

Director's Report to the National Advisory Mental Health Council

January 12, 2007

I am pleased to welcome members of the National Advisory Mental Health Council (NAMHC) and other participants and guests to our 214th Council meeting. Since our last meeting in September, we have made progress on several fronts, which I share with you in this report.

First, on behalf of the National Institute of Mental Health (NIMH), I would like to welcome four new Council members:

Elizabeth Childs, MD, Commissioner, Department of Mental Health, Commonwealth of Massachusetts since June 2003. She is the first psychiatrist to head the department in two decades and has an extensive background in providing services to people with serious mental illness in both the private and public sectors. Prior to her current position, Dr. Childs was Chief and Director of Psychiatry at the Carney Hospital in Dorchester, Massachusetts. She has also held academic appointments at the Massachusetts Institute of Technology (MIT), Harvard University, and the University of Cincinnati.

John March, MD, MPH, Professor of Psychiatry and Chief, Child and Adolescent Psychiatry, Duke University Medical Center. Dr. March has extensive experience developing and testing the efficacy and effectiveness of cognitive-behavioral and pharmacological treatments for pediatric mental disorders. He holds a K24 career development award from NIMH devoted to clinical trials methods, is a member of the Steering Committee of the Multimodal Treatment Study of Children with Attention Deficit Hyperactivity Disorder, and is the principal investigator (PI) on several other NIMH-funded treatment outcome studies.

Dilip Jeste, MD, Estelle and Edgar Levi Chair in Aging, Professor of Psychiatry and Neurosciences, and Chief, Division of Geriatric Psychiatry, University of California, San Diego (UCSD)/VAMC. Dr. Jeste is Director of the NIMH-funded Advanced Center for Interventions and Services Research at UCSD focusing on psychosis in late-life and is the PI on several research and training grants. He has served as president of the American Association of Geriatric Psychiatry and is editor of the *American Journal of Geriatric Psychiatry*. His research focuses on psychosis and its treatment in late life; studies of clinical, neuropsychological, and neurobiological characteristics of late-onset schizophrenia; and psychosis in Alzheimer's disease.

Enola Proctor, PhD, Frank J. Bruno Professor of Social Work Research, George Warren Brown School of Social Work, Washington University in St. Louis. Dr. Proctor directs the NIMH-funded Center for Mental Health Services Research at Washington University. She has worked to advance knowledge in social work through her roles as board member of the Institute for the Advancement of Social Work Research, chair of the Group for the Advancement of Doctoral Education in Social Work, and chair of George Warren Brown's doctoral program. She also currently directs an NIMH-funded doctoral training program in mental health services research. Her teaching focuses on research and evaluation methodology, and social work in health and mental health care settings.

NIH-Wide Update

Update on Funding

The Grants Management Branch processed approximately 3,687 grant actions totaling over \$1.4 billion in Fiscal Year (FY) 2006.

Update on Electronic Submission

As of February 5, 2007, R01 applications must be submitted electronically through the NIH grants portal. The “Research Project Grant (Parent R01)” funding opportunity announcement for R01 applications has been published (<http://grants.nih.gov/grants/guide/pa-files/PA-07-070.html>) for applicants who are not responding to a specific initiative to obtain the SF424 forms for electronic submission. NIMH has also reissued many of its R01 announcements for specific research areas (<http://www.nimh.nih.gov/grants/pamenu.cfm>); the application packages for these announcements may be downloaded also. The National Institutes of Health (NIH) Guide to Grants and Contracts (<http://grants1.nih.gov/grants/guide/index.html>) and the Electronic Submission website (<http://era.nih.gov/ElectronicReceipt/>) will post the latest news on this continuing process.

Several other notable changes accompanying the conversion to the electronic R01 include:

- (1) As of January 2007, new competing R01s have the following new receipt dates: February 5, June 5, and October 5. Amended applications will be due on March 5, July 5, and November 5. Other grant mechanisms have differing submission dates. Please see <http://grants.nih.gov/grants/funding/submissionschedule.htm> for more details.
- (2) As of January 3, 2007, appendix materials have new limits. One major change is that publications that are publicly available may not be included in full in the appendix, but rather the URLs or NIH PubMed Central submission numbers should be included. For more information, see <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-07-018.html>.
- (3) As of February 5, 2007, NIH will allow applicants and their institutions to identify more than one PI. This new policy has been referred to as the Multiple PI initiative. For more information, go to <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-07-017.html>.

NIH Roadmap – Selected Updates

The NIH Roadmap is an exciting trans-NIH effort to support innovative science, stimulate interdisciplinary research, and reshape clinical research to accelerate medical discovery and improve public health. A full summary of Roadmap activities can be found at <http://www.nihroadmap.nih.gov/>. Here I will review a few highlights especially relevant to NIMH.

Molecular Libraries Roadmap

The Molecular Libraries initiative, led by NIMH and the National Human Genome Research Institute (NHGRI), is one of the largest and most ambitious projects in the Roadmap. The goal of this effort is to develop a new generation of small molecules to facilitate discoveries in cell biology. A major resource created by this initiative is the Molecular Libraries Screening Centers Network (MLSCN) which provides high throughput screening of small molecules for the academic community. To date, 92 assay projects have been assigned to the screening centers. The Molecular Libraries Small Molecule Repository compound collection, a centralized repository that provides consistent storage and distribution of compounds to all centers, currently provides more than 100,000 compounds. As the screening centers have developed, efforts have

been made to include an initial selection of 4,000 natural products compounds, to include novel compounds from non-commercial sources, and to bring the library up to 300,000 compounds in 2007. Results with over 2 million data points have now been posted in PubChem, the database of chemical space developed by this Roadmap initiative.

Patient Reported Outcomes and Measurement Information System (PROMIS)

This initiative seeks to develop a publicly accessible electronic testing system that can measure patient-reported symptoms across a wide variety of chronic diseases and conditions. The Centers for Medicare and Medicaid Services (CMS) recently required that PROMIS item banks and measurement procedures be included in an effort to develop and evaluate a new measure for post-acute care. This represents the first adoption of the PROMIS item banks by another Federal agency and could greatly expand the use of PROMIS in health care facilities. Also, in order to address how PROMIS might be used for claims support by industry, Roadmap team members recently provided the Food and Drug Administration (FDA) with requested information about how the items were developed, derived, and tested for content validity in patient and clinical samples.

Clinical and Translational Science Awards (CTSAs)

In October, NIMH staff met with PIs representing the 12 CTSAs funded in FY 2006 (<http://nihroadmap.nih.gov/clinicalresearch/fundedresearch.asp>). In addition, CTSA Project Team Subcommittees were established to help administer these large awards and include NIMH staff representatives on key subcommittees. The Request for Applications (RFA) soliciting supplements to CTSAs for pilot projects in community engagement (<http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-07-006.html>) was issued in November, with applications due by January 23, 2007.

NIH Director's Pioneer Awards

On September 19, 2006, the 13 latest recipients of the NIH Director's Pioneer Award (NDPA) were announced. Three of them were in neuroscience:

- Kwabena A. Boahen, PhD, Stanford University, associate professor of bioengineering, who will develop a specialized hardware platform for the detailed simulation of the inner workings of the brain's cortex.
- Gary J. Pielak, PhD, University of North Carolina at Chapel Hill, professor of chemistry, who will study proteins involved in neurodegenerative diseases at the atomic level inside living cells.
- Rosalind A. Segal, MD, PhD, Dana-Farber Cancer Institute, associate professor of neurobiology, who will focus on identifying the way complex sugars work to maintain neural stem cells in the developing and adult brain.

The goal of the NDPA is to support individual scientists of exceptional creativity who propose pioneering approaches to major challenges in biomedical and behavioral research. It provides support to individuals who intend to pursue new research directions that are not already supported by other mechanisms. Applications for the FY 2007 NDPA competition are currently being accepted and are due by January 17, 2007. For further information, please visit <http://grants1.nih.gov/grants/guide/rfa-files/RFA-RM-07-005.html>.

NIH Blueprint for Neuroscience Research

The Neuroscience Blueprint (<http://braininfo.us/blueprint/index.html>) is a framework to enhance cooperation among the 15 NIH Institutes and Centers (ICs) that support research on the nervous system. Created in 2004, the Blueprint already has a number of cross-cutting projects funded, from training initiatives to support for knockout mouse resources. Going forward, the Blueprint will focus on neurodegeneration in 2007, neural development in 2008, and neural plasticity in 2009. Since September, several activities under the Blueprint have moved forward:

Neurodevelopment Workshop

To provide guidance for developing Blueprint initiatives for FY 2008, Pat Levitt, PhD, and B.J. Casey, PhD, co-chaired a workshop in November that included 32 invited investigators representing a broad range of expertise in neurodevelopment. Issues were framed by focused plenary lectures and break-out group discussions. Group recommendations echoed several themes, including interest in improving understanding of transitions across the lifespan and finding better ways to translate understanding across species and across health and disorder. A report of this workshop is currently being prepared.

Neurodegeneration Initiatives for FY 2007

Based on recommendations from a March 2006 workshop, four solicitations of research and training grant applications were issued in October, with applications due in December. The solicitations are listed below:

- Therapeutics Delivery for Neurodegenerative Diseases (R21)
<http://grants.nih.gov/grants/guide/rfa-files/RFA-EY-07-001.html>
- Biomarkers for Neurodegeneration (R21)
<http://grants.nih.gov/grants/guide/rfa-files/RFA-NS-07-004.html>
- NRSA for Interdisciplinary Individual Postdoctoral Fellows for Training in Neurodegeneration Research (F32)
<http://grants.nih.gov/grants/guide/rfa-files/RFA-AG-07-004.html>
- Short-Term Interdisciplinary Career Enhancement Awards for Neurodegeneration Research (K18)
<http://grants.nih.gov/grants/guide/rfa-files/RFA-DC-07-005.html>

NIMH Update

Expediting Public Mental Health Science through Clinical Research Networks

For over four decades, NIH has supported networks of clinics and clinicians as a means of supporting clinical trials. NIMH is joining this effort by providing infrastructure support to maintain three large networks that have evolved from the large practical clinical trials of interventions for major depressive disorder (Sequenced Treatment Alternatives to Relieve Depression—STAR*D), for schizophrenia (Clinical Antipsychotic Trials of Intervention Effectiveness—CATIE), and for bipolar disorder (Systematic Treatment Enhancement Program for Bipolar Disorder—STEP-BD) in adults. Because these networks already provide rapid and efficient access to nationwide clinical sites and staff, they are ideally suited for addressing the kinds of real-world “effectiveness” questions that require large and diverse study samples and aim to impact clinical practice.

NIMH is currently reviewing its process for funding future research through these networks, aiming to elicit the best science to improve clinical practice, while at the same time maximizing the efficiency of the conduct of that science. The overarching principle is that the networks will provide the infrastructure for research designed to improve the mental health of the public and to help inform clinicians. To accomplish this, research must be informed by broad scientific and public input. The networks are poised to address the public mental health questions that generally are not addressed by non-government entities, as well as research questions that are beyond the scope and timeframe of the R01 process.

In December 2006, NIMH issued a Request for Information (<http://grants.nih.gov/grants/guide/notice-files/NOT-MH-06-128.html>) to solicit suggestions from investigators, stakeholders, and individuals living with mental illnesses for the most important research directions and projects for the networks. An NAMHC workgroup will review these suggestions and then report its findings on top research areas and approaches to the full NAMHC for consideration. The workgroup had its second meeting on January 10, 2007.

Research Projects Aim to Clarify Connection Between SSRI Use and Suicidality

NIMH is funding five new research projects that will shed light on antidepressant medications, notably selective serotonin reuptake inhibitors (SSRIs), and their association with suicidal thoughts and actions (suicidality). These new, multi-year projects may reveal why and how SSRIs may trigger suicidal thinking and behavior in some people but not others, and may lead to new tools that will help clinicians screen for those who are most vulnerable. Project titles and PIs of the five projects are listed below.

- Cross Design Synthesis: Combining Evidence About Antidepressants and Suicidality – Kelly Kelleher, MD, Columbus Children’s Research Institute
- Antidepressants, Concurrent Treatments, and Completed Suicide in VA Registry Data – Marcia Valenstein, MD, University of Michigan
- SSRI-Induced Activation Syndrome In Pediatric OCD – Wayne Goodman, MD, University of Florida
- Antidepressant Use and Suicidality: Comparative Safety in Children and Adults – Sebastian Schneeweiss, MD, Brigham and Women’s Hospital
- Computerized Screen Adverse Events Associated SSRI’s – Prudence Winslow Fisher, PhD, New York State Psychiatric Institute

Further details on these projects can be found at <http://www.nimh.nih.gov/press/suicidessri.cfm>. In addition to these new projects, NIMH is currently funding other studies to find the best treatments for individuals suffering from depression, and reduce or prevent suicidal behavior. Studies focused on youth depression and suicidal behavior include the Treatment for Adolescents with Depression Study (TADS) (<http://www.nimh.nih.gov/healthinformation/tads.cfm>), the Treatment of SSRI-Resistant Depression in Adolescents (TORDIA) (<http://clinicaltrials.gov/ct/show/NCT00018902>), and the Treatment of Adolescent Suicide Attempters (TASA) (<http://clinicaltrials.gov/ct/show/NCT00080158>).

NIMH Intramural Research Program Launches Autism Trials

Three major clinical studies on autism launched by the NIMH Intramural Research Program (IRP) are the first products of a new research program on autism. Initial studies will define the characteristics of different subtypes of autism spectrum disorders (ASD) and explore possible

new treatments, including the antibiotic minocycline, and chelation therapy. For more information, please visit <http://www.nimh.nih.gov/press/autism.irp.trials.cfm>.

Preventing Relapse in Schizophrenia: Oral Antipsychotics Compared to Injectables—Evaluating Efficacy (PROACTIVE)

NIMH's new PROACTIVE clinical trial seeks to find out whether an injection of a long-lasting antipsychotic medication every two weeks results in better adherence to treatment and better outcomes among people with schizophrenia than do oral medications taken daily. Patients can participate for any 2.5-year period during the five years that the study will be offered. The study will be conducted at seven sites across the country and will include only newer, second-generation antipsychotic medications. The trial began patient recruitment in September. The success of treatment will be measured by comparing how long patients go without relapsing into psychosis. For more information about the PROACTIVE study, please visit <http://www.clinicaltrials.gov/ct/show/NCT00330863>.

Office of Cross-Cutting Science and Scientific Technology

The Office of Interdisciplinary Research and Scientific Technology, within the Division of Neuroscience and Basic Behavioral Science (DNBBS) and directed by Michael Huerta, PhD, reorganized in November to shift the focus of the Office from DNBBS-specific programs to scientific activities conducted on behalf of NIMH that cut across divisions, ICs, and agencies. Newly named the Office of Cross-Cutting Science and Scientific Technology, it remains organizationally housed in DNBBS and continues to provide NIMH coordination of the Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) Programs and to serve as the NIMH lead on a number of scientific activities, such as the NIH Blueprint for Neuroscience Research, BECON (trans-NIH bioengineering consortium), and BISTIC (trans-NIH informatics consortium).

NIMH Director's Innovation Speaker Series

NIMH is hosting a series on innovation and creativity designed to encourage broad, interdisciplinary thinking in the development of scientific initiatives and programs and to press for leaps in science over incremental thinking. The speakers are innovators and leaders within their specific fields and include individuals involved in disciplines such as business, law, technology, and art. The speakers describe their work from the perspective of breaking through boundaries and developing new ideas, as well as working outside their initial expertise areas in ways that have pushed their fields forward. Discussions of the meaning of innovation, creativity, breakthroughs, and paradigm-shifting are encouraged. Speakers thus far include Arthur Molella, PhD, Director of the Jerome and Dorothy Lemelson Center for Invention and Innovation at the Smithsonian Institution's National Museum of American History, who discussed "Innovative Lives;" Karl Deisseroth, MD, PhD, Assistant Professor in the Departments of Bioengineering and Psychiatry & Behavioral Sciences at Stanford University, who presented "Bringing Bioengineering to Psychiatry;" and Martin Seligman, PhD, Fox Leadership Professor of Psychology, Department of Psychology, University of Pennsylvania, who spoke on "Positive Psychology and Positive Interventions."

Science of Note

Benefits to Employers Outweigh Enhanced Depression-Care Costs

A simulation, conducted by Philip Wang of Harvard University (currently at NIMH) and colleagues, based on dozens of studies revealed that providing a minimal level of enhanced care for employees' depression would result in a cumulative savings to employers of \$2,898 per 1,000 workers over five years. Savings from reduced absenteeism and employee turnover and other benefits of the intervention began to exceed the costs of the program by the second year, yielding a net savings of \$4,633 per 1,000 workers. These savings were somewhat reduced in later years based on conservative assumptions that benefits wane after care management ceases, while increased use of treatments continues. Enhanced care had the most benefit in cases of higher-level employees who influenced the productivity of co-workers. The intervention yielded gains when the simulated costs for care were consistent with those charged in the real world, suggesting that providing such programs for workers "appears to be a good investment of society's resources," according to the researchers.

Wang PS, Patrick A, Avorn J, Azocar F, Ludman E, McCulloch J, Simon G, Kessler R. The costs and benefits of enhanced depression care to employers. Arch Gen Psychiatry. 2006 Dec; 63(12).

Common Motion-Sickness Medication May Have Antidepressant Effects

People with major depression or bipolar disorder who had predominantly poor prognoses improved dramatically almost immediately after being treated with a medication more commonly used as a sedative or to treat motion sickness. Maura L. Furey and Wayne C. Drevets, of NIMH's Mood and Anxiety Disorders Program discovered that a single intravenous dose of scopolamine (Scopace®) resulted in a reduction of symptoms suggesting that scopolamine may have strong, fast, long-lasting antidepressant and anti-anxiety effects. According to the researchers, patients in the studies tolerated scopolamine well and reported no serious medical adverse outcomes. Given that antidepressant treatments currently on the market may take at least three weeks to show such results and tend to be ineffective in approximately one in three patients, these findings are significant; they may help scientists develop robust, fast-acting, alternative antidepressant and anti-anxiety treatments.

Furey ML, Drevets WC. Antidepressant Efficacy of the Antimuscarinic Drug Scopolamine. Arch Gen Psychiatry, Oct. 2006;63:1121-1129.

Odds of Beating Depression Diminish as Additional Treatment Strategies Are Needed

An overall assessment of the nation's largest real-world study of treatment-resistant depression—STAR*D—suggested that a patient with persistent depression can get well after trying several treatment strategies, but his or her odds of beating the depression diminish as additional treatment strategies are needed. The researchers, lead by A. John Rush of the University of Texas Southwestern Medical Center, also found two important indicators of treatment success. Participants who became symptom-free had a better chance of remaining well than those who experienced only symptom improvement. Those who needed to undergo several treatment steps before they became symptom-free were more likely to experience a relapse during the one-year follow-up phase, reminding clinicians that even if a patient overcomes the depression, he or she still needs attention. These results underscore both the need for better understanding how individuals respond to different therapies, and the challenges in finding broadly effective, short- and long-term depression treatments.

Rush AJ, Trivedi MH, Wisniewski SR, Nierenberg AA, Stewart JW, Warden D, Niederehe G, Thase ME, Lavori PW, Lebowitz BD, McGrath PJ, Rosenbaum JF, Sackeim HA, Kupfer DJ, Luther J, Fava M. Acute and longer-term

*outcomes in depressed outpatients requiring one or several treatment steps: a STAR*D report. Am J Psychiatry. 2006 Nov;163(11):1905-17.*

U.S. Youth Suicide Rates Lower in Counties with High SSRI Use

For children ages five to 14, suicide rates from 1996 to 1998 were lower in areas of the country with higher rates of antidepressant prescriptions, according to Robert D. Gibbons, University of Illinois at Chicago, and colleagues. Examining suicide data from the Centers for Disease Control and Prevention (CDC) and prescription data from IMS Health, a commercial company that collects global health care information and represents more than half of all retail pharmacies in the United States, the researchers found that counties with the highest SSRI prescriptions generally had the lowest suicide rate—around 0.7 per 100,000 people. The counties with some of the lowest rates of SSRI prescriptions had the highest suicide rate of 1.7 per 100,000 people. Although the data are compelling, they do not prove any causal relationship between SSRI use and suicide rates. Gibbons and colleagues note that their results are consistent with other studies that report a decline in suicide attempts and completed suicides among adults and adolescents who are prescribed antidepressant medications.

Gibbons RD, Hur K, Bhaumik DK, Mann JJ. The relationship between antidepressant prescription rates and rate of early adolescent suicide. Am J Psychiatry. 2006 Nov;163(11):1898-904.

New Data on Suicidal Behaviors in Black Americans May Guide Interventions

Examining a subset of study population from the NIMH-funded National Survey of American Life, Sean Joe, of the University of Michigan, Ann Arbor, and colleagues reviewed data from 5,181 African Americans and Caribbean Americans ages 18 and older, and found that the lifetime estimate for attempted suicide is 4.1 percent, higher than previously reported, but similar to the 4.6 percent reported for the general population (ages 15-54). The presence of an anxiety disorder was the strongest risk factor compared with other mental or substance use disorders, which differs from other studies in the general population where depression is often the strongest predictor. The researchers also found that the majority of blacks who attempted suicide sought treatment from a health professional. Further research on the transition from planning to attempts may provide better methods of screening for and preventing suicide in at-risk individuals.

Joe S, Baser RE, Breeden G, Neighbors HW, Jackson JS. Prevalence of and Risk Factors for Lifetime Suicide Attempts Among Blacks in the United States. JAMA. 2006 Nov 1;296(17):2112-2123.

Mouse Model May Reveal Anxiety Gene, Marker for Antidepressant Failure

Studies of a new mouse model suggest that a specific gene variation plays a role in the development of anxiety disorders and in resistance to common medications for anxiety and depression. Francis Lee of Cornell University and colleagues created mice with a variation in the brain-derived neurotrophic factor (BDNF) gene, which produces a protein crucial to growth and maintenance of brain cells. The mice exhibited increased anxiety-like behaviors and some resistance to the SSRI fluoxetine (Prozac®) only if the variant was present in both copies of the gene (each gene has two copies, one from each parent). The scientists also found that mice with the variant had defective brain-cell secretion of the BDNF protein and changes in shape of the brain cells that produce it. These alterations may form part of the basis of BDNF's role in anxiety, SSRI resistance, and depression. The new mouse model appears to be the first report of researchers successfully adding a specific gene variation in animals to purposely induce characteristics similar to those caused by the variation in humans. Further research may help

explain some of the genetic underpinnings of anxiety disorders in humans and lead to biological markers that predict whether SSRI treatment will be effective for a given patient.

Chen ZY, Jing D, Bath KG, Ieraci A, Khan T, Siao CJ, Herrera DG, Toth M, Yang C, McEwen BS, Hempstead BL, Lee FS. Genetic variant BDNF (Val66Met) polymorphism alters anxiety-related behavior. Science. 2006 Oct 6;314(5796):140-3.

Experience Sculpts Brain Circuitry to Build Resiliency to Stress

In a recent study, Steven Maier, University of Colorado, and colleagues unraveled the workings of the brain circuitry that immunizes a rat from developing a depression-like syndrome when it later encounters a stressor that it cannot control. Having a sense of control activated the brain's executive hub—the prefrontal cortex—and altered it so that the prefrontal cortex later activated even when the stressor was not controllable. This activation turned off mood-regulating cells in the brainstem's alarm center. The immunizing effect was so powerful that even a week later, when confronted with an uncontrollable stressor, the cells behaved as if the stressor was controllable, and the rat was protected from developing depression-like symptoms. Lack of control over stressful life experiences has been implicated in mood and anxiety disorders. Understanding how the brain encodes the experience of control to protect against such adverse consequences may lead to better treatments for these disorders.

Amat J, Paul E, Zarza C, Watkins LR, Maier SF. Previous Experience with Behavioral Control over Stress Blocks the Behavioral and Dorsal Raphe Nucleus Activating Effects of Later Uncontrollable Stress: Role of the Ventral Medial Prefrontal Cortex. J Neurosci. 2006 Dec 20;26(51):13264-72.

Older Medication May Be More Cost-Effective for Some Patients with Schizophrenia

An analysis of the economic implications of the CATIE study concluded that the older (first generation) antipsychotic medication perphenazine (Trilafon®) was less expensive and no less effective than the newer (second generation) medications used in the trial during initial treatment, suggesting that older antipsychotics still have a role in treating schizophrenia. Robert Rosenheck, of Yale University, and colleagues analyzed costs and quality-of-life factors associated with each of the five medications used in Phase 1 of the CATIE trial—olanzapine (Zyprexa®), quetiapine (Seroquel®), risperidone (Risperdal®), ziprasidone (Geodon®), and perphenazine. They found that total monthly health costs were up to 30 percent lower for those taking the perphenazine than for those taking the second generation medications. In addition, the researchers found no statistically significant difference in overall effectiveness with regard to symptom relief and side effect burden. However, it is important to note that not all patients respond the same to different medications. In addition, the CATIE study lasted 18 months—long enough to determine how patients *initially* tolerate the drugs, but not long enough to consider serious long-term side effects, such as the movement disorder tardive dyskinesia, diabetes, cardiovascular problems, or other medical conditions that can develop even years after a patient with chronic schizophrenia starts taking an antipsychotic medication. Despite these caveats, the results suggest new ways of thinking about medication treatments for schizophrenia.

Rosenheck RA, Leslie DL, Sindelar J, Miller EA, Lin H, Stroup TS, McEvoy J, Davis S, Keefe R, Swartz M, Perkins D, Hsiao JK, Lieberman J. Cost-effectiveness of Second Generation Antipsychotics and Perphenazine in a Randomized Trial of Treatment for Chronic Schizophrenia. Am J Psychiatry. 2006 Dec;163 (12): 2080-89.

Antipsychotic Medications Used to Treat Alzheimer's Patients Found Lacking

Antipsychotic medications commonly prescribed to treat Alzheimer's patients with delusions, aggression, hallucinations, and other similar symptoms can benefit some patients, but they appear to be no more effective than a placebo when adverse side effects are considered,

according to the first phase of a large-scale, practical clinical trial known as the CATIE-Alzheimer's disease (CATIE-AD) trial. In this phase, 421 participants were randomized to receive olanzapine, quetiapine, risperidone—newer antipsychotic medications—or a placebo. Lon Schneider, University of Southern California, and colleagues at 42 trial sites judged each medication's overall benefits by measuring how long a patient stayed on the medication. On average, patients discontinued treatment after about eight weeks, regardless of whether they were taking an active medication or placebo, indicating no major differences in effectiveness. Some participants did benefit from the treatment; 26 to 32 percent of those taking the active medications improved, compared to 21 percent of those taking placebo. But the antipsychotic medications also were more often associated with troubling side effects, such as sedation, confusion, and weight gain, compared to placebo. Fifteen to 24 percent of those taking active medications discontinued use because of side effects, compared with five percent of those taking placebo. The 82 percent of participants who discontinued their medications went on to subsequent phases of the CATIE-AD trial in which other treatment options were tested; results of these phases are currently being analyzed.

Schneider LS, Tariot PN, Dagerman KS, Davis SM, Hsiao JK, Ismail MS, Lebowitz BD, Lyketsos CG, Ryan JM, Stroup TS, Sultzer DL, Weintraub D, Lieberman JA; CATIE-AD Study Group. Effectiveness of atypical antipsychotic drugs in patients with Alzheimer's disease. N Engl J Med. 2006 Oct 12;355(15):1525-38.

Preschoolers with ADHD Improve with Low Doses of Medication

The Preschool ADHD Treatment Study (PATS) is the first long-term, large-scale study designed to determine the safety and effectiveness of treating preschoolers who have attention deficit/hyperactivity disorder (ADHD) with methylphenidate (Ritalin®). Of the 303 preschoolers ages 3 to 5 enrolled in the study, only those with the most extreme ADHD symptoms who did not improve after a behavioral therapy course and whose parents agreed to have them treated with medication were included in the medication study. Researchers lead by Laurence Greenhill, Columbia University, found that children taking methylphenidate had a more marked reduction of their ADHD symptoms than children taking a placebo, and that different children responded best to different doses. Overall, low doses were effective. However, children this age are more sensitive than older children to the medication's side effects and therefore should be closely monitored. Furthermore, similar to results from earlier studies, the medication appeared to slow the preschoolers' growth rates. Over the 70-week study period, the children grew about half an inch less in height and weighed about three pounds less than expected, based on average growth rates. A follow-up study is underway to track the children's physical, cognitive, and behavioral development, as well as health care services the family is using to care for the child. Those data will be available in two to three years.

Greenhill L, Kollins S, Abikoff H, McCracken J, Riddle M, Swanson J, McGough J, Wigal S, Wigal T, Vitiello B, Skrobala A, Posner K, Ghuman J, Cunningham C, Davies M, Chuang S, Cooper T. Efficacy and safety of immediate-release methylphenidate treatment for preschoolers with ADHD. J Am Acad Child Adolesc Psychiatry. 2006 Nov;45(11):1284-93.

Wigal T, Greenhill L, Chuang S, McGough J, Vitiello B, Skrobala A, Swanson J, Wigal S, Abikoff H, Kollins S, McCracken J, Riddle M, Posner K, Ghuman J, Davies M, Thorp B, Stehli A. Safety and tolerability of methylphenidate in preschool children with ADHD. J Am Acad Child Adolesc Psychiatry. 2006 Nov;45(11):1294-303.

McGough J, McCracken J, Swanson J, Riddle M, Kollins S, Greenhill L, Abikoff H, Davies M, Chuang S, Wigal T, Wigal S, Posner K, Skrobala A, Kastelic E, Ghuman J, Cunningham C, Shigawa S, Moyzis R, Vitiello B. Pharmacogenetics of methylphenidate response in preschoolers with ADHD. J Am Acad Child Adolesc Psychiatry. 2006 Nov;45(11):1314-22.

Kollins S, Greenhill L, Swanson J, Wigal S, Abikoff H, McCracken J, Riddle M, McGough J, Vitiello B, Wigal T, Skrobala A, Posner K, Ghuman J, Davies M, Cunningham C, Bauzo A. Rationale, design, and methods of the Preschool ADHD Treatment Study (PATS). *J Am Acad Child Adolesc Psychiatry*. 2006 Nov;45(11):1275-83.

Swanson J, Greenhill L, Wigal T, Kollins S, Stehli A, Davies M, Chuang S, Vitiello B, Skrobala A, Posner K, Abikoff H, Oatis M, McCracken J, McGough J, Riddle M, Ghuman J, Cunningham C, Wigal S. Stimulant-related reductions of growth rates in the PATS. *J Am Acad Child Adolesc Psychiatry*. 2006 Nov;45(11):1304-13.

ADHD Treatment Linked to Volume Changes in Brain's Anterior Cingulate

Chronic treatment with stimulant medications appears to normalize the volume of the brain's anterior cingulate cortex (ACC) in children with ADHD, in whom ACC volume otherwise likely would have been smaller than normal. The ACC is believed to play a role in monitoring performance, and activity in this area has been shown to be decreased in ADHD. In this study, Steven Pliszka and colleagues at University of Texas Health Science Center at San Antonio compared children with ADHD who had been on stimulant medication for at least a year with those who had never been on the medication, and with children who did not have ADHD. Children with ADHD who had never taken stimulants had smaller ACC volumes, compared with children who had taken the medications and with healthy children. The medications did not appear to normalize volume of another brain area, the caudate (involved in learning and memory), also known to be smaller in children with ADHD. These findings may indicate plasticity in the ACC region, which is thought to serve as a common pathway for cognitive and emotional regulation of behavior. However, further research is needed to confirm these results. Pliszka SR, Lancaster J, Liotti M, Semrud-Clikeman M. Volumetric MRI differences in treatment-naive vs chronically treated children with ADHD. *Neurology*. 2006 Sep 26;67(6):1023-7.

Specific Networks Are Thin in Adult ADHD Cortex

Recent studies of ADHD in adults suggest that persistent structural brain abnormalities are involved, and implicate altered integrity of cell arrangement within specific networks of the cerebral cortex. The networks of nerve cells in question regulate attention and executive functions. Using magnetic resonance imaging (MRI) in adults with ADHD, but who had not been treated for ADHD as children, Nikos Makris, Larry Seidman, and colleagues from Harvard Medical School and Massachusetts General Hospital measured cortical thickness. Compared with healthy adults with similar demographics and IQ, people with ADHD had thinning in these networks, particularly in the right inferior parietal, dorsolateral prefrontal, and anterior cingulate cortices. In a previous study by the researchers, the same group of patients were shown to have smaller cortical gray matter (bundles of brain cells that process information), prefrontal, and anterior cingulate volumes, compared with controls. Studies show that the impairments of ADHD continue from youth into adulthood in at least 50 percent of cases, but little is known about the neuroanatomy of ADHD in adults.

Makris N, Biederman J, Valera EM, Bush G, Kaiser J, Kennedy DN, Caviness VS, Faraone SV, Seidman LJ. Cortical Thinning of the Attention and Executive Function Networks in Adults with Attention-Deficit/Hyperactivity Disorder. *Cereb Cortex*. 2006 Aug 18; [Epub ahead of print]

Seidman LJ, Valera EM, Makris N, Monuteaux MC, Boriel DL, Kelkar K, Kennedy DN, Caviness VS, Bush G, Aleardi M, Faraone SV, Biederman J. Dorsolateral prefrontal and anterior cingulate cortex volumetric abnormalities in adults with attention-deficit/hyperactivity disorder identified by magnetic resonance imaging. *Biol Psychiatry*. 2006 Nov 15;60(10):1071-80.

Targeting the Most Aggressive Children May Be Cost-Effective Prevention of Later Conduct Disorders

To determine whether targeted interventions to reduce conduct problems may be cost-effective, researchers lead by E. Michael Foster, University of North Carolina at Chapel Hill, assessed the NIMH-funded Fast Track program, a 10-year intervention designed to reduce aggression among at-risk children. The Fast Track evaluation enrolled 55 schools which were grouped into nine matched pairs and then randomly assigned as intervention or control groups. According to their schools' assignment, a total of 445 at-risk children, identified through parent and teacher reports, and their families received the intervention, and 446 served as controls. Previous results showed significant differences in outcomes only among high-risk children. By weighing the costs of providing the intervention relative to the costs of crime and delinquency found among the study participants, the researchers concluded that this early prevention program was cost-effective in reducing conduct disorder and delinquency, but only for those who were at high-risk as young children. In light of the disproportionate costs to society in crime and delinquency caused by a relatively small number of youth, the researchers concluded that the Fast Track intervention program is likely cost-effective for high-risk children, but not for moderate-risk children.

Foster EM, Jones D. Can a Costly Intervention Be Cost-effective?: An Analysis of Violence Prevention. Arch Gen Psychiatry. 2006 Nov;63(11):1284-91.

Different Families, Different Characteristics – Different Kinds of Bipolar Disorder?

People with bipolar disorder tend to share similarities in certain characteristics with other members of their families, according to Francis J. McMahon, MD, and Thomas G. Schulze, MD, of the NIMH Mood and Anxiety Disorders Program, and colleagues. Quality of social functioning, whether good or poor, was among the strongest similarities between members of each family. The researchers found that about 20 percent of the difference in social functioning had a genetic basis, although influence of shared family environment could not be ruled out as a contributor. Other characteristics included the levels of substance abuse, alcoholism, psychosis, and suicide attempts within families. As with social functioning, some families tended to share high levels of these characteristics, while other families shared low levels. In either case, the level “ran in the family” of the person with bipolar disorder. Because the levels of similarity vary from family to family, the findings suggest the existence of different subtypes of the illness and may help determine if the subtypes have different causes. Further research may scientists pinpoint specific characteristics to focus on in studies seeking genetic and other biological underpinnings of bipolar disorder. Ultimately, this may lead to better diagnosis and treatment.

Schulze TG, Hedeker D, Zandi P, Rietschel M, McMahon FJ. What is familial about familial bipolar disorder? Resemblance among relatives across a broad spectrum of phenotypic characteristics. Arch Gen Psychiatry. 2006 Dec;63(12):1368-76.

Preschoolers with Bipolar Disorder Show Distinct Symptoms

Recent findings provide initial data for identifying and validating the existence of a bipolar syndrome in preschoolers. NIMH-funded researchers reported that 26 children met adult diagnostic criteria for bipolar disorder, based on parents' reports of mania symptoms adjusted for age-specific symptom expression. These children were highly distinguishable from those with depression or disruptive behavior problems and from children without mood or behavioral problems, in that they were more likely to display all of the core mania symptoms (thus ruling out “typical” preschooler irritability, elation, etc.) and were more highly impaired in many areas of functioning. This finding strengthens growing evidence of a childhood bipolar phenotype,

contrary to the long-held belief that mania does not occur before adolescence. Given the chronicity and disability of adult bipolar disorder, it is imperative that this disorder be identified as early as possible and that intervention begin early.

Luby J, Belden A. Defining and validating bipolar disorder in the preschool period. Dev Psychopathol. 2006 Fall;18(4):971-88.

Rapid Cognition Enhances Positive Mood

The racing thoughts characteristic of manic states raise questions about how cognitive and affective processes interact within both normal and disordered conditions. To examine this relationship, Emily Pronin, Princeton University, and Daniel Wegner, Harvard University, asked healthy, non-manic young adults to read aloud a series of printed statements previously shown to induce either positive or negative mood. The statements were presented at either fast or slow rates. As expected, positive mood was enhanced by exposure to positive statements and reduced by exposure to negative statements. The researchers also found that a rapid rate of presentation—and thus thinking—enhanced positive mood, independent of the content of the statements. In addition, rapid rate of presentation led to higher self-reported feelings of power, creativity, and grandiosity, even when the statements had a negative content. Based on these findings, the researchers plan to investigate whether rapid thinking and other aspects of cognition are among the core features of mania that drive other symptoms. The role of slow thinking in depression also will be examined. Manipulating the speed of thinking may also be a useful cognitive behavioral therapy. Current therapies focus only on the contents of thinking.

Pronin E, Wegner DM. Manic thinking: Independent effects of thought speed and thought content on mood. Psychol Sci. 2006 Sept; 17(9): 807-13.

Brain's Fear Center Shrinks in Autism's Most Severely Socially Impaired

The brain's fear hub, the amygdala, appears to shrink in the most severely socially impaired males with ASD, an MRI study by Richard Davidson and colleagues from the University of Wisconsin shows. Young males who had the least eye contact and were slowest at differentiating emotional and neutral expressions—signs of social impairment—had smaller-than-normal amygdalae. The researchers also linked amygdala shrinkage to impaired nonverbal social behavior in early childhood. The findings suggest that social fear in autism may initially trigger a hyperactive, abnormally enlarged amygdala, which gives way to a toxic adaptation that kills amygdala cells and shrinks the structure. A related MRI study revealed that healthy siblings of people with autism share some of the same differences in amygdala volume and in the way they look at faces and activate social/emotional brain circuitry. Together, the results (1) provide the first evidence linking objective measures of social impairment and amygdala structure with related brain function in autism and (2) suggest that measures such as eye contact may prove useful in clarifying the link between genes, brain, and behavior in ASD.

Nacewicz BM, Dalton KM, Johnstone T, Long MT, McAuliff EM, Oakes TR, Alexander AL, Davidson RJ. Amygdala volume and nonverbal social impairment in adolescent and adult males with autism. Arch Gen Psychiatry. 2006 Dec;63(12).

Dalton KM, Nacewicz BM, Alexander AL, Davidson RJ. Dalton KM, Nacewicz BM, Alexander AL, Davidson RJ. Gaze-Fixation, Brain Activation, and Amygdala Volume in Unaffected Siblings of Individuals with Autism. Biol Psychiatry. 2006 Oct 24; [Epub ahead of print]

Gene Linked to Autism in Families with More Than One Affected Child

While most autism genetic studies have focused on genes expressed in the brain, Pat Levitt, of Vanderbilt University, and colleagues saw a clue in the fact that some people with autism also

have gastrointestinal, immunological, or neurological symptoms in addition to behavioral impairments. They focused on the MET receptor tyrosine kinase gene, which affects such peripheral functions, as well as the development of brain areas disturbed in autism, and is located in a suspect area of chromosome 7 that has been previously linked to ASD. The researchers looked for associations between autism and nine markers in the MET gene, sites where letters in the genetic code vary among individuals, in a large sample totaling 1,231 cases. One marker, the C version, emerged as over-transmitted at “highly significant” levels in people with ASD. The C version was significantly less prevalent in a group of unrelated controls than in individuals with autism or their parents. In cell culture tests, the researchers determined that the C version is weak at making the MET receptor protein, resulting in a two-fold reduction in gene expression with presumably adverse consequences on brain development. Inheriting two copies of the C version boosted risk for ASD 2.26-fold, while inheriting one copy increased risk 1.54-fold. The researchers proposed that in some individuals with ASD who also develop digestive and immune system or non-specific neurological problems, the MET gene variant may play a role in impairing brain and organ development.

Campbell DB, Sutcliffe JS, Ebert PJ, Militerni R, Bravaccio C, Trillo S, Elia M, Schneider C, Melmed R, Sacco R, Persico AM, Levitt P. A genetic variant that disrupts MET transcription is associated with autism. Proc Natl Acad Sci USA. 2006 Nov 7;103(45):16834-9.

Corticotropin-Releasing Hormone Implicated in Rett Syndrome

People with Rett syndrome have behavioral abnormalities, including autistic features and deficits in social behavior. Understanding the regulation of corticotropin-releasing hormone (CRH) in Rett syndrome is an important step toward enabling scientists to evaluate pathway-specific genetic and pharmacologic interventions for these abnormalities. Mutations in the methyl-CpG-binding protein 2 (MeCP2) gene are known to be responsible for most cases of Rett syndrome. Mice in which the MeCP2 gene has been knocked out have increased anxiety, suggesting that anxiety is an important component of the syndrome’s behavioral phenotype. However, where and how this gene acts in the brain to alter behavior is not well understood. Bryan McGill, Huda Zoghbi, and colleagues at Baylor College of Medicine generated a specific Mecp2-knockout mouse, the Mecp2^{308/Y} mouse that models many aspects of human Rett syndrome. These mice show both an increased level of anxiety-like behavior and an enhanced physiological response to stress, compared to normal mice. Mecp2^{308/Y} mice overexpress the gene for CRH in two brain regions critical for behavioral and physiological responses to stress. These results identify the CRH gene as a target for the MeCP2 gene and link specific components of the Rett syndrome phenotype to the CRH gene.

McGill BE, Bundle SF, Yaylaoglu MB, Carson JP, Thaller C, Zoghbi HY. Enhanced anxiety and stress-induced corticosterone release are associated with increased Crh expression in a mouse model of Rett syndrome. Proc Natl Acad Sci USA. 2006 Nov 28;103(48):18267-18272.

Social Interactions Modulate Activity of Specific Brain Cells

Vasopressin is known to function as an important neuropeptide neurotransmitter in the mammalian brain. The distribution of receptors for this neuropeptide has been linked to differences in pair-bonding in animals. However, relatively little is known about the actual modulation of vasopressin-containing neurons during specific social interactions. James Goodson and Yiwei Wang, UCSD, investigated the avian homologue of vasopressin (vasotocin) in a series of experiments with five species of birds that differ in innate tendencies to group together or live in isolation. They found that vasotocin-containing neurons in a specific

brain region, the bed nucleus of the stria terminalis, were differentially activated by social interactions according to whether the species was more or less gregarious (i.e., whether they had a greater or lesser tendency to gather in social groups). Not only were there differences in the activity of these neurons when evoked by specific social situations, but there were also baseline differences in the number of activated neurons in the absence of social interactions across these different species. This suggests that the more gregarious species might normally be predisposed to respond positively to social stimuli.

Goodson JL, Wang Y. Valence-sensitive neurons exhibit divergent functional profiles in gregarious and asocial species. Proc Natl Acad Sci USA. 2006 Nov 7;103(45):17013-7.

Delaying Intervention Facilitates Fear Reduction After Traumatic Event

Considerable controversy exists over whether early or delayed treatment is most effective for preventing fear-related disorders after traumatic events, such as those leading to post-traumatic stress disorder (PTSD). Stephen Maren and Chun-hui Chang of the University of Michigan, Ann Arbor used a rat model to test whether early or delayed extinction training was more effective in inhibiting memory of a fearful event. Rats were trained to associate a previously harmless tone with delivery of a foot shock. Later, animals that had received extinction training soon after the event exhibited just as much fear of the tone as did control rats who did not receive extinction training. In contrast, animals given extinction training after a 24-hour delay showed significantly less fear, indicating that the fear response remained inhibited. Additional experiments demonstrated that level of fear before extinction training also has an impact on long-term reduction in fear responses after extinction. Reduced levels of fear result in more robust and longer-lasting suppression of fear memories, whereas heightened levels interfere with long-term extinction. These results indicate that extinction training is less effective when conducted shortly after fear-inducing trauma, which may be due to the heightened level of arousal that occurs immediately after a trauma. These findings have significant implications for the timing of interventions following traumatic events.

Maren S, Chang CH. Recent fear is resistant to extinction. Proc Natl Acad Sci USA. 2006 Nov 21;103(47):18020-5.

Amygdala Facilitates Emotional Enhancement of Memory

Humans are more likely to form more vivid memories of emotion-packed events than of ordinary experiences, which may underlie conditions such as PTSD. Studies of this phenomenon have shown that emotional arousal causes a long-lasting increase in activity of the basolateral nuclei of the amygdala (BLA)—the amygdala being an important emotional and memory center in the brain—but the link between this activity and memory consolidation has been little explored. Via electrophysiological studies in an animal model, Denis Paré, Rutgers University, and colleagues demonstrated that enhanced activation of the rhinal cortex, the main pathway transmitting impulses from the amygdala to the hippocampus, a key brain structure in consolidating memories, occurs only after BLA neurons are activated. The interaction was strongest in response to unexpected rewards and decreased as the animals learned to expect rewards after a conditioned stimulus. Following this learning, BLA activity occurred when the animals anticipated the reward. The researchers suggest that the BLA may enhance processing of sensory stimuli after behaviorally arousing events by activating the rhinal cortices. This could facilitate formation of memories in emotionally charged situations.

Paz R, Pelletier JG, Bauer EP, Pare D. Emotional enhancement of memory via amygdala-driven facilitation of rhinal interactions. Nat Neurosci. 2006 Oct;9(10):1321-9.

Brain Protein KIBRA May Influence Human Memory

Memory functions are influenced by multiple, unknown genes. Screening the entire human genome, Eric Reiman, University of Arizona, and colleagues found that a genomic locus encoding the brain protein KIBRA was consistently associated with episodic memory, but not with other cognitive functions, such as attention or working memory. The researchers focused on two types of KIBRA alleles, T and C. Functional magnetic resonance imaging studies of brain activation during a memory retrieval task showed that people who did not carry the T allele at the KIBRA locus required increased activation in memory-related brain regions (the hippocampus, temporal lobe, and others) to achieve episodic memory performance levels comparable to those of people with the T allele. The cumulative evidence from these studies, which were conducted in cognitively normal adult cohorts, indicates a significant role for KIBRA in human memory. KIBRA's known linkages to other variables suggest various lines of further research that can be pursued to clarify its mechanisms of action.

Papassotiropoulos A, Stephan DA, Huentelman MJ, Hoerdli FJ, Craig DW, Pearson JV, Huynh KD, Brunner F, Corneveaux J, Osborne D, Wollmer MA, Aerni A, Coluccia D, Hanggi J, Mondadori CR, Buchmann A, Reiman EM, Caselli RJ, Henke K, de Quervain DJ. Common Kibra alleles are associated with human memory performance. Science. 2006 Oct 20;314(5798):475-8.

Receptor Helps Neurons Grow in Right Direction

Using the rodent brain as a model, researcher lead by Susan K. McConnell of Stanford University identified a receptor (Boc) for a key protein (Sonic Hedgehog or Shh) that helps guide nerve cells called commissural axons into the correct position as the nervous system develops—a vital part of a process that enables the brain to receive sensory input from the environment and to send messages to the rest of the body via the spinal cord. Axons serve as highways that carry electrical impulses in the nervous system, the biological messages crucial to brain function. If these axon highways are “built” in the wrong directions, electrical impulses might be misdirected, potentially affecting nervous-system function. The researchers found that when the growing tips of the axons bring the Boc receptor close to Shh found in areas around nerve cells, Boc and Shh bind together. This vital interplay causes the axons to turn toward the correct positions in their long journeys toward the brain. Discovering how the nervous system develops can help scientists understand where and how to intervene when defects occur.

Okada A, Charron F, Morin S, Shin DS, Wong K, Fabre PJ, Tessier-Lavigne M, McConnell SK. Boc is a receptor for sonic hedgehog in the guidance of commissural axons. Nature. 2006 Nov 16;444(7117):369-73.

More Direct Way to Map Brain Activity Deemed Feasible

MRI can be used to directly detect the electrical activity emitted by neurons, NIMH physicists Natalia Petridou, Peter Bandettini, and colleagues have demonstrated. Their findings suggest the feasibility of a more direct and reliable method of mapping brain activity through functional magnetic resonance imaging (fMRI) than has been available up to now. Currently, fMRI measures neuronal activity only indirectly by tracing the flow of oxygenated blood. Since the hardest working brain areas need more oxygen, this signal is a close approximation of neuronal activity, albeit with some mismatches. In this study, the researchers eliminated the confounding effect of blood flow by scanning rat brain cultures devoid of blood vessels. These cultures nonetheless emitted bursts of neuronal activity. MRI readings of the ebb and flow of neuronal activity matched a direct, independent measure of neuronal electrical activity via electroencephalography (EEG). Both the MRI and the EEG signals stopped when the researchers chemically blocked neuronal activity. This suggested that magnetic resonance signal changes

were most likely due to the electrical discharges of neurons. The challenge that lies ahead will be to find a way to similarly separate electrical from blood flow signals in the living human brain, say the researchers.

Petridou N, Plenz D, Silva AC, Loew M, Bodurka J, Bandettini PA. Direct magnetic resonance detection of neuronal electrical activity. Proc Natl Acad Sci USA. 2006 Oct 24;103(43):16015-20.

Researchers Call for Consideration of Outcome Moderators in Randomized Clinical Trials

Researchers funded by NIMH and the National Institute on Aging made a case for requiring that exploratory analyses of treatment outcome moderators be included in randomized, controlled clinical trials (RCT), the current gold standard for evaluating efficacy and effectiveness of treatments. Treatment outcome moderators are factors that differ from person to person or subpopulation to subpopulation, such as age, race, gender, or genotype. Helena Kraemer, of Stanford University, Ellen Frank and David Kupfer, both of University of Pittsburgh School of Medicine, asserted that while clinical decisions rest largely on results of RCTs, most are designed such that their results apply only to “average” patients in study cohorts. The same clinical decisions are likely to be imposed on subpopulations and individuals for whom the RCT results may not hold true. The authors call for a requirement that exploratory analyses of treatment outcome moderators be included in RCTs, a low-cost approach in which results of the analyses would indicate (1) which factors should be stratified in future studies of a given intervention, and (2) when studies should be powered adequately to test the outcome moderators that had been detected.

Kraemer HC, Frank E, Kupfer DJ. Moderators of treatment outcomes: clinical, research, and policy importance. JAMA. 2006 Sep 13;296(10):1286-9.

Gene Therapy May One Day Prevent AIDS-Related Brain-Cell Death

Scientists have shown that gene therapy has potential for treating brain pathology triggered by the human immunodeficiency virus (HIV), which causes acquired immunodeficiency syndrome (AIDS). Although brain damage is among the most common complications of AIDS, there is no recognized therapy for preventing the underlying HIV-induced cell death. D.S. Strayer and colleagues from Thomas Jefferson University loaded a harmless type of virus with genes engineered to produce antioxidant enzymes and allowed the virus to carry the loaded genes into brain cells exposed to a toxic substance (gp120) released by HIV. When the genes took hold in both human brain cells in lab dishes and in brain cells in living rats, the genes began producing the antioxidant enzymes, and the rate of brain-cell death dropped dramatically. This finding presents a possible gene therapy strategy for people with HIV-related brain-cell death.

Agrawal L, Louboutin JP, Reyes BA, Van Bockstaele EJ, Strayer DS. Antioxidant enzyme gene delivery to protect from HIV-1 gp120-induced neuronal apoptosis. Gene Ther. 2006 Dec;13(23):1645-56.

HIV/AIDS Disclosure and Social-Support Intervention Improve Medication Adherence

About one in five participants in a randomized, controlled trial of people with HIV/AIDS skipped doses of antiretroviral therapy due to concerns that taking the medications could reveal their HIV-positive status to others, according to research by Michael Stirratt, Program Officer in NIMH Center for Mental Health Research on AIDS, and colleagues. The researchers were among the first to document that a patient’s disclosure of his HIV status results in greater adherence to medication. They also developed and tested SMART Couples, an intervention that enhanced social support to improve adherence to antiretroviral therapy, with clients in two

hospital HIV/AIDS outpatient clinics. Among the findings was that the SMART Couples intervention significantly improved short-term adherence to therapy.

Stirratt MJ, Remien RH, Smith A, Copeland OQ, Dolezal C, Krieger D, & the SMART Couples Study Team. The role of HIV serostatus disclosure in antiretroviral medication adherence. AIDS Behav. 2006 Sept; 10(5):483-493.

Remien RH, Stirratt MJ, Dognin J, Day E, El-Bassel N, & Warne P. Moving from theory to research to practice: Implementing an effective dyadic intervention to improve antiretroviral adherence for clinic patients. J Acquir Immune Defic Syndr. 2006 Dec 1; 43(S1): 69-78.

Meta-Analysis Finds Interventions for HIV Treatment Adherence Efficacious

Patients must maintain high levels of adherence to HIV/AIDS medication regimens to optimize treatment outcomes, but this is a challenge for many. The first meta-analysis of RCTs of interventions designed to improve adherence provides evidence that those tested are generally efficacious. A team led by Jane Simoni, University of Washington, synthesized results 19 RCTs with cohorts of more than 1,800 participants. Those who received an adherence intervention were 1.5 times as likely to report 95 percent adherence and 1.25 times as likely to achieve an undetectable viral load as participants in comparison conditions. Results were based on data collected immediately post-intervention or after brief follow-up; thus, further research is needed to determine the efficacy of interventions that sustain adherence over longer periods.

Simoni JM, Pearson CR, Pantalone DW, Marks G, Crepaz N. Efficacy of interventions in improving highly active antiretroviral therapy adherence and HIV-1 RNA viral load: A meta-analytic review of randomized controlled trials. J Acquir Immune Defic Syndr. 2006 Dec 1; 43(S1):S23-S35.

Associated commentary: Gordon, CM. Commentary on meta-analysis of randomized controlled trials for HIV treatment adherence interventions: Research directions and implications for practice. J Acquir Immune Defic Syndr. 2006 Dec 1; 43(S1): 36-40.

Broad HIV Screening Valuable Even in Communities with Low Infection Rates

An HIV/AIDS screening program may be cost-effective even in communities and populations at low risk for HIV infection. Using a simulated model, David Paltiel, of Yale University, and colleagues found that a one-time, rapid-test HIV screening program appears to be economically advantageous, even in communities with an HIV prevalence rate as low as 0.28 percent and an annual incidence rate at low as 0.03 percent. Until recently, CDC guidelines had recommended that a community implement a screening program only if HIV prevalence was greater than 1 percent. The results of the study also indicated that repeated HIV screening every five years may be optimal for communities with low prevalence and incidence rates. The study provides practical guidance to public health officials for determining new screening thresholds. These findings and related studies were highly influential in the CDC's recent issuance of revised community HIV screening guidelines, which recommended that HIV testing be made routine in all health care settings for U.S. residents ages 13 to 64.

Paltiel AD, Walensky RP, Schackman BR, Seage GR, Mercincavage LM, Weinstein MC, Freedberg KA. Expanded HIV screening in the United States: Effect on clinical outcomes, HIV transmission, and cost. Ann Intern Med. 2006 Dec 5; 145(9): 797-806.

New NIMH Initiatives

NIMH-Administered RFAs

- *Limited Competition for Applications to Analyze Whole Genome Association Data for NIMH*
NIMH is holding a limited competition open to successful applicants to the Genetic Association Information Network (GAIN) initiative. This limited competition will be for one time, one-year awards to help fund direct costs for analyses of whole genome association data for clinical phenotypes of interest to the NIMH.

Release Date: September 13, 2006; Expiration Date: January 23, 2007

<http://grants.nih.gov/grants/guide/rfa-files/RFA-MH-07-060.html>

Scientific Program Director: Thomas Lehner, PhD, MPH, Office of Human Genetics & Genomic Resources, DNBBS, NIMH

- *Disaster Mental Health Research Center (DMHRC)*
NIMH seeks to support a pre-positioned team of interdisciplinary researchers to plan epidemiological and pilot clinical research protocols in conjunction with public health authorities *in advance* of unforeseen emergencies. The overarching goal of the DMHRC is to create a ready response group to track key public health indicators and to lay the foundation for high impact clinical/services research projects.

Release Date: December 15, 2006; Expiration Date: April 24, 2007

<http://grants.nih.gov/grants/guide/rfa-files/RFA-MH-07-070.html>

Scientific Program Director: Farris K. Tuma, ScD, MHS, Division of Adult Translational Research and Treatment Development (DATR), NIMH

- *Center for Genomic and Phenomic Studies in Autism*
A specific goal of the Center for Genomic and Phenomic Studies on Autism, under the rubric of the NIMH Human Genetics Initiative and the National Database for Autism Research (NDAR), will be to collect data and biomaterials from autistic probands and their relatives for utilization in interdisciplinary genomic, basic, and translational neuroscience research, including clinical trials. The Center will initially leverage available resources, such as an NIH-funded hospital-based General Clinical Research Center (GCRC) to provide bridging infrastructure and expertise in efficient clinical screening and systematic nationwide recruitment, database management, bioinformatics, high-throughput diagnostic assessments, quantitative dysmorphology utilizing state-of-the-art 3D morphometry and scanning of the craniofacial surface, cytogenetic analysis, clinical trials and regulatory issues, bioethics and human consent issues, and rapid data sharing.

Release Date: November 29, 2006; Expiration Date: January 27, 2007

<http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-07-006.html>

Scientific Program Director: Thomas Lehner, PhD, DNBBS, NIMH

Collaborative RFAs

- *Facilitating Interdisciplinary Research via Methodological and Technological Innovation in the Behavioral and Social Sciences*
The purpose of this funding opportunity is to advance the understanding of health through development of new/innovative methodologies and technologies to support the interdisciplinary integration of social and/or behavioral scientific disciplines with other disciplines. This announcement supports proposals that integrate across various levels of analysis, ranging from sub-individual to population levels.

Release Date: October 25, 2006; Expiration Date: February 24, 2007

<http://grants1.nih.gov/grants/guide/rfa-files/RFA-RM-07-004.html>

Scientific Program Director: Patricia L. Mabry, PhD, Office of Behavioral and Social Sciences Research (OBSSR)

- *Mind-Body Interactions and Health: Restricted Competition for Research Infrastructure Programs*

The primary purposes of the Mind-Body and Health Research Infrastructure Program are to provide resources to support and advance research that will improve the understanding of mind-body interactions and health, facilitate interdisciplinary collaboration among investigators conducting health-related mind-body research, and promote innovative approaches to mind-body and health research questions. An additional goal is to facilitate interaction among scientists in locations throughout the United States in order to contribute to the integration and coordination of mind-body and health research.

Release Date: November 15, 2006; Expiration Date: January 13, 2007

<http://grants1.nih.gov/grants/guide/rfa-files/RFA-OD-06-005.html>

Scientific Program Director: Ronald P. Abeles, PhD, OBSSR

- *Methods of Analysis of Gene-Environment Interactions in Complex Diseases: The Genes and Environment Initiative*

The purpose of this RFA to develop and test innovative, informative, and cost-effective methods and analytical strategies for identifying gene-environment interactions in genome-wide association studies, sequencing studies, linkage analyses, or candidate gene approaches with broad applicability in complex diseases.

Release Date: November 20, 2006; Expiration Date: January 30, 2007

<http://grants1.nih.gov/grants/guide/rfa-files/RFA-HL-07-010.html>

Scientific Program Director: Cashell E. Jaquish, PhD, Division of Prevention and Population Sciences, National Heart, Lung, and Blood Institute (NHLBI)

- *Neuroimaging Informatics Software Enhancement for Improved Interoperability and Dissemination*

This Neuroscience Blueprint initiative, complementary to NIH Notice NOT-EB-07-002, aims to support modification and enhancement of neuroimaging informatics tools and resources developed through Blueprint activities that are or will be hosted in the NIH Neuroimaging Informatics Tools and Resources Clearinghouse (NITRC). The NITRC will facilitate dissemination of these tools and resources to neuroimaging researchers and provide opportunities for researchers to improve their usability.

Release Date: December 22, 2006; Expiration Date: February 23, 2007

<http://grants1.nih.gov/grants/guide/rfa-files/RFA-EB-07-002.html>

Scientific Program Director: Yantian Zhang, PhD, Division of Applied Science and Technology, National Institute of Biomedical Imaging and Bioengineering (NIBIB)

- *Integration of Food and Nutrition into Prevention, Care, and Treatment of HIV Infection and AIDS*

NIMH and the National Institute for Child Health and Human Development (NICHD) are soliciting applications that will examine the impact of new programs/guidance intended to fully integrate food and nutrition including on prevention, care, and treatment of HIV infected and affected women, infants, and children. This RFA seeks to stimulate and strengthen a multidisciplinary approach to a complex, under-researched, and rapidly evolving area and to form a basis for future research and clinical care.

Release Date: December 22, 2006; Expiration Date: March 30, 2007

<http://grants.nih.gov/grants/guide/rfa-files/RFA-HD-07-001.html>

Scientific Program Director: Daniel J. Raiten, PhD, Endocrinology, Nutrition and Growth Branch, NICHD

Research Conferences and Workshops

Developing New Treatments for Tourette Syndrome: Clinical and Basic Science Dialogue

In September, NIMH, the National Institute on Neurological Disorders and Stroke (NINDS), the NIH Office of Rare Diseases (ORD), and the Tourette Syndrome Association jointly sponsored a workshop to develop new and improved treatments for children and adults afflicted with Tourette syndrome (TS). The workshop included approximately 100 scientists, clinicians, and industry representatives in the fields of basic neurobiology, behavioral sciences, neurogenetics, neuroimaging, neurological disorders, motor disorders, and child psychiatry. Attendees convened with the express purpose of bridging the communication and information gap between basic and clinical science disciplines to evaluate existing TS treatments and to understand recent updates in the neurobiology of TS, in order to define new therapeutic directions. Barriers to progress were identified, and suggestions for facilitating drug discovery were discussed. *For more information, please contact Ann Wagner at awagner@mail.nih.gov.*

Northeast Regional Meeting on Connecting Science and Service

NIMH, the Center for Mental Health Services (SAMHSA), and the National Association of State Mental Health Program Directors (NASMHPD), held this two-day meeting in September in Baltimore, Maryland, to identify relevant research and service development agendas to improve the public mental health system in the region. The meeting brought together mental health services researchers with state commissioners, consumers, providers, and other key representatives of public mental health. The attendees discussed current and future efforts to perform research studies relevant to service systems and projects to implement evidence-based practices within public mental health systems. State teams discussed new initiatives to use research findings to influence service provision, and developed strategies to facilitate the integration of research activities into clinical and community care settings. *For more information, please contact David Chambers at dchamber@mail.nih.gov.*

Current Issues in Psychosocial Intervention Research in Late-Life Mental Disorders

NIMH's Geriatrics Research Branch in the Division of Adult Translational Research and Treatment Development (DATR) organized this multidisciplinary workshop, held in Arlington, Virginia in September. Participants evaluated the current state of research and formulated suggestions for new research directions that would substantially advance the field. Topics considered included: clinical gaps in the current knowledge base; opportunities for developing new therapies and researching new target populations; increased attention on cognitive impairment as a variable in intervention development and outcome studies; improved inclusion of ethnic minorities; adaptation and dissemination of interventions to geriatric care settings; integration of neuroscience research into geriatric psychosocial intervention studies; and methodological refinements to better handle factors such as patient treatment preferences and assessments of cost-effectiveness. The workshop also resulted in the establishment of a listserv among the workshop participants that will be expanded into a larger email network to facilitate communication and collaboration among psychosocial intervention researchers in geriatric mental health. *For more information, please contact George Niederehe at gniedere@mail.nih.gov.*

Meeting-based Publications

Assessment of Community Functioning in People With Schizophrenia and Other Severe Mental Illnesses: A White Paper Based on an NIMH-Sponsored Workshop

People with schizophrenia frequently have significant problems in community functioning. Progress in developing effective interventions to ameliorate these problems has been slowed by the absence of reliable and valid measures that are suitable for use in clinical trials. NIMH convened a workshop in September 2005 to examine this issue and to make recommendations to the field that would foster research in this area. A summary of the workshop discussion, including evaluation of commonly used assessment approaches, and presentation of different models of functional outcomes in schizophrenia, has been published online.

Bellack AS, Green MF, Cook JA, Fenton W, Harvey PD, Heaton RK, Laughren T, Leon AC, Mayo DJ, Patrick DL, Patterson TL, Rose A, Stover E, Wykes T. Assessment of Community Functioning in People With Schizophrenia and Other Severe Mental Illnesses: A White Paper Based on an NIMH-Sponsored Workshop. Schizophr Bull. 2006 Aug 24; [Epub ahead of print]

Budget

FY 2007 Congressional Action:

On December 9, 2006, the President signed a Continuing Resolution through February 15, 2007. This spending measure funds FY 2007 programs at the lowest of the House-passed, Senate-passed and FY 2006 levels. Attachments 1 and 2 represent NIMH's FY 2007 budget estimate that restricts funding levels to FY 2006 Appropriated levels.

Based on the FY 2007 funding levels, NIMH has developed the following principles for funding Research Project Grants (RPGs) in the coming year:

- (1) Non-competing awards will not be allowed inflationary increases.
- (2) Number of competing awards will be similar to that of FY 2005.
- (3) Average cost for competing RPGs will be restricted to FY 2006 average cost.
- (4) Number of new investigators will be maintained comparable to the average of the most recent five years.

The Full Senate Committee on Appropriations reported its FY 2006 Appropriations Bill for Labor-HHS-Education, including NIH, on July 20, 2006. The Senate bill provides a total program level of \$28.8 billion for NIH, an increase of \$202 million or +0.7 percent over the comparable FY 2006 level (see Attachment 2). Funding for NIMH in the Senate bill is \$1.4 billion, an increase of \$8.7 million over the President's Budget Request and \$36,000 over the FY 2006 comparable level.

On June 20, 2006, the House of Representatives accepted the President's Budget Request of \$28.6 billion (see Attachment 2). The funding amounts provided in the House version were essentially identical to the President's Budget Request for all NIH components, except the House reduced the President's request for the National Institute of Allergy and Infectious Diseases (NIAID) by \$25 million and increased NCRR by \$25 million. The House provided an NIMH program level of \$1.4 billion, the same as the President's Budget Request.

The FY 2007 President's Budget Request for NIH was submitted to the Congress on February 6, 2006. The President's Budget proposed a total NIH program level of \$28.6 billion, the same as

the FY 2006 comparable level. The President's request for NIMH was \$1.4 billion, a decrease of \$8.7 million or -0.6 percent below the FY 2006 comparable level.

FY 2008 President's Budget Request

The FY 2008 President's Budget Request will become public on February 5, 2007.

Major Awards for NIMH Grantees

Aaron T. Beck, MD, Professor Emeritus of Psychiatry at the University of Pennsylvania, the founder of cognitive therapy, and a long-time NIMH grantee, received the Lasker Award for Clinical Medical Research in September 2006. The Lasker Foundation recognizes "scientists, physicians, and public servants whose accomplishments have made major advances in the understanding, diagnosis, prevention, treatment, and even cure of many of the great crippling and killing diseases of our century." Seventy-one recipients of the Lasker Award have gone on to win the Nobel Prize for their work, most within two years of receiving the Lasker Award.

Dr. Beck has received NIH support for more than 40 years, with a total of 13 grants, of which NIMH awarded 11. Trained as a psychiatrist and interested in neurology, Dr. Beck is perhaps most noted for developing cognitive therapy and building the evidence-base for its use in mental health. Through his work spanning more than 50 years, he developed and demonstrated the efficacy of cognitive therapy, used to treat a variety of illnesses, including depression, anxiety disorders, panic disorders, alcoholism, drug abuse, eating disorders, suicidal behavior, and personality disorders. Dr. Beck also helped develop 19 diagnostic scales for measuring symptom severity, including one of the most widely used scales in clinical practice and research, the Beck Depression Inventory. These scales have been critical in bringing about greater rigor in basic research as well as in clinical trials.

Dilip Jeste, MD, received the first Recovery Research Inspiration Award from the Board of Directors of the National Alliance on Mental Illness (NAMI) San Diego, presented at the group's "Recovery in Action" event in September. Dr. Jeste, who directs an NIMH-funded Advanced Center on Interventions and Services Research at the University of California San Diego that focuses on schizophrenia and psychotic disorders in older adults, was recognized for his and his colleagues' work in this center on geriatric research.

Todd Sacktor, MD, Peter A. Serrano, PhD, André A. Fenton, PhD, and colleagues at the State University of New York Downstate Medical Center; as well as **Marshall G. Shuler, PhD**, and **Mark F. Bear, PhD**, along with colleagues at MIT and Brown University, were among the cited authors in *Science Magazine's* top 10 "Breakthrough of the Year" findings of 2006. Drs. Shuler and Bear were noted for their work that showed for the first time that learning triggers a brain process called long-term potentiation (LTP), a sustained increase in synaptic transmission thought to play a role in information storage. In related research, Dr. Sacktor's group found that the enzyme PKMzeta played a critical role in establishing the link between LTP and the storage of memories. By inhibiting PKMzeta, the scientists were able to selectively "erase" information the rats had learned the day before without affecting the learning process.

Major NIMH Staff Awards

Rebecca Claycamp, NIMH Grants Management Officer, was reappointed to the Distinguished Faculty of the Society for Research Administrators (SRA) International. Among the many purposes of this designation is the recognition of SRA International members who are outstanding teachers, researchers, or exemplary professionals in research administration.

Ellen Leibenluft, MD, Chief of the Unit on Affective Disorders in the Pediatrics and Developmental Neuropsychiatry Branch, Mood and Anxiety Disorders Program was granted tenure in October.

Denise Juliano-Bult, MSW, Program Chief of the Division of Services and Intervention Research (DSIR) Systems Research Program, as NIMH representative to the cross-Institute NIH Social Work Research Working Group, received the Office of the Director Merit Honor Award in November 2006. This group award was given “In recognition of outstanding contributions in developing and implementing a trans-NIH program to support research on social work practice and concepts in health.”

Husseini Manji, MD, Chief of the Laboratory of Molecular Pathophysiology and the director of the Mood and Anxiety Disorders Program recently accepted the position of deputy editor of *Biological Psychiatry* in September. Also, in December Dr. Manji was appointed as editor of *Neuropsychopharmacology Reviews*, an official publication of the American College of Neuropsychopharmacology (ACNP) which replaces the ACNP’s *Psychopharmacology: A Generation of Progress* volumes.

Dietmar Plenz, PhD, chief of the Unit of Neural Network Physiology, Laboratory of Systems Neuroscience was granted tenure in October.

Judith L. Rapoport, MD, Chief of the Child Psychiatry Branch, started her term as President Elect of ACNP in January 2007 and will take the role of President starting in 2008.

Daniel Weinberger, MD, and **Andreas Meyer-Lindenberg, MD, PhD, MSc**, were named the inaugural recipients of the Roche-Nature Medicine Award for Translational Neuroscience in September. Dr. Weinberger, Director of the Genes, Cognition and Psychosis Program received the Senior Prize in recognition of his work, which helped define dysfunctional neural systems in the brain that appear to underlie clinical symptoms of schizophrenia, and his influence in focusing research on the role of abnormal brain development as a risk factor for the illness. Dr. Meyer-Lindenberg, sharing the Junior Prize with NIMH grantee Jay Adam Gingrich, MD, PhD, of Columbia University, was recognized for his research contributions to understanding the pathophysiology of schizophrenia, identifying an imaging marker of schizophrenia, as well as his significant discoveries about the childhood disorder known as Williams Syndrome.

Staff Changes

Arriving:

Lauren Baskir, PhD, joined the Division of Pediatric Translational Research and Treatment Development (DPTR) as a Society for Research in Child Development (SRCD) Executive

Branch Fellow. Dr. Baskir received her PhD in Applied Developmental Psychology from Fordham University in May 2006. Her research interests include developmental neuropsychology, specifically the connection between observed behavior and anatomical brain functioning in children and adolescents.

Lauren Choate joined the Office of the Director (OD) in June 2006 as a Research Assistant to Marlene Guzman. Ms. Choate also works on multiple projects in the Office of Science Policy, Planning, and Communications (OSPPC) and with the Office of Resource Management (ORM).

Wen Chen, PhD, joined the Office of Cross-Cutting Science and Scientific Technology and DNBBS as a contractor program analyst. She previously worked at *Neuron* as a Scientific Editor. Dr. Chen completed her postdoctoral work in the Biological Engineering Division of MIT, with a particular interest on DNA damage-mediated signal transduction, using quantitative proteomic approaches. She received her PhD from Harvard Medical School, working in Dr. Michael Greenberg's laboratory on protein phosphorylation-mediated transcription in the nervous system.

Joanna Chisar, RN, joined the Clinical Trials Operations and Biostatistics Unit, DSIR, in September as a contractor and part-time consultant to DATR and DNNBS on operations of their ongoing clinical studies.

Stephen Foote, PhD, former director of DNBBS, re-joined DATR in the Experimental Therapeutics Branch in December as a part-time contractor. He is working on developing the division portfolio and initiatives related to the Foundation for NIH.

Stephen Gerber joined DSIR in November as a contractor to serve as primary contact on PLANET for Mental Health, a web portal aimed to connect NIMH epidemiology, intervention and services research with the mental health practice community.

Su Koester, PhD, joined DNBBS as Deputy Director in December, returning to her extramural NIMH roots after serving as Associate Director for Science in the NIMH IRP from 1998-2006. In her new position, Dr. Koester will be involved with trans-NIH and cross-divisional initiatives, special projects, and neuroscience research policy issues. She will serve as a liaison to build closer ties between the intramural program and extramural efforts.

Nicole Ma joined DNBBS as a program analyst for the Molecular Libraries and Imaging Roadmap Initiative. Ms. Ma is a recent graduate of the University of Richmond with a degree in biology.

Mary Partlow joined the Science Writing and Press Branch of OSPPC, in November as contractor for media relations and science editing. She is a senior strategic health communications professional with expertise in media relations, awareness campaign design and implementation, patient recruitment, and strategic planning. Most recently, she was the project lead at Matthews Media Group in Rockville, Maryland on a contract to manage media relations for announcing results of several of NIMH's large clinical trials.

Phyllis Quartey joined the Office of Constituency Relations and Public Liaison (OCRPL) in December as a program analyst. Ms. Quartey is a graduate of the University of Rochester and received her master's degree in Public and Community Health Education from the University of Maryland in 2005. She most recently worked at BRI Consulting Group on contracts with the CDC, the Federal Emergency Management Agency (FEMA), and the National Institute of Standards and Technology (NIST).

Vijaya Rao joined the OD in September 2006 as Dr. Richard Nakamura's assistant. Prior to her arrival at NIMH, she conducted research at the Institute of Neuroscience and Department of Cell and Molecular Biology at Northwestern University, as well as at the Medical College of Wisconsin. She recently received her undergraduate degree from Northwestern University and plans to go on to medical school.

Michael Schoenbaum, PhD, joined DSIR in November as a Senior Advisor and will be heading up the Institute's internal analytical team. Also, along with Division Director Dr. Philip Wang, Dr. Schoenbaum will be leading the effort to compile burden of disease statistics and create datasets for NIMH to facilitate analyses on the impact and costs of mental disorders.

Tawnie Silva joined OSPPC in November, to assist in coordination of various aspects of the Neuroscience Blueprint, the NIH Roadmap, as well as the NIMH clearance process for manuscripts. Prior to arriving at NIMH, Ms. Silva served as a laboratory manager in the Department of Neurobiology at UCLA.

Anne Sperling, PhD, a Science and Technology fellow from American Association for the Advancement of Science (AAAS), joined OSPPC in September. Dr. Sperling recently completed her post-doctoral fellowship at the Neurology Department at Georgetown University Medical, where she had been studying the neural mechanisms responsible for reading and language, concentrating on the mechanisms underlying dyslexia. She graduated from Cornell University and earned her PhD in Neuroscience from the University of Southern California.

Lesley Whipp joined the Grants Management Branch as a junior grants management specialist with DNBB, having previously served at the National Institute of Neurological Disorders and Stroke (NINDS).

Tricia (Moore) Zarfoss joined NIMH in November, working as a Program Advisor in the Management Analysis and Services Branch (MASB) of ORM. Ms. Moore's background in human resources will help her serve as the primary NIMH advisor on workforce issues and performance activities.

Departing:

Leslie Boggs left the Division of Extramural Activities (DEA) Grants Management Branch to accept a position at the National Institute of Allergies and Infectious Diseases (NIAID). She had served NIMH for more than four years.

Cyndi Shannon-Weickert, PhD, departed from her tenure track position in the Genes, Cognition and Psychosis Program in IRP for a post in Australia.

Regina Smith James, MD, left NIMH in October 2006 to transition to her new role at NICHD, where she is a Medical Officer in the Division of Special Populations. Over the past two years at NIMH, Dr. James headed up the eating disorder and bipolar disorder programs in the Affective and Regulatory Disorders Branch, DPTR.

Monica Radford left in NIMH in October after nearly three years of dedicated service with OSPPC. She accepted a position as Executive Assistant to the Deputy Director of the National Institute of Biomedical Imaging and Bioengineering NIBIB.

Dawn Walker, of the DEA Grants Management Branch, retired from Federal government following almost two years of service in order to pursue personal and career goals.

Marilyn Weeks, Press Officer, Science Writing and Press Branch, OSPPC, retired from the Federal government in September 2006. Over her 16-year tenure at NIMH, Ms. Weeks played a key role in managing the Institute's media relations, which included developing media campaigns to disseminate information on NIMH research and programs; creating, reviewing, and distributing press releases on research advances; and responding to numerous press inquiries. She was also devoted to her duties as the Institute's chief Freedom of Information Act (FOIA) officer. Ms. Weeks is currently enjoying her retirement in North Carolina.

Transfers and Other NIMH Staff Changes:

Mary Blehar, PhD, is on detail with the Extramural Review Branch as a Scientific Review Administrator.

Nancy Desmond, PhD, who has a dual role in the Office of Research Training & Career Development and the Molecular, Cellular, and Genomic Neuroscience Research (MC) Branch in DNBBS, will assume leadership of the Neuroendocrinology and Neuroimmunology Program within the MC.

A. Roger Little, PhD, is serving a part-time detail in OSPPC where he is helping to coordinate the NIH Roadmap and Neuroscience Blueprint activities for the Institute.

Marc Mopsick is on detail to the Extramural Policy Branch as an Information Technology Specialist.

Laurie Nadler, PhD, joined the MC Branch in DNBBS to assume leadership of the Neuropharmacology Program and will serve as the coordinator for the Basic Neuroscience Centers program.