# Director's Report to the National Advisory Mental Health Council

February 6, 2004

# **Director's Opening Remarks**

I'm pleased to welcome members of the National Advisory Mental Health Council (NAMHC), and other participants and guests to our 205<sup>th</sup> Council meeting. Since we last met in September 2003, we have seen progress on many fronts at the National Institute of Mental Health (NIMH). Below I summarize recent scientific accomplishments and provide updates on various initiatives, outreach efforts, conferences, and personnel changes. Since getting your feedback in September we have established a new Aging Treatment and Preventive Interventions Research Branch and a new Global Mental Health Office, which will coordinate and initiate non-AIDS international activities within NIMH. We have also made significant progress on a number of NIH Roadmap activities. The budget for 2004 has now been approved and the President's budget for 2005 has just been released. For both years, the increase is far less than we received in the previous five years, requiring serious attention to setting priorities. A workgroup of Council has been reviewing our basic science portfolio to suggest priority areas. Details of the budget are provided later in this report. I look forward to your comments at our meeting with respect to all of these issues.

#### Science of Note

# Mental Illness Genetics Among Science's Top Breakthroughs for 2003

Research on the genetics of mental illness was named the number two scientific "breakthrough of the year" by *Science* magazine in its December 19, 2003 issue. Most of the studies listed were conducted by either the Institute's intramural scientists or NIMH-funded investigators. The prestigious journal selected the mental health studies collectively as the first of nine runners-up, second only to newfound insights into the nature of the cosmos. It cited progress in identifying genes that increase one's risk of developing schizophrenia, depression and bipolar disorder, as well as advances in "unraveling" how the genes work in the brain to influence vulnerability.

Among studies specifically mentioned is the finding by NIMH grantees Avshalom Caspi and Terrie Moffitt, University of Wisconsin, that a variant of the serotonin transporter gene doubles the risk of depression following life stresses in early adulthood.

NIMH intramural researchers from the laboratory of Daniel Weinberger were also specifically mentioned. Papers by Michael Egan, Venkata Mattay, Mayada Akil, and Joel Kleinman describe the role of the COMT gene in schizophrenia. They found a slightly increased risk for schizophrenia among people who inherit one of two common versions of the COMT gene, which codes for the enzyme that metabolizes neurotransmitters like dopamine and norepinephrine. The gene appears to impair prefrontal function and thus

bias the brain toward a pattern of neurochemical activity associated with psychosis and poorer performance on tasks requiring activation of the prefrontal cortex.

Work by Egan and colleagues is also credited for showing how the BDNF gene, which has been linked to bipolar disorder, affects memory in humans through effects on the hippocampus. Also listed was the finding by NIMH's Ahmad Hariri and Daniel Weinberger that the same gene variant biases the amygdala's response toward increased anxiety when viewing frightening faces.

Breakthroughs of the Year: The Runners Up. The News and Editorial Staffs, <u>Science</u>, Dec 19 2003: 2039-2045.

#### **Mutant Gene Linked to Obsessive Compulsive Disorder**

Analysis of DNA samples from patients with obsessive compulsive disorder (OCD) and related illnesses suggests that these neuropsychiatric disorders affecting mood and behavior are associated with an uncommon mutant, malfunctioning gene that leads to faulty transporter function and regulation. NIMH grantee Norio Ozaki, collaborating with NIMH intramural scientist Dennis Murphy and colleagues, reported their findings in Molecular Psychiatry. The collaborative study revealed a mutation in the human serotonin transporter gene, hSERT, in families with OCD. A second variant in the same gene suggests a genetic "double hit," resulting in greater biochemical effects and more severe symptoms. There are few known instances where two variants within one gene have been found to alter the expression and regulation of the gene in a way that appears associated with symptoms of a disorder. SERT allows neurons, platelets, and other cells to accumulate serotonin, which affects emotions and drives. Drugs that reduce the binding of serotonin to transporters (SSRIs) treat mental disorders effectively. Although about half of patients with OCD are treated with SSRIs, those with the hSERT gene defect do not seem to respond, according to the study. However, the researchers say that any vulnerability to OCD from gene effects most likely interacts with events in the environment such as stresses, and other factors like gender, and treatments. Ozaki, N, Goldman, D, Kaye, WH, Plotnicov, K, Greenberg, BD, Lappalainen, J, Rudnick, G, Murphy, DL. Serotonin transporter missense mutation associated with a complex neuropsychiatric phenotype. Molecular Psychiatry, 8(11): 895, 933-6, 2003.

#### Panic Disorder Patients Deficient in Emotion-Regulating Receptor

Three brain areas of panic disorder patients are lacking in a key component of a chemical messenger system that regulates emotion, according to a new study by researchers in NIMH's Mood and Anxiety Disorders Program. Brain scans using a new radioactive tracer revealed that a type of serotonin receptor is reduced by nearly a third in three structures straddling the center of the brain that mediate anxiety. The finding is the first in living humans to show that the 5-HT1A receptor, which is pivotal to the action of anti-anxiety medications, may be abnormal in the disorder, and may help to explain how genes might influence vulnerability. NIMH intramural scientists Alex Neumeister and Wayne Drevets report on their findings in the January 21 issue of the *Journal of Neuroscience*. Although animal experiments have shown that cortisol secretion triggered by repeated stress reduces expression of the 5-HT1A gene, such stress hormone

elevations are usually not found in panic disorder. Other animal studies reported in 2002, by NIMH grantee Dr. Rene Hen, Columbia University, found that a strain of gene "knockout" mice, engineered to lack the receptor during a critical period in early development, exhibits anxiety traits in adulthood, such as a reluctance to begin eating in an unfamiliar environment. More recent experiments with the knockout mice show that a popular SSRI drug produces its anti-anxiety effects by stimulating the formation of new neurons in the hippocampus via the serotonin 5-HT1A receptor. Noting the recent discovery of a variant of the 5-HT1A receptor gene linked to major depression and suicide, the researchers suggest that reduced expression of the receptor "may be a source of vulnerability in humans, and that abnormal function of these receptors appears to specifically impact the cortical circuitry involved in the regulation of anxiety."

Neumeister A, Bain E, Nugent AC, Carson RE, Bonne O, Luckenbaugh DA, Eckelman W, Herscovitch P, Charney DS, Drevets WC. Reduced Serotonin Type 1A Receptor Binding in Panic Disorder. Journal of Neuroscience, 24(3): 589-591, 2004.

# **Suppressing Unwanted Memories**

More than a century ago, Freud proposed that unwanted memories could be excluded from awareness, a process called repression. It is unknown, however, how repression occurs in the brain. In a study reported in the January 9 issue of *Science*, grantee Michael Anderson and colleagues at the University of Oregon and Stanford University used functional magnetic resonance imaging to identify the neural systems involved in keeping unwanted memories out of awareness. Controlling unwanted memories was associated with increased dorsolateral prefrontal activation, reduced hippocampal activation, and impaired retention of those memories. Both prefrontal cortical and right hippocampal activations predicted the magnitude of forgetting. These results confirm the existence of an active forgetting process and establish a neurobiological model for guiding inquiry into motivated forgetting.

Anderson, MC, Ochsner, KN, Kuhl, B, Cooper, J, Robertson E, Gabrieli SW, Glover, GH, Gabrieli, JDE Neural Systems Underlying the Suppression of Unwanted Memories. <u>Science</u>, 303 Vol 5655: 232-235, 2004

#### Monkey Talk, Human Speech Share Left-Brain Processing

Scans have pinpointed circuits in the monkey brain that could be precursors of those in humans for speech and language. As in humans, an area specialized for processing species-specific vocalizations is on the left side of the brain, report Amy Poremba, Mortimer Mishkin, and colleagues at NIMH, Warren G. Magnuson Clinical Center, and the University of Iowa. An area near the left temple responded significantly more than the same area on the right only to monkey calls, not to other animal calls, human voices or various other sounds. The researchers published their findings in the January 29 issue of *Nature*. The researchers note that their results open up the possibility of characterizing such neuronal responses in a cortical region of the monkey that is not only a higher-order auditory processing area, but also one that could be a precursor for an acoustic language area in humans.

Poremba, A, Malloy, M, Saunders, RC, Carson, RE, Herscovitch, P, Miskin, M, Species-specific calls evoke asymmetric activity in the monkey's temporal poles. <u>Nature</u>, 427: 448-451, 2004.

Sleep Linked to Increased Gene Expression; Study Provides Clues to Function

Inadequate sleep is the predominant complaint by patients visiting psychiatrists. Nevertheless, the functions of sleep are not known. Understanding these functions will lead to better diagnosis and treatment of many psychiatric illnesses and behavioral disorders. Through the use of gene microarray techniques, NIMH grantee Chiara Cirelli and colleagues from University of Wisconsin discovered that sleep (and behavioral quiescence) is associated with increased expression of many genes specific to brain tissue. About 1500 genes are differentially expressed in the cerebral cortex due to changes in day and night; half of these do so because of changing between waking and sleep. They also determined that molecular correlates of sleep and wakefulness are found in the cerebellum, an area not associated with electrographic signs of sleep. Thus sleep may engage the cellular machinery of brain structures that are not known to generate circadian changes. They conclude that a function of sleep may include a relatively specific role for membrane trafficking and maintenance.

Cirelli, C, Gutierrez, CM, Tononi, G. Extensive and Divergent Effects of Sleep and Wakefulness on Brain Gene Expression. <u>Neuron</u>, 41: 35-43, 2004.

# **Healthy Living Project**

Two important studies of risk behavior and HIV treatment adherence among persons living with HIV/AIDS have emerged from the NIMH-funded cooperative agreement called the "Healthy Living Project." The risk behavior study determined that out of nearly 4,000 HIV infected persons, most unprotected sexual activity took place in the context of relationships with other HIV-positive individuals. However, approximately 19% of women, 15.6% of homosexual men, and 13.1% of heterosexual men engaged in unprotected intercourse with partners who were HIV-negative or whose serostatus was unknown. About 30 new infections would be expected during the 3-month reporting period. In the adherence study of more than 2,750 patients, 32% self-reported less than 90% adherence in the prior three days. The following factors were associated with greater likelihood of non-adherence: being African-American, being in a primary relationship, and having a history of injection drug use or homelessness in the previous year. Overall, results supported the need for multi-focused interventions to improve adherence that address logistical barriers, substance use, attitudes and expectancies, as well as skills building.

Weinhardt, L.S., Kelly, J.A., Brondino, M.J., et al. HIV Transmission Risk Behavior Among Men and Women Living With HIV in Four U.S. Cities. <u>Journal of Acquired Immune Deficiency Syndromes</u> (in press).

Johnson, M.O., Catz, S.L., Remien, R.H., et al. Theory-Guided, Empirically Supported Avenues for Intervention on HIV Medication Nonadherence: Findings from the Healthy Living Project. <u>AIDS Patient Care & STD</u>, 17: 645-656, 2003.

# NIMH Publications

#### Schizophrenia Bulletin

For several decades, the NIMH has published *Schizophrenia Bulletin* to provide a forum for research concerning this severe and often disabling mental disorder. The Bulletin has served its original purposes well, but in this electronic age, the Institute needs to consider

new ways to inform scientists, clinicians, patients and families, and the general public about schizophrenia research findings. NIMH has been exploring web-based methods to disseminate such information, and anticipates the development of a new system to communicate important recent findings in a timely and efficient manner. NIMH conducts an ongoing review of all its programs, and has recently decided to phase out Institute sponsorship of this journal. Our goal is to implement this decision in a way that will be least disruptive to the field, and to the authors, reviewers, editorial board, staff, and subscribers. While we will no longer accept new submissions for publication, we do expect to publish articles already accepted. We are also exploring ways in which the Bulletin might be privatized, so that it could continue to exist. We are proud of the accomplishments of the *Schizophrenia Bulletin*, but in this rapidly changing scientific environment it is time to develop communication mechanisms that are equally rapid.

# **NIH Roadmap Progress**

The NIH Roadmap is a planning process for trans-NIH initiatives that will develop science and technology to enable rapid progress in biomedical research. The Roadmap is now in the implementation stage, with the nine working groups adopting 27 of the proposed initiatives. Dushanka Kleinman was named the Assistant Director for NIH Roadmap Coordination. Her office will coordinate the implementation of the initiatives with the help of a committee consisting of the nine working group chairs and representatives from six central NIH offices. Each Institute has a designated liaison to the Roadmap, with Mayada Akil acting as the NIMH liaison. NIMH has representatives on eight of the nine implementation groups and is the lead institution on the Molecular Libraries initiative described below. Akil's role is to represent NIMH in the Roadmap process, to communicate with Institute staff, the research community, and the public about Roadmap activities and to participate in the evaluation of the Roadmap over time. Several Roadmap requests for applications (RFAs) and other funding opportunities have been issued. For this and other useful information on the NIH Roadmap see <a href="http://nihroadmap.nih.gov">http://nihroadmap.nih.gov</a>.

Molecular Libraries initiatives: A request for proposals (RFP) has been issued to establish a publicly available repository of chemically diverse small organic molecules of both known and unknown activities. The anticipated award date for the contract is in the spring of 2004. The collection of small molecules will consist of compounds assembled, arrayed, and screened for possible new activities and applications within the screening centers and by the scientific community. The NIH Chemical Genomics Center, the first of a network of screening centers, is being established in the Intramural Research Program at the National Human Genome Research Institute (NHGRI). An RFA will be issued to establish a network of extramural centers that are expected to begin screening in late 2005. The National Center for Biotechnology Information is in the process of establishing PubChem, a public sector database that will contain chemical structures and biological data obtained for small molecules tested in assays within each of the screening centers. An RFA has been issued to stimulate the development of innovative assays that can be automated and used for use in basic research and within the screening centers (http://grants1.nih.gov/grants/guide/rfa-files/RFA-RM-04-012.html).

**Molecular Probes initiative**: An RFA was issued in late 2003 to facilitate the development of high sensitivity, high resolution probes for cellular imaging; other initiatives are planned for 2005. The Imaging Probe database is in the planning stages, and will be linked to the PubChem database. A core synthesis facility to produce imaging probes is in the process of being established in the NIMH Intramural Research Program (<a href="http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-04-001.html">http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-04-001.html</a>).

# **National Advisory Mental Health Council Workgroup**

Over the past five years, there have been unparalleled advances in the basic sciences relevant to mental health. Maintaining this momentum is a challenge, but one that our patients and their families, as well as the research community, cannot afford to lose. With decelerating budget growth at NIMH, progress requires that we set clear priorities. A workgroup of the NAMHC has been formed to assist us in priority setting for the basic sciences in mental health. Specifically, this workgroup has been charged with reviewing the existing NIMH portfolio in molecular, cellular, and behavioral neuroscience, basic behavioral, and basic cognitive science and, considering relevance to mental disorders, recommending priority areas for research funding. The workgroup charge and membership can be found at http://www.nimh.nih.gov/council/bsworkshop.cfm. The first meeting of the workgroup was held on January 13. Additional meetings will be held during February and March, with a draft final report anticipated at the May 2004 NAMHC meeting.

# **New NIMH Programs**

A new branch has been created within the Division of Services and Intervention Research: the Aging Treatment and Preventive Interventions Research Branch, led by Barry Lebowitz. The Adult Treatment and Preventive Interventions Research Branch will be led by Matthew Rudorfer, who will serve as acting director until we complete a national search for a permanent director. Jane Pearson has agreed to provide active assistance in the management of the Adult Branch. These two branches will replace the current Adult and Geriatric Treatment and Preventive Interventions Research Branch. Lebowitz will assume leadership of the NIMH-wide Aging Consortium, which has been so ably managed by Bruce Cuthbert since the departure of Jason Olin.

NIMH has established a new Office of Global Mental Health, which will coordinate our grants that have an international component. The program will seek opportunities to engage in global clinical and services research that aids in understanding shared and culturally unique attributes that affect mental disorders, providers, and delivery systems. It will seek to build the capacity of U.S. and foreign researchers to conduct global mental disorders- related research, and to work with international organizations and institutes of mental health on shared goals and exchange of resources, from neuroinformatics to studies of the burden of disease. Karen Babich will direct the office, working with Javier Escobar.

# **NIMH Public Outreach**

A five-part series on depression on CNN's primetime news show, *Anderson Cooper 360*, more than doubled calls to the NIMH toll-free number during the week of January 12, 2004. The series, "Conquering Depression," featured NIMH phone numbers and website addresses so viewers could get more information. One of the mental health experts interviewed was NIMH Director Tom Insel, who was included in two of the segments. The final segment devoted to men and depression featured the NIMH **Real Men Real Depression** education campaign and New York firefighter, Jimmy Brown, a participant in the campaign. The Office of Communications assisted CNN producers with resources and materials for the series.

The Real Men Real Depression campaign is one of five finalists in the PRWeek awards for Campaign of the Year in the category of Social Education and Philanthropy. This campaign is also a finalist in the video news release category for Best Use of Broadcast. A panel of 75 judges of top public relations professionals from both agency and corporate backgrounds reviewed nearly 800 entries. The winners will be announced at a gala in New York on March 4.

The new NIMH schizophrenia research initiative announced at the September 2003 Advisory Council meeting was featured in *Science* magazine and the *Washington Fax* articles; Tom Insel and Daniel Weinberger were interviewed for the stories. Other articles in *Science* included a story on diagnosis of psychiatric illnesses with Dennis Charney and Wayne Fenton; depression treatment strategies with Philip Gold and Husseini Manji, and Trey Sunderland on Alzheimer's disease research. Children and mental illness was the topic of the September 19, 2003 cover of *Newsweek*; Daniel Pine and Susan Swedo were quoted in the article.

Twenty-five journalists attended the two-day national Autism Summit where the federal Interagency Autism Coordinating Committee (IACC) announced a 10-year research plan to fight the serious brain disorder. Stories about the conference and research plan and interviews with Tom Insel and Steve Foote appeared in *The New York Times*, The *Washington Post, Washington FAX, JAMA Medical News, USA Today*, and were carried by the Associated Press, Reuters, and CBS Network Radio.

The NIMH pamphlet *Attention Deficit Hyperactivity Disorder* (ADHD) has been updated with the latest information on available medications and treatments and the results from the Multimodal Treatment Study of Children with ADHD. The NIMH-funded study is the largest study to date comparing medication to behavioral treatment.

#### **Outreach Partnership Program**

NIMH is committed to delivering science-based information about mental illness research to the public, health professionals, constituency groups, and other key stakeholders in a nationwide effort to make real progress toward improving identification, diagnosis and treatment for the benefit people with mental illness and their families. The NIMH Outreach Partnership Program is a primary way of reaching this goal. The Program has recently undergone significant change, including new leadership and focus.

Although the program's size remains the same (with 51 NIMH Outreach Partners in all 50 States and the District of Columbia), there is a new concentration on building multiple partnerships with local, State, national and government organizations. Each of these groups will contribute their expertise and strength in collaborative activities with our 51 key Outreach Partners, thus bringing together diverse groups to work together toward reducing stigma and discrimination too often associated with mental illnesses. There has been a special focus on children, older adults and underserved members of minority and ethnic populations. The key goal for the program for this year is "Partnering across the Nation to improve American's mental health."

#### Research Conferences

Autism Summit Conference: Developing a National Agenda for Research in Autism As the lead agency for the Interagency Autism Coordinating Committee (IACC), NIMH played a critical role at the conference "Autism Summit Conference: Developing a National Agenda," which was held in November 2003, in Washington, DC. About 650 people attended the meeting, which was a joint effort of the Department of Health and Human Services and the Department of Education. The summit addressed three major areas of emphasis: biomedical research, implementing early screening and diagnosis, and improving the accessibility and coordination of services. The involvement of members of Congress, public officials, scientific investigators, practitioners, and community members provided a forum for highlighting the Federal government's interest in autism and for the mobilization of resources. Speakers included several members of Congress, the Secretary of Health and Human Services, and the Secretary of Education. A key focus of the meeting was the introduction of a 10-year national research agenda, developed by an IACC appointed science panel. A review of the Autism Summit was published in the Journal of the American Medical Association 2004; 291, 29-31. For a summary of the conference go to: http://www.tvworldwide.com/events/nimh/031119/.

#### NIMH Schizophrenia Initiative

The recent identification of several susceptibility genes for schizophrenia provides an exciting opportunity for a better understanding of the pathophysiology of the disorder that should bring us closer to understanding risk profiles and improving diagnosis and treatment. NIMH is expanding its intramural schizophrenia research program to follow up on these findings at an accelerated pace with an interdisciplinary team ranging from molecular to clinical scientists. To help provide guidance on the scientific and recruitment strategies most likely to advance the understanding of schizophrenia, an international group of scientists met with representatives from the NIMH team in January 2004. Several of the advisors suggested that the field is still in an early stage of discovery and more susceptibility genes should be identified in order to appoint a more complete picture of the genetic underpinning for schizophrenia. Suggested strategies for reaching this goal included using larger and better characterized cohorts. Members of the group suggested that cell biology techniques be employed to identify genes biologically related to those associated with endophenotypes of schizophrenia, and then testing these genes in clinical association studies. Advisors agreed that there is a need to recruit cell biologists to gain a deeper understanding of the biology of the genes involved. They recommended

using cell culture, transgenic mice, and other approaches to understand the biology of each gene and to test the effects of gene-gene and gene-environment interactions.

#### Fostering Collaboration Among Prodromal Schizophrenia Researchers

Seven NIMH-funded prodromal schizophrenia researchers came together for a one-day meeting in January 2004 to explore the scientific benefits of expanding collaboration among existing projects. Discussion focused on four major issues: (1) Can current studies be integrated in a manner that creates a large pool of similarly diagnosed at-risk subjects? (2) Can a common assessment protocol be established that captures important predictor variables and tracks clinical and functional outcomes longitudinally? (3) What modifications to site-specific diagnostic and assessment practices would be necessary to join a multi-site collaboration? (4) What additional resources--technical, personnel, and financial--would be necessary to facilitate these changes? A strong consensus developed regarding the feasibility of merging existing data sets and the positive impact this could have on hastening scientific progress in this area of research. In conference calls in February and March, extramural scientists and program staff will detail plans for a collaborative research initiative.

# **Government-Industry Collaboration Meeting**

Federal and academic researchers and industry representatives came together in January 2004 to examine potential directions for NIMH in medication development for mental illness. Co-chairs for the meeting included Tom Insel of NIMH, Herbert Pardes of New York-Presbyterian Hospital, and Ed Scolnick of Merck. Discussion centered on three issues: (1) Across the spectrum of discovery and development, what useful and non-redundant role might NIMH play in hastening the availability of new treatments for mental illness? (2) Can large NIMH-sponsored clinical trial networks evolve into a resource for public-private partnerships? (3) What are the major barriers to better collaboration (industry/intramural research and industry/extramural research) in drug development and how might they be overcome? A report on the meeting will be forthcoming.

#### **Neuroscience Satellite Symposium**

The Eleventh Annual Neuroscience Satellite Symposium of the Society for Neuroscience Annual Meeting was held in November 2003. This year's meeting, "Neuronal Variability and Noise," brought together a select group of experts in various aspects of neural data analysis to assess the current state of the field and provide insights into the development and application of new data analytic tools.

#### RAND Panel Meeting on Cognition in Schizophrenia

As part of the NIMH treatment development initiative focused on improving the assessment and treatment of cognitive symptoms in schizophrenia, a RAND panel meeting in September 2003 examined 35 neuropsychological tests of cognition for inclusion in a test battery that will undergo psychometric testing for use in clinical trials of medications.

# **Federal Child Neglect Research Consortium Meeting**

NIMH hosted the Federal Child Neglect Research Consortium meeting in January 2004 along with OBSSR, NIDA, NICHD and other NIH Child Abuse and Neglect Working Group members. This consortium is now in its fifth year and consists of nineteen NIH research sites on psychobiological, services, intervention, and clinical research on child neglect (<a href="http://www.nimh.nih.gov/canwg/canrfaupdate3.cfm">http://www.nimh.nih.gov/canwg/canrfaupdate3.cfm</a>). This year's meeting highlighted the impact of neglect on neurobiological, cognitive, and psychiatric functioning and behavior using both animal and human models. Methodological and measurement innovations, including the latest construct and statistical modeling, cortisol measurement and geocoding, were also discussed. Two special journal issues and a book on the definitional challenges of child maltreatment are currently in preparation from the consortium members.

#### Safety Assessment of Psychiatric Treatments for Children

How to improve research on the safety of psychiatric treatments for children, especially psychotropic medications, was the topic of a research forum at the annual meeting of the American Academy of Child and Adolescent Psychiatry in Miami in October 2003. The heterogeneity of methods used across pediatric psychopharmacology studies was identified as a major limitation of the current databases, and possible approaches to standardizing how adverse events are elicited, defined, and classified were discussed.

# **Preventing Suicide**

NIMH, the Center for Disease Control and Prevention (CDC), and the Center for Mental Health Services (CMHS), part of the Substance Abuse and Mental Health Services Administration (SAMHSA), convened a workshop on "The Science of Public Messages for Suicide Prevention," in October 2003. Suicide prevention advocates in the field, evaluation specialists, and experts in suicide contagion, public health message development, mental health literacy, stigma, and marketing were brought together to discuss research on public messaging campaigns, and address specific issues in suicide prevention. The purpose of the workshop was to consider safe and effective ways of raising public awareness that suicide is a preventable public health problem. In breakout sessions, participants were asked to discuss three examples of current public awareness campaigns from state and regional efforts, and to consider ways of testing assumed "active ingredients," market penetration, and proposed outcomes.

#### **Mouse Atlas Workshop**

The NIMH Office on Neuroinformatics sponsored a workshop in November 2003, to examine current approaches to the structure and annotation of mouse neuroanatomical atlases with the goal of exploring compatibility with each other. Options were discussed that could enable different mouse maps and atlases, either existing now or under development, to be compatible with each other and share a common data structure. Workshop participants described their current approaches and goals, and examined issues of compatibility in order to maximize community utility of these maps and atlases. A report is in preparation and will soon be available at: http://www.nimh.nih.gov/neuroinformatics/wmaw03.cfm.

# **NIH/Society for Neuroscience Collaboration**

The NIMH, together with NINDS and NIDA, is working with the Society for Neuroscience (SFN) to develop a neuroinformatics portal to catalyze the integration and dissemination of neuroscience information via the use of readily accessible neuroscience databases. The plan has three phases for the first nine months: in phase I, the SFN will establish the portal; in phase II, Society membership will evaluate the portal; and phase III will establish plans for the future. This approach is proposed by the Brain Information Group (BIG), a special committee established by the SFN Council in 2003, chaired by Floyd Bloom, and charged to define the database needs of the field of neuroscience.

#### **International Cooperation in Science and Technology**

The Organization for Economic Cooperation and Development (OECD), Committee for Scientific and Technological Policy, met with Science Ministers from the 30 member countries in January 2004 in France. The Ministers concluded that greater international co-operation in science and technology is vital to meet a broad range of global challenges related to economic growth, better health, sustainable development, and enhanced safety and security, as well as for implementing large science projects in a growing range of disciplines. The Ministers adopted a declaration intended to strengthen international cooperation for sustainable development and endorse efforts to support and promote scientific cooperation in neuroinformatics.

#### Site Visit to China

In November, NIMH representatives traveled to China to conduct a site visit and provide technical expertise related to AIDS and suicide prevention. The site visit was conducted to monitor an international HIV/STD prevention project in Fuzhou, China, that is part of the NIMH International HIV Prevention Trial, a five-nation trial of the Popular Opinion Leader HIV prevention intervention. The visit included a two-day meeting in Beijing with government leaders and experts in suicide prevention, including representatives from WHO and the Association for Suicide Prevention, to aid in developing a national suicide prevention plan for China. NIMH staff made presentations on cross-agency collaborations and the government's role in developing the U.S. national suicide plan. NIMH staff also provided models of strategic planning that have been valuable in other areas, such as HIV prevention.

#### Workshops on Co-Morbidities Associated with HIV/Hepatitis-C Co-Infection

Two companion workshops related to the emerging co-morbidities associated with HIV/Hepatitis C Co-infection were held in October 2003. The first defined the burden of neurologic and neuropsychiatric disease in the setting of HIV/HCV co-infection and identified future research priorities in the areas of neuropathogenesis as well as treatment. The second workshop built on the most current information to provide a clearer focus for mental health and drug abuse-related research on the behavioral and clinical aspects of HIV/HCV co-infection (risk and prevention; services; treatment). The meetings were co-sponsored by NIDA, NINDS, and the NIH Office of AIDS Research. Proceedings will be published in a special supplement issue of *AIDS*.

# Depression, Cognitive Impairment, and Cognitive Decline in Late Life

The NIMH Aging Research Consortium sponsored a meeting in November 2003, "Perspectives on Depression, Mild Cognitive Impairment, and Cognitive Decline." It brought together investigators supported by NIMH, NIA, and NINDS to examine ways to better integrate the diverse perspectives on the associations among depression, mild cognitive impairment, and cognitive decline in late life and to illuminate the common and/or distinct mechanisms involved in these associations. Two broad questions were addressed: What are the gaps in our knowledge, the answers to which will have the greatest public health significance, and how can we more efficiently use our research?

#### American Academy of Child and Adolescent Child Psychiatry

At the 50th Annual Meeting of the American Academy of Child and Adolescent Child Psychiatry, held in Miami in October 2003, staff presented the NIMH perspective and plans regarding recruitment and training of child mental health researchers, with a particular focus on physician-scientists with training in child and adolescent psychiatry. Additional scientific presentations included a symposium on clinical implications of emotion regulation in young children and an update on pediatric obsessive-compulsive disorder research.

# 2nd Annual Conference on Mental Health and People of Color

The 2nd Annual Conference on Mental Health and People of Color: Overcoming Stigma Through Mind, Body and Spirit was sponsored by the Mental Health Association in Delaware in November 2003. NIMH researchers presented an overview for patients and their families of medications used in the treatment of mental health problems.

#### **Improving Training in Clinical Psychology**

In January, staff from NIMH, NIDA, and other institutes met with representatives of the Academy of Psychological Clinical Science. The Academy was formed several years ago to foster a strong emphasis on training future clinical scientists in clinical psychology graduate programs. The purpose of the meeting was to discuss models of training in clinical science in psychology and to exchange views between the institutes and the Academy as to how such training can best be supported. Topics discussed included training in translational research; the need for training in other disciplines; the need to begin a proper foundation of relevant coursework at the undergraduate level; and the problem of training sufficient numbers of students in evidence-based psychological therapies. NIMH training and program staff plan an ongoing dialogue with Academy members about these important issues.

# Budget

# **FY 2004 Congressional Action:**

After almost four months of Continuing Resolutions that held the National Institutes of Health (NIH) to its FY 2003 funding level, the Congress passed an FY 2004 appropriation for the NIH as part of the FY 2004 Omnibus Appropriations Bill on January 22, 2004. As indicated on Attachment 1, the Bill provides a total of \$27.9 billion for the NIH. This total NIH amount represents an increase of 3.0% over the FY 2003

NIH total of \$27.1 billion and also marks the first year of Congressional Action following the 5-year doubling of the NIH appropriation that took place between FY 1999 and FY 2003.

The NIMH FY 2004 appropriation of \$1.381 billion is an increase of \$42 million or 3.1% over FY 2003. NIMH currently projects an FY 2004 success rate of about 23% for Research Project Grants (RPGs) compared to 27% in FY 2003. The NIH as a whole estimates a higher aggregate success rate of 27% in FY 2004 compared to 30% in FY 2003.

# **FY 2005 President's Budget Request:**

The FY 2005 President's Budget Request was submitted to the Congress on February 2. This request would provide a total budget of \$28.6 billion for the NIH, representing an increase of 2.6% over the FY 2004 Appropriation. NIH spending exclusive of Biodefense and AIDS will increase by 2.5% while NIH funding for Biodefense and AIDS will increase by 4.4% and 2.8%, respectively. The FY 2005 NIH request also provides for an aggregate 1.3 % increase in average cost for Research Project Grants, consistent with the government's Gross Domestic Product Deflator.

The request of \$1.421 billion for NIMH is an increase of \$39 million or 2.8% over FY 2004. At the FY 2005 President's Budget level, the NIMH success rate for RPGs would be about 25% compared to an NIH average of about 27%. NIMH actual expenditures by mechanism for FY 2003 and estimates for FY 2004 and 2005 are displayed on Attachment 2.

# **Major Awards**

"Genes for Mental Disorders" was *Science* magazine's runner-up breakthrough of the year. Included in this breakthrough were several papers from the **NIMH Clinical Brain Disorders Branch** in the Intramural Research Program (*see Science of Note*). NIMH staff and grantees were among the 65 newly elected members of the National Academy of Science's Institute of Medicine. IOM members are elected in recognition of major contributions to the advancement of the medical sciences, health care, and public health. Election is considered one of the highest honors in the fields of medicine and health. New IOM members include:

Tom Insel, M.D., National Institute of Mental Health, Arthur Reingold, M.D., University of California, Berkeley Alan F. Schatzberg, M.D., Stanford University Shelley E. Taylor, Ph.D., University of California, Los Angeles Helena C. Kraemer, Ph.D., Stanford University

IOM also awarded the 2003 Rhoda and Bernard Sarnat International Prize to NIMH grantee **Aaron T. Beck, M.D.**, University of Pennsylvania, in recognition of the international scope and significance of his contributions to psychiatry and mental health, particularly his development of cognitive therapy.

**Stephen Foote, Ph.D.**, Director, Division of Neuroscience and Basic Behavioral Science, was among 348 elected as fellows of the American Association for the Advancement of Science (AAAS). Fellowship in the AAAS is an honor bestowed upon AAAS members by their peers.

**Husseini Manji, M.D.**, Chief, Laboratory of Molecular Pathophysiology, was awarded the Joel Elkes Award for outstanding clinical contributions. Dr. Manji provides a stellar example of translational research in psychiatric disorders, as he has probed basic mechanisms of the elusive action of mood stabilizers and tested these hypotheses in clinical studies.

**Michael D. Ehlers, M.D.**, **Ph.D.**, a grantee from Duke University Medical Center, received the Eppendorf & *Science* Prize for Neurobiology for 2003. This annual international honor, awarded by the AAAS journal *Science* and Eppendorf AG, a German molecular biology development and manufacturing firm, provides \$25,000 for outstanding neurobiological research performed during the past three years.

**Nancy Petry**, **Ph.D.**, University of Connecticut, received the Award for Distinguished Early Career Contributions to Psychology from the American Psychological Association for her "groundbreaking work on the problem of gambling ..."

**Seth Pollak**, **Ph.D.**, an NIMH research investigator on child emotion and trauma at the University of Minnesota, received the 2003 Boyd McCandless Award from the American Psychological Association to acknowledge his distinguished and significant contributions made to developmental psychology at an early career stage. Dr. Pollak's research study, originally presented in the August issue of *Journal of Abnormal Psychology* (Vol. 112, No. 3), reported that an increase in brain electrical activity might explain the kinds of emotion-processing differences observed in abused children, such as anger fixation.

**Nnamdi Pole, Ph.D.**, University of Michigan, received the APA/APAGS Award for Distinguished Professional Contributions by a Graduate Student in recognition of his "contributions to his graduate program, university, and community..." while at the University of California, Berkeley.

NIMH grantee **Roberta Diaz Brinton**, **Ph.D.**, was identified in the December 29, 2003, issue of *US News and World Report* as one of the "Best Minds" addressing current problems based on her work on estrogen regulation of brain function.

NIMH grantee **David S. Bredt, Ph.D.**, received the ACNP Daniel H. Efron Research Award. The Efron award is for outstanding basic/translational research contributions to neuropsychopharmacology. Dr. Bredt also received the Society for Neuroscience Young Investigator Award at the annual Society for Neuroscience meetings in New Orleans in October.

Roberto Malinow, M.D., Ph.D., at Cold Spring Harbor Laboratory, and Thomas C. Sudhof, M.D., at University of Texas Southwestern Medical Center, were the co-

recipients of this year's MetLife Foundation's Award for Medical Research in Alzheimer's Disease. The awards were presented in Washington, DC in January in recognition of their efforts and contributions to understanding Alzheimer's disease (AD).

**John G. Miers, M.B.A.**, Director of the Office of Diversity and Employee Advocacy Programs, was awarded the F. Michael Taff Award by the City of Rockville for efforts towards improving the quality of life for citizens with disabilities.

# **Staff Changes**

# **Arriving:**

Marina Broitman, Ph.D., joined the Review Branch as a Scientific Review Administrator in December. She received her graduate degree from George Washington University and completed a clinical internship in pediatric psychology at DuPont Hospital for Children in Wilmington, DE. She has experience in mental health services research, having worked at the Center for Health Services Research and Development in the Department of Health Policy and Management at the Johns Hopkins University School of Public Health.

**Cynthia Shannon-Weickert, Ph.D.**, will establish a unit within the Clinical Brain Disorders Branch to look at the etiology of schizophrenia from a developmental viewpoint. Dr. Shannon-Weickert has been a Research Fellow at NIMH.

**Marina Volkov, Ph.D.**, joined the Office of Science Policy and Program Planning to serve as a Health Scientist Administrator in Planning and Evaluation. Dr. Volkov most recently served as a Scientific Review Administrator at NIDA, with previous service in the NIH Office of Behavioral and Social Sciences Research and the Office of Extramural Research.

#### **Departing:**

**Richard Weise, Ph.D.**, who served as a Scientific Review Administrator in the Review Branch of the Division of Extramural Activities, retired from NIMH after 26 years of exemplary government service.

**Gene Souder**, who was the Audio Visual Officer in the Office of Communications (OC) for 15 years, retired in January. In addition to serving as branch manager, Gene directed the production of graphics, slides, posters, and PowerPoint presentations for the NIMH Director. He also assisted with video production and coordination of printed materials developed by the OC to answer public requests for information about mental health.

**Constance Burr**, Public Affairs Specialist and Writer/Editor with NIMH since January 1996, will retire at the end of February. She will be a freelance writer and an applicant to the Capitol Fellowship Program for a grant to research and publish on the architectural history of the U.S. Capitol complex.

**Anne Maney, Ph.D.**, Social Science Analyst in the Office of Prevention, retired after 41 years of service. She served as advisor on prevention of mental disorders and the promotion of mental heath.

# **Closing Remarks**

With 3,597 grants and 2,911 extramural investigators, as well as an outstanding intramural research program, it is impossible for me to acknowledge all of the exciting science we are currently supporting. I hope this overview has given you a sense of the diversity and the promise of our research to carry out our mission of reducing the burden of mental illness and behavioral disorders through research on mind, brain, and behavior. In an era of smaller budget increases each year, we will need to set priorities for future funding—identifying areas with relevance, traction, and innovation that can really have an impact on our public health mission. I look forward to working with you on this important process.



