National Institute of Mental Health

NATIONAL INSTITUTES OF HEALTH

DEPARTMENT OF HEALTH AND HUMAN SERVICES

FY 2005 Budget

6001 Executive Blvd., Bethesda, Maryland 20892

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH • NATIONAL INSTITUTE OF MENTAL HEALTH

NIMH
National Institute of Mental Health

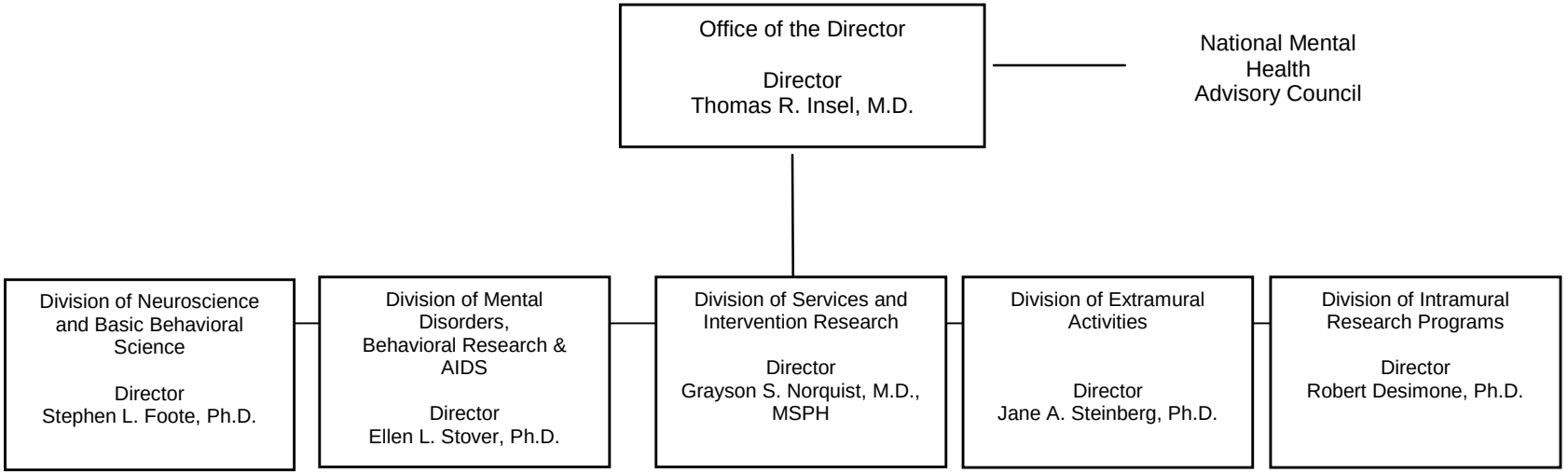
DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

National Institute of Mental Health

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health
National Institute of Mental Health



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, [$1,390,714,000] *$1,420,609,000*.

[Departments of Labor, Health and Human Services and Related Agencies Appropriations Act, as enacted by the Omnibus Consolidated Appropriations Act for Fiscal Year 2004]

National Institutes of Health
National Institute of Mental Health

Amounts Available for Obligation 1/

Source of Funding	FY 2003 Actual	FY 2004 Final Conference	FY 2005 Estimate
Appropriation	$1,349,788,000	$1,390,714,000	$1,420,609,000
Enacted Rescissions	(8,774,000)	(8,940,000)	---
Subtotal, Adjusted Appropriation	1,341,014,000	1,381,774,000	1,420,609,000
Comparative transfer from: Fogarty International Center for International Services Branch	47,000	0	0
Comparative transfer to NIBIB for Radiology Program	(101,000)	(102,000)	0
Comparative transfer to Buildings and Facilities	(402,000)	(406,000)	0
Comparative transfer to Office of the Director for program changes	(1,275,000)	0	0
Subtotal, adjusted budget authority	1,339,283,000	1,381,266,000	1,420,609,000
Unobligated Balance, start of year	0	0	0
Unobligated Balance, end of year	0	0	0
Subtotal, adjusted budget authority	1,339,283,000	1,381,266,000	1,420,609,000
Unobligated balance lapsing	0	---	---
Total obligations	1,339,283,000	1,381,266,000	1,420,609,000

1/ Excludes the following amounts for reimbursable activities carried out by this account:
FY 2003 - $5,837,435; FY 2004 - $5,895,000; FY 2005 - $5,971,000
Excludes $117,252 in FY 2003 and $120,928 in FY 2004 for royalties.

Justification

National Institute of Mental Health

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

Budget Authority:

FY 2003 Actual		FY 2004 Final Conference		FY 2005 Estimate		Increase or Decrease	
FTEs	BA	FTEs	BA	FTEs	BA	FTEs	BA
771	$1,339,283,000	748	$1,381,266,000	746	$1,420,609,000	(2)	$39,343,000

This document provides justification for the Fiscal Year 2005 activities of the National Institute of Mental Health (NIMH), including HIV/AIDS activities. Justification of the National Institutes of Health (NIH)-wide FY 2005 AIDS activities can be found in the NIH section entitle "Office of AIDS Research (OAR)."

INTRODUCTION

The National Institute of Mental Health faces an enormous challenge: to reduce the burden of mental and behavioral disorders through research on mind, brain, and behavior. To do so, the current mental health care system must be transformed, as called for in the recent report from the President's New Freedom Commission on Mental Health. The report describes the dire need for improving the delivery of evidence-based treatments that already exist directly to communities, as well as development of new treatments that more effectively reduce suffering and improve recovery for people with mental illnesses such as schizophrenia, bipolar disorder, depression, anxiety disorders, and autism.

The need is vast: mental disorders account for four of the top five causes of premature death and disability among 15-44 year olds in the Western world. For many of the disorders, there is some form of treatment; for most, there is no cure. Even for the disorders for which treatment can be extremely successful, many are still not getting access to them. For instance, about 16 percent of Americans ages 15-54 have experienced major depression in their lifetime.[1] Just over half of those experiencing it in the past year received treatment. While this is an improvement from previous years, it indicates the need for progress in treatment delivery. Suicide is another threat. While suicide rates are lower than they were 30 years ago, they are still alarming. With 30,000

[1] Kessler, RC, Berglund, P, Demler, O, Jin, R, Koretz, D, Merikangas, KR, Rush, JA, Walters, EE, and Wang, PS, The Epidemiology of Major Depressive Disorder: Results From the National Comorbidity Survey Replication (NCS-R) JAMA. 2003: 289:3095-3105.

people dying each year, far more Americans die from suicide than homicide. Suicide is high among several ethnic minority groups, and is rising in youth.[2]

NIMH recognizes the need for the research enterprise to partner with other organizations to link research findings directly to services in the community. NIMH is now working with government partners, such as the Substance Abuse and Mental Health Services Administration (SAMHSA), to fund states to determine the most effective ways to spread the impact of new treatments in "real world" settings. NIMH is also collaborating with the Centers for Medicare and Medicaid Services (formerly HCFA), to advise state Medicaid directors to support evidence-based community treatment programs for people with schizophrenia. Mental health care is now being given where it was not before: in primary care offices, community clinics, nursing homes, and schools, where it is truly needed.

In addition to applying what we already know, NIMH recognizes that to make significant progress in improving recovery and finding cures for mental illness, we must continue the search for the mechanisms of disease that lead to the development of better, more rational treatments. To develop superior treatments, both pharmacologic and behavioral, we first need to determine both the genetic and the environmental causes of these major disorders. Rapid-paced advances in neuroscience are yielding astonishing discoveries about the basic biological and behavioral components of major mental illness, thanks to new technological tools in genetics and imaging combined with sophisticated behavioral paradigms. The completion of the mapping of the human genome this year has set the stage for scientific discovery with a huge public health impact. The value of cutting-edge imaging methods now allows us to visualize the brain at work and was recently recognized with two scientists winning the Nobel Prize for their contributions to the development of MRI technology. These fields offer new hope for treatments, and even cures for mental disorders, just as they hold great promise for cancer and heart disease.

To help realize the promise of dramatically improved treatments and continue striving for prevention and cure, NIMH established several initiatives this year that will enable significant progress towards overcoming autism, schizophrenia, depression, and suicide, among others.

Autism: NIMH plays a major role in a broad-based NIH effort to create a network of autism research centers focusing on biomedical and behavioral aspects of the disease. Five institutes at NIH are coordinating their research efforts in an initiative called the Studies to Advance Autism Research and Treatment (STAART) Centers program. This commitment to autism research responds to the Children's Health Act of 2000. This year, the institutes awarded grants to support six new autism research centers, in addition to the two that were funded last year. Each STAART center will contribute to understanding the underlying brain abnormalities, causes, diagnosis, early detection, prevention, and treatment of individuals with autism. For instance, imaging studies of the brain currently underway aim to improve early diagnosis and differentiation of various forms of autism; with the results, researchers are building a database

[2] Institute of Medicine, National Academy of Sciences, Reducing Suicide: A National Imperative. Committee on Pathophysiology & Prevention of Adolescent & Adult Suicide, Board on Neuroscience and Behavioral Health, National Academies Press, Washington, DC, 2002

differentiating brain development in autistic children compared to healthy children. In addition, the process of identifying specific genes that confer vulnerability to autism is underway. Once autism-linked genes are identified, scientists can search for what activates them, what brain components they code for, and how they affect behavior. The prospect of acquiring such molecular knowledge holds great hope for the engineering of new therapies. The six new centers include University of Washington, University of California, Los Angeles, Boston University, University of Rochester, Kennedy Krieger Institute, and Mt. Sinai Medical School. Plans for collaborative projects include multi-site clinical trials within the STAART network, as well as interaction with the Collaborative Programs of Excellence in Autism, ten major research programs funded by the NICHD/NIDCD Network on the Neurobiology and Genetics of Autism.

Schizophrenia: Schizophrenia research at NIMH this year has seen exceptional progress, revealing at least a partial blueprint of the genes that place individuals at an increased risk for the disease. NIMH intramural researchers have made some of the seminal discoveries in this area, with studies of COMT, BDNF, and several glutamate receptor-related genes that appear to contribute to the development of schizophrenia. However, it is clear that the road from gene discovery to prevention and treatment is neither simple nor rapid. To accelerate this process, NIMH has laid the groundwork for a new initiative within the intramural program. An interdisciplinary team ranging from geneticists and molecular biologists to clinical scientists will lead a broad effort to understand how various gene variations alter cellular function, neural chemistry, and neural circuitry – ultimately changing brain activity and behavior. The team will work to identify the role of these vulnerability genes, including their individual contributions to risk, severity of the disease, and drug response. Their efforts complement those of a large and vibrant extramural community of basic and clinical researchers following up on the promise of susceptibility genes in schizophrenia.

Suicide: Suicide is a tragic and potentially preventable public health problem, affecting all ages. Each year, about 30,000 people in the U.S. commit suicide,[3] with an estimated eight to 25 attempted suicides per every suicide death[4]. More teenagers and young adults die from suicide than from cancer, heart disease, AIDS, birth defects, stroke, pneumonia and influenza, and chronic lung disease *combined*[5]. In youths, the rates are rising, but the very highest rates are for white men age 65 and up.[6] The alarming numbers of suicide deaths and attempts emphasize the need for carefully designed prevention efforts. Nearly 90 percent of suicide deaths are related to a mental illness, such as depression and/or a substance abuse disorder.[7] Studies show that

[3] Institute of Medicine, National Academy of Sciences, Reducing Suicide: A National Imperative. Committee on Pathophysiology & Prevention of Adolescent & Adult Suicide, Board on Neuroscience and Behavioral Health, National Academies Press, Washington, DC, 2002

[4] World Health Organization, ICD-10 International Statistical Classification of Diseases and Related Health Problems, 1989 Revision, Geneva,1992.

[5] U.S. Public Health Service, The Surgeon General's Call To Action to Prevent Suicide. Washington, DC, 1999.

[6] World Health Organization, ICD-10 International Statistical Classification of Diseases and Related Health Problems, 1989 Revision, Geneva, 1992.

[7] U.S. Public Health Service, The Surgeon General's Call To Action to Prevent Suicide. Washington, DC, 1999.

approximately 70 percent of the older people who committed suicide have seen their primary care doctors within a month of their deaths.[8] This year, an NIMH study (in press) on preventing suicide in the elderly showed that interventions in primary care settings were successful in decreasing the frequency of significant suicidal thoughts and improving treatment of depression. The key elements were the inclusion of families in the care, as well as the addition of a nurse or other professional staff member to work with the physician in educating patients, implementing treatment, monitoring side effects, and modifying therapy when needed. However, many depressed older people live in isolation, do not see physicians on a regular basis, and are never identified. Many of the most severely ill of older adults are treated in home care, nursing homes, rehabilitation facilities, and other institutional settings. With appropriately focused research, we can develop models to increase the access of these patients to treatment and improve their care. NIMH also co-sponsored a workshop this year on the effects of suicide on family and friends. Scientists, clinicians and members of the suicide survivors' community identified areas for future research including the impact of suicide on family functioning and suicide risk, individual vulnerability to distress after suicide, and differences in special populations.

Increasingly, NIMH will be addressing its many opportunities and challenges collaboratively with the other NIH institutes focused on brain and behavior. In addition to new leadership at NIMH, the National Institute on Drug Abuse, the National Institute of Neurological Disorders and Stroke, and the National Institute on Alcohol Abuse and Alcoholism also have recently brought new directors on board. We are working together to help improve treatment and services for mental disorders. Our part of the bold vision stated in the President's New Freedom Commission on Mental Health is to achieve the promise of research, transforming through science both treatment and prevention for people with mental disorders.

SCIENCE ADVANCES AND STORIES OF DISCOVERY

In the last year, NIMH-sponsored studies have revealed new and exciting candidate genes for mental disorders and highlighted the real challenge in understanding mental illness: to discover how genes and the environment interact to produce vulnerability to disease. This year has been remarkable in its wealth of discoveries of genes as well as gene-environment interactions.

Unraveling the Mysteries of the Brain Through Genetics

Many mental disorders are known to have a genetic component. However, the genetics are complicated by the fact that many genes, rather than just one, are likely to predispose to each disorder, and each gene that confers susceptibility only contributes a small amount of the risk. This past year has finally moved us from the generation of linkage studies -- a broad approach to searching for disease genes that only reveals those genes with large effects -- to a new era of association studies and other strategies that have proven successful in identifying genes for susceptibility to mental disorders. With the discovery of vulnerability genes and possible

[8] As cited in: U.S. Public Health Service, The Surgeon General's Call To Action to Prevent Suicide. Washington, DC, 1999. (Pearson JL, Conwell Y, Lyness JM. Late-life suicide and depression in the primary care setting. In: Schneider LS, editor. Developments in geriatric psychiatry. New directions for mental health services (no. 76). San Francisco: Jossey-Bass:1997:13-38.)

cellular pathways involved in schizophrenia and fear disorders, we have made unprecedented progress on the genetic risk architecture for these diseases. We still need to learn how common variations in these genes confer vulnerability, but we are already discovering how they alter brain function, even in the healthy relatives of those suffering from mental disorders. This roster of genes should bring us closer to diagnostic tests for early detection, new strategies for prevention, and even new targets for treatment.

Schizophrenia Genes. Schizophrenia is a profoundly disabling disorder, typically manifesting in young adulthood, characterized by hallucinations, delusions, social withdrawal, flattened emotions, and loss of social and personal care skills. The genetic susceptibility to schizophrenia is complex and likely to arise from the combined effects of multiple genes and their interactions with environmental factors.

Possible Genetic Marker for Schizophrenia Found in Siblings. In schizophrenia, genes do not appear to code directly for symptoms such as hallucinations and delusions. However, patients and their unaffected family members share subtle abnormalities in cognition and data processing that may be closely linked to biological systems influenced by genes. These abnormalities may serve as biological markers for this disorder. For example, previous studies have shown that some abnormalities in working memory that are present in patients with schizophrenia are also present in their unaffected family members at a rate much higher than the general population. In this study, the authors wanted to determine whether abnormalities in the physiological pattern underlying working memory are heritable in families with schizophrenia. The NIMH researchers compared the physiology of working memory in cognitively unimpaired and clinically unaffected siblings of schizophrenic patients to healthy comparison subjects. Tests for working memory were given to the subjects while their brain activity was observed with functional magnetic resonance imaging (fMRI). As expected, the siblings, like the healthy comparison subjects, had no apparent problems with successfully performing the memory tasks. However, unlike the healthy comparison subjects, the healthy siblings showed an abnormal pattern of activity in the dorsolateral prefrontal cortex, similar to the pattern seen in their siblings with schizophrenia. This brain region is involved in working memory and information processing. Abnormal information processing in this region appears to be a component of biological susceptibility to schizophrenia. Although formal estimates of heritability remain to be determined, fMRI measures of activity in the dorsolateral prefrontal cortex likely represent a promising approach to identifying candidate genes associated with an increased risk for schizophrenia.

Human Gene Found to Affect Memory; Provides Clues About Brain Function, Diseases, Aging. Clinical studies suggest that certain forms of human memory, especially the ability to recall specific past events (episodic memory), are mediated by the hippocampus. The protein BDNF, long known to be critical for the growth and survival of neurons, has also recently been shown to play a key role in learning, memory, and hippocampal function in animals. To find out if BDNF has a similar role in humans, NIMH researchers explored the consequences of a variance in the sequence of the human BDNF gene. Each individual inherits two copies of the BDNF gene, one from each parent, in either of two versions. Slightly more than a third inherit at least one copy of a version called met while two thirds inherit a version called val. To examine the effects of this single variation in the BDNF gene on memory, people with two copies of the

met gene and those with two copies of the val gene were given a test for episodic memory. On average, people with only the met version of the gene performed worse in tests for episodic memory, but had no difficulty with working memory, which involves general knowledge not tied to a specific experience or event. In the first study of its kind, the researchers then looked at the effect of the variation of the BDNF gene on hippocampal activation. Functional magnetic resonance imaging (fMRI) scans revealed that those with just one copy of met showed a pattern of diffuse activation along the sides of the hippocampus, in contrast to more focused activation among those with two copies of val. People with the BDNF met allele required more extensive activation to achieve an equal level of performance on memory tasks. This finding demonstrates the power of new imaging techniques to reveal individual differences not detected by traditional psychological tests. In related studies met and val alleles also affected the function of the BDNF protein. This study not only confirms that BDNF plays a role in human memory, it also reveals potential molecular and cellular mechanisms for individual differences in memory. Along with findings from the same researchers on variations in the COMT and SERT genes, these findings with BDNF open up an exciting new horizon of research using non-invasive brain imaging techniques that link memory, brain function, and genes with remarkable specificity. In the future, this area of research will give us a deeper understanding of how subtle, common variations in a number of genes contribute to the various forms of brain dysfunction that underlie psychiatric disorders.

Genes Influence Response to Drug Commonly Given for Psychiatric Illnesses.
Psychostimulants such as amphetamines are effective in the treatment of some patients with attention deficit hyperactivity disorder and other psychiatric illnesses, such as schizophrenia. These drugs increase alertness and attention and enhance mood and cognitive performance presumably by optimizing the levels of dopamine in the brain – since too much or too little dopamine is thought to impair cognition. There is evidence that the effects of these drugs vary from person to person. This variation in response has been difficult to predict and its biological basis was unclear. An enzyme called COMT is responsible for breaking down dopamine. The activity level of the enzyme is altered if there is a variation in the gene that codes for it. Previous research has shown that healthy people with the val version of the COMT gene have higher levels of COMT and less dopamine in the brain, whereas healthy people with the met version have lower activity of COMT and more dopamine. An NIMH study asked two questions: 1) is it true that too much or too little dopamine is deleterious to cognitive performance? 2) Does this genetic variation in the COMT enzyme alter the response to psychostimulants? Using fMRI technology, the researchers show that amphetamine improved cognitive function at all levels of task difficulty in healthy study participants with the val version of the gene. This is presumably because a lower baseline level of dopamine is increased by amphetamine administration, which renders it optimal for cognitive performance. In contrast, amphetamine had no effect on the cognitive performance of subjects with the met version of the gene on the easy and intermediate tasks. However, during difficult tasks, these subjects experienced negative effects with amphetamine; their accuracy, efficiency, and reaction time decreased dramatically. The researchers interpret this result as an indication that these healthy controls with the met gene had an "optimal" level of dopamine at baseline and amphetamine produced "too much" dopamine for ideal cognitive function. This provides the first demonstration in humans of a genetic explanation for individual differences in the brain's response to psychostimulants. In addition, it

appears that genetic differences can interact with other factors such as task difficulty to influence the optimal level of dopamine for cognitive performance. Because cognitive dysfunction is characteristic of many psychiatric disorders such as schizophrenia and attention deficit disorder, the COMT genotype may be an important determinant in understanding the mechanism of these cognitive disturbances and predicting a person's response to treatment.

Protein Expressed During Development May Be Linked to Schizophrenia. The cerebral cortex is the locus of higher cognitive and executive and integrative functions. The neuronal processes allowing communication between cells in the cerebral cortex are abnormal in schizophrenia, and this deficiency is thought to arise very early in life. A mutation in the gene DISC-1 in a Scottish family with a 47 percent prevalence of major psychiatric disorders has been shown to increase susceptibility to schizophrenia. Using rodents, NIMH-sponsored scientists observed that the normal DISC-1 gene is associated with other proteins that regulate neuron growth and migration, ultimately leading to the formation of normal cerebral cortical folds. The mutant form of the DISC-1 protein, in contrast, fails to associate with these other proteins, resulting in a pattern of reduced neuronal growth similar to that seen in schizophrenics. These studies link the DISC-1 gene with the pathology of schizophrenia. Further studies of DISC-1 and its role in brain development may provide researchers with concrete targets for the eventual development of effective early interventions for individuals at high risk for developing schizophrenia.

Anxiety Disorders/Fear Genes

Fear is a normal emotional reaction to threatening or traumatic life experiences. When an individual is faced with traumatic circumstances, fear can trigger a defensive response necessary for survival. However, prolonged memories of fearful events can cause people to overreact to seemingly non-threatening situations–a hallmark of anxiety disorder and post-traumatic stress disorder (PTSD). To learn more about the biological bases of these disorders scientists have been working to understand how fear is processed in the brain. Their studies focus on the amygdala, a key brain region critically involved in the acquisition, storage, and expression of fear responses.

How Fearful Memories Are Made. NIMH-funded researchers have now identified a molecular and cellular pathway in the brain that is important in imprinting fear-related experiences to memory. First, the research team identified a gene in the amygdala that codes for a neurochemical signal called GRP. When certain nerve cells, called principal cells, are activated in response to an emotional event, GRP is released. The GRP is then detected by other nerve cells, called interneurons. The interneurons send a signal back to the principal cells to halt their activation, thus controlling the overall fear response. When GRP activity was removed altogether (by creating mice lacking GRP receptors) the mice showed greater and more persistent long-term memory of fear than did normal mice. This finding demonstrates that the GRP pathway serves to keep learned responses to fear in check. The findings highlight the importance of a finely tuned balance between excitation and inhibition in an individual's overall reaction to fearful events. Further studies also indicate that instinctive fear is different from acquired fear, and point to either drugs that activate GRP, or drugs that act upon the biochemical process

initiated by GRP, as potential therapeutic targets for treatment. This study aids in understanding the brain mechanisms underlying human anxiety and post-traumatic stress disorder, and could lead to the development of new treatments for people who suffer from these conditions.

Reducing Fear in Anxiety Disorders. Little is known about the neural mechanisms that allow us to overcome fear responses. Psychological studies suggest that this process, known as extinction of fear, does not erase the original fear association from memory, but instead generates a new memory for safety. The brain region(s) involved in learning these new safe memories had not been conclusively identified. However, in a recent animal study, NIMH-funded researchers found that the prefrontal cortex is the site of storage for new extinction memory and that activation of this region inhibits the original fear response. These findings suggest that therapies stimulating the prefrontal cortex may strengthen extinction memory in people suffering from anxiety disorders. Current treatments for anxiety disorders -- cognitive and behavioral therapy as well as medications -- can be effective, but the rates of relapse of the original fear response remain high. To develop more effective treatments for anxiety disorders, it is important not only to understand how fear responses are acquired but also how they can be eliminated when the eliciting stimulus no longer represents a threat.

Autism Genes

Autism is a developmental brain disorder that affects social, communicative, and behavioral functioning, usually beginning within the first three years of life. There is no known cure or cause, although genetic factors clearly play a role. Autism describes the most severe of a broad range of disorders called autism spectrum disorders (ASD).

Gene Is Found to Increase Vulnerability for Autism. A previous study of 110 families showed evidence of ASD vulnerability in genes on several chromosomes. In a follow-up analysis of 345 families, each with at least two siblings affected with autism or ASD, the most significant genetic variations were found near the gene 5-HTT, known to regulate the neurotransmitter serotonin. This is the same gene that was recently linked to vulnerability for depression and to increased anxiety in response to fear stimuli. The finding fits with other studies, which show evidence of elevated serotonin levels both in patients with autism and in their unaffected first-degree relatives, and studies which show that drugs targeting 5-HTT can improve some autism-related symptoms. Thus, the neural circuits and pathways involved with serotonin transport may provide targets for developing new drugs for autism. Information on this large group of families has been included in the NIMH Human Genetics Initiative and will have tremendous value as a community resource for mapping vulnerability genes and for studying gene-environment interactions.

Story of Discovery: Life Stress and Genes Inextricably Linked in Depression

For generations, the main scientific question in mental health involved the age-old battle of nature vs. nurture. Were genes or environmental stresses responsible for sending one to the depths of a clinical depression? And which was most effective at treating the disorder: pharmacological or behavioral therapy?

Now, the field, and indeed the question itself, have evolved. Studies in the last decade have suggested that genetics and environment cannot be examined separately; the environment sculpts our biological responses as surely as our genetics influence behavior. Most mental health scientists are no longer concerned with simply choosing between the two, but with discovering specifically how they influence one another – to make us more or less vulnerable to mental disorders – and identifying the mechanisms of action that are involved.

Depression is currently the leading cause of disability and second leading cause of disease burden in America. It is a complex disorder in which gene-environment interaction occurs – where the combination of a particular gene profile and exposure to particular environmental factors result in illness. The difficulty in finding an effective psychiatric treatment for depression has been the wide individual differences among patients: which genes are involved? Which types of life events are stressful enough to trigger the disease? Why doesn't it get triggered in everyone? As each generation of drugs has been developed, from the MAO inhibitors in the early 1950s to the tricyclics to the selective serotonin reuptake inhibitors (SSRIs) in the 1990s, clinicians and researchers have grappled with the fact that what works for some people is ineffective for others. Behavioral therapies have had the same problem, starting with Albert Ellis' rational-emotive therapy in the 1950s and Aaron Beck's cognitive therapy in the 1970s, and the many variations since: they have not proven successful for all patients. It has become apparent that there are different biologies for depression, each reacting to the differences in the various types of treatment.

The current challenge for the mental health sciences is discovering how genes and the environment interact to produce these individual biological differences. Understanding the biological consequences of these interactions will likely be essential for developing an effective personalized treatment for each patient – and even for finding ways to maintain resiliency and prevent depression in the first place.

This year, the study of genes and environment has produced exciting results. NIH-sponsored researchers found a link between a gene and the development of depression. But unlike all previous genetic studies, they found the connection only because they looked at the stress history of the study participants. Their results suggest that measuring pivotal environmental events – from psychosocial traumas like a job loss or the death of a loved one, to exposure to infections and toxins – could be the key to unlocking the secrets of psychiatric genetics.

The scientists followed 847 New Zealanders, born in the early 1970s, from birth into adulthood. They looked at the gene for a chemical transporter called 5-HTT, which regulates transmission of serotonin, the neurotransmitter affected by fluoxetine (Prozac) and other SSRIs. The gene has been a prime suspect in mood and anxiety disorders. Yet its link to depression eluded detection in eight previous studies.

The gene comes in two versions: a long version and a short version. Since every human has one gene from each parent, they could have two long, two short, or one of each version. Previous studies in mice and monkeys, as well as brain imaging studies in humans, indicated that in stressful situations, people with two long versions were better able to handle stress than those with two short versions.

Of the human study participants, 17 percent carried two copies of the short version of the gene; 31 percent carried two copies of the protective long version, and 51 percent carried one copy of each version. The researchers charted study participants' stressful life events for five years from ages 21-26. These included debt problems, homelessness, abuse history, a disabling injury or other health issue, joblessness, and relationship woes. Thirty percent had no stressful events, 25 percent had one, 20 percent had two, 11 percent three, and 15 percent four or more such stressful life experiences.

Interestingly, individuals who had no major life stressors had the same low chance of developing depression no matter which versions of the gene they had. However, individuals with two short versions were more likely to develop depression as they experienced more major life stressors; those with four or more life stressors were six times as likely to develop depression than people with no major life stressors. Thus, there was a clear interaction between genetic vulnerability and environmental events that determined risk for depression.

Among individuals who had experienced multiple stressful events, 11 percent with the short variant thought about or attempted suicide, compared to 4 percent with two copies of the long variant. Interestingly, this study fits with related research showing that people with the short 5-HTT gene show more intense brain reactions to fearful stimuli than do those without this version.

The results suggest that effects of genes in complex disorders like psychiatric illnesses are most likely to be uncovered when life stresses are measured, since differences in a gene's effects may only become critical in people exposed to the requisite environmental risks. With success now in examining the interplay of genes and environment in depression, future research can apply this information to develop more refined treatments that either target genes or the environment, or both.

Diagnosis and Treatment

A major goal of NIMH research is to harvest scientific data from the lab to produce clinical diagnostic tools and novel treatments. For many diseases, early diagnosis can improve outcomes by enabling those affected to obtain early treatment and monitoring. Learning about early stages of a disease can also lead to a better understanding about prevention. For disorders that often occur late in life, such as Alzheimer's, prevention by as little as five years can save enormous personal, financial, and societal costs. Developing more effective treatments, and ensuring that they reach those who need them, helps reduce the enormous burden of mental and behavioral disorders on individuals, families, and society.

Screening Tool For Alzheimer's Disease Looks Promising. Alzheimer's disease is a progressive, degenerative disorder resulting in loss of memory and eventually, loss of mental and physical function. Alzheimer's disease is usually diagnosed on the basis of medical history, cognitive symptoms, brain scans, and by ruling out other disorders. The physical hallmarks of Alzheimer's disease are characteristic deposits of protein in the brain: beta amyloid deposits form in plaques within neurons and tau deposits strangle neurons in tangled filaments. So far, these can only be detected in the brain after death. The challenge for scientists is to develop a way to detect these physical hallmarks before death, for the purposes of accurate diagnosis and treatment. Previous studies have suggested that beta amyloid and tau proteins can be detected in cerebral spinal fluid (CSF), although results have not been consistent. In a major advance, NIMH investigators have confirmed that levels of beta amyloid and tau in spinal fluid distinguished clinically diagnosed Alzheimer's patients from controls with 89-92 percent accuracy. Like many previous studies, the new research found that CSF beta amyloid levels drop, while tau levels rise in Alzheimer's. Results also suggest that these changes may be present early in the disease process. By establishing a person's baseline protein levels and tracking them over time, patients with predictive indicators might then be able to benefit from the early-stage medications currently available, which have been shown to provide some improvement in cognitive and activity measures. Long-term studies now underway will determine if these biomarkers can eventually be widely used as predictive and diagnostic tools.

Lithium Blocks Development of Alzheimer's Disease in Mice. NIMH-funded researchers have discovered that the enzyme called GSK-3 alpha is crucial to formation of the beta amyloid plaques and tangles characteristic of Alzheimer's disease. In mouse cells, they tried blocking the enzyme using lithium, and it significantly reduced production of beta amyloid. Lithium also markedly reduced beta amyloid production in an animal model of Alzheimer's disease -- mice carrying mutations that are known to cause inherited Alzheimer's disease in humans. When they raised GSK-3 alpha levels, beta amyloid production increased. Since certain non-steroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen, behave like lithium in reducing beta amyloid levels, though by a slightly different mechanism, the researchers suggest that combination therapy with lithium and NSAIDs could have an enhanced effect in reducing beta amyloid accumulation. Lithium also protects neurons from stimuli that trigger programmed neuronal cell death in Alzheimer's disease. Although widely used to treat bipolar disorder, lithium's propensity to cause side effects may limit its use in older people. Thus, it will be important to develop new agents that specifically target GSK-3 alpha, but do not have the side effects. Pending development of these new medications, researchers suggest that lithium might be considered for the prevention of Alzheimer's disease especially in younger patients with an inherited form of the disease. The new findings have also spurred interest in whether patients taking lithium for bipolar disorder might have a lower incidence of Alzheimer's disease.

New Diagnostic Tool Speeds Research on Earliest Phases of Schizophrenia. Evidence suggests schizophrenia is a developmental disease, likely involving interaction of several genes, some form of prenatal insult to the developing brain, and stressful life events. Results from the past 15 years suggest that disease mechanisms are active long before obvious psychotic symptoms first appear. International interest has grown in early identification and intervention in the very earliest phase of psychotic illness, with the hope of interrupting the disease process before neurobiological, cognitive, and behavioral impairments become permanent. To date, a major obstacle to conducting research in this area has been the lack of an accurate measure by which to diagnose the earliest phases and the transition from early illness to the onset of psychosis. The Structured Interview for Prodromal Syndromes (SIPS) is a semi-structured diagnostic interview with well-defined measures for evaluating pre-psychotic symptoms. Two recent studies indicate that mental health professionals can be trained to use SIPS to reliably assess risk for the onset of psychosis. Studies across six research sites in the US and Canada successfully identified individuals at imminent risk for developing psychotic symptoms. Translated into 14 languages, the SIPS is now used at more than a dozen early-schizophrenia research centers internationally, including seven NIH-supported programs. Identifying the disease processes underlying the early phases of schizophrenia requires diagnostic tools that reliably identify individuals at clinical high risk. Knowledge of the disease mechanisms will permit creation of preventive treatments designed specifically for the early phase of the disease.

New Light Is Shed On HIV Medication Adherence and Drug Resistance. The efficacy of antiretroviral drug therapy has dramatically altered the landscape of HIV treatment. Medication can inhibit virus replication and reduce virus load to undetectable levels—with much improved clinical outcomes. But not all patients are willing or able to maintain complex medication regimes, and partial or poor adherence can lead to the resumption of rapid viral replication, poorer survival rates, and the mutation of treatment-resistant strains of HIV. However, until

recently, the relationship between level of medication adherence and development of drug resistance has not been well characterized. A team of NIMH-funded researchers sought to address this question by looking at different levels of adherence among 148 HIV-positive, low-income, urban individuals. They measured treatment duration, viral suppression, and the rate of accumulating new drug-resistant mutations. They measured adherence by conducting unannounced pill counts at the participant's homes. They found that the longer people had been on treatment, the better they could stick to the pill regimen, and the more effectively the virus was suppressed in the blood. However, it was surprising that those adhering most closely to the pill regimen developed more drug resistant mutations than occasional or inconsistent pill-takers. About 50 percent of all drug resistant mutations occurred in those who were taking at least 80 percent or more of their pills – which is typically accepted as excellent adherence. These findings raise questions about what leads to drug resistance and should encourage the field to rethink the argument that life-saving antiretroviral drugs should be restricted in some populations because poor pill-taking behavior might accelerate the creation of resistant mutations of HIV. Nevertheless, good adherence to antiviral regimens remains the best way to prevent becoming ill or dying with HIV/AIDS.

Behavioral Science Findings Inform New Treatment Approach for Schizophrenia.
Historically, only about 10-20 percent of people with schizophrenia have been successful at landing a competitive job. More recently, supported employment interventions have helped approximately 40 percent of those with schizophrenia to obtain competitive employment, usually on a part-time basis. However, among those receiving supported employment services, only half maintain their jobs for more than six months. Recent findings suggest that cognitive performance is an important predictor of job tenure among patients with severe mental illness, and that patients with marked cognitive deficits may require additional forms of support to sustain employment. Since conventional medications and behavioral therapies are generally ineffective in restoring cognitive functioning in schizophrenia, novel treatment approaches that directly target impaired cognition are essential. NIMH-funded researchers have developed a new psychiatric rehabilitation approach designed to offset the cognitive deficits that can impede acquiring and performing job-related skills. "Errorless learning" is a skills training method that minimizes demands on verbal memory, which is impaired in schizophrenia, and capitalizes on procedural-learning capabilities, which remain relatively intact. Results from two initial studies show that errorless learning is better than conventional instruction at improving schizophrenia patients' accuracy on index card filing and assembly tasks, as well as work productivity during training sessions. People in the errorless learning group performed well regardless of their degree of impairment in verbal memory and executive functioning, while performance by those in the conventional instruction group closely corresponded to the degree of their cognitive impairment. This is a clear indication that the errorless learning approach can successfully compensate for otherwise rate-limiting cognitive deficits. The approach can be applied to a wide variety of job tasks, particularly those provided to seriously mentally ill clients at entry-level positions. Ongoing studies will test the efficacy of embedding errorless learning training within a supported employment intervention, testing its impact on schizophrenia clients' job tenure, productivity, and satisfaction with work.

Tailored Outreach Efforts Help Low-Income, Young Minority Women Overcome Depression. Impoverished ethnic minority patients are less likely to obtain care for depression than white patients, and are less likely to receive appropriate treatment when they do seek care. Young minority women, a group at high risk for depression, often have histories of trauma as well as financial and child care burdens, making it personally and logistically difficult to receive care. Results from a randomized clinical trial show that over a six-month period, low-income minority women benefited from depression treatment (medication or cognitive behavior therapy) when it was paired with intensive outreach and encouragement to support the interventions. Not only did women achieve lower levels of depressive symptoms, but they also gained higher levels of social and personal functioning in daily life. Outreach support—including transportation, child-care, flexible scheduling, translation into Spanish, and repeated phone contacts to gain the trust of the participants—was an essential part of the study. In comparison to referral to community care, medications were more effective in reducing depressive symptoms, improving personal functioning, and increasing ability to care and interact with others. Cognitive behavior therapy was better than community care in reducing depressive symptoms and increasing the ability to care and interact with others, but had no effect on personal functioning. Most depression treatment efficacy trials are based on samples of predominantly white patients in academic psychiatric settings, but it has never been clear whether such treatment benefits the underserved. This effort demonstrates that with additional outreach efforts, depressed young ethnic minority women with financial and family care burdens and histories of trauma can clearly benefit from treatment.

Behavior Therapy Is Key to Reducing Depression, Anxiety, and Disability in Older Adults. Depression and anxiety disorders are very common among older adults. For many, the commonly prescribed antidepressant and anti-anxiety medications are either insufficient or unsuitable due to other medications being given. Some depressed seniors also have some degree of impairment in executive intellectual function, and these individuals often respond poorly to the drugs. To find relief for these populations, NIMH researchers tried cognitive-behavioral therapy (CBT). For the depressed patients, in separate studies researchers tried different variations of CBT. One, known as Problem-Solving Therapy (PST), appeared to be particularly useful for older adults with depression and executive dysfunction. It was far more effective than regular psychotherapy in reducing both depressive symptoms and overall disability by helping patients acquire better skills in decision-making and in problem-solving. The other kind of CBT, known as Dialectical Behavior Therapy (DBT), was very effective at enhancing the effects of antidepressant medication. Those getting medications in addition to DBT showed significant improvements in self-rated depression, dependency, and adaptive coping skills. Those receiving DBT alone also showed improvement, though not as much as the group getting both. In a third study, CBT was also far more effective in reducing symptoms of worry and anxiety and in improving overall quality of life than was the usual clinical care. The treatment gains were well maintained over a one-year follow-up. These three studies suggest that cognitive behavioral forms of psychotherapy may be useful as alternative or supplemental treatments for depressed older adults when medications alone are insufficient or contraindicated due to other medications. CBT should be considered as a key component in reducing the degree of disability as well as depressive symptoms in the older adult population.

Creation of New Neurons Is the Key to Antidepressant's Action. Depression and anxiety are most commonly treated with medications called selective serotonin reuptake inhibitors (SSRIs). However, why they work and why they take three to four weeks to have a perceivable effect, has been largely unknown. Although the biochemical effects of antidepressants occur rapidly, it is thought that longer-term adaptive changes in brain neurochemistry and structure (in limbic and cortical areas) might be responsible for the therapeutic effect of antidepressants. To establish a cause and effect relationship between brain structural changes and antidepressant drug action, NIMH-funded researchers studied the effects of chronic antidepressant treatment in mice. Mice treated with chronic antidepressants (four weeks) showed less fearfulness. In addition, these mice showed a 60 percent increase in the birth of new neurons (neurogenesis) in the hippocampus, an area involved with learning and memory. The researchers then tested whether blocking the brain's ability to generate new neurons would block the effectiveness of antidepressants. They exposed mice to x-rays targeted at the hippocampus to destroy the capability of generating new neurons. When the irradiated mice were treated for four weeks with antidepressants, they did not re-grow neurons and did not show the expected decrease in fearfulness. These findings are the first to indicate that hippocampal neurogenesis contributes to the behavioral effects of antidepressant drugs. One implication is that strategies aimed at stimulating neurogenesis in the hippocampus, using pharmacological growth factors or environmental manipulations such as exercise, could provide novel avenues for the treatment of mood disorders.

NIH ROADMAP INITIATIVE

The Molecular Library Project. Despite the recent rapid discovery of biological targets with research and therapeutic potential, the identification of chemically diverse small molecules that selectively interact and alter these targets, providing a starting point for therapeutic intervention, has lagged significantly. This situation is likely to worsen as the discovery of new targets accelerates due to advances in genomics and functional proteomics. Small molecule libraries and resources for screening those libraries are the most important tools currently in demand by biomedical researchers, according to participants in the Roadmap planning process. This need arises in part by the lack of collaboration and coordination between public and private sectors. It is proposed that NIH exploit its unique resources to develop molecular libraries for research and therapeutic development. These libraries will represent: consolidated and comprehensive databases that integrate existing database systems from NIH, academic, and private sectors (e.g., pharmaceutical and biotechnology companies); and repositories of compounds that can be used as research tools and for therapeutic development. These libraries will be dynamic with the capacity to evolve through the addition of: molecules synthesized de novo; small molecules, peptides, and proteins discovered and characterized through chemical genetics; and compounds already included in the libraries that have been further characterized. This NIH effort will empower multi-disciplinary academic teams to use small molecules in basic biology and translate basic research findings into novel therapeutics in disorders not attractive to the private sector. The sharing of small molecule reagents and data derived from these centers with the larger scientific community represents a new paradigm that promises to facilitate the understanding of basic biological mechanisms and shorten the timeline for drug development for various mental disorders, with resulting benefits to public health.

NIMH NEW INITIATIVES

New Program Builds on Successes in Schizophrenia Research. The recent discovery of several vulnerability genes for schizophrenia offers an unprecedented opportunity for progress in understanding the pathophysiology of this disease and in reducing its enormous burden on patients, families and society. Over the next decade, a new multi-disciplinary initiative in the intramural program will expand upon the findings of the genetics research to reveal how these genetic alterations affect the neurobiology and ultimately lead to impaired cognition and psychosis. Using the newly identified susceptibility genes as a starting point, this multidisciplinary team will use mouse and cell culture models, postmortem human tissue, clinical studies, and brain imaging to examine the role of these genes at the molecular, cellular, and systems levels. For example, using genetically engineered mice, they will explore the cellular mechanisms by which variations in the genes lead to deficits. The team can then test each gene variant for gene-gene and gene-environment interactions at the level of behavior, pharmacology, electrophysiology, and molecular biology. Gene-gene interactions will also be studied at the level of clinical illness and brain information processing in humans. Findings emerging from the fast-track intramural effort will serve to stimulate spin-off studies by extramural researchers. The plan tentatively calls for recruitment of at least seven new senior scientists to the intramural program, each of whom will bring in unique expertise and head up teams composed of post-doctoral fellows and other support personnel. The schizophrenia program will also gain new laboratories on genetics and cell biology and a new MRI scanner.

Improving Cognition in Schizophrenia. Current medications can often effectively manage the "positive" symptoms of schizophrenia, such as delusions and hallucinations. However, cognitive problems can remain a significant barrier to a productive life for people with schizophrenia. Cognitive deficits, such as trouble with memory, attention, executive function (abstract thinking and problem solving), verbal fluency, working memory and social cognition (ability to understand social situations and respond effectively) are core features of schizophrenia, and remain largely unaffected by medications or changes in severity of positive symptoms. There has been a lack of scientific consensus on which cognitive impairments should be targeted and which tools are best for measuring them. As a result, the FDA has not yet been able to recognize cognition in schizophrenia as a valid treatment endpoint for industry-sponsored research and drug registration. To address these issues, NIMH has launched the Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) program through a contract with UCLA. Through this program, academic, industry, and regulatory agencies will convene to develop a comprehensive assessment tool to measure cognitive functioning in people with schizophrenia. MATRICS will also review pre-clinical models of neurocognition to identify potential molecular targets for new compounds, develop models for industry/government/ academic collaboration to test compounds for improving cognition, and identify potential lead compounds. Once the new instrument to assess cognition is completed, NIMH will award a contract to create a network of Treatment Units for Neurocognition in Schizophrenia (TURNS), which will include four to six new research sites nationwide. These sites will further refine experimental methods needed to assess compounds, identify and obtain promising treatments, and conduct clinical trials. A significant goal of these efforts is to help clarify the issues obstructing regulatory acceptance of cognition in schizophrenia as a valid clinical target for drug

registration. Drug registration would provide a compelling incentive for academic and industry investment to focus on an important but neglected clinical area.

Ten-Year Plan Laid Out For Autism Research. The Children's Health Act of 2000 established the Interagency Autism Coordinating Committee (IACC) to coordinate research and other efforts on autism within the HHS. The IACC, at the request of the House and Senate, convened a panel of scientists to assess the field and identify roadblocks hindering progress in understanding the causes of autism and developing the best treatment options for the disease. The final product was a list of roadblocks and the autism research matrix, which includes goals and activities for the next 10 years to overcome these challenges. The goals in the matrix begin with identification of disease vulnerability genes. A large consortium of autism researchers, including those using biomaterials from the Autism Genetic Resource Exchange will conduct a genome-wide scan of more than 1,200 pedigrees collected worldwide to identify several candidate genomic regions containing vulnerability genes. Data and biomaterials generated under this initiative will be incorporated in the NIMH Human Genetics Initiative and will be widely distributed to the scientific community. Other matrix goals are directed toward developing improved early detection through behavioral and biological markers, increased efficacy of early pharmacological and psychosocial interventions, understanding of the biological basis of core deficits, better school and community interventions, and clinical trials for pharmacotherapy. These efforts will be carried out through the centers of excellence within the Studies to Advance Autism Research and Treatment network. This is a time of unparalleled opportunity as multiple government agencies and private foundations are starting to work in a concerted way to stimulate autism research.

Establishing Clinical Networks for Chronic Mental Disorders. Most mental health conditions are of long duration, often for life, and have important implications for general health and functional status. However, therapeutic studies have tended to be of short duration and limited to assessment of clinical symptoms. Few longitudinal observational studies of chronic mental health conditions have been conducted, leaving gaps in our understanding of these relapsing and often disabling disorders. For instance, we recognize that depression is common, with a lifetime prevalence of 16 percent, reduces function and quality of life, has major associated co-morbidity, and may recur. Although episodes of depression usually have at least a four-month duration and co-morbidity is frequent, studies of depression are traditionally limited to 8-week efficacy studies of patients without co-morbidities. Relapse and failure to respond to treatment are not unusual. To address these problems in previous short-term studies, over the past five years NIMH has initiated large scale, long-term studies that compare therapeutic approaches for several severe mental disorders. These studies will be completed over the next two years. The experience gained by the staff, investigators, industry and patient advocacy groups has forged collaborative and cohesive groups that share a vision of large, long-term studies of mental health conditions seen in community populations and their treatment. Using these new collaborations as a foundation, NIMH hopes to develop clinical networks that will undertake comprehensive studies of schizophrenia, major depression, bipolar disorder, and eating disorders. These networks would: follow patients long-term to identify targets for treatment and ways to prevent relapse; and determine the long-term effectiveness and safety of common therapies, including those used in combination and in vulnerable populations such as

children, adolescents, and the elderly; develop new diagnostic measures and measures of functional change over time; identify risk factors for relapse; facilitate collaborative studies across agencies and with industry, providing opportunities for collaborations on co-morbid conditions that accompany mental illness; determine how best to implement treatments in community practice.

Understanding the Major Mental Health Disorders Through mRNA Profiling. Schizophrenia, major depression, bipolar disorder, autism and other major psychiatric illnesses are complex diseases with high genetic variation and largely unknown pathophysiology. Microarray technology can be used to evaluate either variations in gene expression (mRNA profiling), or variations in DNA sequence (gene profiling). Efforts to identify alterations in DNA for these diseases are underway, but require some time for success. However, mRNA profiling in postmortem human brain may be a more rapid approach to assess the expression of thousands of genes at once and to point to molecules that may be involved in the pathophysiology of these disorders. This approach holds the promise of uncovering molecular mechanisms that heretofore have not been considered and can jump-start studies of the neural basis of these disorders. This initiative seeks to foster accelerated mRNA profiling in major psychiatric disorders using microarray technology and to attract more researchers to this endeavor. Large data sets will be quickly generated and, with appropriate expertise and well-planned experimental design, can provide leads to further investigation of disease mechanisms and treatment targets.

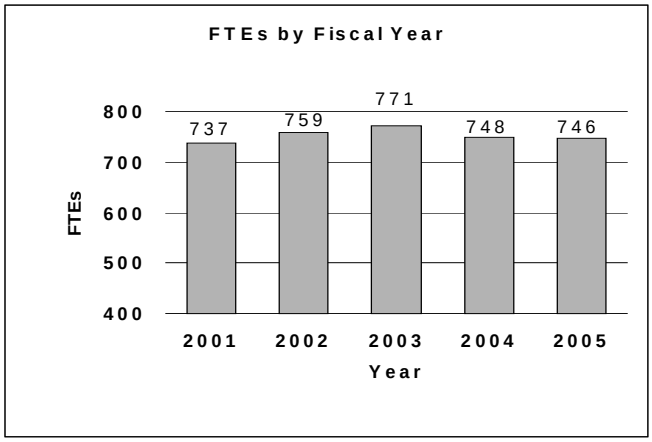
Depression. Many individuals experience mental disorders concurrent with other physical disorders. Their suffering plus the cost in lost productivity and health expenditures far exceeds losses associated with either mental or other physical disorders alone. Examples include depression and heart disease, anxiety disorders and cancer, panic disorder and asthma, post-traumatic stress disorder and chronic physical disability caused by serious injury, and schizophrenia and diabetes. Little is known about the mechanisms that link co-morbid mental and other physical disorders. Thus, our ability to intervene to prevent or treat them is currently limited. The proposed initiative would include: 1) epidemiological studies on the frequency and distribution patterns of co-morbid mental and other physical disorders; 2) studies of biological, behavioral, and psychosocial risk and protective processes to determine targets for intervention; 3) investigations to discover potentially modifiable biological substrates that link co-morbid mental and other physical disorders; 4) safety, efficacy, and long-term outcome studies of innovative pharmacological, behavioral, psychosocial, or environmental interventions; and 5) clinical trials and intervention studies targeting functional and symptomatic outcomes adapting pharmacological, psychosocial, behavioral, or environmental approaches individually or in combination. Within these broad research areas, emphasis on better understanding of basic behavioral processes is encouraged, including motivation, decision-making, adherence, emotion, cognition, and social interactions between health care providers and consumers.

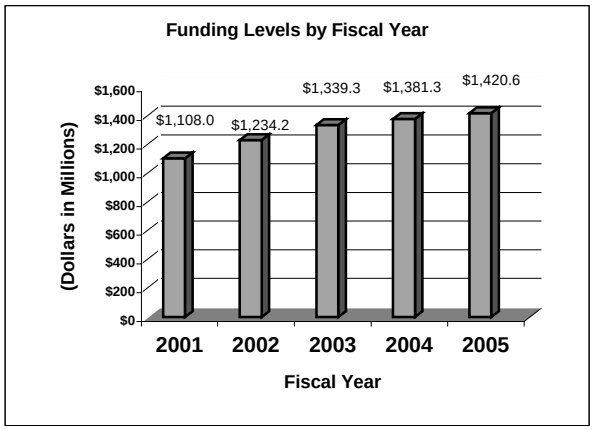
NIMH BUDGET POLICY

The Fiscal Year 2005 budget request for the NIMH is $1,420,609,000, an increase of $39,343,000 and 2.8 percent over the FY 2004 Final Conference Level. Also included in the FY 2005 request, is NIMH's support for the trans-NIH Roadmap initiatives, estimated at 0.63% of

the FY 2005 budget request. This Roadmap funding is distributed through the mechanisms of support, consistent with the anticipated funding for the Roadmap initiatives. A full description of this trans-NIH program may be found in the NIH Overview.

A five year history of FTEs and Funding Levels for NIMH are shown in the graphs below. Note that the Fiscal Year 2001 FTE figure is not comparable to the figures in the succeeding years due to NIH's consolidation of its Human Resources function in FY 2003.





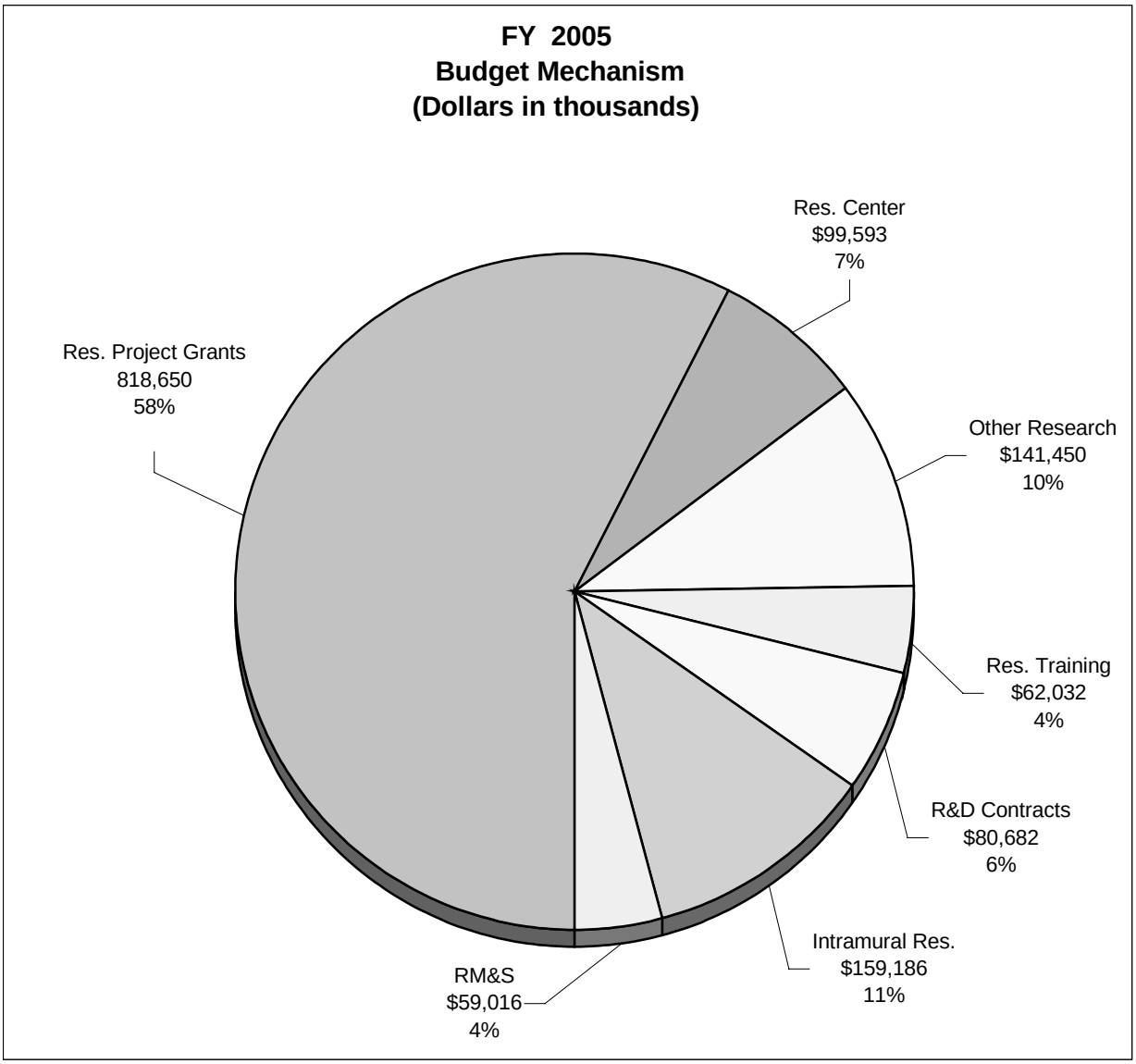
Support for RPGs allows NIH to sustain the scientific momentum of investigator-initiated research while providing new research opportunities. The FY 2005 NIH request provides for an aggregate 1.3 percent increase in average cost for Research Project Grants, consistent with the Gross Domestic Product deflator. The NIMH is providing an average cost increase of 1.9 percent for direct recurring costs in noncompeting continuation awards. Competing RPGs are based on an average cost increase of 1 percent.

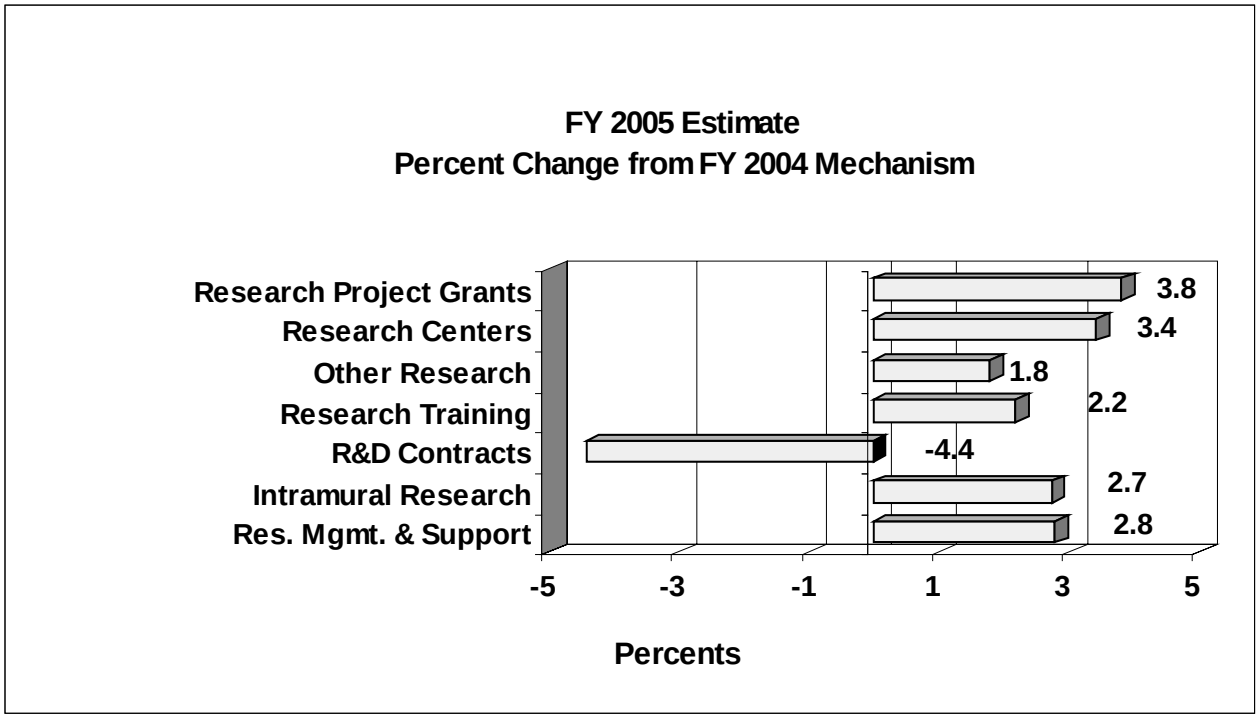
Advancement in medical research is dependent on maintaining the supply of new investigators with new ideas. In the Fiscal Year 2005 request, NIMH will support 1,594 pre- and postdoctoral trainees in full-time training positions. Stipend levels for pre-doctoral and post-doctoral recipients supported through the Ruth L. Kirschstein National Research Service Awards will remain at FY 2004 levels.

The Fiscal Year 2005 request includes funding for 64 research centers, 703 other research grants, including 534 clinical career awards, and 181 R&D contracts. Intramural Research and Research Management and Support receive increases to support increased pay and estimated inflationary increases in FY 2005.

In support of the trans-NIH Obesity Task Force plans for FY 2005, NIMH is requesting $1,146,000 to fund research on mechanisms underlying the comorbidity of mental disorders and obesity, weight-gain related to psychotropic medication, and the development of preventive or treatment interventions for these conditions. Additionally, NIMH will support translational research efforts of scientists studying the mechanisms underlying compulsive over- and under-eating in order to further the understanding of and develop treatments for severe eating disorders.

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




FY 2005 Estimate
Percent Change from FY 2004 Mechanism
Research Project Grants
Research Centers
Other Research
Research Training
R&D Contracts
Intramural Research
Res. Mgmt. & Support
3.8
3.4
1.8
2.2
-4.4
2.7
2.8
-5
-3
-1
1
3
5
Percents

NATIONAL INSTITUTES OF HEALTH

National Institute of Mental Health

Budget Mechanism - Total

MECHANISM	FY 2003 Actual		FY 2004 Final Conference		FY 2005 Estimate	
Research Grants:	No.	Amount	No.	Amount	No.	Amount
Research Projects:						
Noncompeting	1,586	$545,971,000	1,626	$581,330,000	1,603	$584,315,000
Administrative supplements	(61)	5,402,000	(61)	5,490,000	(62)	5,760,000
Full funded	12	1,812,000	14	2,184,000	14	2,206,000
Single year	587	183,390,000	549	177,630,000	625	203,741,000
Renewal	132	52,500,000	123	50,682,000	136	56,599,000
New	451	129,660,000	422	125,690,000	484	145,554,000
Supplements	4	1,230,000	4	1,258,000	5	1,588,000
Subtotal, competing	599	185,202,000	563	179,814,000	639	205,947,000
Subtotal, RPGs	2,185	736,575,000	2,189	766,634,000	2,242	796,022,000
SBIR/STTR	75	21,490,000	91	21,949,000	92	22,628,000
Subtotal, RPGs	2,260	758,065,000	2,280	788,583,000	2,334	818,650,000
Research Centers:						
Specialized/comprehensive	62	92,055,000	62	95,696,000	63	98,692,000
Clinical research	0	0	0	0	0	0
Biotechnology	0	0	1	593,000	1	901,000
Comparative medicine	0	0	0	0	0	0
Research Centers in Minority Institutions	0	0	0	0	0	0
Subtotal, Centers	62	92,055,000	63	96,289,000	64	99,593,000
Other Research:						
Research careers	483	67,397,000	528	74,657,000	534	76,079,000
Cancer education	0	0	0	0	0	0
Cooperative clinical research	22	26,808,000	22	26,866,000	22	27,215,000
Biomedical research support	0	0	0	27,000	0	33,000
Minority biomedical research support	0	0	0	0	0	0
Other	145	39,536,000	146	37,397,000	147	38,123,000
Subtotal, Other Research	650	133,741,000	696	138,947,000	703	141,450,000
Total Research Grants	2,972	983,861,000	3,039	1,023,819,000	3,101	1,059,693,000
Research Training:	FTTPs		FTTPs		FTTPs	
Individual awards	352	11,967,000	352	12,291,000	352	12,451,000
Institutional awards	1,223	46,770,000	1,232	48,417,000	1,242	49,581,000
Total, Training	1,575	58,737,000	1,584	60,708,000	1,594	62,032,000
Research & development contracts	201	93,255,000	197	84,401,000	181	80,682,000
(SBIR/STTR)	(37)	(7,369,000)	(35)	(9,130,000)	(35)	(9,248,000)
	FTEs		FTEs		FTEs	
Intramural research	490	148,273,000	468	154,928,000	468	159,186,000
Research management and support	281	55,157,000	280	57,410,000	278	59,016,000
Cancer prevention & control	0	0	0	0	0	0
Construction		0		0		0
Total, NIMH	771	1,339,283,000	748	1,381,266,000	746	1,420,609,000
(RoadMap Support)		(0)		(4,744,000)		(8,947,000)
(Clinical Trials)		(141,868,000)		(146,315,000)		(150,277,000)

NATIONAL INSTITUTES OF HEALTH
National Institute of Mental Health

Budget Authority by Activity
(dollars in thousands)

ACTIVITY	FY 2003 Actual		FY 2004 Final Conference		FY 2005 Estimate		Change	
	FTEs	Amount	FTEs	Amount	FTEs	Amount	FTEs	Amount
Extramural Research:								
Extramural research and training		$1,135,853		$1,168,928		$1,202,407		$33,479
Subtotal, Extramural research		1,135,853		1,168,928		1,202,407		33,479
Intramural research	490	148,273	468	154,928	468	159,186	0	4,258
Research management & support	281	55,157	280	57,410	278	59,016	(2)	1,606
Total	771	1,339,283	748	1,381,266	746	1,420,609	(2)	39,343

NATIONAL INSTITUTES OF HEALTH
National Institute of Mental Health

Summary of Changes

FY 2004 Final Conference				$1,381,266,000
FY 2005 Estimated Budget Authority				1,420,609,000
Net change				39,343,000
	FY 2004 Budget Base		Change from Base	
CHANGES	FTEs	Budget Authority	FTEs	Budget Authority
A. Built-in:				
1. Intramural research:				
a. Within grade increase		$56,970,000		$789,000
b. Annualization of January 2004 pay increase		56,970,000		584,000
c. January 2005 pay increase		56,970,000		641,000
d. One less day of pay		56,970,000		(224,000)
e. Payment for centrally furnished services		26,449,000		793,000
f. Increased cost of laboratory supplies, materials, and other expenses		71,509,000		1,675,000
Subtotal				4,258,000
2. Research Management and Support:				
a. Within grade increase		29,658,000		505,000
b. Annualization of January 2004 pay increase		29,658,000		304,000
c. January 2005 pay increase		29,658,000		334,000
d. One less day of pay		29,658,000		(116,000)
e. Payment for centrally furnished services		6,302,000		189,000
f. Increased cost of laboratory supplies, materials, and other expenses		21,450,000		606,000
Subtotal				1,822,000
Subtotal, Built-in				6,080,000

NATIONAL INSTITUTES OF HEALTH
National Institute of Mental Health

Summary of Changes--continued

CHANGES	FY 2004 Budget Base No.	FY 2004 Budget Base Amount	Change from Base No.	Change from Base Amount
B. Program:				
1. Research project grants:				
a. Noncompeting	1,626	$586,820,000	(23)	$3,255,000
b. Competing	563	179,814,000	76	26,133,000
c. SBIR/STTR	91	21,949,000	1	679,000
Total	2,280	788,583,000	54	30,067,000
2. Research centers	63	96,289,000	1	3,304,000
3. Other research	696	138,947,000	7	2,503,000
4. Research training	1,584	60,708,000	10	1,324,000
5. Research and development contracts	197	84,401,000	(16)	(3,719,000)
Subtotal, extramural				33,479,000
	FTEs		FTEs	
6. Intramural research	468	154,928,000	0	0
7. Research management and support	280	57,410,000	(2)	(216,000)
Subtotal, program		1,381,266,000		33,263,000
Total changes	748		(2)	39,343,000

NATIONAL INSTITUTES OF HEALTH
National Institute of Mental Health

Budget Authority by Object

	FY 2004 Final Conference	FY 2005 Estimate	Increase or Decrease
Total compensable workyears:			
Full-time employment	748	746	(2)
Full-time equivalent of overtime & holiday hours	2	2	0
Average ES salary	$142,500	$144,638	$2,138
Average GM/GS grade	11.2	11.2	0.0
Average GM/GS salary	$72,141	$73,223	$1,082
Average salary, grade established by act of July 1, 1944 (42 U.S.C. 207)	$87,468	$90,529	$3,061
Average salary of ungraded positions	106,011	107,601	1,590

OBJECT CLASSES	FY 2004 Final Conference	FY 2005 Estimate	Increase or Decrease
Personnel Compensation:			
11.1 Full-Time Permanent	$38,227,000	$39,342,000	$1,115,000
11.3 Other than Full-Time Permanent	21,044,000	21,697,000	653,000
11.5 Other Personnel Compensation	1,421,000	1,463,000	42,000
11.7 Military Personnel	1,558,000	1,605,000	47,000
11.8 Special Personnel Services Payments	8,554,000	8,823,000	269,000
Total, Personnel Compensation	70,804,000	72,930,000	2,126,000
12.1 Civilian Personnel Benefits	14,766,000	15,209,000	443,000
12.2 Military Personnel Benefits	1,058,000	1,090,000	32,000
13.0 Benefits for Former Personnel	0	0	0
Subtotal, Pay Costs	**86,628,000**	**89,229,000**	**2,601,000**
21.0 Travel & Transportation of Persons	3,128,000	3,241,000	113,000
22.0 Transportation of Things	298,000	309,000	11,000
23.1 Rental Payments to GSA	0	0	0
23.2 Rental Payments to Others	261,000	268,000	7,000
23.3 Communications, Utilities & Miscellaneous Charges	1,697,000	1,752,000	55,000
24.0 Printing & Reproduction	1,230,000	1,296,000	66,000
25.1 Consulting Services	2,263,000	2,336,000	73,000
25.2 Other Services	5,302,000	5,474,000	172,000
25.3 Purchase of Goods & Services from Government Accounts	112,509,000	110,012,000	(2,497,000)
25.4 Operation & Maintenance of Facilities	2,665,000	2,752,000	87,000
25.5 Research & Development Contracts	59,096,000	59,897,000	801,000
25.6 Medical Care	1,056,000	1,086,000	30,000
25.7 Operation & Maintenance of Equipment	1,461,000	1,506,000	45,000
25.8 Subsistence & Support of Persons	0	0	0
25.0 Subtotal, Other Contractual Services	**184,352,000**	**183,063,000**	**(1,289,000)**
26.0 Supplies & Materials	8,884,000	9,144,000	260,000
31.0 Equipment	10,260,000	10,581,000	321,000
32.0 Land and Structures	0	0	0
33.0 Investments & Loans	0	0	0
41.0 Grants, Subsidies & Contributions	1,084,527,000	1,121,725,000	37,198,000
42.0 Insurance Claims & Indemnities	0	0	0
43.0 Interest & Dividends	1,000	1,000	0
44.0 Refunds	0	0	0
Subtotal, Non-Pay Costs	**1,294,638,000**	**1,331,380,000**	**36,742,000**
Total Budget Authority by Object	**1,381,266,000**	**1,420,609,000**	**39,343,000**

NATIONAL INSTITUTES OF HEALTH
National Institute of Mental Health

Salaries and Expenses

OBJECT CLASSES	FY 2004 Final Conference	FY 2005 Estimate	Increase or Decrease	Percent Change
Personnel Compensation:				
Full-Time Permanent (11.1)	$38,227,000	$39,342,000	$1,115,000	2.9
Other Than Full-Time Permanent (11.3)	21,044,000	21,697,000	653,000	3.1
Other Personnel Compensation (11.5)	1,421,000	1,463,000	42,000	3.0
Military Personnel (11.7)	1,558,000	1,605,000	47,000	3.0
Special Personnel Services Payments (11.8)	8,554,000	8,823,000	269,000	3.1
Total Personnel Compensation (11.9)	**70,804,000**	**72,930,000**	**2,126,000**	**3.0**
Civilian Personnel Benefits (12.1)	14,766,000	15,209,000	443,000	3.0
Military Personnel Benefits (12.2)	1,058,000	1,090,000	32,000	3.0
Benefits to Former Personnel (13.0)	0	0	0	0.0
Subtotal, Pay Costs	**86,628,000**	**89,229,000**	**2,601,000**	**3.0**
Travel (21.0)	3,128,000	3,241,000	113,000	3.6
Transportation of Things (22.0)	298,000	309,000	11,000	3.7
Rental Payments to Others (23.2)	261,000	268,000	7,000	2.7
Communications, Utilities and Miscellaneous Charges (23.3)	1,697,000	1,752,000	55,000	3.2
Printing and Reproduction (24.0)	1,230,000	1,296,000	66,000	5.4
Other Contractual Services:				
Advisory and Assistance Services (25.1)	2,147,000	2,219,000	72,000	3.4
Other Services (25.2)	5,302,000	5,474,000	172,000	3.2
Purchases from Govt. Accounts (25.3)	80,095,000	76,997,000	(3,098,000)	-3.9
Operation & Maintenance of Facilities (25.4)	2,665,000	2,752,000	87,000	3.3
Operation & Maintenance of Equipment (25.7)	1,461,000	1,506,000	45,000	3.1
Subsistence & Support of Persons (25.8)	0	0	0	0.0
Subtotal Other Contractual Services	**91,670,000**	**88,948,000**	**(2,722,000)**	**-3.0**
Supplies and Materials (26.0)	8,882,000	9,142,000	260,000	2.9
Subtotal, Non-Pay Costs	107,166,000	104,956,000	(2,210,000)	-2.1
Total, Administrative Costs	**193,794,000**	**194,185,000**	**391,000**	**0.2**

National Institutes of Health

National Institute of Mental Health

SIGNIFICANT ITEMS IN HOUSE AND SENATE APPROPRIATIONS COMMITTEE REPORTS

FY 2004 House Appropriations Committee Report Language (H. Rpt. 108-188)

Item

Alzheimer's disease - The Committee encourages NIMH to enhance this Alzheimer's portfolio. (p. 84)

Action taken or to be taken

NIMH continues to place significant priority on studies of Alzheimer's disease. In 2003 NIMH initiated funding of a five-site trial of antidepressant medications in the treatment of depression in patients with Alzheimer's disease. This trial of medications to treat behavioral problems completed recruitment of approximately 200 subjects in January 2004. Initial results should be available late in 2004. In a major advance, NIMH intramural researchers identified a promising new method for early detection of Alzheimer disease. Long-term studies now underway will determine if this biomarker can eventually be widely used as predictive and diagnostic tools.

FY 2004 Senate Appropriations Committee Report Language (S. Rpt. 108-81)

Item

Autism - The Committee is also encouraged by grants from the NIMH to investigate treatment options, including pharmaceutical research targeting the unique needs of the autism community in both children and adults. 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. 151)

Action taken or to be taken

The Research Units on Psychopharmacological and Psychosocial Interventions (RUPP-PI) were renewed and expanded in 2002. Five sites focus on autism treatment. Recent publications include "Risperidone in Children with Autism and Serious Behavioral Problems" (RUPP Autism Network, 2002, New England Journal of Medicine, 347, 314-21); and "Parent-defined target symptoms respond to Risperidone in RUPP Autism Study: Customer Approach to Clinical Trials" (Arnold et al, in press, Journal of the American Academy of Child and Adolescent Psychiatry, 42, 1-8). Additional medication trials are nearing completion, and a combined medication/parent training study is underway. NIMH also took the lead (with NICHD, NINDS, NIDCD, NIEHS) in establishing eight centers of excellence in autism research, the Studies to Advance Autism Research and Treatment (STAART) Centers. Each Center is required to conduct clinical as well as basic research, including at least one intervention study. A meeting in 2002 addressed "Research on Psychosocial and Behavioral Interventions in Autism: Confronting

the Methodological Challenges." NIMH has continued this initiative with on-going workgroups that meet monthly by teleconference and has plans for a follow-up meeting in 2004.

Item

Depression and Bipolar Disorder - The Committee urges the NIMH to continue its efforts to understand depression, to develop new treatments, to decrease the impact of depression on comorbid illnesses, and--because depression and bipolar disorders are prominently associated with suicide--to reduce suicide. The Committee is pleased with NIMH's leadership in public education campaign entitled Real Men. Real Depression and encourages the institute to continue these education and information dissemination efforts. (p. 152)

Action taken or to be taken

NIMH continues to do research to unravel the mystery of the causes of depression, to determine risk factors for developing depression, to explore tools and biological markers for accurate diagnosis, and to determine the most cost-effective treatments that will decrease the possibility of relapse and achieve a durable recovery. Our public education campaigns are used to make the public aware of symptoms of the disease, assure them that there are effective treatments and, hopefully, decrease stigma related to mental illnesses. To date, the Real Men, Real Depression campaign has been extremely successful in reaching millions of people and carrying the message to a previously hard to reach population—men.

To close the gap between knowledge of effective treatments and its use in the public domain, NIMH has instituted a research program that supports studies designed to understand the facilitators and barriers to the dissemination and implementation of new practices. One such study examines whether readily available computerized information is a useful way of increasing physician use of guidelines for treating depression. Moving from a local level to a larger systems level, a set of studies by nine state mental health departments are designed to provide information on the most effective means to disseminate and insure implementation of research-based practice information widely throughout a state system.

Item

Down Syndrome - Persons with Down syndrome have a greater risk of developing disorders such as autism, attention deficit disorder, obsessive-compulsive disorder, anxiety and depression. The Committee urges NIMH to conduct research on the mental health symptoms of persons with Down syndrome and to investigate effective treatments. The Committee also urges the Institute to include Down syndrome in its studies of related disorders and to coordinate its work with NICHD, NINDS and the National Center on Birth Defects and Developmental Disabilities at the Centers for Disease Control. (p. 152)

Action taken or to be taken

NIMH supports research on mental illness that occurs in the context of intellectual disability (mental retardation), including Down Syndrome. A program announcement Research on Psychopathology in Intellectual Disabilities (Mental Retardation) (TPA-03-129) encourages research in this field. In the last three years, to expand research in mental retardation, the NIMH has co-funded several workshops, such as the meeting, "Emotional and Behavioral Health in

Persons with Mental Retardation/Developmental Disabilities", which was convened by the National Institute of Neurological Disorders and Stroke, the National Institute of Child Health and Human Development, the National Institute of Mental Health, the National Institutes of Health Office of Rare Diseases, and the Joseph P. Kennedy Jr. Foundation on November 29 - December 1, 2001; and, a conference entitled, "Closing the Gap: A National Blueprint to Improve the Health of Persons with Mental Retardation (2001)", which was convened by the United States Surgeon General.

Item

Drug Metabolism - The Committee urges NIMH to create a major research focus on the relationship between drug metabolism variation and patients' response to psychiatric medications. (p. 152)

Action taken or to be taken

The effect of heredity on the responses of individuals to drugs is a topic of exceptional scientific interest. In September, 2003 NIMH, in partnership with NIGMS, issued a Request for Applications (RFA) to solicit applications to perform high-quality research studies that correlate responses to drugs used to treat mood or anxiety disorders with genetic variation, and create a valuable knowledge base populated with reliable information that links drug response phenotypes to genotypes. This RFA focuses on studies that examine genetic influences on inter-individual differences in response to therapeutic drugs used to treat mood or anxiety disorders. Data and biomaterials collected and produced in projects supported under this RFA will be included in the NIMH Human Genetics Initiative (http://nimhgenetics.org) and PharmGKB (http://www.pharmgkb.org), a public database for pharmacogenetics information, and distributed to the wider scientific community. Such studies may help elucidate basic mechanisms of drug effects and adverse reactions and facilitate optimal selection of therapy in individual patients, as well as mitigate serious adverse response or lack of response to therapy. The participating ICs intend to commit $3 million in FY 2004 to fund three to five new and/or competitive continuation grants in response to this RFA, and the application due date was February 12, 2004.

Item

Frontier Mental Health Needs - The Committee encourages 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 including depression, suicide and co-occurring disorders with substance abuse. The Committee encourages NIMH to continue its outreach efforts such as those in Alaska and in its recent "Dialogue Four Corners" meeting in Albuquerque, New Mexico which focused on minority populations in the four States comprising that area: Arizona, Colorado, New Mexico and Utah. These efforts have involved bringing research knowledge to the public in local communities, but also in establishing the dialogue between local communities and NIH that is so important to public participation in the NIH priority-setting process. The Committee encourages NIMH to continue these efforts that have been focused on historically underserved populations. (p. 153)

Action taken or to be taken

NIMH investigators are examining various types of service interventions being implemented in rural areas to determine their adequacy to deliver effective care to socially and culturally diverse populations in rural and frontier areas across the U.S. Included in these efforts are some studies that are examining the effectiveness of telemedicine interventions for people living in remote areas.

NIMH considers these dialogue meetings to be a central part of its mission, particularly given the importance of this issue as outlined by the Institute of Medicine in 1998, and again in 2003. NIMH will continue these and other outreach efforts and, given the high priority it places on finding remedies for health disparities, intends to continue its recent focus on historically underserved populations. NIMH has already conducted follow-up activities with respect to several of its recent Dialogue meetings, including collaborating with other institutes at NIH to encourage young people from the various communities to pursue careers in research. One such activity was held in Albuquerque, NM with a focus on Hispanic and Native American students and prominent biomedical researchers. Through its Outreach Partnership Program, NIMH engages in continuous communication with specific partners located in all 50 states, who – as a part of their various ongoing partnership activities–come together in an annual meeting. At the meeting and throughout the year, the partners discuss recent research findings and their relevance, learn about NIMH programs, provide input to NIMH on its research agenda, and share information and assistance with each other to improve outreach and delivery of mental health-related information to individuals and groups in each of the states and the District of Columbia.

Item

Late Life Mental Health Research - The Committee continues to be concerned about funding for late life mental health research at NIMH but is encouraged by some of the positive steps the Institute has taken to address this issue. Furthermore, the Committee expects the NIMH to provide substantial resources to promote aging research or provide data on existing funds targeted toward geriatric mental health research. Therefore, this Committee strongly encourages NIMH to expand research in this area extramurally through all available mechanisms and to provide adequate resources to the NIMH Aging Research Consortium to advance the geriatric mental health research agenda. (p. 153)

Action taken or to be taken

The Aging Consortium was formed in early 2002 to coordinate and foster NIMH's research on late-life mental disorders. This year the Institute has worked to increase the breadth and depth of its portfolio in this domain. The Consortium sponsored a number of workshops and symposia to promote aging research, including a conference addressing issues of attracting and training young scientists, and a conference on the relationships between mild cognitive impairment and depression. This meeting brought together for the first time researchers considering these relationships from differing perspectives of psychiatry, neurology, and neuropsychology. The Consortium also spearheaded the initiation of NIMH Program Announcement 03-014, Research On Mental Illnesses In Older Adults (released in October 2002), to intensify investigator-

initiated research in the area, attract new investigators to the field, and enhance interdisciplinary approaches to research; virtually every area of mental health research in aging populations is encouraged to participate. In addition, a formal National Advisory Mental Health Council workgroup engaged in a yearlong study of the NIMH aging research portfolio and made a number of recommendations regarding the structure and focus of the program. These are contained in a report issued in October 2003. The report is accessible on the NIMH website at: <http://www.nimh.nih.gov/council/agingreport.cfm>. Implementation of the recommendations is already under way and will continue over the next several years.

Item

Learning Disabilities - The committee commends NIMH for the work conducted to explore the neurological and behavioral aspects of learning disabilities. The Committee looks forward to learning the results of this work and encourages the Institute to continue to coordinate with other Institutes working on related activities. (p. 153/154)

Action taken or to be taken

The National Institute of Mental Health is working in collaboration with the National Institute of Child Health and Human Development to support a multidisciplinary research center on the study of learning disabilities. One of the research projects will assess the genetic and environmental etiologies of reading deficits and Attention Deficit/Hyperactivity Disorder (ADHD). The NIMH also provides partial support for the ADHD Interdisciplinary Research Networks – a group of basic scientists and clinical researchers who are piecing together the relationship between brain and behavior in children and adolescents with attentional problems and learning difficulties. One new grant will examine how a child's individual characteristics and classroom environment affect the development of reading skills, and how the interplay between the three may affect the emergence of depressive symptoms and behavior problems among elementary school children. Grant-supported investigators will also evaluate the use of a combination of medical and educational interventions to treat co-occurring ADHD and dyslexia.

Item

Outreach - The Committee encourages NIMH to continue these efforts that have been focused on historically underserved populations, with an emphasis on the co-occurrence of mental disorders with substance abuse and with other physical illnesses such as diabetes and heart disease- an area that the committee encourages NIMH to continue to explore. (p. 154)

Action taken or to be taken

NIMH considers these Dialogue meetings to be a central part of its mission, particularly given the importance of this issue as outlined by the Institute of Medicine in 1998, and again in 2003. NIMH will continue these and other outreach efforts and, in keeping with the high priority it places on finding remedies for health disparities, will continue its recent focus on historically underserved populations heavily affected by co-occurring disorders like diabetes and heart disease. NIMH has already conducted follow-up activities with respect to several of its recent Dialogue meetings, including taking steps in collaboration with other institutes at NIH to encourage young people from the various communities to pursue careers in research. One such

activity was held in Albuquerque, NM with a focus on Hispanic and Native American students and prominent biomedical researchers. Through its Outreach Partnership Program, NIMH engages in continuous communication with specific partners located in all 50 states, who–as a part of their various ongoing partnership activities – come together in an annual meeting. At the meeting and throughout the year, the partners discuss recent research findings and their relevance, learn about NIMH programs, provide input to NIMH on its research agenda, and simply share information and assistance with each other to improve outreach and delivery of mental health related information to individuals and groups in each of the states and the District of Columbia.

Item

Psychological Impacts of Terrorism - The Committee supports NIMH research related to the psychological impact of both acute and chronic exposure to threats of violence, including terrorism, bioterrorism, and war, with particular emphasis on vulnerable populations, such as trauma survivors, children and older adults. The Committee encourages NIMH to expand its research portfolio to include research related to factors that promote detection or prediction, prevention, and post-exposure recovery and resilience. (p. 154)

Action taken or to be taken

In response to the terror attacks of September 11 in New York and Washington D.C., steps were taken to accelerate NIMH-supported research on: 1) identifying populations and individuals most vulnerable to severe trauma responses; 2) interventions to help reduce incidence, duration, and severity of acute stress disorder, post-traumatic stress disorder, and depression; and 3) interventions to sustain resilience among children, adolescents and adults. This research encompasses efforts to develop and test strategies to reduce anxiety/distress and promote resilience, develop tools for conducting needs assessments, refine models of triage, and treat psychiatric disorders that arise after exposure to mass trauma. Beyond supporting this new research, NIMH has been actively collaborating with other DHHS agencies (CDC, SAMHSA, HRSA) and government departments (VA, DOD) to pursue novel research collaborations, conduct scientific reviews, and generate and disseminate guidance on enhancing the Nation's preparedness and response to the psychological consequences of terrorism and other traumatic events.

Item

Research Portfolio - The Committee is pleased with NIMH's progress in fashioning its research portfolio, which has balanced the urgent need to focus on severe mental disorders with the obligation to support the basic neuroscience and behavioral research that will ultimately uncover the mechanisms responsible for human behavior and for the development of the entire spectrum of mental disorders. (p. 154)

Action taken or to be taken

The mission of the National Institute of Mental Health (NIMH) is to reduce the burden of mental illness and behavioral disorders through research on mind, brain, and behavior. In fulfilling this mission, NIMH has a strong portfolio in clinical and services research - research that is most clearly associated with and has the most immediate benefit for those suffering from mental disorder. However, just as important to our mission – and equally crucial if there is to be hope of

curing or preventing mental illness – is the basic neuroscience and behavioral research that allows us to understand the brain mechanisms and environmental conditions that, when combined in specific ways, result in the aberrant behaviors and disordered thinking manifest in mental illness. Over the past five years, we have witnessed unparalleled advances in the basic sciences relevant to mental health. To help us maintain this momentum, workgroups of the National Advisory Mental Health Council are assisting us in setting priorities for our research portfolio. We hope this will enable us to accelerate vital basic and clinical research that will advance the field and aid us in fulfilling our mission.

Item

Suicide - The Committee is aware of the recent Institute of Medicine [IOM] study on suicide- "Reducing Suicide: A National Imperative" - which noted that nearly 30,000 people die by suicide each year in the United States alone. Many, many more attempt suicide. More than 90 percent of people who commit suicide suffer from some form of mental disorder, which emphasizes the severe emotional pain and suffering caused by some forms of mental illness. While the body of evidence pointing to specific risk factors has grown, and the number of NIMH grants focused on treating suicidal patients has increased, there are no intervention centers focused on advancing the scientific methods necessary to efficiently test approaches to the reduction of suicide risk. The Committee encourages NIMH's leadership in responding to the IOM report and urges it to address the need for building a sufficient research infrastructure to adequately reduce the burden of suicidality (suicide deaths, attempts and serious ideation). (p. 154/155)

Action taken or to be taken

In response to the 2002 IOM report, “Reducing Suicide: A National Imperative,” the NIMH recognized that there was insufficient research infrastructure to adequately reduce the burden of suicidality (suicide deaths, attempts and serious ideation). To address this need, NIMH invited NIDA and NIAAA to collaboratively issue the Request for Applications, "Developing Centers on Interventions for the Prevention of Suicide (DCIPS) in August 2003. The purpose of this initiative is to establish core support for building research infrastructure for the study of preventive and treatment interventions for suicidality related to mental and substance use disorders, and alcohol use disorders. Awards for at least three centers are anticipated in July 2004. The particular goals for these centers are to: 1) build networks to conduct intervention/ prevention trials and/or evaluate community practice and service systems; 2) foster interdisciplinary collaboration; 3) develop new research methods; 4) develop, pilot and test novel treatments for suicidal behavior, with particular emphasis on interventions translated from basic science and/or neuroscience; and 5) cultivate training opportunities for new and established investigators. To better leverage knowledge generated from the anticipated funded centers, applicants were asked to include additional travel support to attend at least one annual meeting each year where information on their progress can be shared with other funded centers, as well as with the field at large. Additional efforts to address issues raised in the IOM report include a workshop conducted on safe and effective approaches to developing public messages on suicide prevention and a workshop planned on the role of culture in suicide risk.

NATIONAL INSTITUTES OF HEALTH
National Institute of Mental Health

Authorizing Legislation

	PHS Act/ Other Citation	U.S. Code Citation	2004 Amount Authorized	2004 Final Conference	2005 Amount Authorized	2005 Budget Estimate
Research and Investigation	Section 301	42§241	Indefinite	$1,320,558,000	Indefinite	$1,358,577,000
National Institute of Mental Health	Section 464R	42§285p	Indefinite		Indefinite	
National Research Service Awards	Section 487(d)	42§288	a/	60,708,000	b/	62,032,000
Total, Budget Authority				1,381,266,000		1,420,609,000

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/
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 /3
1998	628,739,000 /2	744,235,000	759,956,000	750,241,000
1999	699,679,000 /2/4	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	1,359,008,000	1,359,008,000	1,350,788,000	1,349,788,000
Rescission				(8,774,000)
2004	1,382,114,000	1,382,114,000	1,391,114,000	1,390,714,000
Rescission				(8,940,000)
2005	1,420,609,000			

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 $478,000.
4/ 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 2003 Actual	FY 2004 Final Conference	FY 2005 Estimate
Office of the Director	106	105	103
Division of Neuroscience and Basic Behavioral Science	39	39	39
Division of Mental Disorders, Behavioral Research and AIDS	46	46	46
Division of Services and Intervention Research	37	37	37
Division of Extramural Activities	53	53	53
Division of Intramural Research Programs	490	468	468
Total	771	748	746
FTEs supported by funds from Cooperative Research and Development Agreements	(0)	(0)	(0)

FISCAL YEAR	Average GM/GS Grade
2001	10.9
2002	11.1
2003	11.2
2004	11.2
2005	11.2

NATIONAL INSTITUTES OF HEALTH
National Institute of Mental Health

Detail of Positions

GRADE	FY 2003 Actual	FY 2004 Final Conference	FY 2005 Estimate
ES-6	1	1	1
ES-5	1	1	1
ES-4	7	6	6
ES-3	1	1	1
ES-2	0	0	0
ES-1	0	0	0
Subtotal	10	9	9
Total - ES Salary	$1,425,000	$1,318,125	$1,301,738
GM/GS-15	52	49	49
GM/GS-14	90	83	83
GM/GS-13	69	66	66
GS-12	79	76	75
GS-11	94	90	89
GS-10	1	1	1
GS-9	77	74	74
GS-8	41	40	40
GS-7	43	43	43
GS-6	9	9	9
GS-5	5	5	5
GS-4	6	6	6
GS-3	0	0	0
GS-2	0	0	0
GS-1	0	0	0
Subtotal	566	542	540
Grades established by Act of July 1, 1944 (42 U.S.C. 207):			
Assistant Surgeon General	0	0	0
Director Grade	12	12	12
Senior Grade	3	3	3
Full Grade	1	1	1
Senior Assistant Grade	0	0	0
Assistant Grade	0	0	0
Subtotal	16	16	16
Ungraded	191	191	191
Total permanent positions	550	527	525
Total positions, end of year	783	758	756
Total full-time equivalent (FTE) employment,end of year	771	748	746
Average ES level	ES-4	ES-4	ES-4
Average ES salary	$142,500	$142,500	$144,638
Average GM/GS grade	11.2	11.2	11.2
Average GM/GS salary	$69,300	$72,141	$73,223