Director's Report to the National Advisory Mental Health Council

September 21, 2007

I am pleased to welcome members of the National Advisory Mental Health Council (NAMHC) and other participants and guests to our 216th Council meeting. Since our last meeting in May, the National Institute of Mental Health (NIMH) has made progress on several fronts, which I share with you in this report.

NIH-Wide Update

Update on Electronic Submission

The change to electronic submission for grant programs originally targeted to transition after May 2007 has been delayed; these include applications for Career Development (K), Fellowship (F), Training & Development (T&D), and complex mechanisms grants. Although all agencies were expected to transition to the new Adobe-based forms by the end of fiscal year 2007 (FY07), Grants.gov has extended the deadline into 2008. For more information, see the Electronic Submission web site at http://era.nih.gov/ElectronicReceipt/index.htm.

Secretary's Advisory Committee on Human Research Protections (SACHRP)

During the past year, the SACHRP began to focus on Consent Capacity (impaired decision-making abilities). A recently formed subcommittee is looking at the issue broadly, focusing on the perspective of this vulnerable population, the need to improve procedures for involving legally-authorized representatives, and approaches that would be too restrictive. The subcommittee is co-chaired by David Strauss and Laurie Flynn, and includes as members Paul Appelbaum, Laura Roberts, Tim Walsh, and others. David Shore, NIMH Associate Director for Clinical Research, serves as a National Institutes of Health (NIH) liaison to this group. The Department of Health and Human Services' (HHS) Office of Human Research Protections (OHRP) issued a Request for Information in September (http://www.hhs.gov/ohrp/documents/20070905.htm) regarding whether guidance or additional regulations are needed to adequately protect adults with impaired decision-making capacity who are potential subjects in research. The deadline is December 4, 2007.

NIH Roadmap—Selected Updates

The NIH Roadmap is a trans-NIH effort to support innovative science, stimulate interdisciplinary research, and reshape clinical research to accelerate medical discovery and improve public health. Currently, workgroups co-chaired by the Directors of NIH Institutes and Centers (ICs) and populated by nominees from interested Institutes are developing initiatives for "Roadmap 1.5." A full summary of Roadmap activities can be found at http://www.nihroadmap.nih.gov/, and an update on Roadmap 1.5 at http://nihroadmap.nih.gov/roadmap15update.asp.

Epigenomics

Epigenetics is an emerging frontier of science that involves the study of changes in the regulation of gene activity and expression that are not dependent on gene sequence. Epigenomics refers to more global analyses of epigenetic changes across the entire genome. The overall hypothesis of the NIH Roadmap Epigenomics Program is that the origins of health and susceptibility to disease are, in part, the result of epigenetic regulation of the genetic blueprint. This program will transform biomedical

research by developing comprehensive reference epigenome maps and developing new technologies for comprehensive epigenomic analyses. More information on the Epigenomics Program can be found at http://nihroadmap.nih.gov/epigenomics/.

Microbiome

Within the body of a healthy adult, microbial cells are estimated to outnumber human cells by ten to one. These communities, which comprise the human microbiome, remain largely unstudied, leaving almost entirely unknown their influence upon human development, physiology, immunity, and nutrition. The NIH Roadmap initiated the Human Microbiome Project (HMP) with the mission of generating resources enabling comprehensive characterization of the human microbiome and analysis of its role in human health and disease. The NIH HMP also will continue the practice established by the Human Genome Project of international collaboration to create a comprehensive and publicly available data set. For more information, see http://nihroadmap.nih.gov/hmp/.

Ongoing NIH Roadmap Initiatives

Interdisciplinary Research Consortia

Roadmap funds were awarded in September to nine interdisciplinary consortia which will each address health challenges that have been resistant to traditional research approaches. The objectives of the consortia range broadly: deciphering the basis of neuropsychiatric disorders, developing new approaches to drug discovery and targeted gene therapy, preserving fertility in women with cancer, understanding the fundamentals of the aging process, developing a coordinated and systematic approach to regenerative medicine and obesity, probing the relationship between self-control and addictive behavior, and developing targeted molecular therapies for neurodegenerative disorders.

Bioinformatics and Computational Biology

In June, a blue-ribbon panel of scientists assessed this initiative, which supports a network of National Centers for Biomedical Computing and projects that collaborate with that network. Their report was supportive, and NIH IC directors are currently considering the future of this initiative within the context of the NIH Roadmap.

Patient Reported Outcomes Measurement Information System (PROMIS)

Work from the first two years of the PROMIS Initiative was highlighted in a special issue of *Medical Care* in May 2007. The issue included articles on domain concept development, qualitative item review, a psychometric evaluation plan, applications of item response theory to the Medical Outcomes Study and Pediatric Quality of Life Inventory items, and administration interface considerations for individuals with disabilities. The PROMIS network is currently analyzing item responses from more than 20,000 respondents to calibrate item banks measuring pain, fatigue, physical functioning, depression, anxiety, anger, and social functioning and/or participation. Upon completion, this project is expected to produce patient-reported outcome measures that are efficiently administered and more precise than existing measures.

Clinical and Translational Science Awards (CTSAs)

The CTSAs are a new consortium to transform how clinical and translational research is conducted, ultimately enabling researchers to provide new treatments to patients more quickly and efficiently. The consortium is designed to:

- Encourage the development of new methods and approaches to clinical and translational research

- Improve training and mentoring to ensure that new investigators can navigate the increasingly complex research system
- Design new and improved clinical research informatics tools
- Assemble interdisciplinary teams that cover the complete spectrum of medical research
- Forge new partnerships with private and public health care organizations

Twelve CTSAs were funded in FY06, and the National Center for Research Resources (NCRR) plans to fund an additional 12 Centers in FY07.

Molecular Libraries Screen Centers Network (MLSCN)
The MLSCN (http://mli.nih.gov) is in the final year of its three-year funding period and has made significant progress toward finding biologically active compounds that can be used as research tools. As of August 2007, MLSCN advances include identification of three new classes of small molecules that may be useful for treating Gaucher disease (an inherited metabolic disorder), and guidelines for reporting small-molecule high throughput screening data. These advances will have high impact on future studies in chemical biology and bio-molecular screening.

In response to a Molecular Libraries Probe Production Centers Network program announcement issued in April, 31 pre-applications for screening and probe generation centers were received. Highly meritorious pre-applications will be invited to apply for the formal Request for Applications (RFA) using the U54 cooperative agreement mechanism in January 2008. There were 29 publications attributed to funding from the Molecular Libraries and Imaging Initiative during 2007.

NIH Blueprint for Neuroscience Research
The Neuroscience Blueprint (http://braininfo.us/blueprint/index.html) is a framework to enhance cooperation among the 15 NIH ICs that support research on the nervous system and NIH's Office of Behavioral and Social Science Research (OBSSR). Created in 2004, the Blueprint now has more than 20 project teams steering a variety of initiatives that provide tools, resources, and training to the neuroscience research community in ways that cut across boundaries of individual ICs. The Blueprint focused on neurodegeneration in 2007, and will focus on neural development in 2008, and neural plasticity in 2009. The Blueprint IC directors recently decided to continue the Blueprint initiative beyond FY09. Since May, several activities under the Blueprint have moved forward:

Blueprint Neurodegeneration Project Team
Team leaders: Bob Baughman, National Institute of Neurological Disorders and Stroke (NINDS); Diane Murphy, NINDS; Michael Oberdorfer, National Eye Institute (NEI); Andrew Monjan, National Institute on Aging (NIA); and Dan Sklare, National Institute on Deafness and Communication Disorders (NIDCD)
In response to RFAs issued for research on biomarkers for neurodegeneration and on new approaches to drug delivery to the central nervous system (CNS), 28 R21 grants were awarded. In response to RFAs regarding interdisciplinary training and interdisciplinary career development, respectively, three F32s and three K18 awards were approved for funding.

Neurodevelopment Workshop Team
Team leaders: Beth-Anne Sieber, NIMH; and Bob Riddle, NINDS
The November 2006 Blueprint workshop on neurodevelopment is now bearing fruit in the form of several funding initiatives for FY08.

Neuroplasticity Workshop Team

Team Leaders: Nancy Pilotte, National Institute on Drug Abuse (NIDA); and Chiiko Asanuma, NIMH

To seek input from the extramural community on opportunities for neuroplasticity research, a three-day workshop was held in August 2007 on the NIH campus in Bethesda, Maryland. The workshop, which will inform plans for FY09 funding initiatives, was co-chaired by Dr. Carol Barnes, of the University of Arizona, and Dr. Richard Tsien, of Stanford University.

Blueprint Informatics Team

Team leader: Michael Huerta, NIMH

Two Blueprint-affiliated program announcements were issued to promote the sharing of data and tools in ways that would be useful to the broad neuroscience community. The first (http://grants.nih.gov/grants/guide/pa-files/PAR-07-425.html) encourages sharing data through the development of common vocabularies to integrate two or more significant datasets. The second announcement (http://grants.nih.gov/grants/guide/pa-files/PAR-07-426.html) encourages scientists to make their data or tools more broadly available by using two large NIH supported infrastructures, the caBIG™ program and the Biomedical Informatics Research Network (BIRN).

Clearinghouse for Neuroimaging Software and Data

Team leader: Yantian Zhang, National Institute of Biomedical Imaging and Bioengineering (NIBIB)

The project team re-issued two announcements soliciting applications to enhance the interoperability and adoptability of existing neuroimaging informatics tools and resources: Neuroimaging Informatics Software Enhancement for Improved Interoperability and Dissemination (http://grants.nih.gov/grants/guide/pa-files/PAR-07-417.html) and Administrative Supplements for Neuroimaging Informatics Software Enhancement for Improved Interoperability and Dissemination (http://grants.nih.gov/grants/guide/notice-files/NOT-EB-07-006.html). The Neuroimaging Informatics Tools and Resources Clearinghouse (NITRC) website, which aims to offer comprehensive information on functional magnetic resonance imaging (fMRI) tools through comments and ratings from users in the research community, is available at: http://www.nitrc.org/

NIMH Update

NIMH Autism Team

In July, NIMH established an Autism Team within the Office of the NIMH Director to support the work of the Interagency Autism Coordinating Committee (IACC). The Combating Autism Act of 2006 established a new IACC that will be responsible for coordinating autism spectrum disorder (ASD) research activities across several Federal agencies, including developing a national strategic plan for ASD research. The new IACC will have its inaugural meeting in November 2007 and aims to approve its first strategic plan at its subsequent meeting in May 2008. The IACC will update the ASD research strategic plan annually. The Team will also coordinate and produce Congressionally-mandated reports and provide oversight of the National Database for Autism Research (NDAR), a web-based tool that autism researchers around the world can use to collect and share information. The NIMH Division of Developmental Translational Research and Treatment Development (DDTR—formerly the Division of Pediatric Translational Research and Treatment Development) will continue to provide programmatic support for NIMH-funded ASD research, and the NIH Autism Coordinating Committee will continue to provide NIH-wide program coordination of ASD activities. The Team members are Joyce Chung, MD, Autism Coordinator; Steve Foote, PhD,

Senior Science Advisor; Diane Buckley, MA, Program Chief for Autism Reports and Evaluation; Dan Hall, MBA, NDAR Manager; and Takea Herbert, Program Assistant.

NIH Pediatric MRI Data Repository

The NIH-sponsored study of healthy pediatric brain development had its first data release to the scientific community in June 2007. The study is following more than 500 typically-developing children, from newborns to young adults, over three or more data points using structural MRI scans and correlated clinical and behavioral data. In addition, ancillary projects are collecting diffusion tensor imaging (DTI) and spectroscopy data on a significant number of children. The study is unique in its inclusion of infants and very young children, its use of a variety of imaging modalities, its inclusion of a significant amount of clinical/behavioral data, and its epidemiologically-based sampling strategy. Data collection ended in August 2007, and all data are expected to become available in 2008 to biomedical and biobehavioral researchers.

Science of Note

Global Survey Reveals Significant Gap in Meeting World's Mental Health Care Needs

Mental disorders rank among the top 10 illnesses causing disability, yet the world's mental health care needs are largely going unmet, according to Philip S. Wang, MD, DrPH, currently director of the NIMH Division of Services and Intervention Research (DSIR), and colleagues. In a survey of 17 countries conducted as part of the World Mental Health Survey Initiative, the researchers analyzed data from 84,848 adults across all economic spectrums. The survey found that, overall, fewer people with mental disorders in less-developed countries sought services compared with people in developed countries. In addition, people in countries spending more of their gross national product on health care used services more often. The US population used services more than any other country, at 18 percent. By comparison, 11 percent of France's population used services. The lowest rate of services use was 1.6 percent in Nigeria. In all countries surveyed, women were more likely than men to seek mental health services. Most people who sought care received help from the general medical sector (primary care doctors, nurses) rather than specialized mental health services (psychiatrists, psychologists), religious or community counselors, or complementary and alternative medicine providers (including traditional healers). Inadequate services were most commonly found in low-income countries, but even in some high-income countries, people received inadequate services. For example, in the United States, only 18 percent received minimally adequate services—much lower than any other high-income country. "Minimally adequate services" was defined as at least eight visits to any service sector, being in ongoing treatment at the time of the study, or receiving a medication for at least one month with four or more visits to a medical professional over a 12-month period. The next lowest level of minimally adequate services in a high-income country was 32 percent, in Japan. France and Germany had the highest level of adequate services, at 43 percent each. The study results show evidence of a striking disconnect in the US mental health care system, as well as the need to help developing countries implement more effective mental health care services.

Wang PS, Aguilar-Gaxiola S, Alonso J, Angermeyer MC, Borges G, Bromet EJ, Bruffaerts R, de Girolamo G, de Graaf R, Gureje O, Haro JM, Karam EG, Kessler RC, Kovess V, Lane MC, Lee S, Levinson D, Ono Y, Petukhova M, Posada-Villa J, Seedat S, Wells JE. Use of mental health services for anxiety, mood, and substance disorders in 17 countries in the WHO world mental health surveys. Lancet. 2007 Sep 8;370(9590):841-50.

Studies Refine Understanding of Treatments for Bipolar Disorder

Two articles on the NIMH-funded Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD) provide additional details on best practices for treating people with bipolar disorder, a sometimes debilitating illness marked by severe mood swings between depression and mania. In one of the papers, Joseph Goldberg, MD, of Mount Sinai School of Medicine, and colleagues, reported that among STEP-BD participants who experienced manic symptoms while also in the midst of a depressive episode, those who received antidepressant medication along with a mood stabilizer recovered no faster than those who received a mood stabilizer plus placebo (sugar pill). The results are consistent with earlier STEP-BD results published in March 2007. Moreover, Goldberg and colleagues found that at the three-month follow-up, manic symptoms were more severe among those who had received the antidepressant, compared with those who had received the placebo. Hence, the researchers caution that adding antidepressant medication to a bipolar treatment routine may actually worsen existing manic symptoms.

In the second article, David Miklowitz, PhD, of the University of Colorado, and colleagues evaluated STEP-BD participants' improvements in relationship, life, and work skills over a nine-month period of psychotherapy in addition to medication treatment. Participants were randomly assigned to receive either 30 sessions over the nine months (intensive psychotherapy) or three sessions (brief therapy). Those who received an intensive psychotherapy in addition to medication reported better life satisfaction and better relationship skills than those who received only brief therapy and medication. However, people receiving intensive psychotherapy fared no better in vocational skills than those in other therapy groups. Miklowitz and colleagues suggest that a different approach that targets specific vocational skills may be necessary.

Goldberg JF, Perlis RH, Ghaemi SN, Calabrese JR, Bowden CL, Wisniewski S, Miklowitz DJ, Sachs GS, Thase ME. Adjunctive Antidepressant Use and Symptomatic Recovery Among Bipolar Depressed Patients With Concomitant Manic Symptoms: Findings From the STEP-BD. Am J Psychiatry. 2007 Sep;164(9):1348-55.

Miklowitz DJ, Otto MW, Frank E, Reilly-Harrington NA, Kogan JN, Sachs GS, Thase ME, Calabrese JR, Marangell LB, Ostacher MJ, Patel J, Thomas MR, Araga M, Gonzalez JM, Wisniewski SR. Intensive psychosocial intervention enhances functioning in patients with bipolar depression: results from a 9-month randomized controlled trial. Am J Psychiatry. 2007 Sep;164(9):1340-7.

Manic Phase of Bipolar Disorder Benefits from Breast Cancer Medication

Current medications for bipolar mania take a week or more to begin working, during which a person's symptoms may lead to risky behaviors and other consequences. The medication tamoxifen (Nolvadex), best known as a treatment for breast cancer, can dramatically reduce manic symptoms in bipolar disorder more quickly than many standard medications, found NIMH researcher Carlos Zarate, MD, and colleagues. An enzyme called protein kinase C (PKC) that regulates activities in brain cells is thought to be overactive during the manic phase of bipolar disorder, and tamoxifen blocks this enzyme. In this study, patients having a manic episode were treated with either tamoxifen or a placebo. Sixty-three percent of tamoxifen patients had reduced symptoms, compared with only 13 percent of placebo patients. Tamoxifen patients responded by the fifth day, corresponding with the amount of time needed to reach levels sufficient to inhibit PKC. However, tamoxifen itself might not become a treatment of choice because it also blocks estrogen—the property that makes it useful as a treatment for breast cancer—and prolonged use raises risk of endometrial cancer. However, targeting PKC directly in developing new medications holds promise for getting this risky phase of bipolar disorder under control faster.

Zarate CA Jr, Singh JB, Carlson PJ, Quiroz J, Jolkovsky L, Luckenbaugh DA, Manji HK. Efficacy of a protein kinase C inhibitor (tamoxifen) in the treatment of acute mania: a pilot study. Bipolar Disord. 2007 Sep;9(6):561-70.

Only Half of Bipolar Patients Take Medications as Prescribed

Lithium (sometimes called Eskalith) and anticonvulsant medications are the primary treatments for bipolar disorder, but prior research estimated that around 40 percent of bipolar patients do not take medications as prescribed. In the largest study of treatment adherence in people with bipolar disorder, Martha Sajatovic, of Case Western Reserve University, and colleagues reviewed Department of Veterans Affairs (VA) patient registries and pharmacy data for 44,637 bipolar patients. Patients who received 80 percent or more of the total amount of medications necessary to take the medications as prescribed were considered fully adherent, those who receive 50–80 percent were considered partially adherent, and those who received less than 50 percent were considered nonadherent. Based on this classification, 54.1 percent of bipolar patients were fully adherent, 24.5 percent were partially adherent, and 21.4 percent were nonadherent. Those who were nonadherent were more likely to be homeless, unmarried, were more likely to be a minority, and were more likely to have a substance abuse disorder and fewer outpatient psychiatric visits. Those taking two mood stabilizing medications had better adherence than those taking only one. These findings underscore the importance of improving treatment adherence, and suggest subgroups of patients who are more likely to be nonadherent and may be in need of intensive efforts to ensure adequate treatment adherence.

Sajatovic M, Valenstein M, Blow F, Ganoczy D, Ignacio R. Treatment adherence with lithium and anticonvulsant medications among patients with bipolar disorder. Psychiatr Serv. 2007 Jun;58(6):855-63.

National Survey Indicates Higher Prevalence of Bipolar Disorder Than Previously Thought

Historically, three major types of bipolar disorder (BP) have been recognized psychiatric diagnoses: bipolar I (BP-I), bipolar II (BP-II), and bipolar not otherwise specified (BP-NOS). There is growing recognition, however, that the illness has a spectrum of expression that is substantially more common than the 1 percent BP-I prevalence traditionally found in population surveys. Using data and methods from the National Comorbidity Survey Replication (NCS-R), NIMH researcher Kathleen Merikangas, PhD, and colleagues assessed lifetime and 12-month prevalence of major mental disorders in 9,282 American adults ages 18 and older. Indicators of clinical severity included age at onset, chronicity, symptom severity, role impairment, comorbidity, and treatment. The data show that lifetime (and 12-month) prevalence estimates are at 1.0 percent (0.6 percent) for BP-I, 1.1 percent (0.8 percent) for BP-II, and 2.4 percent (1.4 percent) for subthreshold BP. For this study, subthreshold BP was defined as recurrent hypomania without a major depressive episode or with fewer symptoms than required for threshold hypomania. Most respondents with threshold and subthreshold BP had lifetime comorbidity with other major mental disorders, particularly anxiety disorders. Clinical severity and role impairment are greater for threshold than for subthreshold BP, and for BP-II episodes of major depression than for BP-I depressive episodes. Neverthelesss, subthreshold cases still have moderate to severe clinical severity and role impairment. Although most people with BP receive lifetime professional treatment for emotional problems, use of antimanic medication is uncommon, especially in general medical settings.

Merikangas KR, Akiskal HS, Angst J, Greenberg PE, Hirschfeld RM, Petukhova M, Kessler RC. Lifetime and 12-month prevalence of bipolar spectrum disorder in the National Comorbidity Survey replication. Arch Gen Psychiatry. 2007 May;64(5):543-52.

Rates of Bipolar Diagnosis in Youth Rapidly Climbing, Treatment Patterns Similar to Adults

Examining 10 years of data from the National Ambulatory Medical Care Survey, Mark Olfson, MD, MPH, of New York State Psychiatric Institute at Columbia University, NIMH researcher Gonzalo Laje, MD, and colleagues estimated that in the United States from 1994–2003, the number of office visits resulting in a diagnosis of bipolar disorder for youths ages 19 and younger jumped 40-fold,

from 25 to 1,003 per 100,000 people. Over the same time period, for adults ages 20 and older, the number of office visits resulting in a bipolar disorder diagnosis nearly doubled, from 905 to 1,679 per 100,000 people. The causes for this increase are unclear. Also, despite limited evidence on treatments for children with bipolar disorder, the researchers found similar treatment patterns for adults and younger patients in terms of use of psychotherapy and prescription medications, suggesting that doctors may be basing their treatment choices for bipolar youth on prescribing practices for adults with the disorder. Given the relative lack of studies on appropriate treatments for youth with bipolar disorder, the researchers noted the urgent need for more research on the safety and effectiveness of medication treatments for this age group.

Moreno C, Laje G, Blanco C, Jiang H, Schmidt AB, Olfson M. National trends in the outpatient diagnosis and treatment of bipolar disorder in youth. Arch Gen Psychiatry. 2007 Sep;64(9):1032-9.

Parents' Diagnoses Help Distinguish Bipolar Disorder from Severe Mood Dysregulation

Children with bipolar disorder have manic episodes of elated mood and/or irritability and increased activity, in addition to episodes of depression. In contrast, children with a related disorder called severe mood dysregulation (SMD) are chronically irritable and hyperactive, without clear-cut manic episodes. However, because both children with SMD and those with bipolar disorder can be irritable and hyperactive, children with SMD may be thought to possibly have another form of bipolar disorder, which can affect treatment decisions. Given that bipolar disorder is known to run in families, one way to test whether SMD is a type of bipolar disorder is to study the family's mental health. In their study, NIMH researcher Melissa Brotman, PhD, and colleagues suggested that if SMD is a broadly defined type of bipolar disorder, then parents of children with SMD should have bipolar disorder as often as parents of children with strictly-defined bipolar disorder. They found that about 33 percent of parents of children with bipolar disorder had bipolar disorder themselves. In comparison, only about 2.7 percent of parents of children with SMD had bipolar disorder. Bipolar disorder was the only mental illness diagnosed at significantly different rates between the two parent groups. According to the researchers, these findings suggest that children with symptoms of SMD may not have a type of bipolar disorder.

Brotman MA, Kassem L, Reising MM, Guyer AE, Dickstein DP, Rich BA, Towbin KE, Pine DS, McMahon FJ, Leibenluft E. Parental Diagnoses in Youth With Narrow Phenotype Bipolar Disorder or Severe Mood Dysregulation. Am J Psychiatry. 2007 Aug;164(8):1238-1241.

Bipolar Youth Show Distinct Pattern of Brain Development

The first pictures of the brain changing before-and-after the onset of pediatric bipolar disorder reveal a distinct pattern of development, when compared to that seen in healthy youth or in childhood onset schizophrenia. Repeated MRI brain scans of youth, ages 7–22, followed over time as they developed symptoms of mania and depression, showed asymmetrical gains and losses of the brain's working tissue, or gray matter, reported NIMH researcher Nitin Gogtay, MD, and colleagues. Some pruning of gray matter, neurons and their connections, is normal as the brain matures and circuitry is streamlined for efficiency. Cases of childhood onset schizophrenia, which are very rare, show an exaggeration of this normal pattern of pervasive gray matter loss, with affected teens losing gray matter in the prefrontal cortex—an area at the front of the brain responsible for judgment and decision-making skills—at four times the normal rate. By contrast, children with bipolar disorder showed a more complicated pattern of gray matter gains in certain areas in the left half of the brain, and losses in the right half and in mood regulating circuitry in the mid-front part of the brain. A developmental pattern was shared by youth diagnosed as "multi-dimensionally impaired." These children had neither bipolar disorder nor schizophrenia, but experienced short psychotic episodes, attention problems, and—like their bipolar peers—unstable

moods. The latter indicates that the shared developmental pattern might reflect a tendency toward mood instability in general. These findings help put to rest speculation that pediatric bipolar disorder and childhood onset schizophrenia might stem from the same underlying illness process, despite overlapping symptoms and genetics.

Gogtay N, Ordonez A, Herman DH, Hayashi KM, Greenstein D, Vaituzis C, Lenane M, Clasen L, Sharp W, Giedd JN, Jung D, Nugent III TF, Toga AW, Leibenluft E, Thompson PM, Rapoport JL. Dynamic mapping of cortical development before and after the onset of pediatric bipolar illness. J Child Psychol Psychiatry. 2007 Sep; 48(9):852-62.

Drops in SSRI Prescriptions Rates Coincide with Increases in Youth Suicide

A 2004 spike in suicide rates coincided with a drop in antidepressant prescriptions for youth, following warnings from US and European regulatory agencies that the medications might trigger suicidal thoughts. In making a case for a possible link between these events, Robert Gibbons, PhD, of the University of Illinois at Chicago, and J. John Mann, MD, Columbia University, and colleagues, reported that SSRI (serotonin selective reuptake inhibitor) prescriptions for youth dropped by 22 percent in both the United States and the Netherlands during 2003-2004. In the Netherlands, youth suicides increased by 49 percent during 2003-2005. In the United States, such rates increased by 14 percent in 2004—the largest change since data collection began in l979. However, a more definitive analysis must wait until later in 2007, when the US suicide rates for 2005 become available. The pattern of decreasing SSRI prescription rates coinciding with increasing suicide rates held regardless of age. The researchers predicted more increases in suicides if current trends continue.

Gibbons RD, Brown CH, Hur K, Marcus SM, Bhaumik DK, Erkens JA, Herings RM, Mann JJ. Early Evidence on the Effects of Regulators' Suicidality Warnings on SSRI Prescriptions and Suicide in Children and Adolescents. Am J Psychiatry. 2007 Sep;164(9):1356-63.

Discovery of Likely Antidepressant Binding Site May Lead to Better Medications

Nobel Laureate Julius Axelrod showed decades ago that tricyclic antidepressants work by shutting molecular pumps, on brain cells, called sodium-coupled transporters. This action prevents neurotransmitters from flooding into the cells, thus helping to relieve major depressive disorder. Recently, Eric Gouaux, PhD, of the Oregon Health & Science University, and colleagues identified a likely scenario of how the medications shut these pumps at the molecular level. In experiments with a similar pump in bacteria, the researchers showed that when tricyclic antidepressants bind to the pump, they change its molecular structure in a way that plugs it. The researchers caution against direct comparisons for now; the binding site for tricyclic antidepressants on human brain cells and that on bacteria may differ in some ways, although they operate in a virtually identical manner and are part of the same large family of pumps. But now that scientists know that plugging the pump appears to be one of the ways that antidepressant medications work, they may be able to develop medications that target these kinds of pumps more directly and efficiently, and perhaps with fewer side effects. The findings extend beyond depression to the development of better medications for treating depression and other mental illnesses in which pump dysfunction plays a role, such as autism and OCD.

Singh SK, Yamashita A, Gouaux E. Antidepressant binding site in a bacterial homologue of neurotransmitter transporters. Nature. 2007 Aug 23;448(7156):952-6.

Ketamine Relieves Depression in Just Hours, Points to Targets for New Medications

Previous NIMH research showed that the medication ketamine, when used experimentally for major depression, could relieve symptoms of the disorder in hours instead of the weeks or months it takes for current antidepressants to take effect. A study led by NIMH researcher Husseini K. Manji, MD,

helped clarify a possible mechanism behind this finding. An earlier study in humans showed that ketamine blocks a receptor called NMDA on brain cells, but the new study in mice shows that this is an intermediate step. Blocking NMDA increases the activity of another receptor, AMPA, and apparently, this boost in AMPA is crucial for ketamine's rapid antidepressant actions. Both NMDA and AMPA are receptors for the neurotransmitter glutamate, one of the chemical messengers that enables brain cells to communicate with each other. The glutamate system has been implicated in depression recently, leading to efforts to unravel its molecular machinery in search of abnormalities and of better targets for antidepressant medications. While ketamine itself probably won't come into use as an antidepressant because of its side effects, the new finding moves scientists considerably closer to understanding how to develop faster-acting antidepressant medications.

Maeng S, Zarate CA Jr, Du J, Schloesser RJ, McCammon J, Chen G, Manji HK. Cellular Mechanisms Underlying the Antidepressant Effects of Ketamine: Role of alpha-Amino-3-Hydroxy-5-Methylisoxazole-4-Propionic Acid Receptors. Biol Psychiatry. 2007 Jul 20; [Epub ahead of print]

Success or Failure of Antidepressant Citalopram Predicted by Gene Variation

NIMH researcher Francis J. McMahon, MD, and colleagues reported that a variation in the gene GRIK4 appears to make people with major depression more likely to respond to the antidepressant medication citalopram (Celexa) than are people without the variation. The researchers examined the genetic material of 1,816 participants from the recently completed NIMH clinical trial, the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) study. By using an advanced technique called "SNP tags," the researchers used fewer resources, in less time, than usually required for these kinds of studies. They discovered that people with the variation in the GRIK4 gene, which makes a protein that acts as a receptor in the glutamate system, had a higher likelihood of response to citalopram. The increased likelihood was small, but when people had both this variation and one in a different gene shown in an earlier study to have a similarly small treatment effect, they were 23 percent more likely to respond to citalopram than were people with neither variation. The finding addresses a key issue in mental health research: that some patients respond to the first antidepressant they try, but many don't. Each medication takes weeks to exert its full effects, during which a patient's depression may worsen. Genetic studies such as conducted by McMahon and colleagues may lead to a better understanding of which treatments are likely to work for individual patients.

*Paddock S, Laje G, Charney D, Rush AJ, Wilson AF, Sorant AJ, Lipsky R, Wisniewski SR, Manji H, McMahon FJ. Association of GRIK4 with outcome of antidepressant treatment in the STAR*D cohort. Am J Psychiatry. 2007 Aug;164(8):1181-8.*

Depression Intervention in Primary Care Reduces Risk for Death in Older Adults

Some studies have shown that depression is independently associated with an increased risk of death. However, few studies have examined whether a depression-focused treatment may modify this risk. Joseph Gallo, MD, MPH, University of Pennsylvania, and colleagues analyzed the relationship between a depression-care management intervention and risk for death among older primary care patients over a five-year period. The investigators looked at data from the Prevention of Suicide in Primary Care Elderly: Collaborative Trial (PROSPECT) in conjunction with supplementary records obtained from the National Death Index. They found that after a four-year follow-up period, patients who received the depression care management intervention were less likely to have died than those in usual care practices. This reduction in risk for death was observed in patients with major depression, but not among those with clinically significant minor depression, and was almost entirely attributable to a reduction in deaths due to cancer. The results suggest that a collaborative care model for depression treatment in the primary care setting may have some

benefits for reducing the risk of death in older patients; however, the mechanism of this effect is unclear and needs further study.

Gallo JJ, Bogner HR, Morales KH, Post EP, Lin JY, Bruce ML. The effect of a primary care practice-based depression intervention on mortality in older adults: a randomized trial. Ann Intern Med. 2007 May 15;146(10):689-98.

Gene Variants Linked to Suicidal Thoughts in Some Men Starting Antidepressant Treatment

Recent studies have indicated that antidepressant treatment may increase the risk of suicidal thinking and behaviors in people up to age 25. Roy Perlis, MD, of Massachusetts General Hospital, and colleagues analyzed DNA samples of 1,447 STAR*D participants who reported no suicidal thinking or behavior prior to treatment and who received up to 12 weeks of the antidepressant citalopram. Perlis and colleagues focused on the participants' genetic variations—known as single nucleotide polymorphisms (SNPs)—that reside within or nearby the CREB1 gene, which scientists suspect is linked with major depression and possibly related to suicidal thinking and behavior, and also may be involved in how antidepressants work. Among the participants, 124 (8.6 percent) developed suicidal thinking after starting treatment, including 54 men. Two of the five SNPs studied were significantly and strongly associated with the onset of suicidal thinking in the men, but not in the women. In previous studies, the same two SNPs appeared to be associated with anger among men with major depression—a symptom commonly associated with suicide. Further analyses indicated that none of the five SNPs were linked to suicidal thought and behaviors in men before they began treatment. The authors conclude that if the results can be replicated, they will have tremendous potential for identifying a subset of people at greater suicidal risk during initial antidepressant treatment.

*Perlis R, et al. Association between treatment-emergent suicidal ideation with citalopram and polymorphisms near cyclic adenosine monophosphate response element binding protein in the STAR*D study. Arch Gen Psychiatry. 2007 Jun;64(6):689-697.*

New Imaging Technique Pinpoints Depression Circuits at Work in Real Time

To overcome the limitations of existing functional brain imaging techniques, Karl Disseroth, MD, PhD, of Stanford University and colleagues, developed a new high-speed technique called voltage-sensitive dye imaging. This technique reveals the split-second pace of brain circuits at work in real time and at the cellular level, as their electrical discharges make them glow. The researchers then used their new technique to pinpoint in rats a possible "final common pathway" where different causes of, and treatments for, major depression appear to converge. The Stanford team first created a depression-like state in rats by applying chronic mild stressors, and then looked for any resultant changes in the hippocampus, which regulates memory and mood and has been implicated in depression. Using the new imaging technique revealed that a smaller part of a hippocampal area called the dentate gyrus glowed in the samples from "depressed" rats than in samples from normal rats. The glowing circuitry expanded to normal size in "depressed" rats that had been treated with the antidepressant fluoxetine (Prozac). This was accompanied by increased birth of new neurons in the dentate gyrus, adding to evidence from previous studies that such neurogenesis is required for behavioral improvement following antidepressant treatment. Yet inhibiting neurogenesis failed to induce a depression-like state. Such studies can help link behavior to real-time brain circuit information and provide the foundation for understanding depression as a brain disorder.

Airan RD, Meltzer LA, Roy M, Gong Y, Chen H, Deisseroth K. High-speed imaging reveals neurophysiological links to behavior in an animal model of depression. Science. 2007 Aug 10;317(5839):819-23.

Antipsychotic Medications for Schizophrenia on Equal Footing in Improving Patients' Thinking Skills

Problems in thinking and reasoning (neurocognition) are often a central feature of schizophrenia, and can be the disease's most troublesome and difficult-to-treat symptoms. But current medications for schizophrenia do not target neurocognitive symptoms specifically. In the NIMH-funded Clinical Antipsychotic Trials for Intervention Effectiveness (CATIE), participants were randomly assigned to take either perphenazine (Trilafon)—an older, first-generation, antipsychotic medication—or one of several newer, second-generation medications—olanzapine (Zyprexa), quetiapine (Seroquel), risperidone (Risperdal), or ziprasidone (Geodon). Richard Keefe, PhD, of Duke University, and colleagues assessed the neurocognitive skills of 817 CATIE participants who completed an initial evaluation before the study began and, after being on the same medication for two months, had a second evaluation. The researchers measured neurocognitive change by comparing pre- and post-test results from 11 examinations designed to test thinking, memory, reasoning, and problem-solving abilities. They found a small rate of improvement among all the treatment groups, but no treatment group appeared to benefit more than the others. The results run contrary to previous studies and to the widely held belief that the newer, second-generation antipsychotics are better than the older medications in improving schizophrenia patients' cognitive skills. The researchers concluded that there was a need for new treatments that could more effectively address neurocognitive impairment in schizophrenia.

Keefe RS, Bilder RM, Davis SM, Harvey PD, Palmer BW, Gold JM, Meltzer HY, Green MF, Capuano G, Stroup TS, McEvoy JP, Swartz MS, Rosenheck RA, Perkins DO, Davis CE, Hsiao JK, Lieberman JA; CATIE Investigators; Neurocognitive Working Group. Neurocognitive effects of antipsychotic medications in patients with chronic schizophrenia in the CATIE Trial. Arch Gen Psychiatry. 2007 Jun;64(6):633-47.

Violence More Likely in Schizophrenia Patients with Past Childhood Conduct Problems

Some people with schizophrenia who become violent may do so for reasons unrelated to their current illness, according to Jeffrey Swanson, PhD, of Duke University, and colleagues. Using data from 1,445 participants in the CATIE study, the researchers found that, overall, 19 percent of participants committed acts of violence. Those with a history of childhood conduct problems reported violence twice as frequently (28 percent) as those without conduct problems (14 percent). In both groups, violence was more likely among those who were unemployed or underemployed, living with family or in restrictive settings (such as a halfway house or hospital), had been recently arrested, or involved with the police. Violence was associated with alcohol and substance abuse in both groups, but in the group with childhood conduct problems, violence was associated even with levels of alcohol and substance use considered below the threshold for abuse. The researchers also found that psychotic symptoms were not significantly associated with violence among participants with a history of childhood conduct problems. In contrast, the presence of psychotic symptoms was associated with an increase in violence among participants without a history of childhood conduct problems. Swanson and colleagues theorize that there may be two pathways in which adults with schizophrenia may become violent—one in which pre-existing conditions like that of antisocial conduct in childhood, regardless of the presence of psychotic symptoms, may link to violence, and one in which psychotic symptoms of schizophrenia themselves may link to violence. Based on their theory, antipsychotic medications used to treat psychosis may not be sufficient to treat violent symptoms in people who are at a higher risk due to pre-existing antisocial conduct problems.

Swanson JW, Van Dorn RA, Swartz MS, Smith A, Elbogen EB, Monahan J. Alternative Pathways to Violence in Persons with Schizophrenia: The Role of Childhood Antisocial Behavior Problems. Law Hum Behav. 2007 Jun 30; [Epub ahead of print]

Suspect Schizophrenia Genes Act Together to Thwart Working Memory

Schizophrenia is thought to stem from complex interactions among multiple genes and environmental factors. Two gene variants implicated in schizophrenia, COMT "Val" and GRM3 "A," interact to degrade the brain's ability to process information, discovered NIMH researcher Joseph Callicott, MD, and colleagues. Using fMRI, which shows how active parts of the brain are at any given moment by tracking the destination of oxygenated blood, the researchers scanned 29 healthy subjects while they performed working memory tasks to gauge how the genes affected information processing. The brain scans revealed an interaction during the task between COMT "Val" and GRM3 "A" that produced inefficient activity and poor connectivity in a key thinking circuit during a working memory task. The COMT "Val" version is associated with weaker signals transmitted via the messenger chemical dopamine, while the "A" version of GRM3 is associated with weaker glutamate activity. The researchers suggested that interacting genes can affect key chemical messenger systems to impair the efficiency of communications signals in a circuit implicated in schizophrenia. Imaging these interactions deepens the understanding of disease mechanisms and may help point the way to improved treatment.

Tan HY, Chen Q, Sust S, Buckholtz JW, Meyers JD, Egan MF, Mattay VS, Meyer-Lindenberg A, Weinberger DR, Callicott JH. Epistasis between catechol-O-methyltransferase and type II metabotropic glutamate receptor 3 genes on working memory brain function. Proc Natl Acad Sci USA. 2007 Jul 24;104(30):12536-41.

Faulty MicroRNA Expression May Underly Cognitive Impairment in Schizophrenia

A type of genetic material called ribonucleic acid (RNA) helps create proteins essential for vital functions of the body, from development to digestion to thinking and memory. It's now known that RNAs can have other functions as well. Small RNAs, including microRNAs, regulate gene expression, the turning on-and-off of genes to produce proteins. Recently, researchers led by Diana Perkins, MD, MPH, University of North Carolina, uncovered the first evidence that expression of microRNAs may be altered in schizophrenia. When comparing the brains of 15 deceased schizophrenia and schizoaffective-disorder patients with the brains of 21 deceased people who did not have psychiatric disorders, the researchers found differences in the prefrontal cortex, which regulates such functions as thinking and decision-making and has been implicated in schizophrenia. Among 264 microRNAs screened in brains of those who had schizophrenia, levels of 15 were lower—and one higher—than normal. This finding suggests that there may be glitches in the formation of microRNAs in schizophrenia that could affect protein production.

Perkins DO, Jeffries CD, Jarskog LF, Thomson JM, Woods K, Newman MA, Parker JS, Jin J, Hammond SM. microRNA expression in the prefrontal cortex of individuals with schizophrenia and schizoaffective disorder. Genome Biol. 2007;8(2):R27.

DISC-1-Carrying Mice May Be Useful Model for Studying Schizophrenia

Disrupted-in-Schizophrenia-1 (DISC-1) is a suspected genetic risk factor for several psychiatric illnesses, particularly schizophrenia. In mice genetically altered to carry the form of the gene that confers brain-specific abnormal DISC-1 function, researchers led by Akira Sawa, MD, PhD, of Johns Hopkins University, found promising results that this mouse model could be useful for studying schizophrenia. The animals developed several neural and behavioral characteristics similar to the human disease, including abnormal neural development, hyperactivity, and a depression-like syndrome. These findings and the creation of the transgenic animals represent a new advance in the molecular dissection of the genes and proteins suspected to be involved in schizophrenia.

Hikida T, Jaaro-Peled H, Seshadri S, Oishi K, Hookway C, Kong S, Wu D, Xue R, Andrade M, Tankou S, Mori S, Gallagher M, Ishizuka K, Pletnikov M, Kida S, Sawa A. From the Cover: Dominant-negative DISC1 transgenic mice display schizophrenia-associated phenotypes detected by measures translatable to humans. Proc Natl Acad Sci USA. 2007 Sep 4;104(36):14501-6.

Risk Factors for Psychosis Identified in 22q11.2 Deletion Syndrome

Studies of children with 22q11.2 deletion syndrome (also known as velocardiofacial syndrome or DiGeorge syndrome), which is associated with congenital malformations and cognitive deficits, suggest that one-third to one-half demonstrate sub-syndromal psychotic symptoms. Children with this disorder also have a high rate of co-morbid non-psychotic disorders, including attention deficit hyperactivity disorder (ADHD), anxiety and mood disorders, autism, and obsessive-compulsive disorder (OCD). Doron Gothelf, MD, of Schneider Children's Medical Center of Israel, and colleagues sought to identify early risk factors for the development of psychotic disorders in 22q11.2 deletion syndrome. They conducted genotyping, neuroimaging, and clinical evaluations of children ages 9–16 with 22q11.2 deletion syndrome, none of whom had developed a psychotic disorder. Clinical evaluations of the study participants were conducted 4–5 years later. Consistent with prior research, 32 percent developed a psychotic disorder prior to the follow-up evaluation. The presence of sub-threshold psychotic symptoms at baseline interacted both with a version of the COMT gene previously linked with increased risk for schizophrenia (which is also associated with psychotic symptoms) and with baseline symptoms of anxiety or depression to dramatically increase the rate and severity of psychotic symptoms at follow-up. Lower baseline verbal IQ was also associated with more severe psychotic symptoms at follow-up. More research is needed to determine whether early treatment of internalizing symptoms in children with 22q11.2 deletion syndrome would prevent or reduce the severity of psychosis.

Gothelf D, Feinstein C, Thompson T, Gu E, Penniman L, Van Stone E, Kwon H, Eliez S, Reiss AL. Risk factors for the emergence of psychotic disorders in adolescents with 22q11.2 deletion syndrome. Am J Psychiatry. 2007 Apr;164(4):663-9.

Improvement Following ADHD Treatment Sustained in Most Children, but Linked Problems Persist Into Adolescence

Four articles on a major follow-up study to the Multimodal Treatment Study of Children with Attention Deficit Hyperactivity Disorder (MTA) revealed outcomes of treatment for ADHD, three years after the original study. For the follow-up, a multi-site research team evaluated 485 children, at ages 10–13, from those originally enrolled in MTA. In the first follow-up paper, Peter Jensen, MD, Columbia University, and colleagues reported that 45–71 percent of the youth in the original treatment groups were taking medication. However, continuing medication treatment was no longer associated with better outcomes by the third year. To understand this change, the researchers examined medication use patterns that emerged after formal treatment in the study ended. They found that children who had been assigned to intensive behavioral treatment were more likely to begin taking medication, while those who had been taking medication were more likely to stop. The researchers emphasized that "it would be incorrect to conclude…that treatment makes no difference or is not worth pursuing."

In a secondary analysis of the data, researchers led by James Swanson, PhD, University of California (UC) at Irvine, reported on substantial variability in responses to medication. They identified three groups of children with different patterns of response. One group, about a third of the children, showed a gradual, moderate improvement; a second group, about half of the children, showed larger initial improvement, which was sustained through the third year; a third group, about 14 percent of the children, responded well initially, but then deteriorated as symptoms returned during the second and third years. Swanson and colleagues suggested "trial withdrawals" for some children to determine if they still need to take medications.

Another report by Swanson and colleagues confirmed an earlier finding from the MTA study that taking medication slowed growth. A group of 65 children with ADHD who had never taken

medication grew somewhat larger—about three-fourths of an inch and 6 pounds more, on average—than a group of 88 peers who stayed on medication over the three years. Growth rates normalized for the children on medication by the third year, but they had not made up for the earlier slowing in growth.

Finally, Brooke Molina, PhD, University of Pittsburgh, and colleagues reported that, despite treatment, children with ADHD showed significantly higher-than-normal rates of delinquency (27.1 percent vs. 7.4 percent) and substance use (17.4 percent vs. 7.8 percent) after three years. Earlier evidence of lower substance use rates among children who had received intensive behavioral therapy had lessened by the third year. The researchers noted that these findings suggest ADHD treatment for one year does not prevent serious problems from emerging later.

Jensen PS, Arnold LE, Swanson JM, Vitiello B, Abikoff HB, Greenhill LL, Hechtman L, Hinshaw SP, Pelham WE, Wells KC, Conners CK, Elliott GR, Epstein JN, Hoza B, March JS, Molina BS, Newcorn JH, Severe JB, Wigal T, Gibbons RD, Hur K. 3-year follow-up of the NIMH MTA study. J Am Acad Child Adolesc Psychiatry. 2007 Aug;46(8):989-1002.

Swanson JM, Hinshaw SP, Arnold LE, Gibbons RD, Marcus S, Hur K, Jensen PS, Vitiello B, Abikoff HB, Greenhill LL, Hechtman L, Pelham WE, Wells KC, Conners CK, March JS, Elliott GR, Epstein JN, Hoagwood K, Hoza B, Molina BS, Newcorn JH, Severe JB, Wigal T. Secondary evaluations of MTA 36-month outcomes: propensity score and growth mixture model analyses. J Am Acad Child Adolesc Psychiatry. 2007 Aug;46(8):1003-14.

Swanson JM, Elliott GR, Greenhill LL, Wigal T, Arnold LE, Vitiello B, Hechtman L, Epstein JN, Pelham WE, Abikoff HB, Newcorn JH, Molina BS, Hinshaw SP, Wells KC, Hoza B, Jensen PS, Gibbons RD, Hur K, Stehli A, Davies M, March JS, Conners CK, Caron M, Volkow ND. Effects of stimulant medication on growth rates across 3 years in the MTA follow-up. J Am Acad Child Adolesc Psychiatry. 2007 Aug;46(8):1015-27.

Molina BS, Flory K, Hinshaw SP, Greiner AR, Arnold LE, Swanson JM, Hechtman L, Jensen PS, Vitiello B, Hoza B, Pelham WE, Elliott GR, Wells KC, Abikoff HB, Gibbons RD, Marcus S, Conners CK, Epstein JN, Greenhill LL, March JS, Newcorn JH, Severe JB, Wigal T. Delinquent behavior and emerging substance use in the MTA at 36 months: prevalence, course, and treatment effects. J Am Acad Child Adolesc Psychiatry. 2007 Aug;46(8):1028-40.

Behavioral Interventions Effective for Preschoolers with ADHD

Two types of early interventions designed to reduce symptoms of ADHD in preschoolers may be effective alternatives or additions to medication treatment, according to Lee Kern, PhD, of Lehigh University and colleagues. The researchers compared a multicomponent intervention (MCI) with a parent education (PE) program using a group of 135 preschoolers (ages 3 to 5) diagnosed with ADHD and their parents. Participants who were randomly assigned to MCI received parent education classes that focused on parenting skills, understanding the child's behavior and development, and ensuring child safety. They also received individualized interventions in the home and at preschool or day care. Participants assigned to PE only received training in parenting skills in a group setting. Both programs lasted for one year and child progress was evaluated every six months. Both groups showed significant improvement after one year. Problem behavior among the children decreased, and their social skills improved. Although the researchers expected to see more improvement among those receiving MCI compared to those receiving only PE, they found no significant differences in improvement rates between the two groups. Regardless of the reasons for the lack of differences, the results indicate that behavioral interventions for preschoolers with ADHD can be effective, and further study will help identify the best approaches.

Kern L, DePaul G, Volpe R, Sokol N, Lutz G, Arbolino L, Pipan M, VanBrakle J. Multisetting assessment-based intervention for young children at risk for attention deficit hyperactivity disorder: Initial effects on academic and behavioral functioning. School Psych Rev. 2007;36(2):237-255.

Gene Predicts Better Outcome as Cortex Normalizes in Teens with ADHD

A particular version of the dopamine D4 receptor gene, called the 7-repeat variant, accounts for about 30 percent of the genetic risk for ADHD, making it by far the strongest candidate gene

implicated in the disorder to date. To determine how this gene variant affects brain development, NIMH researcher Philip Shaw, MD, and colleagues determined the D4 gene types and used MRI to scan the brains of 105 children with ADHD and 103 healthy controls, and then re-scanned them through their teen years. Nearly one-fourth of youth with ADHD and about one-sixth of the healthy controls had at least one copy of the 7-repeat variant. The 7-repeat variant was linked to a thinner cortex in brain areas important for controlling attention in both ADHD and healthy subjects, but it appeared to confer advantage only among youth with ADHD. For example, participants with ADHD who lacked the 7-repeat variant had significantly lower IQs, and more than half of them still had pronounced ADHD symptoms at the follow-up assessment about six years later. In contrast, those with at least one copy of the 7-repeat variant generally had better overall functioning, and only 21 percent had ADHD symptoms at follow-up. The attention-controlling brain areas normalized in thickness during the teen years, coinciding with clinical improvement. The researchers are following up with studies on the relationship between cortex thickness and cognitive features of ADHD, such as working memory and the ability to inhibit responses.

Shaw P, Gornick M, Lerch J, Addington A, Seal J, Greenstein D, Sharp W, Evans A, Giedd JN, Castellanos FX, Rapoport JL. Polymorphisms of the dopamine D4 receptor, clinical outcome, and cortical structure in attention-deficit/hyperactivity disorder. Arch Gen Psychiatry. 2007 Aug;64(8):921-31.

Half of Children with Autism May be Diagnosable Soon After Their First Birthday

ASDs are characterized by impairments in language, communication skills, and the ability to relate to others—and are highly heritable. They are also rarely diagnosed before age 3. Accordingly, Rebecca Landa, PhD, of Kennedy Krieger Institute in Baltimore, and colleagues followed the development of social and communication skills from ages 14 to 36 months in 107 infants who had siblings with the disorder—and were therefore deemed at high risk. They also tracked 18 low-risk healthy controls from unaffected families. By the end of the study, 30 of the high-risk children were diagnosed with ASDs. Half of these children had developed marked signs of disturbed sociability and play behavior by 14 months. Early on, these children exhibited lags in development on multiple measures. In contrast to this early-diagnosis group, a later-diagnosis group showed a very different course. At 14 months, they were distinguishable from healthy children only in that they shifted their gaze less between objects and a person's eyes. However, their social functioning subsequently deteriorated so that by two years, these children behaved similarly to the early-diagnosis group. Children in this later-diagnosis group would likely pass a screening at 14 months, underscoring the importance of re-screenings at age 2. The researchers hope to develop criteria for doctors to use in diagnosing ASDs in one-year-olds, as early intervention holds the best hope for a better outcome.

Landa RJ, Holman KC, Garrett-Mayer E. Social and communication development in toddlers with early and later diagnosis of autism spectrum disorders. Arch Gen Psychiatry. 2007 Jul;64(7):853-64.

Researchers Detect Brainwaves Associated with Human Social Behaviors

Animal studies have shown that certain brain cells called mirror neurons fire when the animal performs a specific action and when the animal simply observes another animal performing the same action. In humans, specific brain areas have been identified as comprising the mirror neuron system. Deficits in the mirror neuron system may contribute to some mental disorders, such as autism. Using a specially designed dual electroencephalogram (EEG) system, J.A. Scott Kelso, PhD, of Florida Atlantic University, and colleagues identified a brainwave complex called phi that is a marker for social coordination in humans. The researchers found this marker by looking at brainwaves in pairs of people engaged, alone and together, in sustained, rhythmic flexing and stretching of their fingers. They sometimes spontaneously coordinated their movements when they were paired with a person and sometimes did not. Different parts of the phi complex were

associated with different behaviors. For example, an increase in the phi_1 part of the complex favored independent behavior, whereas an increase in phi_2 favored coordinated behavior. Another brainwave, mu, was found to contribute to somatosensory awareness (i.e., the part of the nervous system that senses things) in perceiving what somebody else is doing. The researchers indicated that phi may be important to understanding deficits in social coordination, and mu, to understanding problems in perception/awareness of social behaviors.

Tognoli E, Lagarde J, DeGuzman GC, Kelso JA. The phi complex as a neuromarker of human social coordination. Proc Natl Acad Sci USA. 2007 May 8;104(19):8190-5.

Male Veterans Have Double the Suicide Rate of Civilians

To date, most studies on suicide among veterans have relied on data from those getting health care from the VA. However, 75 percent of veterans do not get their health care through the VA. In a large study by Mark S. Kaplan, DrPH, and colleagues from Portland State University and Oregon Health & Science University, 320,890 men age 18 and older in the general population, 104,026 of them veterans, were followed for 12 years. The researchers found that male veterans in the general US population are twice as likely as their civilian peers to die by suicide. Veterans who were white, had at least 12 years of education, or whose daily-life activities were limited by health problems were at highest risk. Those who were overweight had a lower risk. By the end of the study, 197 of the veterans had died by suicide. During the same period, the risk of death from other causes was the same in the veterans as in civilian men. The researchers also noted that the number of veterans with daily-life activity limitations—one of the higher risk factors for suicide listed above—is likely to rise, increasing the need for clinical and community interventions. They further called for clinicians to be alert for signs that veterans might be contemplating suicide and to assess their access to firearms.

Kaplan MS, Huguet N, McFarland BH, Newsom JT. Suicide among male veterans: a prospective population-based study. J Epidemiol Community Health. 2007 Jul;61(7):619-24.

Genetic Technique Enables Mapping of Fear Circuits via Tracking of Neuron Activity

Scientists identified the handful of neurons that were activated in mice learning fearful memories and determined that the same neurons became active again, much later, when the memory of the precipitating event was retrieved. Mark Mayford, PhD, and colleagues at the Scripps Institute generated a new mouse model to overcome a major challenge to conducting this kind of research—not only how to identify specific cells involved in the brief window of learning, but also to tag them in a lasting way that enables the same cells' activity to be tracked after many days, during memory retrieval. The model tracks activity in genetically engineered genes (the c-fos promoter) in the basolateral amygdala, an area of the brain known to be involved in fear processing. This TetTag mouse model will, in the future, enable researchers to manipulate other engineered genes that can further understanding of the physiology and biochemistry that underlie the learning process, a process whose dysfunction may play a role in some mental illnesses.

Reijmers LG, Perkins BL, Matsuo N, Mayford M. Localization of a stable neural correlate of associative memory. Science. 2007 Aug 31;317(5842):1230-3.

Differences in Fear Response Point to Diverging Mechanisms for Fear Conditioning

Past studies on rats have pointed to the important role of the amygdala as a key site for encoding fear memories, with insights into how neural systems are modified to eliminate or reduce the learned fear response. However, a study by David Amaral, PhD, of UC Davis, and colleagues suggests that there are likely to be significant differences between primates and rodents in the neural mechanisms underlying fear conditioning. Their group tested rhesus monkeys using a fear potentiated startle procedure. One group of animals had a complete lesion of the amygdala while the

other group did not. Although animals that had their amygdala lesioned were unable to develop a conditioned fear response when trained after lesioning, the finding was different if the lesion occurred between the training and the testing. In contrast to rodents, monkeys who were first trained to show a learned fear response and then had their amygdala lesioned still showed a learned fear response afterwards. This suggests that, in primates, the long-term memory for fear responses might be stored outside of the amygdala, which has important implications for research on a number of disorders in humans, such as phobias and post-traumatic stress disorder (PTSD).

Antoniadis EA, Winslow JT, Davis M, Amaral DG. Role of the primate amygdala in fear-potentiated startle: effects of chronic lesions in the rhesus monkey. J Neurosci. 2007 Jul 11;27(28):7386-96.

NCS-R Comparison Study Finds Correlation Between Immigration and Mental Illness

Understanding of the relationship between immigration and mental health can be advanced by comparing immigrants pre- and post-immigration with residents of the immigrants' home countries. Researchers working with Joshua Breslau, PhD, ScD, of UC Davis, used identical methods to assess anxiety and mood disorders in representative samples of English-speaking Mexican immigrants to the United States (from a subsample of the NCS-R), and Mexicans (from the Mexican National Comorbidity Survey, MNCS). Retrospective reports of age of onset of disorders, and age of immigration in the immigrant sample, were analyzed to study the associations of pre-existing mental disorders with immigration, and of immigration with the subsequent onset and persistence of mental disorders. The researchers found that Mexicans with pre-existing anxiety disorders were three times as likely to immigrate as mentally healthy Mexicans. Also, immigration predicted subsequent onset of anxiety and mood disorders and the persistence of anxiety disorders. The results are inconsistent with the "healthy immigrant" hypothesis (that mentally healthy people immigrate) and partly consistent with the "acculturation stress" hypothesis (that stresses of living in a foreign culture promote mental disorder). The researchers noted the need to replicate and extend their findings in a larger study sample.

Breslau J, Aguilar-Gaxiola S, Borges G, Castilla-Puentes RC, Kendler KS, Medina-Mora ME, Su M, Kessler RC. Mental disorders among English-speaking Mexican immigrants to the US compared to a national sample of Mexicans. Psychiatry Res. 2007 May 30;151(1-2):115-22.

Compulsive Hoarding Linked to Faulty Information Processing

Compulsive hoarding is generally thought to be a type of OCD associated with stockpiling things that may be of little value or use. To study a possible biological basis for this behavior, Jessica Grisham, PhD, of the University of New South Wales (Australia), and colleagues compared people who exhibited compulsive hoarding with a mixed clinical group (in which some showed hoarding behaviors and others did not), and with a health control group. Study participants were tested on information-processing features thought to be central to hoarding (memory, attention, and decision-making). Hoarding patients demonstrated slower and more variable reaction time, increased impulsivity, greater difficulty distinguishing targets and non-targets, and worse spatial attention relative to comparison groups. Further analyses demonstrated that slower reaction time and increased impulsivity were significantly related to hoarding symptoms over and above the effect of depression, psychosis-related characteristics or experiences, and other OCD symptoms. There were no differences between groups on a test of emotion-based decision-making. Based on these findings, the researchers emphasized that treatment approaches to compulsive hoarding should be supplemented with strategies that address co-occurring neuropsychological deficits, such as impaired attention.

Grisham JR, Brown TA, Savage CR, Steketee G, Barlow DH. Neuropsychological impairment associated with compulsive hoarding. Behav Res Ther. 2007 Jul;45(7):1471-83.

Gene Triggers Obsessive Compulsive Disorder-Like Syndrome in Mice

Using genetic engineering, researchers led by Guoping Feng, PhD, at Duke University, created a set of behaviors in mice resembling OCD and reversed them with antidepressants and genetic targeting of a key brain circuit. First, the researchers bred mice without the gene, SAPAP3, which makes a protein that helps brain cells communicate via the glutamate chemical messenger system. As a result, they found defects in a brain circuit previously implicated in OCD. Much like people with a form of OCD, the mice engaged in compulsive grooming, which led to bald patches with open sores on their heads. They also exhibited anxiety-like behaviors, often associated with OCD. They were slower to venture into—and quicker to exit—risky environments. And like their human counterparts, the animals responded to treatment with fluoxetine, which reduced both the excessive grooming and anxiety-like behaviors. When the missing gene was reinserted, both the behaviors and the defects were largely prevented. According to the researchers, this finding provides the first link between OCD-like behaviors and abnormalities in the glutamate system, and may lead to new targets for drug development.

Welch JM, Lu J, Rodriguiz RM, Trotta NC, Peca J, Ding JD, Feliciano C, Chen M, Adams JP, Luo J, Dudek SM, Weinberg RJ, Calakos N, Wetsel WC, Feng G. Cortico-striatal synaptic defects and OCD-like behaviours in Sapap3-mutant mice. Nature. 2007 Aug 23;448(7156):894-900.

Genetic Risk Factor for Alzheimer's Disease Linked to Decline in Whole Brain Volume in Cognitively Normal Adults

People with Alzheimer's disease (AD) show high rates of decline in both structural and functional measures of brain volume and activity. Previous research has shown abnormal rates of decline among patients with mild cognitive impairment who later went on to develop AD. Kewei Chen, PhD, and colleagues at the Banner Alzheimer Institute and Good Samaritan Medical Center in Phoenix, Arizona, studied cognitively normal adults in their late middle-age over a two-year period to examine possible risk factors for the disorder. Specifically, they examined normal adults with varying levels of genetic risk for late-onset AD: those with two copies, one copy, or no copies of the apolipoprotein E (APOE) ε4 allele, a common AD susceptibility gene. Even though there were no differences in clinical ratings or neuropsychological test scores among the three groups, the study results indicated that whole brain atrophy rates were significantly greater for the group with two ε4 copies than for the group with no copies, and atrophy rates were correlated with the number of copies. The findings suggest that the APOE genetic risk of Alzheimer's disease is associated with accelerated brain atrophy, which occurs before the onset of diagnosable symptoms of the disease.

Chen K, Reiman EM, Alexander GE, Caselli RJ, Gerkin R, Bandy D, Domb A,Osborne D, Fox N, Crum WR, Saunders AM, Hardy J. Correlations between apolipoprotein E epsilon4 gene dose and whole brain atrophy rates. Am J Psychiatry. 2007 Jun;164(6):916-21.

Unpleasant Words Trigger Strong Startle Response in People with Borderline Personality Disorder

Borderline personality disorder (BPD) is a serious mental illness characterized by intense fear of abandonment and/or rejection, problems controlling emotions, troubled relationships, impulsive or reckless behaviors, and other symptoms. Erin Hazlett, PhD, of Mount Sinai School of Medicine, and colleagues presented an objective way to measure the hallmark symptoms of BPD, in a study that assessed the startle eyeblink response, a measure of emotional reactivity. The researchers assessed startle response in 27 people with BPD and 21 healthy people by showing each participant a random series of words, some with neutral emotional meaning (such as "collect," "regular," "actually") and some with unpleasant meanings, particularly for people with BPD (such as "hate," "lonely," "abandon"). The participants would hear a brief startling burst of static noise at

unpredictable intervals—sometimes while a word was shown, sometimes between words, and sometimes not at all. Both groups of participants had similar startle reactions when viewing neutral words. But people with BPD were more startled than healthy adults by the static burst when looking at unpleasant words. Also, people with more BPD symptoms showed a greater difference in startle reaction when viewing unpleasant words vs. neutral words compared to people with less severe BPD. Because the startle reflex is a non-verbal, involuntary, physiological response that appears sensitive to emotional processing, the researchers suggest it may be a useful biomarker to diagnose and assess treatment for people with BPD, in conjunction with a patient's verbal self-report.
Hazlett EA, Speiser LJ, Goodman M, Roy M, Carrizal M, Wynn JK, Williams WC, Romero M, Minzenberg MJ, Siever LJ, New AS. Exaggerated affect-modulated startle during unpleasant stimuli in borderline personality disorder. Biol Psychiatry. 2007 Aug 1;62(3):250-5.

Magnetic Stimulation of the Brain Cortex Evokes Deep Sleep-Like State in Humans
Human sleep consists of two main phases that alternate throughout the night—non-rapid eye movement (NREM) sleep and rapid eye movement (REM) sleep. EEGs of sleep demonstrate that during the deep phase of NREM sleep, cortical neurons exhibit slow, synchronous, up-and-down oscillations. The alternation between up and down states of cortical neurons is thought to have an important role in memory consolidation, maintenance of normal synaptic function, and the restorative function of sleep. Marcello Massimini, MD, PhD, of the University of Wisconsin, and colleagues recently demonstrated that using transcranial magnetic brain stimulation (TMS) at the beginning of sleep triggers slow waves that resemble the pattern of the deepest NREM sleep. This finding indicates that natural sleep rhythms can be triggered non-invasively and without using medications. The practical implication is that TMS could someday be used to improve sleep for people who experience insomnia, sleep restriction, and sleep problems linked to mental disorders.
Massimini M, Ferrarelli F, Esser SK, Riedner BA, Huber R, Murphy M, Peterson MJ, Tononi G. Triggering sleep slow waves by transcranial magnetic stimulation. Proc Natl Acad Sci USA. 2007 May 15;104(20):8496-501.

New NIMH Initiatives

NIMH-Administered RFAs

- *Methods of Statistical Analysis of DNA Sequence Data for Studies Relating Variation to Disease*
  NIMH seeks applications related to the development of novel methods of statistical analysis of DNA sequence data in studies that aim to relate genetic variation to disease. Areas of interest include, but are not limited to, designing sequencing studies and statistical methods for relating the variation to phenotype; assessing the significance of the associations; incorporating population genetic factors such as population history, admixture, and natural selection; and finding sets of variants that may include functional variants.
  Release Date: June 21, 2007; Expiration Date: September 21, 2007
  http://grants1.nih.gov/grants/guide/rfa-files/RFA-MH-08-040.html
  Scientific Program Director: Thomas Lehner, MD, MPH, Division of Neuroscience and Basic Behavioral Science (DNBBS), NIMH

- *Basic and Translational Research Opportunities in the Social Neuroscience of Mental Health*
  NIMH and NIA invite applications that examine the neurobiological bases of social behavior—including its genetic, developmental, cognitive and affective components—at either the basic or translational levels of analysis. It is anticipated that findings derived from these approaches will ultimately aid in understanding of the causes or disease courses of mental disorders, or will add to the knowledge base necessary for developing appropriate biomarkers or identifying key

endophenotypes that will further advance the understanding of the causes and treatments of mental disorders across the developmental lifespan.
Release Date: August 8, 2007; Expiration Date: October 18, 2008
http://grants1.nih.gov/grants/guide/rfa-files/RFA-MH-08-070.html
Scientific Program Director: Kevin J. Quinn, PhD, DNBBS, NIMH

Collaborative RFAs

- *US-India Bilateral Collaborative Research Partnerships (CRP) on the Prevention of HIV/AIDS*
  This Funding Opportunity Announcement (FOA) solicits applications from institutions funded by the United States with partner institution funded by India to establish CRPs in the prevention of human immunodeficiency virus (HIV) and/or acquired immune deficiency syndrome (AIDS), with an emphasis on topical microbicides as well as other modes of HIV/AIDS prevention. The US-India Bilateral CRP Program is designed to develop collaborations between scientists and institutions in the United States and India to conduct high quality HIV/AIDS prevention research of mutual interest and benefit to both countries while developing the basis for future institutional and individual scientific collaborations.
  Release Date: July 18, 2007; Expiration Date: October 19, 2007
  http://grants.nih.gov/grants/guide/rfa-files/RFA-AI-07-031.html
  Scientific Program Director: Willo Pequenat, PhD, Division of Mental Disorders, Behavioral Research and AIDS, Division of AIDS and Health and Behavior Research (DAHBR), NIMH

- *Exceptional, Unconventional Research Enabling Knowledge Acceleration (EUREKA)*
  The purpose of this initiative is to foster exceptionally innovative research that may have an unusually high impact on areas of science that are germane to the mission of one or more participating NIH ICs. The rationale for EUREKA is that for science to move forward in leaps rather than in incremental steps, investigators must have opportunities to test unconventional, potentially paradigm-shifting hypotheses, and to attempt to use novel, innovative approaches to solve difficult technical and conceptual problems that severely impede progress in a field.
  Release Date: July 23, 2007; Expiration Date: October 25, 2007
  http://grants1.nih.gov/grants/guide/rfa-files/RFA-GM-08-002.html
  Scientific Program Director: Ravi Basavappa, PhD, Division of Cell Biology and Biophysics, National Institute of General Medical Sciences (NIGMS)

- *Diagnostic and Pharmacokinetic Research in Pediatric HIV/TB and Effects of Co-infection on the Central Nervous System*
  This FOA, issued by the National Institute of Child Health and Human Development (NICHD) and NIMH, solicits applications that propose improved methods for diagnosing and treating tuberculosis (TB) infection in children with HIV/TB co-infection. Applications are also invited for the evaluation of how first- and second-line anti-TB medications are processed in the body, as well as interactions between these and antiretroviral medications in children with HIV/TB co-infection. Finally, applications are solicited for research to evaluate the effect of HIV/TB co-infection in children on the CNS.
  Release Date: July 23, 2007; Expiration Date: October 28, 2007
  http://grants.nih.gov/grants/guide/rfa-files/RFA-HD-07-006.html
  Scientific Program Director: Carol Worrell, MD, Pediatric, Adolescent and Maternal AIDS Branch, NICHD

- *Collaborative Research to Explore New Uses for Existing Radioligands*
  NIDA, NIA, NINDS, and NIMH, are seeking applications to increase the use of established positron emission tomography (PET) or single photon emission tomography (SPECT) radioligands by reducing barriers to wider distribution, and by expanding their utility to the research on diseases or organs not previously studied with these radioligands. Radioligands are

small molecules that have been tagged with a radioactive tracer that will appear in certain imaging scans, such as PET or SPECT. Applications are expected to propose multi-institutional collaborations between investigators who have the capacity for routine production of a given radioligand for human use and investigators who lack access to the radioligand but wish to demonstrate the feasibility of an innovative use for the radioligand in a novel patient population.
Release Date: August 8, 2007; Expiration Date: January 29, 2008
http://grants.nih.gov/grants/guide/rfa-files/RFA-DA-08-001.html
Scientific Program Director: Steven Grant, PhD, Clinical Neuroscience Branch, Division of Clinical Neuroscience and Behavioral Research, NIDA

- *Genome-Wide Association Studies in the Genes, Environment, and Health Initiative*
  This FOA seeks to support investigative groups that conduct genome-wide association genotyping and/or replication studies, using data and specimens from human subjects on whom information is available for conditions/traits of public health importance and relevant environmental exposures. It includes support for sharing specimens and data and analyzing the resulting data as part of the NIH-wide Genes, Environment, and Health Initiative.
  Release Date: August 9, 2007; Expiration Date: October 19, 2007
  http://grants.nih.gov/grants/guide/rfa-files/RFA-HG-07-012.html
  Scientific Program Director: Emily L. Harris, PhD, National Human Genome Research Institute (NHGRI)

- *Epidemiologic Investigation of Putative Causal Genetic Variants Coordinating Center*
  The purpose of FOA is to provide support for a Coordinating Center to serve as a centralized resource to facilitate and support the investigation, in well-characterized population studies, of genetic variants identified as potentially causally associated with complex diseases in genome-wide association and other genetic studies. It is the aim of this announcement to promote widespread sharing of the resulting population-based descriptive and association data to accelerate the understanding of genes related to complex diseases.
  Release Date: August 17, 2007; Expiration Date: November 20, 2007
  http://grants.nih.gov/grants/guide/rfa-files/RFA-HG-07-015.html
  Scientific Program Director: Erin M. Ramos, PhD, MPH, NHGRI

- *Microbicide Innovation Program (MIP III)*
  The purpose of the Microbicide Innovation Program (MIP III) is to support novel and under-explored strategies in the field of topical microbicides. This broadly based program will support research and development of microbicides with the ultimate goal of facilitating technology or methodology design and development that can advance the field as a whole.
  Release Date: August 17, 2007; Expiration Date: November 21, 2007
  http://grants.nih.gov/grants/guide/rfa-files/RFA-AI-07-034.html
  Scientific Program Director: Jim A. Turpin, PhD, Division of AIDS, National Institute of Allergy and Infectious Diseases (NIAID)

- *International Cooperative Biodiversity Groups (ICBG)*
  NIH, along with the National Science Foundation, the US Department of Agriculture, and the US Department of Energy, invite applications for the establishment or continuation of ICBGs to address the interdependence of biodiversity exploration for potential applications in health, agriculture, and energy, with investments in research capacity that support sustainable use of these resources, the knowledge to conserve them and equitable partnership frameworks among research and development organizations in the US and low- and middle-income countries. This competition of the ICBG program includes several changes from past RFAs, including an increased emphasis on microbial and marine organisms, changes in target health areas, greater involvement of funded consortia with government contract resources, greater use of molecular

and genomic tools, new data dissemination resources, and the opportunity to integrate energy- or agriculture-related discovery research into projects.
Release Date: September 5, 2007; Expiration Date: December 5, 2007
http://grants.nih.gov/grants/guide/rfa-files/RFA-TW-08-003.html
Scientific Program Director: Joshua Rosenthal, PhD, Deputy Director, Division of International Training and Research, Fogarty International Center

Research Conferences and Workshops

Evolving Mechanisms of HIV Neuropathogenesis in the HAART Era: Domestic and Global Issues

In April 2007, NIMH co-sponsored an international meeting in Venice, Italy to discuss research on disease mechanisms that lead to chronic and milder forms of HIV-associated CNS disease following long-term anti-retroviral therapy. Other meeting co-sponsors included the San Raffaele Scientific Institute of Milano, Italy; the National Institute for Infectious Diseases of Rome, Italy; and NIH's Office of AIDS Research and NINDS. A key area of discussion related to understanding the viral and host genetic mechanisms that impact the development of HIV-associated CNS disease from a global perspective. Participants also discussed research on the impact of global diversity of HIV subtypes on the development of HIV-associated CNS disease. The meeting occurred in conjunction with another conference entitled, "Second HIV Infection and the Central Nervous System: Developed and Resource-Limited Settings." *For more information, please contact Jeymohan Joseph at jjeymoha@mail.nih.gov.*

NIMH Special Symposium: Mental Illness, the Person and Prison

In May 2007, NIMH hosted a symposium on the urgent problem of prisoners with serious mental illness. The symposium featured accounts from Pete Earley, former *Washington Post* reporter and author of the book *Crazy*, as well as Clare Dickens. Both are parents of mentally ill individuals who had been incarcerated. The symposium also featured presentations from Denise Juliano-Bult, MSW, from DSIR, as well as Arleen Rogan, PhD, Acting Director of Maryland's Montgomery County Core Service Agency. The symposium addressed the underlying problems in the US jail and prison system that lead to individuals with mental illness becoming incarcerated, current and needed research, and the efforts of one local jurisdiction to find solutions. *For more information, please contact David I. Sommers at dsommers@mail.nih.gov.*

Are Endophenotypes for Genetic Studies of Suicidal Behavior within Reach?

In June 2007, researchers in suicide, neuroscience, genetics, epidemiology, imaging, and related fields met in New York City to review promising findings, discuss research gaps and opportunities, and propose next steps toward identifying relevant endophenotypes for suicidality. The meeting was organized by the NIMH Suicide Research Consortium, NIH Office of Rare Diseases, Columbia University/Research Foundation for Mental Hygiene, Inc. at New York State Psychiatric Institute, and the American Foundation for Suicide Prevention. Issues discussed included the critical and fundamental role of accurately defining and measuring phenotypes, and the complexity inherent in explanations for suicidality. The participants identified promising intermediate phenotypes for suicidality and current findings on potential underlying brain mechanisms. Participants also discussed the challenges associated with appropriate methodologies for measuring genetic and environmental contributions to suicidality, in the context of development. *For more information, please contact Eve Mościcki at em15y@nih.gov or Jane Pearson at jp36u@nih.gov.*

Roundtable on Mood Disorders and Hormonal Transitions
In June 2007, NIMH co-sponsored the roundtable with the Society for Women's Health Research. The meeting brought together experts in the areas of postpartum and perimenopause-related depression, in order to share information regarding research in mood disorders associated with reproductive hormone change. NIMH-funded investigators, along with Dr. Peter Schmidt of the NIMH Intramural Research Program (IRP), participated in the event. *For more information, please contact Catherine Roca at croca@mail.nih.gov.*

Child and Adolescent Onset Schizophrenia: Research Challenges and Opportunities
In June 2007, NIMH and the NIH Office of Rare Diseases convened a meeting of basic, translational, and clinical investigators to review the current knowledge on causes, neurobiology, developmental trajectory, and treatment of child- and adolescent-onset schizophrenia. The scientific workshop identified: (1) opportunities for expanding current knowledge of causes and neurobiology of child- and adolescent-onset schizophrenia; (2) critical "next steps" in order to translate current knowledge into treatment development; and (3) current challenges of conducting research in this area, and strategies to overcome them. Workshop participants identified opportunities for multidisciplinary collaborations to elucidate the pathophysiology of child- and adolescent-onset schizophrenia. *For more information, please contact Ann Wagner at awagner@mail.nih.gov.*

Third Annual Meeting of the Developing Centers for the Intervention and Prevention of Suicide
In July 2007, NIMH, NIDA, and the National Institute for Alcohol Abuse and Alcoholism (NIAAA) co-sponsored a meeting of the Developing Centers for the Intervention and Prevention of Suicide. Representatives attended from the American Foundation for Suicide Prevention (AFSP), the Substance Abuse and Mental Health Service Administration (SAMHSA), the Centers for Disease Control and Prevention (CDC), the Suicide Prevention Resource Center, the University of Pittsburgh Medical College, the University of Michigan Medical Center, VISN 19 Veterans Administration Medical Center in Denver, the VA, and the Indian Health Service (IHS). Investigators and practitioners funded by IHS described their efforts at implementing and evaluating an intervention, delivered by a paraprofessional, to screen and refer White Mountain Apache members at risk for suicide. Primary investigators from the Centers provided progress updates on an AFSP-funded pilot project testing a common protocol for identifying individuals who attempted and sought care in psychiatric emergency rooms at the hospitals affiliated with each of the three Centers. *For more information, please contact Jane Pearson at jp36u@nih.gov.*

Enhancing the Impact of Mental Health Services Research
In July 2007, the Services Research and Clinical Epidemiology Branch (SRCEB) of DSIR sponsored the 19th national conference on mental health services research. Approximately 300 participants from academia, government, and the private sector attended. Highlights included two plenary sessions on Federal and state level mental health policy directions that encouraged researchers to focus on mental health policy relevant issues in their future work. Representative Patrick Kennedy (D-RI) spoke about current Federal mental health insurance parity legislation initiatives. Young investigators who participated in a pre-conference technical assistance workshop also had the opportunity to present their posters at the larger forum. *For more information, please, contact Agnes Rupp at arupp@mail.nih.gov or Denise Juliano-Bult at djuliano@mail.nih.gov.*

NeuroAIDS in Asia and the Pacific Rim
In July 2007, in conjunction with the 4th International AIDS Society Conference on HIV Pathogenesis, Treatment and Prevention held in Sydney, Australia, NIMH co-sponsored a meeting to highlight the current research relating to neurological and neuropsychological complications of HIV infection in the Asia-Pacific region. The meeting also assessed the impact of HIV-associated opportunistic and co-infections on the nervous system. Meeting co-sponsors included NINDS and the Australian Government (AusAID). Leading researchers, all of whom conduct NeuroAIDS research in resource limited settings, attended from Australia, China, Hong Kong, India, Indonesia, Japan, Papua New-Guinea, Thailand, the United Kingdom, the United States, and Vietnam. The agenda included a focus on the clinical experience of NeuroAIDS within the Asia-Pacific Region, a review of the current Asia-Pacific NeuroAIDS research initiatives, updates on several aspects of HIV-related neurological diseases, an update on international neuroscience research programs, and an update on funding programs and opportunities and international clinical research networks. *For more information, please contact Jeymohan Joseph at jjeymoha@mail.nih.gov.*

NIMH Annual International Research Conference on the Role of Families in Preventing and Adapting to HIV/AIDS
In July 2007, NIMH and the Center for AIDS Prevention Studies at UC San Francisco co-sponsored a conference in San Francisco aimed at "Responding to the Social Context of HIV Risk: The Role of Families and Support Networks." The first day, called Community Day, focused on issues developing collaborative research projects involving both researchers and community members. The second and third day focused on recent data on family and HIV/AIDS research. Over 200 people attended the conference, including participants from Africa, Eastern Europe, India, Jordan, and South America. *For more information, please contact Willo Pequegnat at wpequegn@nih.gov.*

Cognition and Stress: Advances in Basic and Translational Research
In July 2007, the NIMH cross-divisional Cognition Working Group held a workshop that gathered leading scientists in Bethesda, Maryland, to identify major current trends, gaps, and opportunities in behavioral and biological research. Specifically, the group addressed the following: the underlying mechanisms of interactions between cognition and stress, and the genetic, hormonal, developmental, experiential, and environmental factors influencing these mechanisms; and how cognition/stress interactions can lead to or influence the course of mental disorders. Suggestions for new directions for intervention development emerged from the discussions. Among other points, participants noted the importance of encouraging collaborations between basic and clinical scientists and of supporting more sophisticated approaches to animal models for human disorders. *For more information, please contact Kathleen Anderson at kanders1@mail.nih.gov*

Novel Methods for Examining Prefrontal Interactions with Cortical and Subcortical Systems that Support Complex Mental Function
In July 2007, NIMH sponsored a workshop to identify the gaps in understanding of the anatomical and functional influences of the prefrontal cortex on circuits supporting complex mental functions, and to assess current technologies that could help achieve a more precise understanding of the organization and function of these brain networks. The workshop highlighted several innovative methods, including the combination of multi-site recording with electrical and pharmacological inactivation and stimulation; *in vivo* imaging of circuits in animals; and genetic and molecular approaches for circuit tracing and manipulation. Participants agreed that the wider adoption of multi-level mechanistic approaches and collaborations between teams of investigators that can merge technical approaches to manipulate cells, synapses, and circuits with behavioral measures of

complex cognitive, social, and emotional behavior would significantly advance our understanding of how the prefrontal cortex interacts with other brain circuits. *For more information, please contact Kathleen Anderson at kanders1@mail.nih.gov*

NIMH Alliance for Research Progress – Summer Meeting
In July 2007, the NIMH Office of Constituency Relations and Public Liaison (OCRPL) convened the Summer Meeting of the NIMH Alliance for Research Progress. The Alliance unites representatives from patient and family-related advocacy organizations directly concerned with mental illnesses. The theme of the meeting, the seventh Alliance meeting to date, was co-occurrence of mental illness and addictive disorders. Updates on the State of NIMH and the State of NIDA were presented by the respective Directors of each Institute. *New York Times* Science Correspondent, Gardiner Harris provided luncheon remarks. *For more information, please contact Alison Bennett at abennet1@mail.nih.gov.*

Mental Health Consideration in Secondary HIV Prevention
In July 2007, the Secondary Prevention and Translation Branch of NIMH's Center for Mental Health Research on AIDS (CMHRA) hosted a meeting in Bethesda, Maryland that focused on identifying target areas for new research on the intersection of secondary HIV prevention and mental health, specifically related to HIV-infected individuals with psychiatric disorders living in the United States. The workshop assembled researchers and staff from CMHRA, DSIR, and the Divisions of Adult Translational Research and Treatment Development (DATR), and AIDS and Health and Behavior Research (DAHBR)to discuss promising research directions to spur scientific advances in understanding how best to intervene to address risk behaviors and the psychological well-being for people living with HIV/AIDS. *For more information, please contact Cynthia Grossman at grossmanc@mail.nih.gov.*

Building Consensus for Functional Endpoints in Schizophrenia Research
In August 2007, NIMH sponsored a meeting to convene a wide array of experts to discuss further measurement development for functional endpoints in schizophrenia research and treatment development in Bethesda, Maryland. The meeting was co-chaired by Drs. Ellen Stover from NIMH, Stephen Marder from the University of California, Los Angeles (UCLA) and Brendon Binneman from Pfizer, Inc. The meeting brought together basic and clinical cognitive neuroscientists, pharmaceutical companies, researchers from academia and industry, clinical trial experts, and staff from the US Food and Drug Administration (FDA) and the European Federal Institute for Drugs and Medical Devices. Following invited talks by basic scientists and breakout groups involving all attendees, meeting participants recommended functional endpoints for further measurement and development of clinical trials. *For more information, please contact Ellen Stover at estover@mail.nih.gov.*

2007 American Psychological Association (APA) Convention
NIMH staff divisions organized several sessions at the APA convention held in August in San Francisco, California. At these sessions, NIMH staff highlighted pediatric translational research, research training opportunities, translational priorities, and health disparities. Child and adolescent mentored K awardees participated in the Rodney Clark Memorial Symposium for Early Career Clinical Science on mentoring. Another session highlighted developmental issues for the study of racial and ethnic minority families and mental health. A special session entitled "*Culture, Race, Ethnicity, and Mental Health: A Dialogue"* provided an update on the landmark report, "*Mental Health: Culture, Race, and Ethnicity—A Supplement to Mental Health: A Report of the Surgeon General,"* which was released at the 2001 APA annual convention. Dr. Richard Nakamura, Deputy

Director of NIMH gave closing remarks at this special dialogue event. *For more information, please contact Cheryl Boyce at cboyce@mail.nih.gov.*

NIH Conference on Building the Science of Dissemination and Implementation in the Service of Public Health

In September 2007, NIH's OBSSR, the National Cancer Institute (NCI), NIDA, NIAAA, NICHD, and NIMH sponsored the first of five annual meetings on the state of the science of dissemination and implementation research. The meeting, with more than 500 registrants, featured a number of presentations from current NIMH grantees, along with other NIH-funded researchers on the theories, methods, processes and outcomes of dissemination and implementation research. This was the first trans-NIH meeting on the science of dissemination and implementation. *For more information, please contact David Chambers at dchamber@mail.nih.gov.*

Meeting-based Publications

Culturally Relevant Research Provides Clues That may Help Reduce Health Disparities

A special issue of *Research in Human* Development published in June examined trends in prevalence and risk factors for mental disorders across the lifespan in diverse US minority populations. Originally presented at a workshop organized by NIMH and the Family Research Consortium IV, the five articles provide insight into NIMH-sponsored national studies of mental health among minority populations in the United States, one of the first major studies of mental illness among ethnically diverse teens, as well as a SAMHSA-funded study on potential cultural risk factors for suicide among Native American youth. Cheryl Boyce, PhD, of NIMH, and Andrew Fuligni, PhD, of UCLA, discussed in an introductory article particular cultural considerations relevant to the mental health of U.S. minority populations. Recommendations for further research may help inform efforts to reduce health disparities.

Boyce CA, Fuligni AJ. Issues for Developmental Research Among Racial/Ethnic Minority and Immigrant Families. Res Hum Dev. 2007 Jun;4(1&2):1-17.

Social Neuroscience: Progress and Implications for Mental Health

Social neuroscience is a new, interdisciplinary field devoted to understanding how biological systems implement social processes and behavior. Social neuroscience capitalizes on biological concepts and methods to inform and refine theories of social behavior, and it uses social and behavioral constructs and data to inform and refine theories of neural organization and function. In an article derived from an Institute sponsored workshop (previously reported to Council), Kevin Quinn, Chief of the NIMH Behavior Science and Integrative Neuroscience Research Branch, aimed to review the development of this field, examine some currently promising approaches, identify obstacles and opportunities for future advances and integration, and consider how this research can inform work on the diagnosis and treatment of mental disorders.

Cacioppo JT, Amaral DG, Blanchard JJ, Cameron JL, Carter CS, Crews D, Fiske S, Heatherton T, Johnson MK, Kozak MJ, Levenson RW, Lord C, Miller E, Ochsner K, Raichle ME, Shea MT, Taylor SE, Young LJ, Quinn KJ. Social neuroscience: progress and implications for mental health. Perspect Psychol Sci. 2007 Jun:2(2);99-123.

Budget

FY 2008 Budget Request

The FY08 President's Budget Request for the NIH was submitted to Congress on February 5, 2007. This request would provide a total NIH program level of $28,858 million, a decrease of $279

million or -1.0 percent below the FY07 Joint Resolution. The FY08 request of $1,405 million for the NIMH is an increase of $927 thousand or +0.1 percent over the FY07 Joint Resolution. NIMH actual expenditures by budget mechanism for FY06 and estimates for FY07 Joint Resolution and FY08 President's Budget are displayed on Attachment 1.

On June 7, 2007 the House of Representatives considered the Chairman's Mark-up of the FY08 appropriations bill (see Attachment 2). The House bill provided an increase to NIH of $750 million or +2.6 percent over the FY07 Joint Resolution to increase the number of new and competing research grants by approximately 545 over last year; lifted a two-year freeze on the average cost of new research grants; and provided $110.9 million for the National Children's Study and $300 million for the global AIDS fund. The House provided an NIMH program level of $1,426 million for an increase of $21 million or +1.5 percent over the FY07 Joint Resolution.

On June 19, 2007 the Senate Appropriations Subcommittee provided $30,137 million to the NIH. This represented an increase of $1,000 million or +3.4 percent over the FY07 level. The Senate provided an NIMH program level of $1,436 million for an increase of $32 million or +2.2 percent over the FY07 level.

Next steps involve dialogue between members of the House and Senate to reconcile these budget proposals.

Extramural Loan Repayment Program
In FY07, NIMH received 222 Clinical and 67 Pediatric Loan Repayment Program (LRP) applications, and funded 133 applications with the $4.9 million budgeted for these programs. This represents a 46 percent success rate for the combined NIMH Clinical and Pediatric LRP applications. Of the 67 Pediatric LRP applications that were submitted, 28 were paid (42 percent success rate), and of the 222 Clinical LRP applications that were submitted, 105 were paid (47 percent success rate). Twenty-three of the Pediatric LRP applications were submitted by MD's or MD/PhD's, of which 13 were paid (57 percent success rate), and of the 57 Clinical LRP applications submitted by MD's or MD/PhD's, 33 were paid (58 percent success rate).

Major Awards for NIMH Grantees

Martha Sajatovic, MD, a recipient of an NIMH career award in the Health and Behavior Branch of DAHBR, received the Gerald L. Klerman Young Investigator Award. The award, bestowed by the Depression and Bipolar Support Alliance (DBSA), recognizes the Young Investigator felt to have made the most important contribution to mood disorder research in 2006-2007. In addition, Dr. Sajatovic has joined the DBSA Scientific Advisory Board.

Major NIMH Staff Awards

Alan Mirsky, PhD, a Scientific Review Administrator in the Scientific Review Branch of the Division Extramural Activities (DEA), is the recipient of the Distinguished Service Award to the Profession of Psychology presented by the American Board of Professional Psychology (ABPP). The award was presented at the 60th Anniversary of the ABPP held August 17, 2007 in San Francisco, California.

Jane Steinberg, PhD, Director of NIMH's DEA, was among eight new members appointed by NIH Director Elias Zerhouni, MD, to the NIH Peer Review Advisory Committee. This committee provides technical and scientific advice on matters related to the procedures and policies governing the scientific and technical evaluation of NIH grant applications.

2007 NIH Director's Awards

The NIH Director annually recognizes individuals and groups whose special efforts and contributions beyond regular duty requirements have resulted in significant benefits to the programs or the people of the NIH and the fulfillment of the NIH mission. The following NIMH staff were honored at a ceremony on the NIH campus in June:

- **Olga Boikess**, Senior Advisor to the Executive Officer, NIMH Office of the Director, received an NIH Director's Merit Award in recognition of "her leadership role in providing privacy protections through Certificates of Confidentiality for research subjects that enable important clinical trials to recruit patients."
- **Daniel S. Pine, PhD**, Chief, Section on Developmental and Affective Neuroscience, Division of Intramural Research Programs (IRP), received an NIH Director's Award for Mentoring in recognition of "exemplary performance while demonstrating significant leadership, skill and ability as a mentor."
- **Ellen Stover, PhD**, Director of DAHBR, received an NIH Director's Merit Award in recognition for "exceptional initiative and extraordinary effort in facilitating NIMH adult translational research and treatment programs."
- **Carlos Zarate, MD**, Chief, Mood and Anxiety Disorders Research Unit, IRP, received an NIH Director's Merit Award in recognition of "his dedication to the cause of helping mankind with his mental health research endeavors."
- **Molecular Libraries and Imaging Project Development Group** received an NIH Director's Merit Award "for extraordinary scientific leadership of the Molecular Libraries and Imaging Roadmap to enable research on new pathways to discovery in health and disease." The group included David Armstrong, PhD; Jing Bao, MD, PhD; Linda Brady, PhD; Jamie Driscoll; Kathy Kopnisky, PhD; Ingrid Li, PhD; A. Roger Little, PhD; and Yong Yao, PhD.
- **NIH Information Security Program Team** received an NIH Director's Merit Award "for sustained contributions to the NIH mission." The team included William Hermach, Kyle C. Christiansen, Douglas Hooper, Hoan Le (contractor), Vincent Tavedi, Derek Toney (contractor), Quang Tran, and Robert Winfield.

2007 NIH Blueprint Awards

The Directors of the 15 ICs participating in the NIH Blueprint for Neuroscience Research recognized the following individuals and groups for their contributions at an awards ceremony on the NIH campus in July 2007:

- **Robert Cox, PhD**, leader of the Scientific and Statistical Computing Core in IRP, received a Blueprint Merit Award "for his scientific contribution to the NITRC contract acquisition process."

- **Michael Huerta, PhD**, Associate Director of the Office of Cross-Cutting Science and Scientific Technology, received a Blueprint Merit Award "in recognition of his leadership contributions to the Blueprint Neuroimaging Project Team."
- **Beth-Anne Sieber, PhD**, Program Director of the DNBBS Developmental Neurobiology Program, received a Blueprint Merit Award "for extraordinary leadership and management of the Neurodevelopment Workshop Project Team."
- **Neurodevelopment Workshop Project Team** received a Group Blueprint Merit Award "for their expertise, dedication, and good humor in planning the NIH Neuroscience Blueprint Workshop on Neurodevelopment." The team included Beth-Anne Sieber, PhD (Co-Team Leader); A. Roger Little, PhD; and Judith Rumsey, PhD.
- **Neuroepidemiology Project Team** received a Group Blueprint Merit Award "in recognition of the outstanding teamwork and extraordinary effort of the architects of the NIH Toolbox for Assessment of Neurological and Behavioral Function." The team included Pim Brouwers, PhD.
- **Neuroscience Information Framework Project Team** received a Group Blueprint Merit Award "for significant administrative contributions and oversight to redirect the NIF project for successful Phase II implementation." The team included Michael Huerta, PhD.

Staff Changes

Arrivals:

Diane L. Buckley accepted a contract position as Program Chief for Autism Reports and Evaluation in June 2007. Prior to joining the NIMH Autism Team, Ms. Buckley held various positions, both federal and contract¸ in the evaluation office within the NIH Office of Director. She received her graduate degree in Educational Psychology from the University of Illinois at Urbana-Champaign.

Rosemary Cerny, a graduate of the 2007 NIH Management Intern class, joined the Grants Management Branch staff in August as a grants specialist. Ms. Cerny came to NIH in August 2004 as the Technology Office Manager for the National Institute of Allergy and Infectious Diseases (NIAID). Prior to that, she spent several years working in a private, managed healthcare company as the Provider Communications and Contracting Manager.

Joyce Y. Chung, MD, began a contract position as Autism Coordinator within the NIMH Office of the Director in July 2007. Dr. Chung will divide her time between NIMH and Georgetown University Medical School where she is an Associate Professor of Psychiatry and an NIH K23 award recipient (DSIR) focused on sociocultural barriers to depression treatment. She received her medical degree from Northwestern University.

James (Jay) Churchill, PhD, joined the Research Training and Career Development Office in NIMH's Division of Neuroscience and Basic and Behavioral Science (DNBBS) as a Health Scientist Administrator in August, 2007. Dr. Churchill received his PhD from Indiana University in neural science and psychology and then did postdoctoral research training at the Beckman Institute, University of Illinois at Urbana-Champaign under the mentorship of William Greenough. He worked previously at St. Louis University as an assistant professor of psychology and an NIMH-funded investigator. His independent research program focused on the influence of experience on

learning and memory. Dr. Churchill has a deep interest in science education and research training and has contributed significantly to the Society for Neuroscience Public Education and Communication Committee, among other related service activities.

Alok Doshi joined the NIMH budget team in July, assisting on finance-related duties. Mr. Doshi will complete his final rotation in the HHS Emerging Leaders program with NIMH. He has previously interned within the Agency for Healthcare Research and Quality (AHRQ), FDA, HHS, and NCI; and has worked on economic analysis, policy research, and other accounting tasks. Prior to those experiences, Mr. Doshi spent six years as a consultant for Booz Allen Hamilton focusing on Information Technology. He also holds an MBA from the University of Maryland.

Steve Foote, PhD, accepted a contract position as Senior Science Advisor for the Autism Team in July 2007. Prior to his retirement in 2006, he served in DNBBS as Acting Director for two years and as Director for six.

Michelle Freund, PhD, joined the Office of Cross-Cutting Science and Scientific Technology as a Health Science Administrator in July. Dr. Freund came to NIMH from the Department of Neurosurgery at Thomas Jefferson University, where her research focused on neurotransmitter function at the levels of cells, circuits, and behavior. Before that, she held faculty or postdoctoral positions at Drexel University, the University of Pennsylvania, and Rutgers University. She received her PhD in Neuroscience from Hahneman University. Her collaborators have included Drs. Elisabeth Van Bockstaele, Rita Valentino, Irwin Lucki, Barry Waterhouse, and Steve Foote. Dr. Freund directs the Molecular Biotechnology Program and will lead efforts to coordinate cross-division and cross-IC activities in which the Office is involved.

Wayne K. Goodman, MD, accepted the position of Director of DATR in July 2007, after a competitive, nationwide search. He is on an intergovernmental personnel action (IPA) from the University of Florida's College of Medicine, where he has served as Chairman of the Department of Psychiatry for the past ten years. He is a pioneering researcher in the field of OCD and is the principal developer of the Yale-Brown Obsessive Compulsive Scale (Y-BOCS), the gold standard for rating OCD. A graduate of Columbia University with a BS in electrical engineering, Dr. Goodman received his medical degree from Boston University and completed his internship, residency, and a research fellowship at Yale University School of Medicine where he remained on faculty until 1993, before joining the University of Florida in Gainesville. Dr. Goodman has published more than 200 articles in scientific journals and has been principal investigator on NIMH-funded grants since 1992. He is a member of the American College of Neuropsychopharmacology and Distinguished Fellow of the American Psychiatric Association.

Kichelle Green accepted a position in September as a management analyst, with responsibilities in areas such as Continuity of Operations, Internal Controls, and 360° evaluations, in the Office of Resource Management (ORM) Management Analysis and Services Branch. Ms. Green completed the NIH Management Intern program two years ago, where she served in various rotational assignments throughout NIH, including NIMH assignments with the Executive Office and the IRP Associate Director for Administration.

Daniel J. Hall, MBA, accepted a contract position in August as the manager of NDAR. He will also continue his contract work at NCI on their clinical data management system.

Takea Herbert accepted a contract position as the Program Assistant for the Autism Team within the NIMH Office of Director in July 2007. Prior to joining the NIMH Autism Team, Ms. Herbert held a position as the Executive Assistant to the NIH Office of Director/Office of Extramural

Research. She is currently enrolled in the Montgomery College Meeting, Conference and Event Management Program.

Shoshana Y. Kahana, PhD, accepted a position as a Visiting Scientist in the Psychosocial Stress and Related Disorders Branch within DDTR. Dr. Kahana received her doctoral degree in Clinical Psychology from Case Western Reserve University and completed postdoctoral work at Case Western, as well as Brown University. Her primary research interest focuses upon the development and provision of appropriate interventions for children and adolescents affected by traumatic stress. In addition, some of her work examines risk and protective factors for treatment noncompliance among youth with chronic health conditions, as well as the effects of treatment choice/preference on outcome among adult sexual assault victims diagnosed with PTSD.

Alan Mirsky, PhD, joined the DEA Scientific Review Branch as Scientific Review Administrator. Previously, Dr. Mirsky served as Chief of the Section on Clinical and Experimental Neuropsychology in the NIMH IRP. Before coming to NIMH, he was professor of Psychiatry, Psychology, and Neurology at Boston University for 20 years, where he was the recipient of a Research Scientist Award from NIMH. He is past president of the International Neuropsychological Society, the Division of Clinical Neuropsychology, and the Division of Behavioral Neuroscience and Comparative Psychology of the American Psychological Association. Dr. Mirsky has received many awards, including the Distinguished Contribution to Psychology from the City University of New York, and honorary lectureships from the International Neuropsychological Society, the American Psychological Association, and many others. He has served on numerous editorial boards and has published over 200 scientific articles.

Tammy Rowe transferred from NIA to NIMH in May to the Office of Science Policy, Planning, and Communication's (OSPPC) Reports and Analysis Branch. At her previous position, Ms. Rowe served as a program assistant, working on a number of grants and reporting issues for NIA.

Kevin Lyn Sisson joined the OSPPC Science Writing, Press & Dissemination Branch in May 2007 as Media Specialist and Editor (contractor). Her previous positions in healthcare communications have included Associate Administrator for Communications at the Centers for Medicare and Medicaid Services (CMS); Communications Director at Group Health Association of America (now America's Health Insurance Plans, AHIP); and Public Affairs Director at Project HOPE. She has a BA from the University of Iowa, and a Masters Certificate in Nonprofit Management from Johns Hopkins University.

Lois Winsky, PhD, was selected in August as Chief of the Molecular, Cellular, and Genomic Neuroscience Research Branch in DNBBS following a competitive search. Dr. Winsky was recruited to NIMH as program officer in 1998 where she played a key role in shaping the long term goals of both the Psychopharmacology and Neuroendocrinology and Neuroimmunology Programs. She has also had a major role in developing the NIMH portfolio in preclinical drug discovery and model development. She brought expertise to NIMH in neuropharmacology and learning and memory from her PhD studies at the University of Iowa. Before joining the NIMH extramural program, Dr. Winsky led a program of molecular studies of brain calcium proteins in the NIMH IRP. Dr. Winsky has served as the Acting Director of the Branch since July 2006.

Yin Yao, PhD, joined the Genomics Research Branch in DNBBS in September and will be responsible for the Genetics & Genomic Research Resources Program. Dr. Yao received her degree in genetic epidemiology from Columbia University studying with Dr. Jurg Ott, a former NIMH merit grantee, and comes from Johns Hopkins University where she held a position as Associate Professor in the Department of Epidemiology.

Departures:

Lauren Baskir, PhD, completed a one-year Society for Research in Child Development Science and Policy Fellowship in DDTR, where she worked with Dr. Judith Rumsey on the NIH MRI Study of Normal Brain Development. Dr. Baskir has accepted a position as Research Fellow at the Zucker Hillside Hospital in New York, where she will investigate neurocognitive aspects of prodromal schizophrenia and will receive additional training in neuroimaging techniques.

Karen Bourdon, Chief Psychopathology Risk and Protective Factors Research Program of DATR retired after 34 years of government service in May 2007.

Bill Fitzsimmons retired in June 2007 after serving 17 years as the Executive Officer of NIMH and a total of 37 years of employment at NIH. Mr. Fitzsimmons' years at NIMH have spanned such moments as the transfer of NIMH from the Alcohol, Drug Abuse and Mental Health Administration to NIH, the move of the NIMH Director's Office and Extramural Research Programs from the Parklawn building to the Neuroscience Center, the first ever NIMH Employee Recognition Day held at Smokey Glen Park, and the tenures of six NIH Directors and seven NIMH Directors and Acting Directors.

John Grossi left NIMH at the end of August to pursue an advanced degree in business, law, and technology transfer at Columbia University. During the past two years, he served as a Program Analyst for the Molecular Libraries and Imaging Roadmap initiative.

Howard Kurtzman, PhD, Chief of the Cognitive Science Program, within the Behavioral Science and Integrative Neuroscience Research Branch in DNBBS, accepted a new position with the APA as Deputy Executive Director for Science.

Susan Matthews, who directed the DEA Office for Special Projects for many years, retired from NIMH at the end of June after more than 30 years of service. Ms. Matthews, who held many positions within the Institute, was tireless in her dedication to NIMH and to the NAMHC in particular. She is spending her retirement with family, having enjoyed most of the summer at her beach house, fishing and crabbing.

Carmi Schooler, PhD, Chief, Section on Socio-Environmental Studies in the NIMH IRP retired after 51 years of service to the government.

Beth-Anne Sieber, PhD, Program Director for the DNBBS Developmental Neurobiology Program since 2000, will be leaving NIMH to take on a position in the Neurodegeneration Cluster at NINDS. Starting in October 2007, she will oversee a portfolio addressing the pathophysiology and treatment of neurodegenerative disorders.

Ichiji Tasaki, PhD, Senior Investigator in the Laboratory of Cellular and Molecular Regulation, in the NIMH IRP will retire in October after 54 years of government service.

Timothy Tosten, Associate Director for Administration, left the NIMH IRP in May to serve as Executive Officer at the NIH Fogarty International Center.

Daisy Whittemore, Director of the Outreach Partnership Program in the Office of Constituency Relations and Public Liaison, left NIMH in June 2007 following eight years of service to the Institute in order to spend more time with her family.

Transfers and Other NIMH Staff Changes:

Kathleen C. Anderson, PhD, has accepted the position of Deputy Director of DDTR in September. Dr. Anderson received her doctorate in neuroscience from Rutgers University and did postdoctoral

research at the Massachusetts Institute of Technology on the neurophysiology of attention and memory. Since 2001, she has been Chief of the Neural Bases of Cognition Program in DNBBS. In her new position, Dr. Anderson will help to build a strong program of extramural research applying basic neuroscience to the understanding of child and adolescent mental disorders.

William (Bill) Riley, PhD, was appointed as Deputy Director of DAHBR in August 2007. Dr. Riley will continue his responsibilities as Chief of the Health Behavior Change and Treatment Adherence Programs in DAHBR and as Coordinator of Sleep Research for NIMH. Dr. Riley also will continue to serve as the Chief Science Officer for PROMIS, an NIH Roadmap initiative.

Patrick Shirdon, formerly the Deputy Executive Officer, assumed the responsibilities of Acting Executive Officer for NIMH in June. Mr. Shirdon has been with NIMH for two years and understands both the Institute's and NIH's administrative functions. Prior to coming to the NIMH, he had worked at NIA as Financial Management Officer, and at both the National Institute of Dental and Craniofacial research (NIDCR) and the NIH Office of the Director in various capacities.

Barbara Vermillion was selected for the position of Associate Director for Administration in NIMH's IRP and started her new position in September 2007. Ms. Vermillion previously served as the Lead Administrative Officer for NIMH's ORM since 1985, and in the past, has worked as an Administrative Officer at the National Heart, Lung and Blood Institute (NHLBI) and NCI. She brings thorough expertise and knowledge of administrative rules, policies, and procedures in the analysis and development of options to further the NIMH IRP goals and objectives.

In Memoriam:

Marian Radke-Yarrow, a research psychologist who served as chief of the laboratory of developmental psychology at NIMH from 1974–1995 and published many books and scholarly articles as a scientist during her 50-year career at NIH and at several universities, died of cancer in May 2007. She was 89 years old.

Dr. Radke-Yarrow's lifelong research on human development and psychological research methodology included a pioneering longitudinal study of children of depressed mothers, as well as influential studies on the development of altruism in children, psychological consequences for various categories of at-risk children, the nature and development of prejudice among children, and many other topics.

National Institute of Mental Health

Attachment 1

FY 2006 Actual, FY 2007 Revised Joint Resolution, FY 2008 President's Budget

(Dollars in Thousands)

	FY 2006 Actuals						FY 2007 Revised Joint Resolution						FY 2008 President's Budget					
	Non-AIDS		AIDS		Total		Non-AIDS		AIDS		Total		Non-AIDS		AIDS		Total	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount	No.	Amount	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Research Grants:																		
Research Projects:																		
Noncompeting	1,459	508,099	160	83,918	1,619	592,017	1,420	482,736	158	80,066	1,578	562,802	1,410	480,037	175	78,732	1,585	558,769
Admin. Suppl	(35)	3,437	(6)	502	(41)	3,939	(55)	5,593	(10)	876	(65)	6,469	(45)	4,616	(10)	821	(55)	5,437
Competing	494	154,726	49	20,972	543	175,698	553	172,695	86	34,101	639	206,796	541	168,873	88	34,594	629	203,467
Subtotal	1,953	666,262	209	105,392	2,162	771,654	1,973	661,024	244	115,043	2,217	776,067	1,951	653,526	263	114,147	2,214	767,673
SBIR/STTR	71	22,656	15	4,579	86	27,235	73	22,312	12	4,511	85	26,823	72	22,037	12	4,485	84	26,522
Subtot.,RPG	2,024	688,918	224	109,971	2,248	798,889	2,046	683,336	256	119,554	2,302	802,890	2,023	675,563	275	118,632	2,298	794,195
Research Centers	67	92,404	8	19,178	75	111,582	68	96,293	8	18,670	76	114,963	67	94,293	8	18,670	75	112,963
Other Research:																		
Res. Careers	444	67,357	31	4,383	475	71,740	453	67,920	31	4,361	484	72,281	462	68,021	31	4,361	493	72,382
Coop. Clin. Res	8	4,115	10	13,120	18	17,235	8	4,094	5	5,918	13	10,012	8	4,094	5	5,918	13	10,012
Biomedical Res.Sup	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Other	136	30,774	7	5,237	143	36,011	136	30,153	7	5,061	143	35,214	136	30,153	7	5,061	143	35,214
Subtot., Other	588	102,246	48	22,740	636	124,986	597	102,167	43	15,340	640	117,507	606	102,268	43	15,340	649	117,608
Total Res.Grants	2,679	883,568	280	151,889	2,959	1,035,457	2,711	881,796	307	153,564	3,018	1,035,360	2,696	872,124	326	152,642	3,022	1,024,766
Research Training:	FTTP		FTTP		FTTP		FTTP		FTTP		FTTP		FTTP		FTTP		FTTP	
Individual	268	9,989	23	834	291	10,823	267	9,939	23	830	290	10,769	267	9,939	23	830	290	10,769
Institutional	977	40,795	79	3,526	1,056	44,321	972	40,591	78	3,508	1,050	44,099	972	40,591	78	3,508	1,050	44,099
Total Training	1,245	50,784	102	4,360	1,347	55,144	1,239	50,530	101	4,338	1,340	54,868	1,239	50,530	101	4,338	1,340	54,868
R&D Contracts	206	64,721	17	10,116	223	74,837	214	76,011	17	10,085	231	86,096	211	70,611	17	10,085	228	80,696
Total, Extramural		999,073		166,365		1,165,438		1,008,337		167,987		1,176,324		993,265		167,065		1,160,330
	FTEs:		FTEs:		FTEs:		FTEs:		FTEs:		FTEs:		FTEs:		FTEs:		FTEs:	
Intramural Res	381	156,926	3	3,000	384	159,926	399	159,200	3	2,992	402	162,192	408	157,481	3	2,964	411	160,445
Res. Mgmt. & Supp	215	57,171	15	7,474	230	64,645	220	58,367	15	7,611	235	65,978	221	58,483	15	7,662	236	66,145
Total, NIMH	596	1,213,170	18	176,839	614	1,390,009	619	1,225,904	18	178,590	637	1,404,494	629	1,209,229	18	177,691	647	1,386,920
% Over Prior Year		-0.6%		-3.2%		-0.9%		1.0%		1.0%		1.0%		-1.4%		-0.5%		-1.3%
Contribution To Roadmap	2	10,946	0	1,596	2	12,542	0	0	0	0	0	0	1/ 4	16,144	0	2,357	4	18,501
% Over Prior Year		22.6%				40.5%		-100.0%		-100.0%		-100.0%						
Total, Including Roadmap	598	1,224,116	18	178,435	616	1,402,551	619	1,225,904	18	178,590	637	1,404,494	633	1,225,373	18	180,048	651	1,405,421
% Over Prior Year		-0.4%		-2.3%		-0.7%		0.1%		0.1%		0.1%		0.0%		0.8%		0.1%

1/ Roadmap is fully funded in the OD under the FY 2007 Joint Resolution.

National Institutes of Health
FY 2008 Senate Full Committee Mark
Dollars In Thousands

		FY 2007 Revised Joint Resolution		FY 2008 President's Budget Amount		FY 2008 House Subcommittee Mark			FY 2008 Senate Full Committee Mark			
		Amount	% > FY06	Amount	% > FY07	Amount	% > FY07	% > FY08 PB	Amount	% > FY07	% > FY08 PB	
NCI	- Cancer	$4,797,639	0.9%	$4,782,114	-0.3%	$4,870,382	1.5%	1.8%	$4,910,160	2.3%	2.7%	NCI
NHLBI	- Heart	2,922,929	1.0%	2,925,413	0.1%	2,965,775	1.5%	1.4%	2,992,197	2.4%	2.3%	NHLBI
NIDCR	- Dental	389,703	1.1%	389,722	0.0%	395,753	1.6%	1.5%	398,602	2.3%	2.3%	NIDCR
NIDDK	- Diabetes 2/	1,705,868	-14.2%	1,708,045	0.1%	1,731,893	1.5%	1.4%	1,747,784	2.5%	2.3%	NIDDK
NINDS	- Neurology	1,535,545	1.0%	1,537,019	0.1%	1,559,106	1.5%	1.4%	1,573,268	2.5%	2.4%	NINDS
NIAID	- Allergy	4,367,708	2.2%	4,592,482	5.1%	4,632,019	6.1%	0.9%	4,668,472	6.9%	1.7%	NIAID
NIGMS	- General Medical	1,935,808	1.0%	1,941,462	0.3%	1,966,019	1.6%	1.3%	1,978,601	2.2%	1.9%	NIGMS
NICHD	- Child	1,254,707 3/	0.2%	1,264,946 3/	0.8%	1,273,863	1.5%	0.7%	1,282,231	2.2%	1.4%	NICHD
NEI	- Eye	667,116	1.0%	667,820	0.1%	677,039	1.5%	1.4%	681,962	2.2%	2.1%	NEI
NIEHS	- Environmental	642,002	-9.5%	637,406	-0.7%	652,303	1.6%	2.3%	656,176	2.2%	2.9%	NIEHS
NIA	- Aging	1,047,260	1.0%	1,047,148	0.0%	1,062,833	1.5%	1.5%	1,073,048	2.5%	2.5%	NIA
NIAMS	- Arthritis	508,240	1.1%	508,082	0.0%	516,044	1.5%	1.6%	519,810	2.3%	2.3%	NIAMS
NIDCD	- Deafness	393,668	1.0%	393,682	0.0%	400,305	1.7%	1.7%	402,680	2.3%	2.3%	NIDCD
NIMH	**- Mental Health**	**1,404,494**	**1.0%**	**1,405,421**	**0.1%**	**1,425,531**	**1.5%**	**1.4%**	**1,436,001**	2.2%	2.2%	**NIMH**
NIDA	- Drug Abuse	1,000,621	1.0%	1,000,365	0.0%	1,015,559	1.5%	1.5%	1,022,594	2.2%	2.2%	NIDA
NIAAA	- Alcohol	436,259	1.0%	436,505	0.1%	442,870	1.5%	1.5%	445,702	2.2%	2.1%	NIAAA
NINR	- Nursing	137,404	1.0%	137,800	0.3%	139,527	1.5%	1.3%	140,456	2.2%	1.9%	NINR
NHGRI	- Human Genome	486,491	1.1%	484,436	-0.4%	493,996	1.5%	2.0%	497,031	2.2%	2.6%	NHGRI
NIBIB	- Bioengineering	296,887	1.0%	300,463	1.2%	303,318	2.2%	1.0%	304,319	2.5%	1.3%	NIBIB
NCRR	- Research Resources	1,133,240 3/	4.1%	1,112,498 3/	-1.8%	1,171,095	3.3%	5.3%	1,177,997	3.9%	5.9%	NCRR
NCCAM	- Alternative Medicine	121,576	1.1%	121,699	0.1%	123,380	1.5%	1.4%	124,213	2.2%	2.1%	NCCAM
NCMHD	- Minority Health	199,444 3/	3.1%	194,495 3/	-2.5%	202,691	1.6%	4.2%	203,895	2.2%	4.8%	NCMHD
FIC	- Fogarty	66,446	1.1%	66,594	0.2%	67,599	1.7%	1.5%	68,000	2.3%	2.1%	FIC
NLM	- Library	320,850 3/	2.9%	312,562 3/	-2.6%	325,484	1.4%	4.1%	327,817	2.2%	4.9%	NLM
OD	- Office/Director	1,046,901 3/	44.4%	517,062 3/	-50.6%	1,114,422	6.4%	115.5%	1,145,790	9.4%	121.6%	OD
B&F	- Bldg. & Fac	81,081	-52.4%	136,000	67.7%	121,081	49.3%	-11.0%	121,081	49.3%	-11.0%	B&F
Subtotal, NIH		**28,899,887**	**1.3%**	**28,621,241**	**-1.0%**	**29,649,887**	**2.6%**	**3.6%**	**29,899,887**	**3.5%**	**4.5%**	**Subtotal, NIH**
Interior/Superfund Res. Prog		79,117	0.0%	78,434	-0.9%	79,117	0.0%	0.9%	79,117	0.0%	0.9%	VA/HUD Approp.
Total, NIH Discretionary B.A		**28,979,004**	**1.3%**	**28,699,675**	**-1.0%**	**29,729,004**	**2.6%**	**3.6%**	**29,979,004**	**3.5%**	**4.5%**	**Total, NIH Disc. B.A.**
Type 1 Diabetes 2/		150,000	0.0%	150,000	0.0%	150,000	0.0%	0.0%	150,000	0.0%	0.0%	Type 1 Diabetes 2/
Total, NIH Budget Authority		**29,129,004**	**1.3%**	**28,849,675**	**-1.0%**	**29,879,004**	**2.6%**	**3.6%**	**30,129,004**	**3.4%**	**4.4%**	**Total, NIH B.A.**
Plus, NLM Planning & Evaluation		8,200	0.0%	8,200	0.0%	8,200	0.0%	0.0%	8,200	0.0%	0.0%	Plus, NLM PE
Total, NIH Program Level		**29,137,204**	**1.3%**	**28,857,875**	**-1.0%**	**29,887,204**	**2.6%**	**3.6%**	**30,137,204**	**3.4%**	**4.4%**	**Total, NIH Prog. Level**

1/ Includes funds to be transferred to the Global Fund for HIV/AIDS, Malaria, and Tuberculosis.

2/ Includes funds for the Type 1 Diabetes Initiative.

3/ Level includes specific amounts identified in P.L. 110-5 plus formula driven amounts for pay cost.