality disturbance. These results build on earlier work that have refined the window of vulnerability and suggest new hypotheses regarding neuro-maturational events that may be related to the etiology of schizophrenia.

New Clues to Risk for HIV-Dementia. Human immunodeficiency virus type I (HIV-1) infects and depletes specific types of cells that are critical to maintaining a healthy immune system. The virus also damages the central nervous system, with 15 to 25% of infected individuals developing dementia and a higher percentage developing encephalitis (brain inflammation). It is unclear exactly how HIV-1 penetrates the brain, but monocytes and macrophages, cells mobilized in response to the infection, attack the virus by making and releasing inflammatory agents such as macrophage chemotactic protein-1 (MCP-1), which can ultimately have toxic effects. NIH-sponsored investigators studied macaque monkeys infected with a strain of HIV known as simian immunodeficiency virus (SIV). The researchers determined that SIV causes a temporary increase in the ratio of MCP in cerebral spinal fluid (CSF) to MCP in blood in all monkeys 10 days after infection. Thereafter, in monkeys that do not develop encephalitis, the CSF-to-blood ratio decreased and remained low. In macaques that developed moderate to severe encephalitis, the ratio escalated to much higher levels approximately 28 days after infection. When the macaques' brains were examined 56 days after SIV infection, the researchers found that the increase in the MCP CSF-to-blood ratio occurred before brain inflammation. This finding suggests that this early predictor of brain inflammation could be used to design treatments that, if used in initial stages of infection, might prevent or lessen the development of the inflammation. Additionally, the investigators identified the types of brain cells that appear to be making and releasing the MCP-1 as macrophages and astrocytes. The findings indicate that MCP is an excellent candidate marker of early brain infection, and it may also indicate individuals who are susceptible to HIV-induced brain inflammation and related complications in humans. Such early predictors could be used to tailor current drug treatment regimens and to develop new drugs that specifically target the brain inflammatory processes for susceptible individuals.

Converting Knowledge into Treatment

An ultimate aim of much NIMH-funded research is to generate knowledge that can be applied to alleviate the burden of mental and behavioral disorders on individuals, families, and society as a

whole. The development of new treatments is an immensely challenging task that typically requires the active participation of patients who volunteer to become members of the research process; the collaboration of scientists in government, academia, and often, industry; and front-line health care providers. Among the most important responsibilities of NIMH is to continuously monitor progress across a broad scientific spectrum to detect opportunities for the development of new psychosocial and biological treatments.

Medication Effective in Reducing Behavioral Disturbances in Autism. Autism, a chronic mental disorder occurring in early childhood, is thought to be caused by abnormalities in brain development, and twin and family studies indicate a strong genetic contribution. Autism spectrum disorders may affect as many as 2-3 children per 1,000 [2]. Autism is characterized by symptoms of impaired social relatedness, delayed language, and restricted patterns of behavior. In addition, children with autism frequently exhibit serious behavior disturbances, such as self-injury, aggression, and tantrums in response to routine demands. Both behavior therapy and medications are used to treat these symptoms, but no study has determined which is most beneficial. Several different medications have been used to treat autism, but each has had limited success. To date, only haloperidol consistently has been shown to be superior to placebo for serious behavior problems. However, many clinicians have concerns about neurological and other side effects with haloperidol and thus avoid its use in children. Atypical antipsychotics, such as risperidone, are medications that have been found to be effective for adults with psychosis, and have also potential therapeutic value for children with autism-associated severe behavioral disturbances. At five clinical sites, 101 children with autism-associated severe behavioral disturbances, 82 boys and 19 girls, ranging in age from 5 to 17, were randomly assigned to receive either risperidone or placebo. The study found risperidone to be significantly more effective than placebo in improving behavior. Using a stringent definition of improvement, 69% of the children on risperidone showed major improvement by the end of the study, as compared with only 12% in the placebo group. This is the most positive improvement from medication observed in children with autism. Overall, the medication was well tolerated with few neurological side effects, but there was substantial weight gain (an average of about a 6 pound increase in the 8-week period).

Work is an Important Component of Mental Health. Reintegration into the workplace, and back into the family and the activities one was involved in before the illness is a priority issue for many people suffering from severe mental disorders. Rather than living a life that focuses mainly around their illness (e.g., medication visits, case management visits, trips to pick up disability payments, and attendance at day programs), they have voiced their preference for programs that allow them to work as a vital step to being more self-reliant. Congress has supported this perspective by passing legislation to eliminate work disincentives (Ticket to Work; Work Incentives Improvement Act 1999). However, most people with severe mental disorders living in community settings do not have jobs and vocational services are not included as part of their treatment plans. A decade of research supports the idea that competitive

[2]http://www.cdc.gov/ncbddd/dd/ddsurv.htm#madds

employment in integrated settings for people with severe mental disorders is possible. One of the most successful models, Individual Placement and Support (IPS), developed at Dartmouth, emphasizes the importance of speedy rather than gradual reintegration into the work environment, with follow-along support given by mental health treatment teams. This model also has proven to be effective in New Hampshire for increasing rates of competitive employment and improving the worker's sense of well-being. When IPS clients were compared with those receiving the State's usual psychosocial treatment program, there were few differences in the number and the length of time jobs were held during the two-year period, the hours worked and the compensation paid, and the time to secure the first job. However, the IPS group was far more likely than those in the standard training group to be employed (42% vs. 11%) and to be employed competitively (27% vs. 7%). The IPS employment model is more successful in getting people into the work force, but now attention must focus on identifying the factors—individual, dyadic, and organizational—that affect whether a person gets and retains a job and is reintegrated into the community.

D-Cycloserine Enhances Extinction of Maladaptive Fear Responses. In the 1990s, an NIH-funded investigator pioneered the use of an animal model for understanding the neural circuitry underlying fear conditioning. Fear conditioning occurs when a previously neutral stimulus (e.g., light) is paired with an aversive stimulus (e.g., foot-shock). After fear conditioning, the previously neutral, or conditioned stimulus (CS), presented alone, generates fear responses in the animal or human. In contrast, extinction is the process by which the association between the CS and the aversive stimulus is uncoupled through repeated presentations of the CS without the associated aversive stimulus. Over time, the fear response diminishes. Extinction training has been used as a treatment for patients who have developed maladaptive fear responses to particular stimuli or events. The amygdala is a brain region known to be involved in the processing and consolidation of emotionally significant events, and neurons in the amygdala and other brain regions contain specific receptors known to be involved in learning. D-Cycloserine, a drug that binds to these receptors, has previously been shown to facilitate learning in animals. Researchers also hypothesized that D-Cycloserine might also facilitate the "unlearning" or extinction of previously learned associations. Using startle amplitude as a measure of fear conditioning and extinction, NIH-funded researchers conditioned animals to expect an aversive stimulus in the presence of a light. The animals were then given extinction training. Just prior to extinction training, half of the animals were given D-Cycloserine. The animals that received D-Cycloserine took significantly less time to extinguish the fear conditioned response than animals that did not receive the drug. D-Cycloserine without extinction training did not reduce the fear conditioned response. A number of debilitating psychiatric disorders such as phobias, anxiety, panic disorder, and post-traumatic stress disorder are characterized by the inability to inhibit maladaptive fear responses. The development of a drug that could enhance extinction learning would be of significant clinical benefit for persons suffering from these disorders. These results suggest that a combination of D-Cycloserine and behavioral training might be more effective in treating anxiety disorders than behavioral or pharmacological treatment alone.

Understanding the Molecular Basis of Antipsychotic Drug-Induced Weight Gain in Schizophrenia. Although new antipsychotic drugs (APDs) have been introduced that improve symptoms and cognitive deficits in schizophrenia, short- and long-term weight gain is an unwanted side effect that can increase the risk of cardiovascular disease and type II diabetes, and can lead to treatment noncompliance. Two recent studies have shed light on the molecular mechanisms underlying APD-induced weight gain, with both studies implicating neurons in hypothalamic areas known to be involved in the control of appetite and food intake. In the first study, investigators measured Fos protein, a marker of neuronal activity, to assess the effects of APDs on the activity of orexin neurons in the hypothalamus. They found that APDs that significantly increase weight gain produced a large increase in Fos protein, whereas APDs with low weight gain liability did not. These findings suggest that orexin neurons in the hypothalamus may be involved in APD-induced weight gain. In a second study, researchers examined the receptor binding profile of atypical and typical APDs to determine which receptors were contributing to APD-induced weight gain. Using statistical analysis to determine the relationship between receptor binding and weight gain, they found a striking correlation for the ability of APDs to bind to the H1 histamine receptor and their propensity to induce significant weight gain. The APDs with high affinity for the H1 histamine receptor were associated with significant weight gain, whereas the APDs with low affinity for the H1 receptor were not. Together, these studies advance our understanding of the molecular basis of APD-induced weight gain. In addition, these studies suggest that the development of APDs with low or no affinity for H1 receptors will lead to a new generation of ADPs with a more favorable side-effect profile.

NEW INITIATIVES

Dissemination of Evidence-Based Behavioral Interventions for HIV/AIDS. NIMH has been a leader in supporting research to reduce the spread of HIV/AIDS by understanding what behaviors put people at risk for HIV infection and by developing and testing interventions to change those behaviors. In controlled trials, NIMH-supported investigators have demonstrated the effectiveness of individually focused prevention models that target at-risk populations and are tailored to varying socio-cultural risk patterns. Active components of these interventions include (1) teaching accurate risk perception, (2) increasing motivation to practice safer HIV-related behaviors, (3) identifying triggers for risk behavior, and (4) practicing negotiation skills that are essential for safer behavior. Although individually targeted interventions are cost-effective and can be incorporated into public health settings, they are insufficient to stop the HIV epidemic. Thus, NIMH also supports intervention trials for couples, families, and communities to reinforce and sustain individual-level change as well as create community norms for healthy behavior. Under this initiative, NIMH will convene funded investigators and appropriate consultants to help design a strategy for disseminating to five developing countries with a high HIV prevalence community-level intervention programs that currently are being refined and tested in the United States.

Research to Facilitate State Adoption of Evidence-Based Practices. A growing number of State mental health commissioners and others are interested in adopting and implementing evidence-

based practices (EPB). Insufficient information exists, however, about what factors contribute to successful adoption by States of EPB. It is clear that States vary widely in their capacity to conduct research or utilize research-based program models or findings that likely were developed and evaluated in controlled academic settings. To help prepare States to use EBPs successfully in pursuit of distinct program goals, NIMH is working with other NIH components (NIDA and NIAAA) and with the Substance Abuse and Mental Health Services Administration to identify well-documented interventions that are ready for dissemination to State program directors. Using a two-phase process, NIMH has issued an RFA designed to make funding available to States for one-year exploratory research grants. These grants allow States to create systems to facilitate adoption of EBPs by clinicians and practices; to enhance collection and aggregation of data about State needs and resources; and to create partnership networks of program administrators, policymakers, and researchers to share information. The principal investigator must be a State official, and it will be incumbent on that person to Apartner@ with researchers. Recipients will be better poised to compete for a variety of research mechanisms, including traditional investigator-initiated research project grant (R01s), to assist in carrying out their individualized State plans. The second phase would fund five of the successful Phase One State grantees to do large-scale implementation projects, as well as fund an additional five State Planning Grants (Phase One).

Mapping Vulnerability Genes for the Major Mental Disorders. Tremendous advances have occurred in mapping and cloning genes for diseases that follow Mendelian patterns in families. In contrast, the discovery of genes that influence vulnerability to mental disorders has proceeded at a much slower pace. The etiologies of these disorders are highly complex, with disease vulnerability likely influenced by multiple genes of small effect interacting with environmental factors. Such complexities present considerable challenges for genetic inquiry, and a serious limitation of past studies has been small sample size. Mapping through linkage, linkage disequilibrium or association studies and subsequent positional cloning of a given gene will require analyses of information collected in hundreds, if not thousands, of affected individuals and family members. NIMH has launched a Human Genetics Initiative to assemble and make available to the scientific community large data sets that contain high statistical power to detect genes producing vulnerability to mental disorders. It is likely that sufficient numbers of individuals/families with schizophrenia have been obtained to proceed with mapping efforts. In FY 2004, NIMH will intensify efforts to obtain requisite numbers of individuals/families with bipolar disorder, major depression, autism, obsessive-compulsive disorder, and attention-deficit hyperactivity disorder. Special emphasis will be placed on fostering large-scale collaborations, by which combined meta-analyses of all available data may occur. Through workshops and other means, the Institute will aggressively "market" within the broad scientific community the availability of these critical research resources for detecting specific genetic mutations involved in the etiology of mental disorders. Characterization of these vulnerability genes will significantly advance drug discovery and individualized treatment selection.

Utilize New Epidemiologic Data to Address Disparities in Mental Health Services. The optimal allocation of societal resources for treating and preventing mental disorders requires an

accurate research-based understanding of the incidence and prevalence of mental disorders, the functional disability associated with these disorders, and current service use patterns. In FY 2004, three NIMH-supported epidemiologic studies of the Nation's principal racial/ethnic minority groups will have been completed. The National Survey of African Americans (N=7,000) and the National Latino (N=3,525) and Asian American (N=3,711). Surveys will complement findings obtained from a replication of the National Comorbidity Survey, which has drawn on a representative sample (N=10,000) of the U.S. population. This initiative will position NIMH to encourage a variety of basic, clinical, and health services research projects that will exploit the findings of the four surveys in the service of reducing the burden of mental disorders among our Nation's citizens. Of high priority will be research to define standard measures – and, particularly, culturally appropriate measures – of "need for treatment." As part of the initiative, NIMH will convene multidisciplinary workshops and actively encourage research to examine potential uses and applications of the new epidemiologic data in basic, clinical, and health services research. An overall goal of the initiative is to enable focused efforts aimed at reducing health disparities on the basis of sound data regarding the prevalence and the use of services for mental disorders among the major racial/ethnic minority groups in the United States.

Discover and Test Novel Molecules as Therapeutic Candidates for Treating Mental Disorders. The goal of this initiative is to identify biological targets, generate libraries of molecules with novel mechanisms that target brain signaling pathways, and test them clinically as candidates for the treatment of mental disorders. This initiative will utilize new strategies and expand the scope of ongoing activities to enhance biomedical discovery in the following areas: (1) identification of gene products as validated targets for drug discovery; (2) generation of new chemical entities; (3) testing existing molecules for new indications; and (4) testing molecules in cellular, genetic, or behavioral models using research grant, cooperative agreement, and contract mechanisms. An important initial activity will be to explore and establish public-private partnerships that will accelerate the identification of new therapeutic candidates and test existing compounds for new indications. Groundwork also will be conducted for establishing a clinical trials network, which will include NIH intramural research programs, to conduct proof of concept studies and to develop and validate models for evaluating novel therapeutics. The initiative will involve the participation of several NIH neuroscience institutes (e.g., NIDA, NINDS, and NIMH) that share common targets of interest and relevant expertise that can be brought to bear in a synergistic manner.

Accelerating the Development of Treatments for Post-traumatic Stress Disorder. Post-traumatic Stress Disorder (PTSD) is an anxiety disorder that occurs after exposure to an extreme stressor (e.g., physical/sexual assault, natural disaster, terrorist attack) in which an individual experiences, witnesses, or is confronted with actual or threatened death or serious injury to self or others. In addition to severe anxiety symptoms, sufferers of PTSD have high co-morbidity rates of depression, substance abuse, and suicide. Children display a wide range of emotional and physiological reactions following exposure to traumatic stressors, with more severe reactions associated with a higher degree of exposure. Events most often associated with PTSD are

physical or sexual assault, childhood neglect or physical abuse, natural disasters, accidents, combat exposure, and most recently, bioterrorism. Given its prevalence, disability level, chronicity, and treatment resistance, PTSD represents a major public health risk. This NIMH initiative will entail issuance of an RFA to solicit applications to:

- Determine the sequence and optimal timing of interventions (pharmacological, psychosocial, and the combination) to reduce the impact of trauma on subsequent neurobehavioral functioning.
- Determine the optimal time to begin intervention after exposure to a traumatic stressor.
- Conduct clinical trials to assess the efficacy of novel drug candidates alone and in combination with psychosocial therapy to reduce clinical symptoms and protect prophylactically against relapse.
- Explore how to encourage individuals who are numb, avoidant, etc., to obtain and follow through with treatment (and/or to participate in research) and determine the best setting for health care delivery and other treatment-related research.

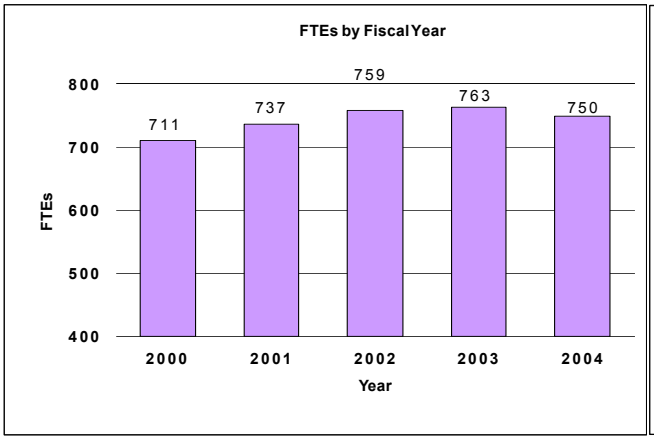
Develop New Prevention and Treatment Approaches to Reduce Suicide. In the United States, deaths by suicide consistently outnumber deaths by homicide. Suicide is the third leading cause of death for 10-24 year olds, and the eighth leading cause of death for males of all ages. While research on risk factors has further refined the social, biologic, and genetic factors associated with suicide, the most consistent factors are major mental illnesses, which affect up to 90% of all people who die by suicide. Despite the high correlation between mental illness and suicide, only a small proportion of persons with mental disorders engage in suicidal behavior, making it difficult to test treatments aimed at preventing or reducing suicidality. Under this FY 2004 initiative, NIMH will support research that further characterizes protective factors against suicide, as well as new treatments to reduce suicidality for various disorders. The ethical and safety challenges of identifying and treating individuals at high risk for suicide also would benefit from further research on ethical issues. The Institute will issue a Program Announcement (PA) to indicate interest in further advancing research on suicidality by highlighting research gaps and opportunities, including measurement (e.g., risk and protective factors, treatment response), biological bases, and interventions for underserved populations (rural, racial/ethnic minority populations). The invitation for research applications also will note the need for studies of safe approaches to providing public health messages about suicide, its risk factors, and how to obtain treatment.

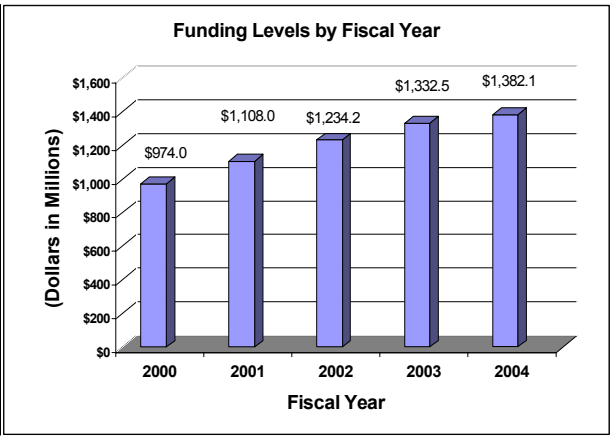
In FY 2004 NIMH will expand its collaboration with the Substance Abuse and Mental Health Services Administration in developing its health services research portfolio to enable a more rapid translation of research findings into the delivery of mental health treatment and prevention services.

NIMH BUDGET POLICY

The Fiscal Year 2004 budget request for the NIMH is $1,382,114,000, including AIDS, an increase of $49,614,000 and 3.7 percent over the FY 2003 amended President's Budget Request.

A five year history of FTEs and Funding Levels for NIMH are shown in the graphs below. Note that Fiscal Years 2001 and 2000 FTEs are not comparable for the NIH Human Resources functional consolidation.





NIH's highest priority is the funding of medical research through research project grants (RPGs). Support for RPGs allows NIH to sustain the scientific momentum of investigator-initiated research while providing new research opportunities. In FY 2004, NIMH will provide an aggregate average cost increase of 2.6 percent for RPGs.

Also in FY 2004, NIMH will fully fund 12 RPG awards. The majority of these grants will be Academic Research Enhancement Awards (AREA) that are designed to enhance the research environment of educational Institutions that are not traditionally recipients of NIH research grants.

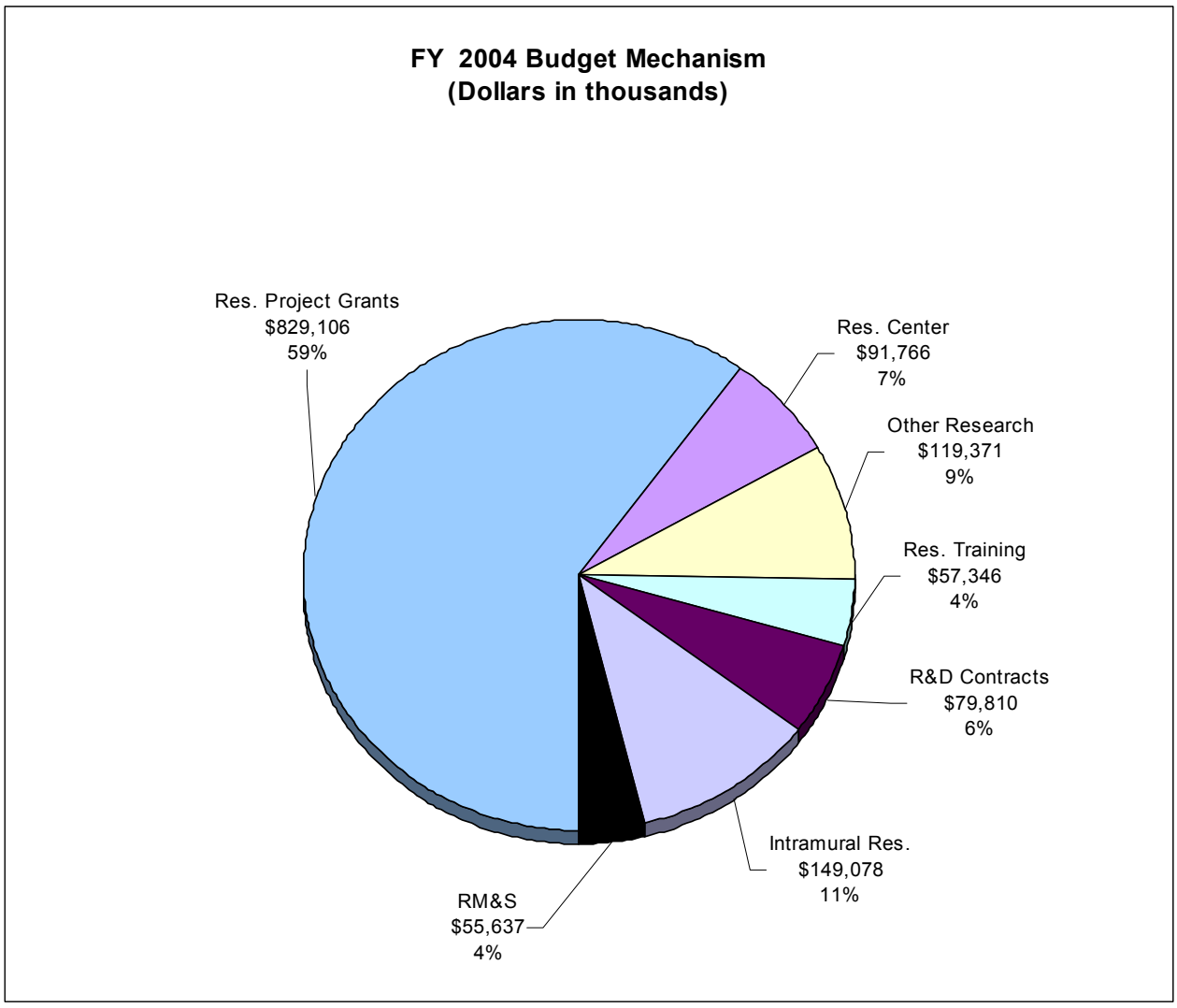
Promises for advancement in medical research are dependent on maintaining the supply of new investigators with new ideas. In the Fiscal Year 2004 request, NIMH will support 1,589 pre- and postdoctoral trainees in full-time training positions, the same number as in FY 2003. Stipend levels for NRSA trainees will increase by 4 percent over Fiscal Year 2003 levels for predoctoral fellows, and from 4-1 percent, based on years of experience, for postdoctoral fellows.

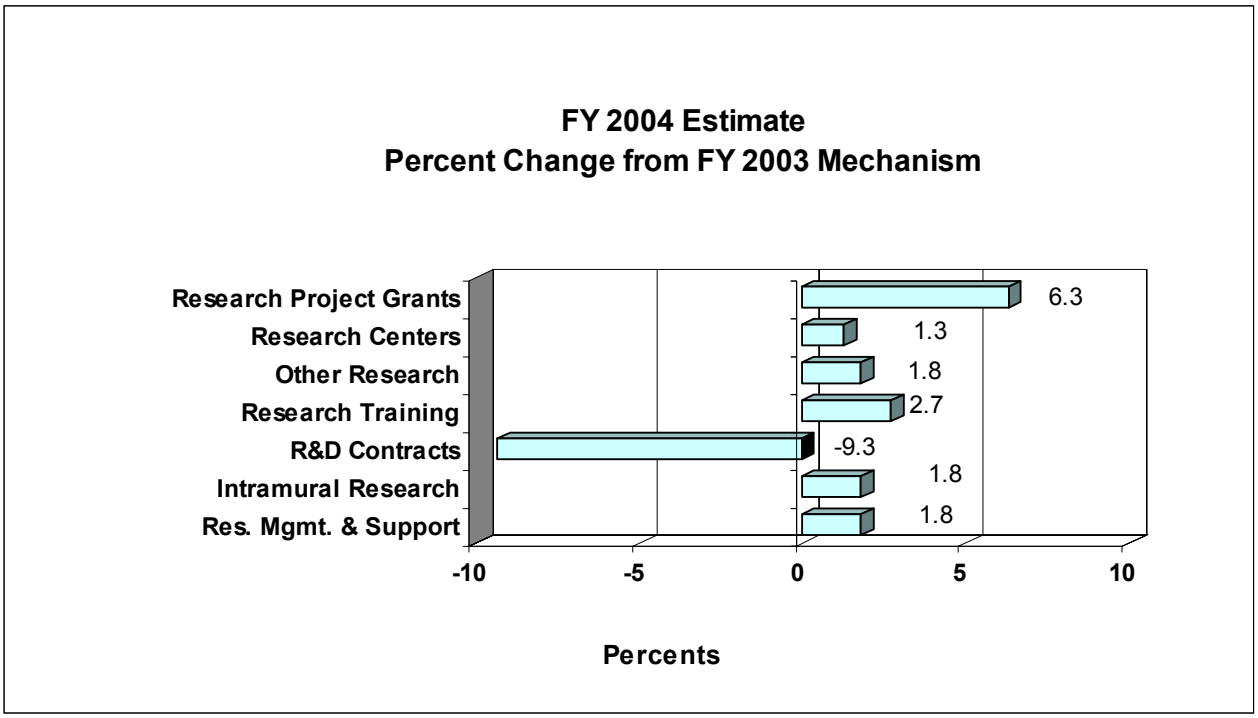
The Fiscal Year 2004 request includes funding for 58 research centers, 589 other research grants, including 146 clinical career awards, and 163 R&D contracts. Intramural Research and Research Management and Support receive increases of 1.8 percent over FY 2003.

The Fiscal Year 2004 request includes funding in the amount of $3,375,000 for the NIMH to support clinical trials in accordance with provisions of the Best Pharmaceuticals for Children Act (BPCA), which calls for clinical trials of off-patent medications that hold promise for the treatment of pediatric disorders. There exist a number of medications that have never been evaluated for clinical utility in a range of childhood psychiatric and behavioral disorders

including, but not limited to, attention-deficit/hyperactivity disorder (ADHD), anxiety disorders, depression, and autism. NIMH proposes to convene a panel of experts to help the Institute identify medications and disorders most appropriate for study, and to initiate clinical trials in FY 2004.

The mechanism distribution by dollars and percent change are displayed below:




FY 2004 Estimate
Percent Change from FY 2003 Mechanism
Research Project Grants
Research Centers
Other Research
Research Training
R&D Contracts
Intramural Research
Res. Mgmt. & Support
6.3
1.3
1.8
2.7
-9.3
1.8
1.8
-10
-5
0
5
10
Percents

NATIONAL INSTITUTES OF HEALTH

National Institute of Mental Health

Budget Mechanism - Total

MECHANISM	FY 2002 Actual		FY 2003 Amended President's Budget		FY 2004 Estimate	
Research Grants:	No.	Amount	No.	Amount	No.	Amount
Research Projects:						
Noncompeting	1,469	$493,882,000	1,596	$552,220,000	1,675	$598,813,000
Administrative supplements	(75)	6,410,000	(75)	6,525,000	(58)	5,258,000
Full funded	0	0	0	0	12	1,608,000
Single year	585	183,638,000	612	200,195,000	606	200,200,000
Renewal	114	51,217,000	119	57,453,000	121	57,441,000
New	468	131,885,000	490	142,079,000	482	142,079,000
Supplements	3	536,000	3	663,000	3	680,000
Subtotal, competing	585	183,638,000	612	200,195,000	618	201,808,000
Subtotal, RPGs	2,054	683,930,000	2,208	758,940,000	2,293	805,879,000
SBIR/STTR	89	22,196,000	83	20,777,000	91	23,227,000
Subtotal, RPGs	2,143	706,126,000	2,291	779,717,000	2,384	829,106,000
Research Centers:						
Specialized/comprehensive	56	85,204,000	59	90,588,000	58	91,766,000
Clinical research	0	0	0	0	0	0
Biotechnology	0	0	0	0	0	0
Comparative medicine	0	0	0	0	0	0
Research Centers in Minority Institutions	0	0	0	0	0	0
Subtotal, Centers	56	85,204,000	59	90,588,000	58	91,766,000
Other Research:						
Research careers	441	59,228,000	441	60,569,000	441	61,660,000
Cancer education	0	0	0	0	0	0
Cooperative clinical research	22	17,827,000	22	18,148,000	22	18,475,000
Biomedical research support	0	0	0	0	0	0
Minority biomedical research support	0	0	0	0	0	0
Other	126	37,864,000	126	38,544,000	126	39,236,000
Subtotal, Other Research	589	114,919,000	589	117,261,000	589	119,371,000
Total Research Grants	2,788	906,249,000	2,939	987,566,000	3,031	1,040,243,000
Research Training:	FTTPs		FTTPs		FTTPs	
Individual awards	365	11,532,000	365	11,846,000	365	12,168,000
Institutional awards	1,224	42,816,000	1,224	43,981,000	1,224	45,178,000
Total, Training	1,589	54,348,000	1,589	55,827,000	1,589	57,346,000
Research & development contracts	126	84,393,000	186	88,011,000	163	79,810,000
(SBIR/STTR)	(15)	(4,649,000)	(26)	(7,991,000)	(26)	(8,135,000)
	FTEs		FTEs		FTEs	
Intramural research	480	139,030,000	482	146,442,000	473	149,078,000
Research management and support	279	50,138,000	281	54,654,000	277	55,637,000
Cancer prevention & control	0	0	0	0	0	0
Construction		0		0		0
Total, NIMH	759	1,234,158,000	763	1,332,500,000	750	1,382,114,000
(Clinical Trials)		(123,764,000)		(133,626,000)		(138,602,000)

NATIONAL INSTITUTES OF HEALTH
National Institute of Mental Health

Budget Authority by Activity
(dollars in thousands)

ACTIVITY	FY 2002 Actual FTEs	FY 2002 Actual Amount	FY 2003 Amended President's Budget FTEs	FY 2003 Amended President's Budget Amount	FY 2004 Estimate FTEs	FY 2004 Estimate Amount	Change FTEs	Change Amount
Extramural Research:								
Extramural research and training		$1,044,990		$1,131,404		$1,177,399		$45,995
Subtotal, Extramural research		1,044,990		1,131,404		1,177,399		45,995
Intramural research	480	139,030	482	146,442	473	149,078	(9)	2,636
Research management & support	279	50,138	281	54,654	277	55,637	(4)	983
Total	759	1,234,158	763	1,332,500	750	1,382,114	(13)	49,614

NATIONAL INSTITUTES OF HEALTH
National Institute of Mental Health

Summary of Changes

2003 Amended President's Budget				$1,332,500,000
2004 Estimated Budget Authority				1,382,114,000
Net change				49,614,000
	2003 Amended President's Budget Base		Change from Base	
CHANGES	FTEs	Budget Authority	FTEs	Budget Authority
A. Built-in:				
1. Intramural research:				
a. Within grade increase		$53,306,000		$758,000
b. Annualization of January 2003 pay increase		53,306,000		413,000
c. January 2004 pay increase		53,306,000		800,000
d. One extra day of pay		53,306,000		211,000
e. Payment for centrally furnished services		25,647,000		513,000
f. Increased cost of laboratory supplies, materials, and other expenses		67,489,000		1,198,000
Subtotal				3,893,000
2. Research Management and Support:				
a. Within grade increase		27,471,000		467,000
b. Annualization of January 2003 pay increase		27,471,000		213,000
c. January 2004 pay increase		27,471,000		412,000
d. One extra day of pay		27,471,000		109,000
e. Payment for centrally furnished services		7,221,000		144,000
f. Increased cost of laboratory supplies, materials, and other expenses		19,962,000		355,000
Subtotal				1,700,000
Subtotal, Built-in				5,593,000

NATIONAL INSTITUTES OF HEALTH
National Institute of Mental Health

Summary of Changes--continued

CHANGES	2003 Amended President's Budget Base		Change from Base	
	No.	Amount	No.	Amount
B. Program:				
1. Research project grants:				
a. Noncompeting	1,596	$558,745,000	79	$45,326,000
b. Competing	612	200,195,000	6	1,613,000
c. SBIR/STTR	83	20,777,000	8	2,450,000
Total	2,291	779,717,000	93	49,389,000
2. Research centers	59	90,588,000	(1)	1,178,000
3. Other research	589	117,261,000	0	2,110,000
4. Research training	1,589	55,827,000	0	1,519,000
5. Research and development contracts	186	88,011,000	(23)	(8,201,000)
Subtotal, extramural				45,995,000
	FTEs		FTEs	
6. Intramural research	482	146,442,000	(9)	(1,257,000)
7. Research management and support	281	54,654,000	(4)	(717,000)
8. Cancer control and prevention	0	0	0	0
9. Construction	0	0	0	0
Subtotal, program		1,332,500,000		44,021,000
Total changes	763		(13)	49,614,000

NATIONAL INSTITUTES OF HEALTH
National Institute of Mental Health

Budget Authority by Object

	FY 2003 Amended Pres. Budget	FY 2004 Estimate	Increase or Decrease
Total compensable workyears:			
Full-time employment	763	750	(13)
Full-time equivalent of overtime & holiday hours	2	2	0
Average ES salary	$142,467	$142,464	($3)
Average GM/GS grade	11.1	11.1	0.0
Average GM/GS salary	$66,920	$68,258	$1,338
Average salary, grade established by act of July 1, 1944 (42 U.S.C. 207)	$82,879	$84,537	$1,658
Average salary of ungraded positions	98,136	100,099	1,963
OBJECT CLASSES	FY 2003 Amended Pres. Budget	FY 2004 Estimate	Increase or Decrease
Personnel Compensation:			
11.1 Full-Time Permanent	$37,490,000	$38,425,000	$935,000
11.3 Other than Full-Time Permanent	18,752,000	19,158,000	406,000
11.5 Other Personnel Compensation	1,229,000	1,260,000	31,000
11.7 Military Personnel	1,567,000	1,603,000	36,000
11.8 Special Personnel Services Payments	6,844,000	6,986,000	142,000
Total, Personnel Compensation	65,882,000	67,432,000	1,550,000
12.1 Civilian Personnel Benefits	13,759,000	14,083,000	324,000
12.2 Military Personnel Benefits	1,136,000	1,162,000	26,000
13.0 Benefits for Former Personnel	0	0	0
Subtotal, Pay Costs	**80,777,000**	**82,677,000**	**1,900,000**
21.0 Travel & Transportation of Persons	2,905,000	2,894,000	(11,000)
22.0 Transportation of Things	369,000	369,000	0
23.1 Rental Payments to GSA	0	0	0
23.2 Rental Payments to Others	2,980,000	2,936,000	(44,000)
23.3 Communications, Utilities & Miscellaneous Charges	1,865,000	1,856,000	(9,000)
24.0 Printing & Reproduction	1,920,000	1,897,000	(23,000)
25.1 Consulting Services	2,849,000	2,763,000	(86,000)
25.2 Other Services	8,972,000	8,898,000	(74,000)
25.3 Purchase of Goods & Services from Government Accounts	92,443,000	94,015,000	1,572,000
25.4 Operation & Maintenance of Facilities	5,581,000	5,592,000	11,000
25.5 Research & Development Contracts	68,290,000	60,457,000	(7,833,000)
25.6 Medical Care	466,000	467,000	1,000
25.7 Operation & Maintenance of Equipment	1,452,000	1,452,000	0
25.8 Subsistence & Support of Persons	0	0	0
25.0 Subtotal, Other Contractual Services	**180,053,000**	**173,644,000**	**(6,409,000)**
26.0 Supplies & Materials	9,550,000	9,566,000	16,000
31.0 Equipment	8,685,000	8,683,000	(2,000)
32.0 Land and Structures	0	0	0
33.0 Investments & Loans	0	0	0
41.0 Grants, Subsidies & Contributions	1,043,393,000	1,097,589,000	54,196,000
42.0 Insurance Claims & Indemnities	0	0	0
43.0 Interest & Dividends	3,000	3,000	0
44.0 Refunds	0	0	0
Subtotal, Non-Pay Costs	**1,251,723,000**	**1,299,437,000**	**47,714,000**
Total Budget Authority by Object	**1,332,500,000**	**1,382,114,000**	**49,614,000**

National Institute of Mental Health

Salaries and Expenses

OBJECT CLASSES	FY 2003 Amended Pres. Budget	FY 2004 Estimate	Increase or Decrease
Personnel Compensation:			
Full-Time Permanent (11.1)	$37,490,000	$38,425,000	$935,000
Other Than Full-Time Permanent (11.3)	18,752,000	19,158,000	406,000
Other Personnel Compensation (11.5)	1,229,000	1,260,000	31,000
Military Personnel (11.7)	1,567,000	1,603,000	36,000
Special Personnel Services Payments (11.8)	6,844,000	6,986,000	142,000
Total Personnel Compensation (11.9)	**65,882,000**	**67,432,000**	**1,550,000**
Civilian Personnel Benefits (12.1)	13,759,000	14,083,000	324,000
Military Personnel Benefits (12.2)	1,136,000	1,162,000	26,000
Benefits to Former Personnel (13.0)	0	0	0
Subtotal, Pay Costs	**80,777,000**	**82,677,000**	**1,900,000**
Travel (21.0)	2,905,000	2,894,000	(11,000)
Transportation of Things (22.0)	369,000	369,000	0
Rental Payments to Others (23.2)	2,980,000	2,936,000	(44,000)
Communications, Utilities and Miscellaneous Charges (23.3)	1,865,000	1,856,000	(9,000)
Printing and Reproduction (24.0)	1,920,000	1,897,000	(23,000)
Other Contractual Services:			
Advisory and Assistance Services (25.1)	1,951,000	1,949,000	(2,000)
Other Services (25.2)	8,972,000	8,898,000	(74,000)
Purchases from Govt. Accounts (25.3)	67,359,000	69,289,000	1,930,000
Operation & Maintenance of Facilities (25.4)	5,581,000	5,592,000	11,000
Operation & Maintenance of Equipment (25.7)	1,452,000	1,452,000	0
Subsistence & Support of Persons (25.8)	0	0	0
Subtotal Other Contractual Services	**85,315,000**	**87,180,000**	**1,865,000**
Supplies and Materials (26.0)	8,083,000	8,095,000	12,000
Subtotal, Non-Pay Costs	103,437,000	105,227,000	1,790,000
Total, Administrative Costs	**184,214,000**	**187,904,000**	**3,690,000**

NATIONAL INSTITUTES OF HEALTH

National Institute of Mental Health

SIGNIFICANT ITEMS IN SENATE APPROPRIATIONS COMMITTEE REPORT

The following section represents FY 2003 Congressional requirements for reports and significant items derived from Senate Report 107-216. These actions discussed below are contingent on inclusion of similar language and funding in the final FY 2003 appropriation and related reports. Additional items may be transmitted at a later date as a result of the final Conference report.

Item

Alzheimer's disease – the NIMH's newly formed Aging Workgroup has undertaken an exhaustive review of its current aging-related research portfolio, with a view toward enhancing coordination and collaboration with other NIH institutes. The Committee is pleased with the steps the NIMH has already taken, and it encourages the Institute to continue its efforts to reduce the psychiatric burden of Alzheimer's disease, including research into the relationship between Alzheimer's and depression. (p. 136)

Action taken or to be taken

In January 2002 NIMH re-established its "aging workgroup" as the Aging Research Consortium, a formal research planning group that includes members from across the Institute divisions. The Consortium also works with other NIH institutes with Alzheimer's disease portfolios. At one of its workshops designed to increase research applications, the Consortium focused on the ethical issues surrounding informed consent for individuals, including those with Alzheimer's disease, who are unable to give their own consent. With respect to ongoing clinical research, NIMH has passed the halfway mark in its recruitment of patients with Alzheimer's disease to participate in the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE). This large-scale clinical effectiveness trial is designed to identify the best medication regimen for treating the behavioral problems that co-occur in Alzheimer's disease. In 2002, NIMH staff orchestrated a successful effort by the Nation's leading investigators in late-life mental health to publish "Provisional Diagnostic Criteria for Depression of Alzheimer Disease." One outcome of the publication has been two newly submitted applications for research on this topic. In sum, through the efforts of the Aging Research Consortium and its collaboration with other NIH Institutes including NIA, NIMH is continuing to expand its efforts to develop effective treatments for reducing the burden of Alzheimer's disease.

Item

Autism – The Committee urges the NIMH to continue to fund behavioral and clinical research as well as other promising areas of research related to autism spectrum disorders. (p. 136)

Action taken or to be taken

NIMH is strongly committed to funding behavioral and clinical research related to autism spectrum disorders. In 2002, NIMH committed to be the primary funding source for the Studies to Advance Autism Research and Treatment (STAART) Centers program mandated by the Children's Health Act of 2000. The Institute awarded grants to develop STAART Centers, with co-funding provided by NINDS, NICHD, NIDCD, and NIEHS. Also, eleven applications were received in response to the initial Request for Applications (RFA) for STAART centers and were reviewed in March 2002. Two centers now have been funded. Applications have been received for the second round of STAART Centers competition, and the collaborating Institutes intend to fund an additional three or more centers in FY 2003. This will complete establishment of the network of at least five centers required by the Act. To compete successfully for funding, centers must include both basic and clinical research activities and at least one treatment project. The first two centers encompass research in the behavioral and clinical domains. It is expected that the full network of centers, for which NIMH will be the primary funding source, will continue to reflect this emphasis. NIMH uses other grant mechanisms to solicit and fund new applications in these areas, in addition to its ongoing support of an extensive portfolio in the genetics and neuroscience of autism.

Item

Borderline personality disorder (BPD) – The Committee understands that failure to recognize and adequately treat BPD can have devastating consequences such as substance abuse, domestic violence, and even suicide. The Committee urges the NIMH to expand its research on this disease. (p. 136)

Action taken or to be taken

Borderline personality disorder (BPD) is a severe mental illness characterized by instability in moods, interpersonal relationships, behavior, and self-image. To forge new directions for research on this disorder, the NIMH is encouraging the application of relevant translational basic behavioral and neuroscience research to the study of BPD. NIMH recently included questions regarding personality disorders, and particularly BPD, in the National Comorbidity Survey replication, a major mental illness epidemiology study that NIMH currently supports. The National Comorbidity Survey is designed to give the Institute an accurate picture of the current prevalence of mental disorders in the Nation. NIMH also convened a workshop in May 2002 to encourage young investigators to conduct BPD research. At this workshop, which was co-sponsored with the Swiss Borderline Personality Disorder Research Foundation (BPD-RF) and

the University of Minnesota, NIMH staff provided technical assistance to potential grantees. In August 2002, NIMH issued a RFA for pilot projects regarding borderline personality disorder. This announcement encourages translational research approaches to BPD, and is designed to support new, innovative exploratory approaches toward understanding the psychopathology of the disorder and devising new preventive and treatment interventions. These approaches are expected to lead to the development and submission of several fully implemented, highly competitive new applications for BPD studies over the next 3 to 5 years. Finally, NIMH is planning a conference in collaboration with the BPD-RF that will explore new issues regarding the core symptoms in BPD, and the best approaches to valid and reliable diagnosis.

Item

Elderly mental health – The Committee is concerned that despite substantial funding increases for the NIMH in recent years, the Institute's sponsorship of extramural research on the mental health of the elderly has not kept pace with its funding of research for other populations. Therefore, the Committee urges the NIMH to expand research in this area through all available mechanisms. (p. 136)

Action taken or to be taken

In 2002, NIMH re-established its "aging workgroup" as the Aging Research Consortium, a formal research planning body that includes members from all of the NIMH Divisions. The Consortium, which meets monthly, has held three workshops. The first focused on the ethical issues surrounding informed consent for individuals who are unable to give consent on their own (e.g., those with Alzheimer's disease, psychotic depression). A second workshop addressed needs for research on mood and anxiety symptoms in late-life. At the third workshop, Consortium members considered the need for expanded and innovative research training models to encourage more investigators to enter the late-life research field. The Consortium will hold a workshop in late-life basic research in 2003. Additional recent NIMH activities include the issuance of a new program announcement focused on aging research; dissemination of a report summarizing NIMH aging research; travel by staff to scientific meetings and other settings to promote aging research; and the use of funds to permit payment of meritorious applications that were on the border of fundability. NIMH also is developing an aging research website that will come on-line in late FY 2003.

Item

Fragile X – The Committee urges the NIMH to conduct research on the neurobiological basis of Fragile X, characterize the mental health symptoms of Fragile X, and investigate effective treatments and promising new psychopharmacologic interventions that target those symptoms. The Committee also urges the NIMH to include Fragile X in its studies of related neuropsychiatric disorders and to work with other Institutes such as the NICHD and the NINDS to develop cooperative research support mechanisms in this area. (p. 137)

Action taken or to be taken

NIMH supports research on the clinical phenomenology (including mental health symptoms), neurobiology, and genetics of Fragile X syndrome. NIMH strongly supports the inclusion of Fragile X syndrome patients in studies of related disorders such as autism and has explored, and will continue to explore, opportunities for such inclusion in specific collaborative funding activities that have been undertaken with NINDS and NICHD. Recent meetings on Fragile X syndrome include a workshop held by NIMH in November 2001 entitled, "Mental Health Aspects Of Fragile X Syndrome: Treatment Research Perspectives" and a workshop held at the Jackson Laboratory in Bar Harbor, ME in January 2003 co-sponsored by NIMH, the FRAXA Research Foundation, NICHD, and NINDS to bring together geneticists, clinicians, and neuroscientists to develop better models of the Fragile X syndrome. The long-term goals of these meetings are to accelerate research on the pathophysiology of Fragile X syndrome and the discovery of new therapeutic approaches.

Item

Frontier mental health needs – The Committee commends the NIMH on its outreach efforts to determine the differences in mental health needs which may exist in remote frontier communities. The Committee encourages the NIMH to expand its research efforts into these communities, which are often ignored in research projects but which continue to suffer from high incidences of mental health problems. (p. 137)

Action taken or to be taken

The NIMH and the NIMH Office of Rural Mental Health Research (ORMHR) support a large portfolio of research grants focused on addressing the mental health needs of rural and frontier communities. In addition, the ORMHR has sponsored several workshops to address specific issues of interest to these communities (e.g., a recent workshop on developing culturally relevant mental health interventions for rural and frontier people). Newly funded grants are looking at methods to reduce barriers to appropriate mental health care. Grants-supported investigators are testing new ways of delivering mental health interventions to remote areas (e.g., telemedicine) and models of disseminating best practices to providers in those areas. The NIMH has focused additional efforts to increase the research capacity for addressing the pressing problems faced by frontier areas, such as Alaska. Such efforts have included technical assistance to researchers and infrastructure support. In April of 2003, the NIMH will sponsor a conference in New Mexico that will bring together people from the Four Corners region to form the NIMH research agenda. Particular emphasis will be placed on research that addresses the health disparities found in traditionally underserved populations living in that region.

Item

Health disparities – The Committee urges the NIMH to act on its strategic goals to achieve a

more ethnic and racially diverse pool of mental health investigators through minority-focused training and career development mechanisms; to ensure inclusion of minority groups in clinical trials funded by the NIMH; to obtain an accurate measurement of the extent of mental health disparities across communities of color; and to use basic behavioral science to determine cultural differences in stress, coping and resilience. (p. 137)

Action taken or to be taken

During FY 2002, NIMH vigorously implemented a variety of initiatives designed to address the strategic goal of achieving greater racial and ethnic diversity among mental health investigators; trainees and post doctoral fellows; and clinical trial participants. The Institute hired an Associate Director for Special Populations and the Office for Special Populations was reorganized to include a neuroscientist for the newly created position of Chief, Research Scientist Development Program. In addition, the appointment was extended for the Special Expert who serves as the Program Official for Training and Infrastructure. NIMH hosted mental health investigators from several Hispanic/Latino organizations; representatives from Native American organizations; and, in December 2002, convened a planning meeting that addressed methods of increasing African American M.D./Ph.D. researchers. There was a 16% increase in the number of grants awarded for training support to colleges and universities with a racial and ethnic minority student population of at least 33%. There was also an 18% increase in the number of mental health research infrastructure support awards for faculty training and developmental research projects at colleges and universities that have predominantly racial and ethnic minority student populations (i.e. Chicago State University, California State University at Fresno, and Howard University). NIMH continued to seek effective ways to increase the inclusion of minority groups in its clinical trials. One method was a $5 million contractual agreement with Howard University to conduct community-based recruitment of human participants. NIMH has also developed a successful Hispanic Research Initiative in its Intramural Program at the NIH Clinical Center, which recently received an award for its developers from the NIH Hispanic Employees Organization. The Pilot Hispanic Research Initiative in Mood Disorder Patients is unique in that the care providers and researchers all speak Spanish, rather than relying upon translators, and are attuned to cultural sensitivities in their research. During FY 2002, NIMH invested $167 million in mental health research specifically related to health disparities. These research projects included studies that used basic behavioral science to examine cultural differences in stress, coping and resilience.

Item

Major Depression and Bipolar Disorder – More than 20 million children and adults in the Nation are affected by major depression or bipolar disorder, and depression has been shown to be a leading cause of disability worldwide. Depression and bipolar disorders are also prominently associated with suicide. The Committee is aware that the NIMH has developed "Breaking Ground, Breaking Through: The Strategic Plan for Mood Disorders Research" in consultation with nationally recognized scientific experts, members of the National Advisory Mental Health Council, and representatives of consumer groups. This plan summarizes the current state of the

science on major depression and bipolar disorder across the life span, provides a vision of achievable scientific goals, and recommends research priorities. It also addresses the causes, diagnosis, and improvement of interventions at the level of individual patients and service systems, as well as prevention. The Committee encourages the NIMH to continue its efforts to understand, treat, and prevent these illnesses. (p. 137)

Action taken or to be taken

The NIMH has undertaken a number of activities this past year to meet goals established in the Strategic Plan for Mood Disorders Research. The activities range from the most basic need of gaining a better understanding of the core components of the complex disease called "depression," to the initiation of clinical research that examines more effective treatments for children with bipolar disorder. In April, 2002, NIMH convened a workshop on "Measurement of Depression" in Washington, DC to discuss problems in the current measurement of depression and the desired outcomes for new tools. Following the workshop, NIMH and NIDA sponsored a call for research on (RFA) on "Development of Tools for the Assessment of Depression" to encourage research on developing tests that discriminate between levels of depression and identify core dimensions of depression. Refined measurement of the heterogeneous complex of depressive disorders is a prerequisite for studies of the association between clinical phenomena and neural substrates of mood and emotion; to link genetic models to particular forms of the disorder; or to tailor future therapeutic to particular subtypes of depression.

The treatment of depression and bipolar disorder by medication, while helpful to many, still is not able to target the actual "cause" of the disease. To advance the development and testing of fundamentally new, rationally designed medications and treatments, NIMH is working in partnership with NIDA and pharmaceutical industry investigators in a National Cooperative Drug Discovery Group Program to accelerate innovative drug discovery, the development of pharmacologic tools for basic and clinical research in mood disorders, and the development and validation of models for evaluating novel therapeutics.

How to effectively treat children with bipolar disorder has perplexed clinicians for decades and now NIMH is addressing these concerns by funding two clinical trials. In the Treatment of Early Age Mania (TEAM) study three medications (lithium, valproate, risperidone) are being compared alone and in combination for the treatment of children age 6-14 with bipolar disorder in manic or mixed state at six different treatment sites. In another study at three sites, the Pediatric Bipolar Collaborative Mood Stabilizer Trial, lithium and valproate are being tested to see if they are helpful in treating children age 8-17 years with bipolar disorder. In addition, activities are also be undertaken to learn more about the natural history of the disorder.

Item

Native Hawaiians – The Committee remains concerned that Native Hawaiians and other

NativeAmerican Pacific Islanders continue to suffer disproportionately from mental health problems. The NIMH is encouraged to continue its efforts to address this area. (p. 137)

Action taken or to be taken

The NIMH has an award in place through the year 2005, to support the Pacific People's Mental Health Research Support Program, located at the University of Hawaii at Manoa. The NIMH has planned a staff visit to the State of Hawaii in Spring, 2003, to identify and promote ways to assist Native Hawaiian and other Native American Pacific Islander constituents in their efforts to produce competitive applications for grants that support mental health research.

Item

Translating behavioral and social sciences research – The Committee supports translational research in the behavioral and social sciences to address how basic behavioral processes inform the diagnosis, treatment, and delivery of services for patients, particularly for young people, with mental disorders. To further the translation of research knowledge into practice, the Committee encourages ongoing collaboration between the NIMH and the Substance Abuse and Mental Health Services Administration to reduce the current lag time between the discovery of an effective treatment or intervention and its availability at the community level. The Committee also promotes the establishment of translational behavioral research as a priority funding area for the NIMH. (p. 138)

Action taken or to be taken

As part of implementing the NIMH Report on Translating Behavioral Science into Action, three Program Announcements (PA) have been issued to this regard: 1) Integrating Behavioral Sciences and Services Research; 2) Translational Research Grants in Behavioral Science; and, 3) Building Translational Research in Behavioral Science. To further the translation of research knowledge into practice, NIMH has released a new Program Announcement on Dissemination and Implementation Research and held three workshops.

The collaboration between NIMH and the Substance Abuse and Mental Health Services Administration (SAMHSA) regarding translating research knowledge into practice continues to be extremely active. NIMH and SAMHSA jointly sponsored a Request for Applications (RFA) "State Implementation of Evidence Based Practices: Bridging Science and Service." NIMH and SAMHSA held a technical assistance workshop for potential RFA respondents. NIMH continues to be an active participant in the cross-agency committee on Bridging Science and Service, and will sponsor, along with NIDA and NIAAA, a technical assistance workshop for SAMHSA grantees. NIMH encourages investigator-initiated research applications that seek to address problems of major public mental health significance in which the opportunity to conduct research is time limited.

NIMH recently funded a Time Sensitive Opportunities research grant on homeless families – one that built on a SAMHSA funded project. Finally, NIMH and SAMHSA now are developing a plan to collaborate on children's issues and homelessness issues.

NATIONAL INSTITUTES OF HEALTH
National Institute of Mental Health

Authorizing Legislation

	PHS Act/ Other Citation	U.S. Code Citation	2003 Amount Authorized	2003 Amended President's Budget	2004 Amount Authorized	2004 Budget Estimate
Research and Investigation	Section 301	42§241	Indefinite	$1,276,673,000	Indefinite	$1,324,768,000
National Institute of Mental Health	Section 417B	42§285	Indefinite		Indefinite	
National Research Service Awards	Section 487(d)	42§288	a/	55,827,000	b/	57,346,000
Total, Budget Authority				1,332,500,000		1,382,114,000

a/ Amounts authorized by Section 301 and Title IV of the Public Health Act.
b/ Reauthorizing legislation will be submitted.

NATIONAL INSTITUTES OF HEALTH
National Institute of Mental Health

Appropriations History

Fiscal Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation 1/
1995 2/	$545,223,000	$541,687,000	$543,687,000	$542,989,000 /3
Rescission				(789,000)
1996	558,580,000 /2	661,328,000	550,632,000 /2	661,328,000
Rescission				(706,000)
1997	578,149,000 /2	701,247,000	589,187,000 /2	701,107,000 /4
1998	628,739,000 /2	744,235,000	759,956,000	750,241,000
1999	699,679,000 /2/5	815,707,000	861,208,000	861,208,000
Rescission				(570,000)
2000	758,892,000 /2	930,436,000	969,494,000	978,360,000
Rescission				(5,214,000)
2001	896,059,000 /2	1,114,638,000	1,117,928,000	1,107,028,000
Rescission				(492,000)
2002	1,238,305,000	1,228,780,000	1,279,383,000	1,248,626,000
Rescission				(533,000)
2003	1,343,728,000			
2004	1,382,114,000			

1/ Reflects enacted supplementals, rescissions and reappropriations.
2/ Excludes funds for HIV/AIDS research activities consolidated in the NIH Office of AIDS Research.
3/ Excludes enacted administrative reductions of $561,000.
4/ Excludes enacted administrative reductions of $478,000.
5/ Reflects a decrease of $2,111,000 for the budget amended for bioterrorism.

NATIONAL INSTITUTES OF HEALTH
National Institute of Mental Health

Detail of Full-Time Equivalent Employment (FTEs)

OFFICE/DIVISION	FY 2002 Actual	FY 2003 Amended Pres. Budget	FY 2004 Estimate
Office of the Director	107	107	103
Division of Neuroscience and Basic Behavioral Science	40	40	40
Division of Mental Disorders, Behavioral Research & AIDS	44	47	47
Division of Services and Intervention Research	37	37	37
Division of Extramural Activities	51	50	50
Division of Intramural Research Programs	480	482	473
Total	759	763	750
FTEs supported by funds from Cooperative Research and Development Agreements	(0)	(0)	(0)

FISCAL YEAR	Average GM/GS Grade
2000	10.6
2001	10.9
2002	11.1
2003	11.1
2004	11.1

NATIONAL INSTITUTES OF HEALTH
National Institute of Mental Health

Detail of Positions

GRADE	FY 2002 Actual	FY 2003 Amended Pres. Budget	FY 2004 Estimate
ES-6	1	1	1
ES-5	2	2	2
ES-4	7	7	6
ES-3	1	1	1
ES-2	0	0	0
ES-1	0	0	0
Subtotal	11	11	10
Total - ES Salary	$1,519,901	$1,567,137	$1,424,637
GM/GS-15	53	53	51
GM/GS-14	86	85	84
GM/GS-13	67	67	67
GS-12	86	86	86
GS-11	92	91	89
GS-10	1	1	1
GS-9	81	80	78
GS-8	43	43	43
GS-7	50	50	50
GS-6	13	13	13
GS-5	8	8	8
GS-4	6	6	6
GS-3	0	0	0
GS-2	0	0	0
GS-1	0	0	0
Subtotal	586	583	576
Grades established by Act of July 1, 1944 (42 U.S.C. 207):			
Assistant Surgeon General	0	0	0
Director Grade	13	13	12
Senior Grade	3	3	3
Full Grade	1	1	1
Senior Assistant Grade	0	0	0
Assistant Grade	0	0	0
Subtotal	17	17	16
Ungraded	186	182	181
Total permanent positions	577	572	570
Total positions, end of year	800	793	783
Total full-time equivalent (FTE) employment, end of year	759	763	750
Average ES level	ES-4	ES-4	ES-4
Average ES salary	$138,173	$142,467	$142,464
Average GM/GS grade	11.1	11.1	11.1
Average GM/GS salary	$64,908	$66,920	$68,258