Director's Report to the National Advisory Mental Health Council

May 12, 2006

I am pleased to welcome members of the National Advisory Mental Health Council (NAMHC) and other participants and guests to our 212th Council meeting. Since our last meeting in February, we have made progress on several fronts, which I share with you in this report.

NIH-Wide Update

National Institutes of Health (NIH) Roadmap

The NIH Roadmap is an integrated vision to deepen the understanding of biology, stimulate interdisciplinary research, and reshape clinical research to accelerate medical discovery and improve public health. The Roadmap is organized into three themes, and much activity involving National Institute of Mental Health (NIMH) staff has taken place in each of them. A full summary of Roadmap activities can be found at http://www.nihroadmap.nih.gov/. Here I will summarize just a few highlights where NIMH has served as the lead Institute.

I. Pathways to Discovery

Molecular Libraries Roadmap

Since January 2006, the 10 fully operational centers of the Molecular Libraries Screening Centers Network (MLSCN) have been screening an initial set of 57 assays selected for implementation in the first two solicitation cycles. Assay descriptions are available at http://nihroadmap.nih.gov/grants/fundedresearch.asp. During the first quarter, the MLSCN generated more then 210,000 screening data points, and active compounds (hits) are being evaluated. Seven centers have deposited screening data into the PubChem database. Because high throughput screening is a new discipline to academic investigators, outreach and education efforts to the research community are essential for the success of the Molecular Libraries Roadmap initiative. All centers are actively involved in outreach to enhance and sustain the MLSCN assay pipeline, and two centers have recently published papers describing molecular screening approaches and identifying bioactive compounds as research tools.[1]

The NIH Molecular Libraries Small Molecule Repository (MLSMR) has deposited the structures of 67,555 compounds into PubChem and distributed these compounds to the screening centers. In 2006, the compound collection in MLSMR will be expanded to 200,000 compounds with greater chemical diversity through acquisitions from commercial vendors, depositions of compounds from the Molecular Libraries Pilot Libraries initiative, and solicitation of novel compounds from the academic community.

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[1] *Bologa CG, Revankar CM, Young SM, Edwards BS, Arterburn JB, Kiselyov AS, Parker MA, Tkachenko SE, Savchuck NP, Sklar LA, Oprea TI, Prossnitz ER. Virtual and biomolecular screening converge on a selective agonist for GPR30. Nat Chem Biol. 2006 Apr;2(4):207-12.*

Wei SH, Rosen H, Matheu MP, Sanna MG, Wang SK, Jo E, Wong CH, Parker I, Cahalan MD. Sphingosine 1-phosphate type 1 receptor agonism inhibits transendothelial migration of medullary T cells to lymphatic sinuses. Nat Immunol. 2005 Dec;6(12):1228-35.

Nanomedicine

The Nanomedicine Development Centers Request for Applications (RFA), originally released in May 2004, was re-issued, but required prior approval before applications could be submitted. Concept approval letters were due in March 2006; the RFA expires on June 24, 2006. NIH staff will approve proposals based upon how well the applicants address the vision and goals of a Nanomedicine Development Center in the context of the network of currently funded centers. For more information on this Roadmap initiative, please see http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-06-007.html.

II. Research Teams of the Future

Interdisciplinary Research

This funding initiative has $2.6 million set aside in Fiscal Year 2006 (FY 2006) to support the development and implementation of novel, interdisciplinary training programs through the T90 mechanism. These grants will support a variety of innovative didactic and research experiences designed to provide students with the knowledge and research experiences necessary to develop interdisciplinary solutions to complex health problems, with the ultimate goal of increasing quality and years of healthy life and eliminating health disparities.

The flagship initiative under this implementation group is the Interdisciplinary Research Consortium initiative. These Consortia were solicited in announcements published in late January. It is expected that, in FY 2007, about eight or nine Interdisciplinary Research Consortia will be awarded, with the aim of each being to address a significant biomedical research problem from a new conceptual perspective that integrates multiple disciplines.

III. Re-Engineering the Clinical Research Enterprise

PROMIS (Patient Reported Outcomes Measurement Information System)

This Roadmap initiative aims to develop ways to measure patient-reported symptoms, such as pain, fatigue, and aspects of health-related quality of life, across a wide variety of chronic diseases and conditions. A primary goal of the project is to leverage item-response theory and computerized adaptive testing to efficiently and reliably assess a range of patient-reported clinical research outcomes in a publicly accessible system. Now in its second year, the six project research sites and statistical coordinating center are reviewing and refining items, and plan to complete their analysis in summer 2006. The resulting item banks will be evaluated with approximately 10,000 participants selected from various medical and normal populations. NIMH is represented on the PROMIS steering committee by two grantees, each of whom serves as science officer for his respective project research sites: 1) Paul Pilkonis, at the University of Pittsburgh, who is developing the emotional distress domain and has an independent project to develop a sleep assessment domain, and 2) Arthur Stone, at the Stony Brook University, who is developing the fatigue domain and has an independent project assessing the relationship of retrospective self-reports to reports from real-time event sampling. William Riley, from NIMH, is the PROMIS project director.

The National Electronics Clinical Trials and Research Network (NECTAR)

The 12 contracts awarded under this initiative are currently in their second year of funding. The aim of these contracts is to design and implement feasibility projects for developing common infrastructure elements to be used in clinical trials across a variety of medical conditions and

clinical settings. One the contracts, headed by Daniel Clauw, at the University of Michigan, has a special emphasis on mental health and is focused on developing integrated academic-community research collaborations, including a depression-in-primary-care network. To this end, several cores (clinical informatics, data management, education, and research and development) have been established and are being pilot tested. Among other projects, a revised adverse event reporting module has been developed, in collaboration with Oracle Clinical software engineers, and a system-security plan was implemented to protect patient privacy. An Inventory and Evaluation of Clinical Research Networks (IECRN) National Leadership Forum is planned for May 31-June 1 in Rockville, where Westat's inventory of clinical research networks will be discussed to identify best practice models of clinical networks.

Clinical and Translational Science Awards

In October 2005, NIH released a RFA soliciting grant and planning grant applications for Institutional Clinical and Translational Science Awards (CTSAs). The purpose of this Roadmap initiative is to assist institutions in forging a uniquely transformative, novel, and integrative academic home for clinical and translational science. By the closing date of the announcement, 34 letters of intent for "full" and 69 for "planning" CTSA applications had been received, exceeding originally projected responses and confirming substantial community interest in the CTSA program. Awards are expected by September 2006.

NIH Blueprint for Neuroscience Research

The Neuroscience Blueprint (http://braininfo.us/blueprint/index.html) is a framework to enhance cooperation among the 16 NIH Institutes and Centers (ICs) that support research on the nervous system. In the second year of funding (FY 2006), Blueprint funds were used to both expand existing activities and create new tools and resources and to support the following initiatives:

- Neuroscience Blueprint Interdisciplinary Center Core Grants
  Forty applications were received in response to this initiative and were reviewed in April. Awards will support centralized resources and facilities shared by neuroscience investigators. Each center will comprise one or more research cores. The applicant institutions are both geographically and scientifically diverse, and many applications include multiple institutions in their plans. Three centers may be funded with the set-aside funds.
- New Ways to Image Neural Activity
  This initiative addresses the need to visualize neural activity with higher spatial and temporal resolution than is currently possible. Twenty-nine applications were submitted, 14 R21s and 15 R01s, which were reviewed in April 2006.
- Clearinghouse for Neuroimaging Software and Data
  Many neuroimaging tools and databases are underutilized, because they are not user-friendly or easy to adopt. This initiative will establish a clearinghouse for neuroimaging tools, vocabularies, and databases to facilitate the dissemination of these resources and the discussion of needs and limitations. It will initially focus on functional magnetic resonance imaging (fMRI). The Small Business Administration has limited competition to small businesses. The Request for Proposals (RFP) was released March 28, 2006, with proposals due in May.

- Neuromouse
  Neuromouse includes two initiatives. The first initiative, entitled "Development of Recombinase-Expressing ('Driver') Mouse Lines for Studying the Nervous System," solicited applications to design, generate, and validate "driver" mouse lines that can be used to study gene functions in distinct cell types and/or useful temporal and spatial patterns in the nervous system. The second initiative supports the distribution ("repatriation") of existing mouse lines to the scientific community.

  Since the first RFA was released, 16 applications were received and evaluated in March. In addition, four supplement applications were received and reviewed by program staff (including four members of the Neuromouse project team). Funding recommendations for two of these were decided following administrative review; payment decisions are scheduled to go before the National Center for Research Resources Council for approval in May. The list of mice to be selected will be circulated within the Neuromouse project team for final approval before being provided to the funded repositories, who will then work to import those lines with high priority.

- Development of the NIH Toolbox for Assessment of Neurological and Behavioral Function
  Many studies collect data on cognitive, sensory, and/or motor aspects of neural function, but there is little uniformity among the measures used. Thus, it is very difficult to draw comparisons or compile data across studies that use unique assessment batteries. This initiative will use the contract mechanism to solicit development of a set of neurological and behavioral measurements appropriate for a variety of project types, particularly longitudinal epidemiologic studies and prevention or intervention trials. The RFP was issued in March 2006 with a deadline for proposals on May 15, 2006. The contract will be awarded by late September 2006.

- Training Initiatives
  These initiatives were developed to ensure the training of a new generation of neuroscientists in translational research, computational neuroscience, and neuroimaging. All FY06 training initiatives have been released. "Training in Translational Research in Neurobiology of Disease" (http://grants.nih.gov/grants/guide/rfa-files/RFA-DA-06-008.html) had a receipt date of February 22, 2006; thirteen applications were received. "Training in Computational Neuroscience: From Biology to Model and Back Again" (http://grants.nih.gov/grants/guide/rfa-files/RFA-DA-06-010.html) and "Training in Neuroimaging: Integrating First Principles and Applications" (http://grants.nih.gov/grants/guide/rfa-files/RFA-DA-06-011.html) both had a receipt date of March 13, 2006.

NIMH Update

Update on Electronic Submission

In April 2006, NIH converted to electronic grant application submission on the SF 424 (Research and Related) forms for Small Business applications (SBIR/STTR), conference grant applications (R13/U13), the dissertation grant program (R36), the Academic Research Enhancement Award (AREA, R15), and the Biomedical Research Support Shared Instrumentation Grant (S10). The

next large scale conversion will occur on June 1, 2006, when all Small Grant (R03), Exploratory/Developmental (R21), and Clinical Trial Planning (Clinical Exploratory/Developmental for NIMH, R34) applications must be submitted electronically. Please see http://era.nih.gov/ElectronicReceipt/index.htm for further details.

Two major changes that were recently announced are that the conversion of R01s to electronic submission has been delayed from October 1, 2006, to February 1, 2007, and that the submission time has changed from 8:00 p.m. Eastern time to 5:00 p.m. local time (of the applicant institution/organization) on the submission date listed in the announcement.

Another significant change is NIH's announcement that the Program Director/Principal Investigator (PD/PI) signature on a grant application has been replaced with an institutional compliance requirement, allowing NIH to simplify the eRA Commons verification process. As of May 10, 2006, NIH no longer requires the verification of grant applications by the institutional signing official and the PD/PI. The previously required verification step is now replaced by a two-business-day period for checking the assembled application in the eRA Commons, after which the submission process is complete. The two-day period will allow PD/PIs and their institutional official to reject an application and submit a corrected application Please see http://grants.nih.gov/grants/guide/notice-files/NOT-OD-06-055.html for further details.

Additional interim changes to PHS398 applications and PHS2590 progress reports, in addition to changes in instructions for SF424 forms, are described on the following web pages, respectively:
http://grants.nih.gov/grants/guide/notice-files/NOT-OD-06-056.html
http://grants.nih.gov/grants/guide/notice-files/NOT-OD-06-058.html
http://grants.nih.gov/grants/guide/notice-files/NOT-OD-06-057.html

Division of Extramural Activities (DEA) Review Branch
The Branch convened a cross-Institute committee, over Summer 2005, to make a recommendation regarding the optimal split of two large NIMH standing committees—the Interventions Research Review Committee (ITV) and the Services Research Review Committee (SRV). The final recommendation for a five-committee structure was presented to and endorsed by Council at its September 2005 meeting. Five new standing subcommittees under the NIMH Initial Review Group were recently chartered and will hold their inaugural meetings in June:

- Interventions Committee for Adult Mood and Anxiety Disorders (ITMA)
  David Sommers, Scientific Review Administrator
  The ITMA has primary responsibility for the scientific merit review of applications concerned with the development and clinical trials of pharmacotherapeutic, psychotherapeutic, and combination treatments as applied to mood and anxiety disorders and related mental health problems.

- Interventions Committee for Schizophrenia Spectrum Disorders, Personality Disorders, and Disorders of Late Life (ITSP)
  Tracy Waldeck, Scientific Review Administrator
  The ITSP Committee has primary responsibility for the scientific merit review of applications concerned with clinical trials of pharmacotherapeutic, psychotherapeutic, and combination treatments as applied to schizophrenia spectrum disorders, personality disorders, and disorders of late life.

- Interventions Committee for Disorders Involving Children and Their Families (ITVC)
  Christopher Sarampote, Scientific Review Administrator
  The ITVC has primary responsibility for the scientific merit review of applications concerned with clinical trials of pharmacotherapeutic, psychotherapeutic and combination treatments as applied to a range of disorders occurring in children.
- Mental Health Services in MH Specialty Settings (SRSP)
  Marina Broitman, Scientific Review Administrator
  The SRSP Committee has primary responsibility for the scientific merit review of applications concerned with clinical services and service systems, such as innovative service delivery systems; studies at the interface of service and interventions, such as studies of treatment guidelines and practice patterns; and policy, cost, and dissemination research, especially assessing service sites that are considered specialty mental health settings, such as mental health clinics, psychiatric hospitals, rehabilitation/reintegration, and mental health-related departments in institutions.
- Mental Health Services in Non-Specialty Settings (SRNS)
  Aileen Schulte, Scientific Review Administrator
  The SRNS has primary responsibility for the scientific merit review of applications that focus on clinical services and service systems, such as innovative service delivery systems; studies at the interface of service and interventions, such as studies of treatment guidelines and practice patterns; and policy, cost, and dissemination research, especially assessing service sites that are considered non-specialty mental health settings, such as primary or specialist medical care, schools, child welfare agencies, criminal justice settings, shelters, and other social service agencies where the primary focus of care is not mental health.

Science of Note

Studies Offer New Information About Treatment Choices for Schizophrenia
Results of the second phase of CATIE—Clinical Antipsychotic Trials of Intervention Effectiveness—can help the 2.4 million U.S. adults with chronic schizophrenia and their doctors determine what to do next when patients need to change medications—a common occurrence in treating schizophrenia. The national clinical trial compared clozapine (Clozaril®) with other new-generation antipsychotic medications for treatment of chronic schizophrenia and showed that people who switched to clozapine were twice as likely to continue treatment as were patients who switched to other antipsychotic medications. However, not all patients can or want to take clozapine, because it may cause serious side effects in some people and requires close monitoring. A companion study found that among people who switched to new-generation antipsychotic medications other than clozapine, those who took olanzapine (Zyprexa®) or risperidone (Risperdal®) continued taking their medication longer than people taking quetiapine (Seroquel®) or ziprasidone (Geodon®). Patients in this companion study had stopped taking their first prescribed medication because of side effects or because they told their doctors they wanted to change medications. Future CATIE reports will address topics such as cost-effectiveness, quality of life, and predictors of response, and will provide a more detailed picture of the interaction between patient characteristics, medications, and outcomes.

McEvoy JP, Lieberman JA, Stroup TS, Davis SM, Meltzer HY, Rosenheck RA, Swartz, MS, Perkins DO, Keefe RSE, Davis CE, Severe J, Hsiao JK, CATIE Investigators. Effectiveness of clozapine versus olanzapine, quetiapine, and risperidone in patients with chronic schizophrenia who did not respond to prior atypical antipsychotic treatment. Am J Psychiatry. 2006 Apr;163(4): 600-610.

Stroup TS, Lieberman JA, McEvoy JP, Swartz MS, Davis SM, Rosenheck RA, Perkins DO, Keefe RSE, Davis CE, Severe J, Hsiao JK, CATIE Investigators. Effectiveness of olanzapine, quetiapine, risperidone, and ziprasidone in patients with chronic schizophrenia following discontinuation of a previous atypical antipsychotic. Am J Psychiatry. 2006 Apr;163(4): 611-622.

New Strategies Help Depressed Patients Become Symptom-Free

Results of the nation's largest depression study show that one in three depressed patients who previously did not achieve remission using an antidepressant became symptom-free with the help of an additional medication, and one in four achieved remission after switching to a different antidepressant. The four-part Sequenced Treatment Alternatives to Relieve Depression (STAR*D) project is the first to examine effectiveness of different treatment strategies for patients who did not become symptom-free after their initial medication, and provides treatment options for mental health clinicians and the millions of Americans who struggle with treatment-resistant depression. STAR*D participants were initially treated with selective serotonin reuptake inhibitor (SSRI) citalopram (Celexa®), a commonly prescribed antidepressant, for 14 weeks. If they did not achieve remission, then participants were offered several other treatment choices, including switching to sertraline (Zoloft®), bupropion-SR (Wellbutrin®), or venlafaxine-XR (Effexor®); or augmenting their citalopram regimen with the addition of buspirone (Buspar®) or bupropion-SR. Further research may help customize treatment to individual patients. Results from levels 3 and 4 of the STAR*D trial will be published later this year.

*Trivedi MH, Fava M, Wisniewski SR, Thase ME, Quitkin F, Warden D, Ritz L, Nierenberg AA, Lebowitz BD, Biggs MM, Luther JF, Shores-Wilson K, Rush AJ, STAR*D Study Team. Medication augmentation after the failure of SSRIs for depression. N Engl J Med. 2006 Mar 23;354(12):1243-52.*

Gene Influences Antidepressant Response

A genetic analysis of response rates in the STAR*D study demonstrates a potential role for genes in predicting who will respond to medication. The HTR2A gene, which encodes the serotonin 2A receptor, has a variation that appears to be associated with treatment response. In screening 1,953 participants treated with citalopram, researchers found that patients with one version of this gene were 18 percent more likely to have a favorable response. This genetic variation favoring response was six times more prevalent in Caucasian than in African American patients. The findings add to evidence that the serotonin receptor plays a pivotal role in the mechanism of antidepressant action. Discovering different genetic and other variations that predispose people to depression helps in the search for treatments that can be individualized to each patient's needs.

McMahon FJ, Buervenich S, Charney D, Lipsky R, Rush AJ, Wilson AF, Sorant AJ, Papanicolaou GJ, Laje G, Fava M, Trivedi MH, Wisniewski SR, Manji H. Variation in the gene encoding the serotonin 2A receptor is associated with outcome of antidepressant treatment. Am J Hum Genet. 2006 May;78(5):804-14.

Depression Rates Are Lower in Children Whose Mothers Are Successfully Treated

When women treated for depression become symptom-free, their children are less likely to be diagnosed with depression, anxiety or disruptive disorders, according to a recent study. The study, called STAR*D-Child (part of the STAR*D study that includes adults), alerts health professionals and patients of the need to vigorously treat depressed mothers and to evaluate their

children for symptoms. Children of mothers who achieved remission of symptoms in this study had an 11 percent drop in diagnosis of depression. There was an 8 percent increase in diagnosis of depression among children whose depressed mothers did not become symptom-free. STAR*D-Child examined 151 mother-child pairs, including children 7-to-17 years old, in 19 clinical settings across the country. The researchers will continue to follow the children for a year after their mothers are in remission, or for two years if their mothers are not in remission.
*Weissman MM, Pilowsky DJ, Wickramaratne PJ, Talati A, Wisniewski SR, Fava M, Hughes CW, Garber J, Malloy E, King CA, Cerda G, Sood AB, Alpert JE, Trivedi MH, Rush AJ, STAR*D-Child Team. Remissions in maternal depression and child psychopathology. JAMA. 2006 March; 295(12):1389-1398.*

Maintenance Treatment Prevents Depression Recurrence in Older Adults
People age 70 and older who continued taking the antidepressant that helped them recover from their first episode of depression were 60 percent less likely to have a recurrence during a two-year study than were those who stopped taking the medication. The study, by Charles Reynolds III and colleagues at the University of Pittsburgh, addresses a major controversy over the benefits and risks of administering long-term antidepressant treatment to elderly patients who have only one lifetime occurrence of major depression. To date, the consensus has been that older patients having their first episode of depression should be treated to full remission, and continue treatment for 6 to 12 months. However, this study demonstrates the benefits of keeping older patients on an antidepressant medication long after they become symptom-free. A form of psychotherapy that focuses on interpersonal relationships did not appear to reduce recurrences in this population. Patients who also had multiple physical illnesses benefited from an antidepressant, but not as much as those without such illnesses.
Reynolds CF 3rd, Dew MA, Pollock BG, Mulsant BH, Frank E, Miller MD, Houck PR, Mazumdar S, Butters MA, Stack JA, Schlernitzauer MA, Whyte EM, Gildengers A, Karp J, Lenze E, Szanto K, Bensasi S, Kupfer DJ. Maintenance treatment of major depression in old age. N Engl J Med. 2006 Mar 16;354(11):1130-8.

Stopping Antidepressant Use While Pregnant May Pose Risks
Pregnant women who discontinue antidepressant medications may be five times more likely to have episodes of depression during pregnancy than those who continue use of these medications. Contrary to the belief that hormonal changes shield pregnant women from depression, a recent study led by Lee Cohen at Massachusetts General Hospital demonstrated that pregnancy itself is not protective. Of the pregnant women who stopped taking antidepressants, 68 percent relapsed during pregnancy, compared to the 26 percent who relapsed despite continued antidepressant use. The results demonstrate the importance of women discussing with their physicians the risks and benefits of continuing antidepressant use during pregnancy.
Cohen LS, Altshuler LL, Harlow BL, Nonacs R, Newport DJ, Viguera AC, Suri R, Burt VK, Hendrick V, Reminick AM, Loughead A, Vitonis AF, Stowe ZN. Relapse of major depression during pregnancy in women who maintain or discontinue antidepressant treatment. JAMA. 2006 Feb 1;295(5):499-507.

ADHD Medication Use Among U.S. Children Held Steady in Recent Years
Results of a study by NIMH and the Agency for Healthcare Research and Quality (AHRQ) indicate that prevalence of stimulant use among U.S. children for treating symptoms of attention deficit hyperactivity disorder (ADHD) remained relatively constant between 1997 and 2002. Data from the Medical Expenditure Panel Survey, which included more than 7,000 children in each of the five years of the study, showed that stimulant use among U.S. children ages 18 and younger had increased sharply from 0.6 percent in 1987 to 2.7 percent in 1997. By 2002, however, use had dropped to 2.9 percent, with rates highest among 6- to 12-year-olds (4.8

percent) and lowest and most stable among children under 6 years old (0.3 percent), countering fears that preschoolers' use of ADHD medications is escalating. Use continued to be more prevalent among white male children, although rates in black children increased, and was more prevalent in the South and Midwest than in the Northeast and West. Income, type of health insurance, and living in an urban or rural setting did not affect the overall rate, although those without health insurance were much less likely to use stimulant medication. Children identified as "functionally impaired" by their disorder were much more likely to take stimulants than children not characterized as such.

Zuvekas SH, Vitiello B, Norquist GS. Recent trends in stimulant medication use among U.S. children. Am J Psychiatry. 2006 Apr;163(4):579-85.

Significant Prevalence of ADHD Symptoms Among Adults

A survey tracking prevalence of ADHD symptoms found that an estimated 4.4 percent of U.S. adults ages 18-44 have symptoms and some disability. The National Comorbidity Survey Replication (NCS-R) is part of a NIMH-supported series, conducted by Harvard Medical School, assessing mental health in English-speaking residents age 18 or older. The results raise awareness that many children who have ADHD may continue to have symptoms as adults, indicating the need for long-term follow-up. Symptomatic adults in this survey were more likely to be divorced, white males who were unemployed or unable to work and to have problems with substance abuse. The study also showed that of people with ADHD treated for other mental disorders or substance abuse, which frequently co-occur with ADHD, a smaller proportion receive treatment for ADHD itself. Symptoms of ADHD tend to be more varied and subtler in adults than in children, suggesting that clinicians may need to consider a wider variety of symptoms for assessing adults. Until biomarkers are identified that will enable clinicians to differentiate between ADHD and other conditions with similar symptoms, diagnosis must depend on careful, comprehensive clinical evaluation.

Kessler RC, Adler L, Barkley R, Biederman J, Conners CK, Demler O, Faraone SV, Greenhill LL, Howes MJ, Secnik K, Spencer T, Ustun TB, Walters EE, Zaslavsky AM. The prevalence and correlates of adult ADHD in the United States: results from the National Comorbidity Survey Replication. Am J Psychiatry. 2006 Apr;163(4): 716-723.

Behavioral Health Care Coverage Does Not Increase Insurance Costs

In 1999, President Clinton ordered equal coverage for mental health and substance abuse services as provided for physical illness in the Federal Employee Health Benefits Program (FEHB), as well as an evaluation of this program to inform Federal policy. This evaluation of parity was a large-scale research project jointly funded by NIMH, the National Institute on Drug Abuse (NIDA), the Department of Health and Human Services' Assistant Secretary for Planning and Evaluation, the Substance Abuse and Mental Health Services Administration (SAMHSA), the Centers for Medicare and Medicaid Services (CMS), and AHRQ. The research team assessed seven FEHB plans for benefits, enrollment, and claims over four years, from 1999-2002, including two years before and two years after the implementation of parity. In addition, these plans were compared against a matched dataset of health plans that did not have parity. Overall, data from a random sample of 20,000 enrollees per plan were analyzed. The researchers found similar increases in mental health service use and spending in both FEHB and non-FEHB plans, indicating that increases in cost were not related to parity requirements. In addition, the researchers concluded that, with management of care, providing equal mental health and substance abuse coverage can improve insurance protections without raising costs.

Goldman HH, Frank RG, Burnam MA, Huskamp HA, Ridgely MS, Normand SL, Young AS, Barry CL, Azzone V, Busch AB, Azrin ST, Moran G, Lichtenstein C, Blasinsky M. Behavioral health insurance parity for federal employees. N Engl J Med. 2006 Mar 30;354(13):1378-86.

Characteristics, Short Term Outcomes of Pediatric Bipolar Disorder Defined in New Study

Recent findings from the multi-site Course and Outcome of Bipolar Illness in Youth (COBY) study, conducted by Boris Birmaher and colleagues at the University of Pittsburg, are helping to shape the understanding of three major subtypes of bipolar disorder that affect children and adolescents and how this diagnosis might affect them as adults. Bipolar disorder (BP) appears to affect children and adolescents more severely than adults, with serious implications for the children's emotional, cognitive, and social development. Children had longer symptomatic stages and more frequent changes from one mood to another or mixed episodes than those previously reported in adults. Children and adolescents also converted from a less severe to a more severe form of BP at a much higher rate. The COBY study is the largest trial of its kind, involving 263 children and adolescents, ages 7-17. Future reports will cover characteristics of BP in children and adolescents, longer-term disease progression, factors predictive of outcome, and effects of different treatments. Understanding the effects of BP early in life may lead to better treatments and improve long-term outcomes as these children and adolescents become adults.

Birmaher B, Axelson D, Strober M, Gill MK, Valeri S, Chiappetta L, Ryan N, Leonard H, Hunt J, Iyengar S, Keller M. Clinical course of children and adolescents with bipolar spectrum disorders. Arch Gen Psychiatry. 2006 February; 63:175-183.

Brain MRI Predicts Depressed Patients' Response to Cognitive Behavioral Therapy

Levels of reactivity in two areas of the brain after unmedicated people with unipolar depression were shown negative words predicted which of them would benefit from cognitive behavioral therapy (CBT), a small fMRI study has shown. Researchers led by Greg Siegle at the University of Pittsburgh found that among 14 depressed patients, those who showed low levels of sustained reactivity in the brain's subgenual cingulate cortex and high levels in the amygdala before CBT had the most improvement in depression after 12 weeks of therapy. Patients with depression sometimes try a number of treatments, including other therapies and medications that take weeks to show if a beneficial effect is emerging, before finding the right one. CBT is a common treatment, but isn't effective for everyone, with a success rate of 40 to 60 percent of patients. The new finding may help determine which patients are likely to benefit from CBT and which are not, avoiding the need for trial and error in many cases.

Siegle GJ, Carter CS, Thase ME. Use of fMRI to predict recovery from unipolar depression with cognitive behavior therapy. Am J Psychiatry. 2006 Apr; 163:735-738.

Aggression-Related Gene Weakens Brain's Impulse Control Circuits

A version of a gene previously linked to impulsive violence appears to weaken brain circuits that regulate impulses, emotional memory, and thinking in humans. Functional and structural MRI brain scans of 97 healthy subjects with no history of violence revealed that people with this version ("L"), especially males, tended to have relatively smaller emotion-related brain structures, a hyperactive alarm center, and under-active impulse-control circuitry. A team of NIMH researchers led by Andreas Meyer-Lindenberg identified neural mechanisms by which this gene likely contributes to risk for violent and impulsive behavior through effects on the developing brain. The gene is one of two common versions that code for the enzyme monoamine oxidase-A, which breaks down key mood-regulating chemical messengers, most notably serotonin. By itself, the gene variant is likely to contribute only a small amount of risk (of violent

behavior) in interaction with other genetic and psychosocial influences. Studying its effects in a large, normal population enables scientists to see how it may predispose the brain to impulsive, aggressive behavior.

Meyer-Lindenberg A, Buckholtz JW, Kolachana B, Hariri AR, Pezawas L, Blasi G, Wabnitz A, Honea R, Verchinski B, Callicott JH, Egan M, Mattay V, Weinberger DR. Neural mechanisms of genetic risk for impulsivity and violence in humans. Proc Natl Acad Sci U S A. 2006 Apr 18;103(16):6269-74.

Cortex Matures Faster in Youth with Highest IQ

Youth with superior IQ are distinguished by how fast the thinking part of their brains thickens and thins as they grow up, according to a recent study by Philip Shaw, Jay Giedd, and fellow NIMH researchers. MRI scans showed that their brains' outer mantle, or cortex, thickens more rapidly during childhood, reaching its peak later than in their peers, perhaps reflecting a longer developmental window for high-level thinking circuitry. It also thins faster during the late teens, likely due to withering of unused neural connections as the brain streamlines its operations. Past studies have shown that people with higher IQs do not have larger brains. This study, which followed the same 307 children and teens, ages 5-19, as they grew up suggests that the way the brain develops may account for the difference. The relationship between cortex thickness and IQ varied with age, particularly in the prefrontal cortex, seat of abstract reasoning, planning, and other "executive" functions.

Shaw P, Greenstein D, Lerch J, Clasen L, Lenroot R, Gogtay N, Evans A, Rapoport J, Giedd J. Intellectual ability and cortical development in children and adolescents. Nature. 2006 Mar 30;440(7084):676-9.

Lithium Blocks Enzyme to Help Cells' Clocks Keep On Tickin'

NIMH-funded researchers have discovered how the medication lithium (Eskalith®) likely fixes body clocks gone awry, stabilizing sleep-wake cycles and other disturbances in daily rhythms and mood that are common in bipolar disorder. For the body's internal, intracellular clock to work properly, clock genes must turn on and off in synchronized, rhythmic, feedback loops—a process that probably is upset in bipolar disorder. Using cultured cells, researchers led by Lei Yin and Peter Klein at the University of Pennsylvania showed that lithium triggers a critical step in synchronizing the rhythmic activities of the clock genes, which produce proteins, including enzymes. Lithium inhibited the enzyme GSK-3ß, causing the receptor Rev-erbα (a protein) to degrade, leading to the rhythmic activation of the protein Bmal1, which starts the clock cycle. The results reveal a pathway by which lithium may act to restore daily rhythms in bipolar disorder and suggest the potential utility of treatments that alter Rev-erbα degradation.

Yin L, Wang J, Klein PS, Lazar MA. Nuclear receptor Rev-erbα is a critical lithium-sensitive component of the circadian clock. Science. 2006 Feb 17;311(5763):1002–10.

Brain Activity Before an Event Predicts Later Recollection

Studies have shown that patterns of brain activity immediately after perception of an event predict whether the event will be successfully encoded in episodic memory (memory of specific events). Now Michael Rugg, at the University of California at Irvine, in collaboration with the University College London, have shown that patterns of brain activity immediately before perception of the event also predict whether it will be encoded—that the brain can prepare itself to encode new material. The researchers mapped brainwaves using an electroencephalogram (EEG) as participants were given cues regarding words they were about to be shown, then shown the words, and later asked to recall them. The waves indicating preparation to encode were detected primarily over an area of the brain, the prefrontal cortex, known to have a role in memory. These findings help tease apart the many mechanisms that contribute to memory

encoding, and have major implications for how scientists will design and interpret fMRI and EEG studies—valuable tools in memory research. To date, such studies may have assumed that the brainwaves on which they were based reflected only encoding-related brain activity that occurred after stimuli. Scientists now can take into account the brain activity that occurs before stimuli, as well.

Otten LJ, Quayle AH, Akram S, Ditewig TA, Rugg MD. Brain activity before an event predicts later recollection. Nat Neurosci. 2006 Apr;9(4):489-91.

Modulating Mouse Memories of Defeat

The social avoidance behavior that normally develops when an individual repeatedly experiences defeat by a dominant individual disappears when the gene for brain-derived neurotrophic factor (BDNF), a molecule related to memory in a brain circuit for social learning, is missing. Eric Nestler and colleagues at the University of Texas Southwestern Medical Center engineered mice to lack BDNF, which then continued to welcome strangers in spite of repeated social defeat. Unaltered mice subjected to the same hard knocks became confirmed loners, unless the researchers treated them with antidepressants. The results reveal neural mechanisms by which social learning is shaped by social experiences and how antidepressants act in a circuit in the ventral tegmental area of the brain, an area linked to the reward system, pleasure, and incentives. This circuit mediates response to emotionally important environmental stimuli via release of the neurotransmitter dopamine, which is regulated by BDNF. In addition to triggering a depression-like social withdrawal syndrome, repeated defeat by dominant animals leaves a mouse with an enduring "molecular scar" in its brain that could help to explain why depression is so difficult to cure. In mice exposed to this animal model of depression, silencer molecules turned off the gene for BDNF in the hippocampus. By activating a compensatory mechanism (acetylation), the antidepressant imipramine (Tofranil®) temporarily restored the animals' sociability and production of the protein, but it failed to remove the silencers. Targeting this persistent stress-induced scar holds promise for developing new medications for treatment of depression in humans. The results also suggest new strategies for treating mood disorders, such as depression, social phobia, and post-traumatic stress disorder, or other illnesses in which social withdrawal is a prominent symptom.

Berton O, McClung CA, Dileone RJ, Krishnan V, Renthal W, Russo SJ, Graham D, Tsankova NM, Bolanos CA, Rios M, Monteggia LM, Self DW, Nestler EJ. Essential role of BDNF in the mesolimbic dopamine pathway in social defeat stress. Science. 2006 Feb 10;311(5762):864-8.

Tsankova NM, Berton O, Renthal W, Kumar A, Neve RL, Nestler EJ. Sustained hippocampal chromatin regulation in a mouse model of depression and antidepressant action. Nat Neurosci. 2006 Apr;9(4):519-25.

To Store Recent Experiences in Memory, Rats Replay Experiences in Reverse

How nerve cells in the brain encode everyday experiences for later memory retrieval is unknown. Studies have shown that during slow-wave sleep in rats, cells in the hippocampus, a brain structure vital for learning and memory, replay patterns of activity that correspond to specific actions the rat engaged in during the day. This may be a way to strengthen circuits that encode an experience. New research by David Foster and Matthew Wilson, at the Massachusetts Institute of Technology, shows that animals also replay behavior-related sequences of neural activity while awake—but in reverse order than when the behavior occurred. The underlying neural activity patterns emerging from the hippocampus during reverse replay were similar to those during slow-wave sleep, suggesting that the mechanism for consolidating memory is the same during sleep and wakefulness. The replaying of sequences in reverse order of importance

while awake may ensure that the behavior immediately before the desired outcome is encoded more strongly than the behaviors that led up to the outcome. This finding provides novel insights into how learning occurs, how it might be facilitated through rest or sleep, and the mechanisms by which recent experiences are consolidated into memory. In humans, several mental disorders are characterized by learning and memory deficits and are associated with hippocampal abnormalities. Understanding mechanisms that facilitate formation of memory informs the search for ways to relieve the cognitive impairments associated with these disorders.
Foster DJ, Wilson MA. Reverse replay of behavioural sequences in hippocampal place cells during the awake state. Nature. 2006 Mar 30;440(7084):680-3.

Genes on Sex Chromosomes Influence Expression of Social Behavior in Mice
Studies of humans and animals have revealed gender differences in expression of some types of social behaviors. Typically, males are more aggressive and females show more parental behavior. In this study, investigators led by Jessica Gatewood at the University of Virginia separated the gene for male gonadal development from other genes present on the sex chromosomes and "knocked it out," resulting in mice that had female gonads, but otherwise were genetically male and had all of the remaining Y (male) chromosome genes. This enabled the researchers to examine whether gender-related differences in social behavior are driven solely by differences in hormones produced by the gonads, or whether other genes on sex chromosomes play a role. The knockout mice were more similar to intact, unaltered male mice than to female mice in their aggression and parental behavior. This suggests that additional genes on the Y chromosome (that is, other than the gene responsible for gonad development) are important in the determination of sexually differentiated social behavior. Because many mental disorders are characterized by social deficits, understanding the genes involved in social behavior is important in understanding the biological basis of these deficits.
Gatewood JD, Wills A, Shetty S, Xu J, Arnold AP, Burgoyne PS, Rissman EF. Sex chromosome complement and gonadal sex influence aggressive and parental behaviors in mice. J Neurosci. 2006 Feb 22;26(8):2335-2342.

Early Life Experiences Confer Lifetime Lower Stress Response
Increased maternal care following repeated stressors early in life appears to have enduring effects on neuroplasticity, or the ability of the brain to recover or "repair" itself after injury or disease. Kristina Fenoglio and colleagues at the University of California at Irvine showed that changes in the brain circuits regulating adult stress responses induced by daily handling of newborn rat pups are evident by the ninth postnatal day (P9). A single handling of rat pups at P5 or P9 also induced changes in maternal behavior (e.g., increased licking, grooming, and nurturing following the pups' return to the cage) and activation of components of the stress circuitry, including the central nucleus of the amygdala and the bed nucleus of the stria terminalis, in the pups' brains. However, this single handling did not result in the same brain changes that seemed to permanently moderate the stress response in repeatedly handled rats. For example, increases in c-Fos, a useful protein marker for neuronal activity, in the paraventricular nucleus of the thalamus required daily handling from P2-9. Furthermore, the researchers found that by P9, the response to an acute stressor was attenuated in the repeatedly handled rats, an effect which endured into adulthood.
Fenoglio KA, Chen Y, Baram TZ. Neuroplasticity of the hypothalamic-pituitary-adrenal axis early in life requires recurrent recruitment of stress-regulating brain regions. J Neurosci. 2006 Mar 1;26(9):2434-42.

Progress on NIMH Initiatives

Schizophrenia Research Forum & Schizophrenia Bulletin

NIMH's recent move to shift funding from the now-privatized *Schizophrenia Bulletin* to the development of the Schizophrenia Research Forum (SRF) website (http://www.schizophreniaforum.org/) has been proceeding smoothly. William T. Carpenter, Editor-in-Chief of the *Schizophrenia Bulletin*, reports that the journal now has more than 2,000 subscribers and is included in the Oxford University Press block subscriptions to a number of libraries. They are keeping subscription prices low, at $50 for individuals or $35 to SRF members and International Congress of Schizophrenia Researchers or Winter Workshop on Schizophrenia Research attendees. The *Bulletin* has included key meeting reports, such as the Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) pre-clinical and the consensus design for cognition, and has produced every issue on time after careful peer review. So far, the *Bulletin* is averaging 29 days from first submission to first decision and 30 days from revised submission to final decision. They are posting all articles online and have nearly completed posting past issues from 1969 onward. They maintain a good relationship with the SRF, which cross-links websites and also features the *Bulletin* and a selected article every two months with free, online access to all SRF members.

Medicare Part D Prescription Drug Benefit

The new Medicare Part D prescription drug benefit is an important research topic for NIMH-supported researchers, regarding the approximately 5.9 million mentally ill people in the Medicare program, including the 2.2 million mentally disabled dually (Medicare/Medicaid) eligible, who are affected by this section of the Medicare Modernization Act (P.L. 108-173). NIMH organized a Research Coordination Roundtable in December 2005, where preliminary findings were presented from NIMH-supported work using econometric microsimulation models predicting the potential impact of the new drug benefit. A research paper by Nancy Morden and Louis Garrison, titled "Implications of Part D for Mentally Ill Dual Eligibles: A Challenge for Medicare," which was presented at the Third NIMH Pharmacoeconomics Workshop in May 2005 and published in the March/April 2006 issue of *Health Affairs*, was also used for technical assistance. The findings were shared with CMS to assist with the successful implementation of the new Part D prescription drug benefit for the highly vulnerable, mentally disabled population.

NIMH Activities in Response to Gulf Coast Hurricanes

Seven months after the initial storms, NIMH continues to contribute to the national response through communication and outreach via dissemination of information (print, electronic and multi-media) and use of existing partner networks, coordination with researchers both within and outside of the region to organize research for improving preparedness and response, and planning for what is likely to be an enormous public mental health burden in the region.

As of March 2006, three new Rapid Assessment Post Impact of Disaster (RAPID) grants have been awarded, and one supplemental award was issued. These research projects are focused on:

- risk for postpartum psychopathology, infant temperament and development;
- the impact of displacement on youth mental health, social behavior, school adjustment, and family functioning;
- the role of caregiver-child relationship in post-disaster emotional, behavioral, and academic functioning of young children; and

- the problems (e.g., mental health, housing, employment) faced by a broad cross-section of people who resided in New Orleans and other parts of Louisiana, as well as Alabama and Mississippi, as they try to reconstruct their lives.

NIMH also coordinated with SAMHSA for a Gulf Coast meeting. In April 2006, the Center for Evidence-Based Policy, the Milbank Memorial Fund, NIMH, and the Reforming States Group sponsored a two-day meeting to assist impacted state leadership. Discussions focused on identifying existing research results that would be useful in informing state policy makers as they decide the next steps to address the mental health effects of the hurricanes; shaping NIMH research priorities to be useful to the states as they address the mental health effects of the hurricanes and prepare for future such disasters; and considering how best to rebuild and evaluate public mental health programs.

Genetic Association Information Network (GAIN) Initiative

The Foundation for the National Institutes of Health, in conjunction with NIH and Pfizer Global Research & Development, recently launched a unique, public-private, medical research partnership—the Genetic Association Information Network (GAIN)—to unravel the genetic causes of common diseases over the next three years. Their genetic analysis will focus on single nucleotide polymorphisms (SNPs), which normally occur in the DNA sequence that makes up a person's genome. SNPs are like single-letter variations in the spellings of a word. Most of these variations are biologically meaningless, but a small fraction alter the function of a gene—often only slightly. Combining the effects of many slightly altered genes may significantly increase the risk of a specific disease, and finding these disease-causing variants is one of the highest priorities of current biomedical research.

In conjunction with this public-private partnership, NIMH is supportive of advancing whole-genome association studies to identify susceptibility genes for mental disorders. The Institute will consider requests from investigators for annotated samples stored in the Center for Collaborative Genetics Studies (CCGS) for the following diseases of interest to the NIMH mission: autism, Alzheimer's disease, bipolar disorder, depression, and schizophrenia. The CCGS was established by the NIMH Human Genetics Initiative as a national resource, with broad data-sharing requirements, for the genetic study of mental disorders. For more information, please visit http://nimhgenetics.org/.

NIMH Human Genetics Initiative

This initiative was founded on the principle that timely access to primary data and biomaterials for human genetic research may stimulate research and development and maximize the benefits afforded to individuals affected with these disorders and their family members. Progress on these efforts is paralleled by growing interest throughout the scientific community in having timely access to the information and resources that may speed the understanding of disease etiology, refinement of diagnostic systems, and development of novel therapeutic agents and preventive interventions. The sample and data repository at the CCGS contains DNA, cell lines, phenotypic data, clinical information, and genotyping data for a large number of fully consenting individuals with mental disorders as well as controls; the repository samples consist of unrelated cases and controls, trios, sibling pairs, and multiplex families. This initiative will accept applications that focus on one of six mental disorders represented in the center: anorexia nervosa, attention deficit hyperactivity disorder, bipolar disorder, depression, obsessive compulsive disorder, and schizophrenia.

The CCGS sample collection continues to expand, with more than 50,000 samples of patients and controls with associated phenotypes stored in its DNA and cell bank repositories as of April 1, 2006. In the first three months of this year, the repository received 2,557 new samples from existing NIMH-supported projects and has also added four new projects (two autism, one schizophrenia, one bipolar disorder) to the repository. These new projects are expected to begin contributing samples to the repository within six months.

NIMH continues to make samples available to the research community and has granted access to 10 new research projects for sample and data access between January–April 2006. The scientific research community is making wide use of existing samples, demonstrated by the more then 25,000 DNA samples sent by CCGS to investigators between January 1 and April 15, 2006.

NIMH-Administered RFAs

- *Treatment Response: Linking Genes with Behavioral Phenotypes of Relevance to Patients, Families, and Policymakers*
  NIMH is seeking applications that integrate what are currently two distinct tracks of research—determining the complex genetic basis of mental disorders, and creating new strategies and tools for assessing individual functioning in the real world. In combining these two areas of research, the goal is to characterize the relationship between genetic risk and functional abilities. This RFA is being funded under four separate mechanisms: R01, collaborative R01, R03 (small research grant), and R34 (exploratory/developmental clinical trial).
  Release Date: March 9, 2006; Expiration Date: May 12, 2006
  http://grants1.nih.gov/grants/guide/rfa-files/RFA-MH-07-010.html
  http://grants.nih.gov/grants/guide/rfa-files/RFA-MH-07-013.html
  http://grants1.nih.gov/grants/guide/rfa-files/RFA-MH-07-011.html
  http://grants.nih.gov/grants/guide/rfa-files/RFA-MH-07-012.html
  Scientific Program Director: Donna Mayo, PhD, Division of AIDS and Health and Behavior Research (DAHBR), NIMH

- *HIV and Psychiatric Comorbidity Research Project*
  This is a re-issuance of RFA-MH-05-010 from NIMH's Center for Mental Health Research on AIDS, inviting applications that address the cellular, molecular, and genetic factors underlying the high comorbidity between HIV-1 infection and psychiatric disorders. This initiative is being funded under two mechanisms, R01 and R21.
  Release Date: March 30, 2006; Expiration Date: May 27, 2006
  http://grants.nih.gov/grants/guide/rfa-files/RFA-MH-07-020.html
  http://grants.nih.gov/grants/guide/rfa-files/RFA-MH-07-021.html
  Scientific Program Director: Kathy L. Kopnisky, PhD, DAHBR, NIMH

Collaborative RFAs

- *Global Partnerships for Social Science AIDS Research*
  NIMH, the National Institute of Child Health and Human Development (NICHD), and the National Institute on Aging (NIA) are calling for partnerships between U.S. (or other developed country) and non-U.S. scientists that will enhance capabilities for rigorous behavioral and social science research in developing countries affected by the HIV epidemic. Investigators undertaking research in response to this RFA should be mindful of the efforts in their country to develop and implement strategic plans on the national and community levels to address local HIV/AIDS-related challenges and problems.

Release Date: April 13, 2006; Expiration Date: December 14, 2006
http://grants.nih.gov/grants/guide/rfa-files/RFA-HD-06-007.html
Scientific Program Director: Susan F. Newcomer, Demographic and Behavioral Sciences Branch, NICHD

- *Institutional Research Training Programs: Increasing Diversity*
  NIMH, in conjunction with NIDA and the National Institute of Neurological Disorders and Stroke (NINDS), are requesting competing renewal applications from current grant recipients of RFA-MH-01-009, "Institutional Training Programs: Increasing Diversity," funded in 2002. The objective of this RFA is to ensure that a diverse and highly trained workforce is available to assume leadership responsibility related to the Nation's biomedical and behavioral research agenda in the scientific domains of the NIMH, and/or NIDA, and/or NINDS. More specifically, the objective is to support national or regional research training programs that will recruit, train, and retain pre- and/or post-doctoral trainees from underrepresented groups.
  Release Date: March 3, 2006; Expiration Date: May 13, 2006
  http://grants.nih.gov/grants/guide/rfa-files/RFA-MH-07-030.html
  Scientific Program Director: Mark Chavez, PhD, Division of Adult Translational Research & Treatment Development (DATR), NIMH

- *Phase II Comprehensive ICOHRTA-AIDS/TB (International Clinical, Operational and Health Services Research Training Award for AIDS and Tuberculosis)*
  This is a re-issuance of RFA-TW-04-002 and is open to Phase I awardees and their partner institutions. The Fogarty International Center, in conjunction with NIMH, seeks to support research training to strengthen the skills at eligible institutions in low-and middle-income countries; training needed to design and conduct AIDS and TB research for the scale-up of promising interventions to the population and healthcare system level.
  Release Date: February 21, 2006; Expiration Date: May 26, 2006
  http://grants1.nih.gov/grants/guide/rfa-files/RFA-TW-06-005.html
  Scientific Program Director: Jeanne McDermott, CNN, MPH, PhD, Division of International Training and Research, Fogarty International Center

- *Novel HIV Therapies: Integrated Preclinical/Clinical Program*
  This is a re-issuance with modifications of PAR-03-138. The National Institute of Allergies and Infectious Diseases (NIAID) and NIMH are seeking to assist researchers interested in HIV therapeutics development to assemble the diverse scientific expertise and resources needed to translate basic laboratory discoveries to applied entities. In the preclinical area, this RFA seeks research on: (1) the development/validation of new therapeutic targets; and (2) the development and evaluation of small-molecule inhibitors of viral or cellular proteins or pathways critical to HIV replication and/or persistence. In the clinical area, the focus is on iterative bench to bedside research to optimize new therapeutic approaches.
  Release Date: March 1, 2006; Expiration Date: June 24, 2006
  http://grants2.nih.gov/grants/guide/rfa-files/RFA-AI-06-009.html
  Scientific Program Director: Sandra Bridges, PhD, Division of AIDS, NIAID

NIMH Public Outreach

Outreach Partnership Program 7th Annual Conference

The NIMH Outreach Partnership Program, which enlists partners from all 50 states and the District of Columbia in conducting outreach and education to help bridge the gap between

mental health research and clinical practice, held its annual conference in Nashville, Tennessee, in March 2006. This conference provides outreach partners with the opportunity to interact directly with NIMH staff and with each other, and to learn about recent scientific advances and other activities surrounding national mental health issues. It is also an important way for NIMH to receive direct feedback from the community. The conference highlighted two topic areas, "Disasters and Traumatic Events" and the "Mental Health and Criminal Justice Systems." Federal, state, and local experts presented the latest findings, and partners shared their own experiences and activities in these areas. Of note, Council Member Renata J. Henry hosted sessions on (1) working with state mental health program directors and (2) outreach to underserved populations.

NIMH Professional Coalition for Research Progress Annual Meeting
In April 2006, a meeting of the NIMH Professional Coalition for Research Progress, which includes representatives of NIMH's major professional constituency organizations, was convened in Washington, D.C. Attendees heard presentations of ongoing research and new findings in areas that are of particular saliency or that are especially promising. Another critical purpose of the meeting was to provide an opportunity for NIMH to get direct feedback about the priorities, plans, and current directions of the Institute from an important segment of its stakeholders. An update on the Institute highlighted findings and other current activities; speakers focused on translational research. Kerry Ressler spoke on "Reducing Fear: Translational Research on Anxiety Disorders" and Karen Berman spoke on "Translating between Genes, Brain, and Cognition with Neuroimaging: Lessons from Schizophrenia and Williams Syndrome." Ron Finch reported on the recently published "Employer's Guide to Behavioral Health Services." A report from the meeting will be posted on the NIMH website.

Pre-doctoral Research Festival
This year, the Intramural Office of Fellowship Training initiated a long-term post-doctoral recruitment strategy, which entailed sponsoring a reception for extramural training directors and pre-doctoral students at the Annual Meeting of the Society for Neuroscience, held in Washington, D.C. Approximately 350 faculty and graduate students attended the reception. A follow-up event, the NIMH-sponsored National Pre-doctoral Research Festival, will be held on the NIH campus in May 2006. The festival will provide an opportunity for pre-doctoral fellows from across the United States to visit the NIH campus to showcase their talents through oral and poster presentations and learn more about the research being conducted at the NIMH. In addition to the scientific agenda, the students will have the opportunity to meet with current post-doctoral Fellows and faculty in an informal setting. Through these outreach activities, the Intramural Office of Fellowship Training hopes to foster relationships with the extramural training community and facilitate the recruitment of outstanding post-doctoral fellows to the NIMH Division of Intramural Research Programs (DIRP).

Diversity and Outreach Activities
The Intramural Office of Fellowship Training aggressively pursued efforts in outreach to enhance the diversity of the DIRP training program. These efforts included participating in an extramural T32 inter-university training award titled "Alliance for Minority Training in Neuroscience" and providing recruitment talks at the NIMH Career Opportunities in Research Symposium and the annual meeting of the American Psychological Association. In addition,

DIRP representatives attended several national meetings, including the Hispanic Association of Colleges and Universities, Society for the Advancements of Chicanos and Native American in the Sciences, American Psychological Association, Annual Biomedical Research Conference for Minority Students, National Medical Association, National Hispanic Medical Association, and National Medical Student Association. As one indicator of success of these efforts, approximately 38 percent of the participants in this year's Summer Research Program were derived from the under-represented, minority, educational community; and approximately 62 percent of these summer trainees were female. In addition, joint NIH/International K99 Training Programs were developed and memoranda of understanding were officially adopted as a result of meetings with the Training Directors and Embassy Representatives from Germany, Belgium, and France.

News Media Highlights

Media coverage of the STAR*D Level 2 clinical trial results published in the March 22 , 2006, *New England Journal of Medicine* reached more than 46 million people. Nearly 30 major media print and broadcast reporters participated in a teleconference briefing about the treatment-resistant depression study with investigators John Rush, Madhukar Trivedi, and Maurizio Fava. More than 200 print and broadcast organizations carried the story, including *The Washington Post*, *The New York Times*, *Wall Street Journal*, Associated Press, Reuters, NPR, and television's CNN, ABC Nightly News, and NBC Washington D.C. affiliate WRC4.

Research pointing to cingulate Area 25 as pivotal in depression was featured in an article in the *New York Times Magazine*, 4/2/06. NIMH grantee Helen Mayberg and intramural researcher Andreas Meyer-Lindenberg were among the experts interviewed.

Intramural findings linking IQ to the trajectory of cortex maturation in children and adolescents, published in *Nature*, 3/30/06, were covered by nearly all major print and broadcast outlets, scoring at least 263 postings in Google News that day. NIMH's Philip Shaw, Judith Rapoport, and Jay Giedd were widely quoted.

Former NAMHC member Eric Nestler's discoveries of the molecular mechanisms by which social defeat leads to a depression-like syndrome in mice, published in *Science*, 2/10/06, and online in *Nature Neuroscience*, 2/26/06, received wide coverage, including *AP, Newsday, Dallas Morning News,* and *Hartford Courant*.

Having a common version of a serotonin receptor gene was found to boost a patient's odds for responding to an antidepressant by 18 percent, intramural researchers Francis McMahon and Husseini Manji reported online in the 3/8/06 *American Journal of Human Genetics*. The story was covered by *Web MD* and *Science,* among others.

Science, Bloomberg News, and *The New York Times* reported on MRI findings by Andreas Meyer-Lindenberg and Daniel Weinberger that a gene previously linked to impulsive violence weakened brain circuitry for impulse control, reported online in the *Proceedings of the National Academy of Sciences* during the week of 3/20/06.

Research Conferences and Workshops

Developmental and Translational Models of Emotion Regulation and Dysregulation: Links to Childhood Affective Disorders

In April 2006, the Division for Pediatric Translational Research and Treatment Development (DPTR) convened a meeting to (1) review the current state of knowledge on emotion regulation and dysregulation and affective disorders from an interdisciplinary and developmental perspective and (2) discuss areas of agreement, identify gaps and challenges, and lay out directions for research. Separate panel presentations and discussion focused on conceptual/developmental issues for research on emotion and emotion regulation, neural and genetic perspectives, links between dysregulation and affective disorders, developmental precursors of dysregulation from toddlerhood through adolescence, and opportunities for translational work. *For more information, please contact Rebecca DelCarmen-Wiggins at rdelcarm@mail.nih.gov.*

NIMH Workshop for Emerging Research Investigators in Pediatric Mental Health: Making a Successful Transition to Research Career Independence

DPTR, in conjunction with the Division on Services and Intervention Research (DSIR), DAHBR, and the Office of Special Populations (OSP), held this two-day workshop in February 2006, in Rockville, Maryland. The workshop focused on providing emerging research investigators with the resources necessary to initiate and continue upon the path of research independence focused on child and adolescent research. The workshop consisted of plenary, practical, and breakout sessions pertinent to attendee interest. Attendees were also given the opportunity for one-on-one consultation with NIMH Program Officials. To increase the dissemination of information to diverse and special populations, the workshop was taped and archived at http://www.videocast.nih.gov/. *For more information, please contact Courtney Ferrell at cferrell@mail.nih.gov.*

Reward Neurocircuitry in Adolescent Development and Decision Making

DPTR cosponsored this workshop with NICHD, NIDA, and NINDS, held in January 2006, in Bethesda, Maryland. The four sessions addressed current knowledge of the functional neuroanatomy and neurochemistry of reward neurocircuitry in adults, changes in reward circuitry over the course of adolescence, how puberty contributes to or affects these changes, and methodological considerations in designing research to address these questions. A widely interdisciplinary group generated ideas for future research in this area. *For more information, please contact Ann Wagner at awagner@mail.nih.gov.*

2006 NIMH/IAPAC International Conference on HIV Treatment Adherence

In March 2006, in Jersey City, New Jersey, NIMH and the International Association of Physicians in AIDS Care (IAPAC) hosted a state-of-the-science conference to examine strategies to understand and enhance adherence to antiretroviral regimens in a variety of settings. Over 340 health and human service professionals attended the conference, which profiled the most current HIV treatment adherence research, programs, and perspectives from over 20 countries. Due to collaborative partnerships in the conference planning and organization, interdisciplinary attendees included those with memberships in the Association of Nurses in AIDS Care, the Society of Infectious Disease Pharmacists, and HIV treatment providers funded by the HIV/AIDS Bureau of the Health Resources and Services Administration. Other contributing

organizations included the National Association of AIDS Education and Training Centers, the University of Medicine & Dentistry of New Jersey, the Office of AIDS Research at NIH, and NIDA. The goals of the conference were to rapidly translate scientific advances into approaches that can make a difference in real-world settings and to strengthen the dialogue among government agencies, treatment providers, and researchers. *For further information, please contact Christopher Gordon at cgordon1@mail.nih.gov.*

Translational Research: Bridging Basic and Applied Perspectives
In May 2006, DAHBR sponsored this two-day meeting in Rockville, Maryland with the purpose of bringing together scientists whose work has focused on prejudice, stereotyping, discrimination, stigma, and related areas to assist NIMH in identifying (1) the most exciting and timely possibilities for translation and integration across basic and applied approaches, (2) the greatest gaps in knowledge, (3) barriers to conducting this kind of translational research, and (4) ways to overcome these barriers. The meeting was jointly planned and co-chaired by Jennifer Crocker, University of Michigan; Bernice Pescosolido, Indiana University; and Emeline Otey, DAHBR. The impetus for this meeting came from the convergence of recommendations from Federal advisory groups. Reports from two NAMHC workgroups—the Behavioral Science Workgroup's "Translating Behavioral Science into Action" and the Workgroup on Basic Sciences' "Setting Priorities for Basic Brain and Behavioral Science Research at NIMH"—both identified prejudice and stereotyping as highly productive areas of research that are now ripe for a shift in focus to addressing issues of concern to individuals with mental disorders, their families, and their providers. Another report, "Transforming Mental Health Care in America – The Federal Action Agenda: First Steps," is the most recent in a series of compelling reports conveying the urgency of mental health care needs in 21st century America. This report also underscores findings from the earlier Surgeon General's Report on Mental Illness and the White House Conference on Mental Health that the stigma and discrimination associated with mental illness and its treatment have substantial negative impact on the lives of individuals, families, and communities, and must be addressed. The converging recommendations from these two lines of reports suggest the opportunity, if not the imperative, for bringing basic behavioral and social science theories, approaches, and findings on prejudice, stereotyping, and discrimination to bear on efforts to reduce the stigma and discrimination associated with mental illness. *For more information, please contact Emeline Otey at eotey@mail.nih.gov.*

International Society for CNS Clinical Trials and Methodology (ISCTM) Meeting
In February 2006, the ISCTM held this meeting by satellite on the NIMH initiative regarding treatment development for negative symptoms of schizophrenia. Participants discussed the conceptual objectives and implementation of the initiative to date, in addition to the epidemiology and long-term course of negative symptoms. Other topics included the identification and management of psychometric challenges to the assessment of negative symptoms, the neurobiology of negative symptoms, and the Food and Drug Administration's (FDA) perspective on negative symptoms as a clinical target. The meeting allowed broad input from industry and regulatory officials in advance of finalizing the battery. *For more information, please contact Wayne Fenton at wfenton@mail.nih.gov.*

FDA-NIMH Partnership
As part of a broad initiative to enhance NIH/FDA cooperation, NIMH staff from DATR and the Division of Neuroscience and Basic Behavioral Science (DNBBS) met with Janet Woodcock,

Associate Director, FDA, to discuss a future collaboration related to the FDA's Critical Path Initiative to enhance the efficiency of the drug development process. An FDA-NIMH Critical Path Committee was formed and Doug Meinecke was asked to serve as the NIMH lead on this effort. *For more information, please contact Doug Meinecke at dmeineck@mail.nih.gov.*

Treating Children and Adolescents with Depression: What We Know, What Else We Need to Know Through Research

In February 2006, NIMH hosted this two-day workshop with the purpose of reviewing the evidence for benefits and risks of existing treatment interventions for youths suffering from depression, identifying knowledge gaps in need of further research, and discussing approaches to future research with respect to design, methods, and implementation. The workshop was organized by DSIR and DPTR and gathered researchers in psychotherapies, psychopharmacology, clinical neuroscience, clinical trial methodology and design, and patient advocates. Among the main topics of discussion were: a) the need to develop evidence-based treatment algorithms for youths with depression by integrating the effective interventions into validated sequential approaches; b) the importance of studying how to individualize treatment by matching intervention to patient and illness characteristics; and c) the heterogeneity of the current construct of major depressive disorder and consequent need to identify more homogeneous and clinically valid subtypes to be more effectively targeted by treatment. *For more information, please contact Ben Vitiello at bvitiell@mail.nih.gov.*

Indigenous Suicide Prevention Research & Programs in Canada and the United States: Setting a Collaborative Agenda

This bi-national conference, held in Albuquerque, New Mexico, in February, brought together representatives from research, service, community programs, and governments (across a range of countries, tribes, and villages) from Canada, the U.S., and U.S. Territories to illuminate the current state of knowledge across indigenous people and to foster collaborative efforts to address suicide. While suicide rates of young, indigenous males are among the highest in the U.S. and Canada, the rates vary dramatically across communities. Conference attendees were synergistically engaged to better understand what research efforts, from the communities' perspectives, need to take place to better address this tragic health disparity. Health Canada and the Canadian Institute of Health Research (CIHR) supported attendance of a Canadian delegation. NIMH (Suicide Research Team) took a lead role in planning the meeting in collaboration with the Indian Health Service, Health Canada and CIHR, and SAMHSA. In addition, the following agencies provided additional meeting support: NIH Office of Rare Diseases, NIDA, National Institute on Alcohol Abuse and Alcoholism, Office of Research on Women's Health, Office of Behavioral and Social Sciences Research, and the National Library of Medicine. *For more information, please contact Jane Pearson at jpearson@mail.nih.gov.*

Meeting-based Publications

Depression and Cognitive Impairment in Late Life

The public health implications of depression and cognitive impairment in late life are enormous. While both late life depression and cognitive impairment short of dementia have been receiving increasing research as well as clinical attention in recent years, these investigations appear to be proceeding along two separate tracks. The meeting, "Perspectives on Depression, Mild Cognitive Impairment, and Cognitive Decline," was organized by NIMH in November 2003 to examine

how researchers might better integrate the varied perspectives on associations among depression, mild cognitive impairment, and cognitive decline. A recently published report of this meeting presents the recommendations from participants for achieving this integration.
Steffens DC, Otey E, Alexopoulos GS, Butters MA, Cuthbert B, Ganguli M, Geda YE, Hendrie HC, Krishnan RR, Kumar A, Lopez OL, Lyketsos CG, Mast BT, Morris JC, Norton MC, Peavy GM, Petersen RC, Reynolds CF, Salloway S, Welsh-Bohmer KA, Yesavage J. Perspectives on depression, mild cognitive impairment, and cognitive decline. Arch Gen Psychiatry. 2006 Feb;63(2):130-8.

MATRICS Neurocognitive Battery
As a product of the MATRICS initiative, the final version of the MATRICS Neurocognitive Battery, created with broad input from academic, industry, and regulatory scientists, was published and is now available through the catalogs of several psychological testing publishers. The FDA has accepted the MATRICS Executive Summary representing guidance for the design of studies to assess pharmacological interventions for cognition in schizophrenia previously reviewed and approved by the NAMHC. *For more information, please contact Wayne Fenton at wfenton@mail.nih.gov.*

Staff Publications

Recognizing that stigma is a major barrier to effective mental health care, Wayne Fenton and Emeline Otey oversaw the team that, along with the NIH Office of Education, developed a five-day middle school curriculum called "**The Science of Mental Illness**," accessible online in March 2006 and available for free distribution to school systems throughout the United States. They integrated a measure of stigma attitudes into the field testing of this curriculum with more than 1,300 middle school students, adding value to the project by generating research demonstrating its impact on both knowledge and stigma reduction. For more information, please visit http://science.education.nih.gov/supplements/nih5/mental/default.htm , or link to the curriculum by going to the "Highlights" section of the NIMH home page, at http://www.nimh.nih.gov/.

Budget

The FY 2007 President's Budget Request for the NIH was submitted to the Congress on February 6, 2006. If approved by the Congress, this request would provide a total NIH program level of $28,587 million, the same amount as the FY 2006 program level (see Attachment 1). Highlights of the total NIH request include:

- NIH Research Project Grants (RPGs)
  The FY 2007 President's Budget would support an estimated 9,337 competing RPGs at the NIH, an increase of 275 RPGs over the FY 2006 amount of 9,062. The President's Budget Request proposes to hold the average cost of competing RPGs at the FY 2006 level, while also allowing no inflationary increases for direct, recurring costs in noncompeting continuation RPGs.
- NIH National Research Service Award (NRSA) Research Training
  In the FY 2007 Request for NIH, stipends for trainees supported by NRSA will remain at FY 2006 levels. No increases are provided for other components of the NRSA training programs, such as tuition or health benefits.

- Intramural Research
  Funding for each Institute's Intramural Research Program will be decreased by –0.5 percent from FY 2006.
- Research Management and Support (RMS)
  RMS funds support the headquarters and extramural program support activities of each NIH Institute. Funding for RMS in FY 2007 at each Institute will receive an increase of +1.5 percent
- NIH Biodefense-Related Research
  NIH biodefense-related research increases from $1,781 million in FY 2006 to $1,891 million in FY 2007. This is an increase of $110 million or +6.2 percent.
- NIH Roadmap for Medical Research
  In FY 2007, NIH will direct $443 million toward the roadmap initiatives, an increase of $113 million or +34 percent over the FY 2006 level of $330 million. Of this total amount, $111 million will be provided by the NIH Director's Discretionary Fund (DDF) and the remaining $332 million will be provided by the ICs. The IC contribution of support for these trans-NIH research goals is estimated to be 1.2 percent of each individual IC's total request for FY 2007.
- NIH Blueprint for Neuroscience Research
  Spending for NIH Blueprint initiatives by the 15 participating ICs will increase from $25 million in FY 2006 to $33 million in FY 2007.

The FY 2007 request of $1,395 million for the NIMH is a decrease of $9 million or –0.6 percent below FY 2006.

- At the FY 2007 President's Budget level, the NIMH would support an estimated 2,185 total RPGs compared to 2,175 total RPGs in FY 2006. Approximately 614 of the 2,185 grants to be funded in FY 2007 will be competing awards, either new or renewal. This compares to an estimated 550 in FY 2006 and 569 in FY 2005.
- The NIMH success rate for RPGs in FY 2007 would be about 21 percent, compared to an NIH average of about 19 percent.
- The NIMH budget request includes funding for two new NIH-wide initiatives in FY 2007:
  - $0.9 million will be used to support 10 awards for the new K/R "Pathways to Independence" program to provide increased support for new investigators, and
  - NIMH will contribute $2.1 million toward the $40 million that NIH will invest in the new Genes, Health, and Environment Initiative to accelerate the discovery of major genetic factors for diseases that have a substantial public health impact.
- The budget will support an estimated 1,387 full-time equivalent NRSA research trainees, a decrease of 6 trainees from FY 2006.
- The FY 2007 President's Budget Request provides no additional funding toward completion of the John Edward Porter Neuroscience Research Center on the NIH campus.

NIMH actual expenditures by budget mechanism for FY 2005 and estimates for FY 2006 and 2007 are displayed in Attachment 2.

Major Awards for NIMH Grantees

In April 2006, the National Academy of Sciences, a private organization of scientists and engineers that "acts as an official adviser to the Federal government, upon request, in any matter of science or technology," elected to membership the following former and current grantees:

- **Wolfhard Almers, PhD**, Senior Scientist, Vollum Institute and Professor of Biochemistry, Oregon Health Sciences University
- **Rochel Gelman, PhD**, Professor of Psychology, Rutgers University (former grantee)

The American Academy of Arts & Sciences selects "the finest minds and most influential leaders from each generation" for membership. In April, the Academy announced the election of 195 new members, including the following former and current NIMH grantees:

- **Laurence Abbott, PhD**, Professor of Physiology and Cellular Biophysics, Columbia University
  (NIMH R01 and 2004 NIH Director's Pioneer Awardee)
- **William T. Greenough, PhD**, Director, Center of Advanced Study, Beckman Institute, University of Illinois at Urbana-Champaign
  (NIMH R01: 1983-present)
- **Reid Hastie, PhD**, Professor, Graduate School of Business and the Department of Psychology, University of Chicago
  (NIMH R01: 1999-2002)
- **E. Tory Higgins, PhD**, Stanley Schachter Professor of Psychology, Columbia University
  (NIMH R01:1990-present)
- **Rachel Keen, PhD**, Professor of Psychology, University of Massachusetts, Amherst
  (NIMH R01 and K05: 1981-present)
- **Joseph E. LeDoux, PhD**, Henry and Lucy Moses Professor of Science, Center for Neural Science and the Department of Psychology, New York University
  (NIMH R01, K02, K05, and MERIT Awardee)
- **Henry A. Lester, PhD**, Bren Professor of Biology, California Institute of Technology
  (Former NIMH grantee and former member of NAMHC)
- **Susan K. McConnell, PhD**, Professor of Biological Sciences, Stanford University
  (NIMH R01: 1994 to present)

Staff Changes

Arriving:

Emily Brown, who previously served as a Grants Technical Assistant in the NIH Office of the Director, Division of Extramural Activities Support, joined the Grants Management Branch as a Grants Management Specialist in April.

Susan Cahill joined the Office of Science Policy, Planning, and Communication (OSPPC) as Writer/Press Officer in February 2006. In addition to having a BS in Journalism, Ms. Cahill brings to the office 14 years of experience in science writing and editing (of which 10 years she has been writing for NIH) and her background as a former critical care RN. She has won awards from NIH and the Maryland-Delaware-DC Press Association. Prior to coming to NIMH, Ms. Cahill held positions at NIA, the National Institute on Alcohol Abuse and Alcoholism, and the National Eye Institute.

Mi Hillefors, MD, PhD, joined the Experimental Therapeutics Branch, DATR, in March 2006. Before joining DATR, she worked with Dr. Barry Kaplan in the NIMH Intramural Research Program's Section on Neurobiology. Dr. Hillefors received her MD and PhD in Neuroscience from Karolinska Institute, Sweden. She has conducted research on dopamine receptors as well as studied effects of protein synthesis on mitochondria in primary neurons. Additionally, Dr. Hillefors is a Board Certified Physician in Sweden and has experience in psychiatry, geriatrics, and family health care. Prior to her work with Dr. Kaplan, she worked with Dr. David Sibley in the Molecular Neuropharmacology Section, NINDS.

Colleen Labbe joined the OSPPC as a Writer/Press Officer in March 2006. Prior to joining NIMH, she was a Communications Specialist and Writer/Editor with the National Oceanic and Atmospheric Administration, and has worked as a writer and editor of science and environmental trade and commercial publications. Ms. Labbe holds an MS in Science Communications from The Ohio State University.

Cheryl Nathaniel joined the Grants Management Branch as a Grants Management Specialist in April. Previously, Ms. Nathaniel held the position of Grants Management Specialist at NICHD.

Takisha Schulterbrandt, PhD, joined the Reports and Analysis Branch in May 2006 as a contractor. Dr. Schulterbrandt earned her PhD in Neuroscience in 2005 from the University of Maryland School of Medicine. Most recently, she served as an academic coordinator within the Department of Obstetrics and Gynecology and Reproductive Sciences at the University of Maryland School of Medicine.

Kimberly Wheat, who previously worked at the National Institute of General Medical Sciences, joined the Grants Management Branch as a Grants Management Specialist in April.

Departing:

David Eskenazi, Chief of the NIMH Contracts Management Branch for 23 years, retired from the Federal government in May 2006 after a total of over 30 years with the Federal government.

Dave will be taking it easy locally for awhile, but eventually plans to move to a house he owns in the San Francisco area.

Steve Foote, PhD, retired in March as the Director of DNBBS. Dr. Foote first came to NIMH in 1972 as a staff fellow, leaving the Institute in 1976 to venture forth to a successful academic and research career, culminating in the position of Professor in Residence in the Department of Psychiatry at the University of California, San Diego. NIMH was able to lure him back in 1996 to serve as Chief of the Behavioral and Integrative Neuroscience Branch, and in 1998 he became the Director of DNBBS. In this role, Dr. Foote advanced the integrative Conte Centers program, providing a unifying framework for basic and clinical neuroscience research relevant to mental disorders. Dr. Foote also helped put the Division at the forefront of genetics research, establishing large genetic repositories long before other research organizations. DNBBS, under his leadership, continues to redefine the basic neuroscience research terrain with its groundbreaking approach to studying molecular and cellular systems, especially with regard to novel therapeutic agents. Of course, none of these accomplishments would have been possible without a tremendously talented and dedicated staff, and Dr. Foote's capacity to train and mentor program staff, and manage a high-performing group, is legendary. Over the course of his distinguished career, Dr. Foote has received numerous honors and recognitions, perhaps most notable election as a Fellow to the American Association for the Advancement of Science.

Steve Moldin, PhD, Director of the DNBBS Office of Human Genetics and Genomic Resources and Associate Director for the Division, retired in March after serving 11 years at NIMH. He has since accepted the position of Executive Director for the University of Southern California's Washington, D.C. Office of Research Advancement.

Rich Pine, NIMH Budget Officer for the past 20 years, retired in May. Mr. Pine entered the Federal government through the Health, Education & Welfare Intern program, and over the course of roughly 35 years, built an impressive career at NIH and the Office of the Assistant Secretary for Health.

Susan Schultz, eRA/IMPAC II Tech Coordinator for the past four years, left her position at NIMH in April to pursue a new position with the Department of Justice.

Robert Silberfarb, MA, MPA, retired from his position as Social Science Analyst in the Reports and Analysis Branch of OSPPC at the end of March 2006. Through 40 years of service to NIMH, beginning in 1960, Mr. Silberfarb served under every NIMH Director since the Institute was established. In 1973, he moved to Israel, where he spent over five years working as a clinical psychologist in a Jerusalem mental hospital, a school psychologist in the Ashdod schools, and consultant for the cities of Ashdod and Rehovoth. He also headed an evaluation unit at a community mental health center. Mr. Silberfarb participated in the coding and classification of research grant applications, which he later supervised; provided analyses and evaluation reports on the program based on the coded data collected, both for internal and external use; and oversaw the development of the classification scheme as it evolved to incorporate growing needs of the Institute. He also helped provide the data that comprised the early sourcebooks issued by the Branch and the report on the research grant programs to NAMHC.

Transferring/Other Changes:

Kathy Anderson, PhD, will be handling the duties of Chief for Behavioral Science and Integrative Neuroscience Research Branch, DNBBS, until a permanent replacement has been selected.

David Chambers, PhD, has accepted the position of Associate Director for Dissemination and Implementation Research, NIMH. Since joining NIMH in 2001 as a Program Officer in the Services Research and Clinical Epidemiology Branch of DSIR, he has built up a strong portfolio of grants that bring scientific findings and effective clinical practices in mental health to real-world practice settings. In this additional capacity, Dr. Chambers will lead the NIMH Science to Service Initiative and serve as the Institute's representative to the Federal Action Agenda Executive Committee. He will also work closely with other NIMH offices, such as OSPPC and the Office of Community Relations and Public Liaison (OCRPL), on these issues.

Thomas Lehner, PhD, MPH, has accepted the position of Acting Director of the Office of Human Genetics and Genomic Resources in DNBBS. Dr. Lehner has been with NIMH since September 2004. He received his PhD in Genetics from the University of Vienna, Austria, and his MPH in Epidemiology from Columbia University in New York. Prior to joining NIMH, Dr. Lehner worked at Rockefeller University, where he had been studying complex traits in the Laboratory of Dr. Jurg Ott, a NIMH MERIT grantee. Dr. Lehner began his career as a postdoc in genetic epidemiology at Columbia University, in the late 1980s. He applied genetic epidemiological methods and worked to identify several disease-causing genes, among them genetic candidates for muscular dystrophy and bipolar disorder. Dr. Lehner's career path reflects his varied scientific, health policy, and entrepreneurial interests, and has included senior positions as an epidemiologist in the New York City Department of Health and as a scientific administrator at Rockefeller University. More recently, he was a co-founder of a personalized medicine company in Cambridge, Massachusetts, that aimed to bring pharmacogenomic research to clinical practice.

Molly Oliveri, PhD, Deputy Director of DPTR, has agreed to serve as Acting Director for the Division until a new Director has been selected.

Kevin Quinn, PhD, agreed to step in as Acting Director for DNBBS at the end of March 2006. Dr. Quinn has been with the NIMH for almost nine years and is well-versed in the extramural program operations.

Susan Swedo, MD, left her position as Director of DPTR to focus on the Intramural Research Program's Autism Program, a new program that is a high priority for the Institute. She will continue in her post as Associate Director for Pediatric Research, with responsibility for helping to guide NIMH priorities and coordinating activities in this area both in the intramural and extramural programs. Dr. Daniel Pine from the Intramural Research Program is chairing the national search for a new Director of DPTR.