Fiscal Year 2006 President's Budget Request for NIMH

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH

Witness appearing before the Senate Subcommittee on Labor-HHS-Education Appropriations

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Mr. Chairman, and members of the Committee, I am pleased to present the Fiscal Year (FY) 2006 President's budget request for the National Institute of Mental Health (NIMH). The FY 2006 budget includes $1,417,692,000, which reflects an increase of $5,759,000 over the 2005 enacted level of $1,411,933,000 comparable for transfers proposed in the President's request. In my statement, I will call to your attention our Nation's immense burden of mental and behavioral disorders and include a brief review of our research activities and accomplishments.

BURDEN OF MENTAL ILLNESS

The mission of the National Institute of Mental Health (NIMH) is to reduce the public health burden of mental and behavioral disorders. New scientific discoveries and powerful new tools are revealing the mechanisms involved in the pathophysiology of mental disorders. This is a vital step in the development of more effective strategies to manage, treat, and even prevent these debilitating disorders.

The report of the President's New Freedom Commission: Achieving the Promise--Transforming Mental Health Care in America defined the challenge. The burden of these disorders is staggering, in terms of both morbidity and mortality. Mental illness represents 4 of the top 6 sources of disability from medical causes for Americans ages 15-44 according to the World Health Organization; suicide accounts for more deaths each year than either homicide or AIDS. Recent estimates in the President's report put the economic costs of treating mental disorders at $150 billion, with elements of these costs increasing beyond 20 percent per year. The report called for a transformation of mental health care, with recovery as a goal. NIMH is working closely with the Substance Abuse and Mental Health Services Administration (SAMHSA) as it seeks to carry out this mandate.

PRIORITY SETTING

This past year NIMH searched for creative ways in which to optimize its impact on public health; the Institute and its stakeholders endeavored to reevaluate priorities for funding research. To help with this process, two workgroups of the National Advisory Mental Health Council were formed: one to review the NIMH extramural clinical treatment portfolio and one to review the basic sciences research portfolio.

The goal of the clinical treatment workgroup was to help NIMH focus strategically in its support of therapeutics and interventions research. The workgroup's report describes clinical areas where more study is essential, and urges increased innovation and a sharpened focus on amplifying the impact of clinical trials on clinical practice. The report also cites the need to expand core resources and clinical trials infrastructure for NIMH to enhance its treatment development capacity.

The workgroup reviewing the basic sciences research portfolio outlined specific tools and areas of research particularly ripe for increased investment, such as the pathophysiology of mental disorders and the translation of basic science discoveries into biomarkers, diagnostic tests, and new treatments.

Translation of basic science to clinical issues and practice is now a major focus of the Institute. This past year, NIMH reorganized its extramural programs into five research divisions (from three) to focus on: basic science, translational research for adults, translational research for children and adolescents, behavioral effects on health (including HIV/AIDS spread and prevention), and psychiatric services and treatments. A key aim of the reorganization is accelerating translation of the best ideas in neuroscience and behavioral research into the clinics and out into the community.

Rapid advances in mental health research are revealing the biological and environmental components of major mental illness. We now recognize that mental disorders are brain disorders, and we now have the tools to identify the brain circuits involved. Of note is recent research on improved detection of disease with biomarkers and development of personalized treatments.

REVEALING THE BIOLOGICAL BASIS OF MENTAL DISORDERS

A major goal for NIMH is to identify the biological basis of mental disorders to more precisely pinpoint targets for prevention and treatment. This means understanding the neural basis of the illness at all levels, from molecular to behavioral. For instance, imaging studies suggest that ischemia (restriction of blood flow in the brain due to a narrowed or blocked artery) may significantly contribute to the development of a form of depression. In a recent clinical trial, more than half of elderly depressed participants met the criteria for this newly recognized form of depression called “ischemic depression.” This realization should help improve diagnosis, and more effectively guide treatment for those with late-life depression.

A recent NIMH study shows that in people with panic disorder, a type of receptor for serotonin (a mood-regulating neurotransmitter) is reduced by nearly a third in several structures of the brain that mediate anxiety. The finding is the first in living humans to show that this specific receptor, which is pivotal to the action of anti-anxiety medications, may be abnormal in the disorder and may help explain how genes might influence vulnerability for panic and anxiety disorders.

A recent translational study on post-traumatic stress disorder (PTSD) was the first to demonstrate in humans the importance of a particular brain region in “fear extinction” – the process by which a previously learned fear is extinguished by a new form of learning, rather than the forgetting of the original fear. The brain region is associated not with emotion, but with the regulation of higher cognitive functions. This will provide important contributions to the understanding and treatment of PTSD and other anxiety disorders.

Several studies on depression have suggested that the formation of new neurons (neurogenesis) might be hindered in those with the disorder. In addition, animal studies have demonstrated that antidepressant medications are likely effective because they help increase neurogenesis. Several genes have been implicated in the susceptibility to schizophrenia and depression. In the past year, we have learned that common genetic variations bias the way the brain works, even in people who have not developed a major mental disorder. For instance, a gene variant that is especially common in people with depression is associated with a higher level of brain activation in response to threat or stress. A variant associated with schizophrenia appears to increase the amount of activity in the frontal lobe needed to perform complex attentional tasks. These kinds of studies reveal how subtle genetic variations may increase vulnerability to mental illness. Ultimately, this may provide a strategy

for early detection and prevention of a psychotic or depressive episode based on identifying individuals at genetic highest risk, just as we routinely intervene in those with high blood pressure and high cholesterol to prevent a heart attack.

Autism continues to be an increasing priority for NIH. We are just beginning to see the pay-offs of cross-Institute investments in several new centers and projects. Previous studies show that on average, autism is not diagnosed in children until after the age of 6, a relatively late age considering that early intervention is critical for the best treatment response. Thus, NIMH research will help develop new tools for detecting autism early, before age two. In addition, NIMH is part of a public/private research consortium focusing on the study of infant siblings of children with autism, to help identify early features and distinguishing characteristics of autism. NIMH and other NIH institutes are collaborating with voluntary and private funding organizations and government agencies internationally to develop a new research initiative ($21.5 million over 5 years) to identify specific gene variants that produce susceptibility to autism.

TREATMENTS FOR RECOVERY

The first of several large, NIMH-funded clinical studies testing various treatment options for those with serious mental illnesses was completed last summer: a 13-site trial aimed at defining the most effective and safe treatment for children and adolescents with major depressive disorder. Depression is an important risk factor for suicide, the third leading cause of death among adolescents; it is also a major risk factor for long-term psychosocial impairment in adulthood. There has been much debate about whether a class of antidepressant medications, selective serotonin re-uptake inhibitors (SSRIs) can actually increase suicidal thinking. At present, fluoxetine (Prozac) is the only FDA-approved medication for depression in children and adolescents, and there have been conflicting results regarding its benefits and risks. The goal of the NIMH trial was to clarify the usefulness of treating adolescent depression with a type of psychotherapy called cognitive behavior therapy (CBT), or fluoxetine, or both. Results of the first 12 weeks found that a combination of fluoxetine and CBT was the most effective treatment (71 percent response rate). Of the other three treatment groups, fluoxetine alone, (60.6 percent response), but not CBT alone (43.2 percent response) was significantly better than placebo (34.8 percent response). Suicidal thinking, which was present in 29 percent of the participants at the beginning of the study, improved significantly in all four treatment groups, with those receiving medication and therapy showing the greatest reduction (below 8 percent). Soon we will know the effectiveness of these treatments over a six-month period from treatment initiation. It is critical for physicians and psychotherapists to closely monitor their young patients on antidepressant medications for signs of hurtful or suicidal behavior, particularly during the early phases of treatment.

A central focus of NIMH treatment research has been finding a more tailored, individual approach to therapy. To personalize treatments, we need to know predictors of treatment response. Recent studies have begun to reveal some predictors that will help clinicians optimize care. For instance, studies of people with major depressive disorder reveal that standard antidepressant medication may be less helpful in those with a history of trauma, or specific genetic variations, or specific patterns of brain activation as seen on imaging scans. These same patients may respond well to cognitive behavior therapy. Similarly, patients with schizophrenia who have poor attentional processing and other cognitive deficits may report less satisfaction with anti-psychotic medications, which were not designed to treat these features of the illness. Ongoing research seeks to find markers that will guide individual treatment to optimize recovery.

Other large trials to be completed within the next year will answer urgent questions about the choice of treatments in people with bipolar disorder, schizophrenia and Alzheimer's, and treatment-resistant major depression. NIMH continues its strong commitment to public dissemination of findings from

these clinical trials by fostering partnerships with national and state organizations via the Outreach Partnership Program. Through this program, NIMH works with the National Institute on Drug Abuse and SAMHSA to bridge the gap between research and clinical practice.

BLUEPRINT FOR NEUROSCIENCE RESEARCH

The NIH Blueprint for Neuroscience is a framework to enhance cooperation among the 15 NIH Institutes and Centers that have common interests in the nervous system. By pooling resources and expertise, the Institutes and Centers can take advantage of economies of scale, confront challenges too large for any single Institute, and develop research tools and infrastructure that will serve the entire neuroscience community. The Blueprint is developing a primary set of initiatives including a gateway to existing databases that permits more effective searches; training enhancement for basic neuroscientists; and expansion of ongoing pediatric imaging, gene microarray, and gene expression database efforts.

NIH ROADMAP

NIMH has assumed a lead role on the Molecular Libraries and Imaging initiative of the NIH Roadmap, whose goal is to provide organic compounds called “small molecules” to scientists to use as tools to improve our understanding of biological pathways in health and disease. The potential of scientific discoveries of clinical relevance is enormous. The NIMH mission can be advanced by the identification of even one novel small molecule with biological activity in the brain, as it could provide invaluable information about brain circuits involved in mental illness and those that are altered by treatment.