Director's Report to the National Advisory Mental Health Council

May 13, 2005

I am pleased to welcome members of the National Advisory Mental Health Council (NAMHC), and other participants and guests to our 209th Council meeting. Since we last met in February 2005 we have made progress on several fronts, which I share with you in this report.

NIH-Wide Update

Congressional Hearings

Senate Appropriations. On April 6, National Institutes of Health (NIH) Director Elias Zerhouni testified on the Fiscal Year (FY) 2006 budget for NIH before the Subcommittee on Labor-Health and Human Services and Education of the Senate Committee on Appropriations. The Subcommittee is chaired by Senator Arlen Specter (R-PA); the Ranking Minority Member is Senator Tom Harkin (D-IA). Dr. Zerhouni was the principal witness, accompanied by several Institute directors. While the hearing primarily concerned the NIH budget and recent research progress, there was also extensive discussion about the interim conflict of interest regulations (see below) proposed for NIH employees. Senators expressed concern that the regulations as currently proposed could have a detrimental effect on NIH in terms of its ability to attract and keep the highest quality scientists. Written testimony is available at the Senate Appropriations Committee web site at http://www.senate.gov/.

House Appropriations. On April 27, the Subcommittee on Labor-Health and Human Services and Education of the House Committee on Appropriations held a "theme" hearing to discuss mental health and substance abuse issues, and the FY 2006 budgets for the National Institute on Drug Abuse (NIDA), the National Institute on Alcohol Abuse and Alcoholism (NIAAA), and the National Institute of Mental Health (NIMH), as well as for the Substance Abuse and Mental Health Services Administration (SAMHSA). The Subcommittee is chaired by Congressman Ralph Regula (R-OH); the Ranking Minority Member is Congressman David Obey (D-WI). The topics addressed at the well-attended hearing included collaboration between the NIH Institutes and SAMHSA; the overall economic, social, and personal burdens caused by mental illness; preparations to deal with mental health problems faced by members of the military returning from Iraq; underage drinking; increasing use of psychotropic medications; and drug abuse in rural areas. Written testimony is available at the House Appropriations Committee web site at http://www.house.gov/.

Conflict of Interest Regulations
In February, the Department of Health and Human Services (DHHS) published new "interim final" conflict of interest regulations for employees, which restrict the personal financial interest holdings and the outside employment activities of NIH staff. While these regulations were technically in effect from the date of their publication, they were established with the idea that they would likely be altered after an official public comment period, which ended March 31. The final form of the regulations has not yet been published; however, following the recent Senate Appropriations Committee hearing on the subject, both the DHHS Secretary and the NIH Director publicly stated that significant changes could be expected. The most likely changes will affect restrictions on employee financial interests in "significantly affected organizations," such as stock holdings in pharmaceutical and biotechnology corporations. Recent news articles have brought attention to the negative effect these restrictions are already having on the recruitment and retention of research scientists at NIH; considerable attention was given to the potential departure of an NIH Institute director due to the new regulations**.**

NIH Roadmap

I. Pathways to Discovery

Molecular Libraries Roadmap
The 38 applications received in response to the Molecular Libraries Screening Centers Network (MLSCN) request for applications (RFA) (http://grants1.nih.gov/grants/guide/rfa-files/RFA-RM-04-017.html) have been peer reviewed. The Council voted concurrence on the applications by mail ballot. Nine extramural screening centers are awaiting approval by the Roadmap Implementation Coordinating Committee. Awards will be issued in June 2005 as U54 cooperative agreements for three years. An external scientific panel of five or six outside scientists will review and evaluate progress of the MLSCN program and recommend mid-course corrections, as appropriate.

A program announcement (PA), "Solicitation of Assays for High Throughput Screening in the Molecular Libraries Screening Centers Network" (http://grants1.nih.gov/grants/guide/pa-files/PAR-05-060.html), was released in the NIH Guide on March 1, 2005. Sixty-four applications were submitted and will be reviewed in June/July.

Bioinformatics and Computational Biology
Four new National Centers for Biomedical Computing (NCBC) are underway, two of which focus on neuroscience issues. Twenty applications were received for the second NCBC competition, aiming to create three additional Centers. Together, the NCBCs will form a national network providing computational underpinnings important to biomedical research.

Nanomedicine
This phased initiative—in which participation in each phase is required for further funding—will lead to a network of centers linking nanoscience and biomedical research. The first phase comprised 20 planning grant awards, seven of which were related to neuroscience.

Building Blocks, Biological Pathways, and Networks

The general aim of metabolomics is to identify, measure, and interpret the complex time-related concentration, activity, and flux of endogenous metabolites in cells, tissues, and other biosamples such as blood, urine, and saliva. In accordance with the Roadmap initiative, 14 grants were awarded for metabolomics technology development, four of which are related to neuroscience.

II. Research Teams of the Future

High Risk Research

The NIH Director's Pioneer Award Program is designed to support individual scientists of exceptional creativity who propose pioneering approaches to major contemporary challenges in biomedical research. The second competition opened in March 2005 for approximately five to ten new awards of up to $500,000 direct costs per year for five years; award selections will be made by the end of September 2005.

Interdisciplinary Research

A new notice, "NIH Roadmap Administrative Supplements to Support Interdisciplinary Research in the Behavioral/Social and Biological Sciences" (http://grants.nih.gov/grants/guide/notice-files/NOT-RM-05-007.html), was issued on April 6 for one-year administrative supplements aimed at stimulating interdisciplinary research in humans that integrates the behavioral or social sciences with the biological sciences. The short-term supplemental funds are intended to support partnerships that foster the melding of these disciplines' typically disparate perspectives and methodologies into interdisciplinary research efforts that will improve the ability to prevent, detect, diagnose, and treat disease and disability and to improve symptom management and health.

III. Re-Engineering the Clinical Research Enterprise

Translational Research

To aid in harmonizing the methods employed across clinical research networks, contracts were recently awarded to the best clinical networks interested in sharing methods and developing common research culture through collaboration. A contract has also been awarded to Westat to create an archive of existing networks in the United States. A central web portal to foster and facilitate communication between participating researchers is being developed under contract with the University of Pennsylvania.

Clinical Outcomes Assessment

The Patient-Reported Outcomes Measurement Information System (PROMIS) network steering committee last met in March at Duke University. Ongoing tasks for participants include conducting qualitative reviews for all items related to physical function, physical symptoms, emotional distress, role participation, and social support, as well as examining item response structure within existing data sets. Primary investigators also carry out independent projects related to PROMIS.

Clinical Research Workforce Training

This initiative was designed to allow training programs the flexibility to provide interested students access to a level of clinical research training appropriate to their career stage and level of interest, and to accommodate changing training needs as they progress through predoctoral training. NIH received 36 applications for review in July.

Neuroscience Blueprint

Fifteen NIH Institutes and Centers (ICs) have collaboratively developed the NIH Blueprint for Neuroscience Research (http://neuroscienceblueprint.nih.gov/) with two broad goals: to accelerate the pace of discovery in, and translation of, neuroscience research; and to increase the payoff on the significant investment made in neuroscience research by the participating ICs. The first goal will be accomplished by creating tools and resources for the neuroscience research community, and developing coherent strategies and policies for sharing tools, resources, and data. The second goal will be accomplished by establishing organizational processes and structures to prospectively plan and coordinate research efforts of common interest to the Blueprint ICs.

In the last four months, the structures and processes for collaborative action and funding have been put in place. Discussions among researchers, professional societies, and voluntary organizations have informed plans for five initiatives for FY 2005 that include: 1) expansion of current efforts to collect longitudinal normative neuroimaging data from children (infants through young adults); 2) issuance of an RFA to support the development of training courses linking basic neuroscience with a wide range of clinical neuroscience; 3) issuance of a Broad Agency Announcement to develop a comprehensive web portal to tools and resources accessible to neuroscience researchers around the world; 4) expansion of the Microarray Consortium that makes gene profiling services available to NIH-funded researchers; and 5) support for the first year of the International Neuroinformatics Coordinating Facility.

Discussions have also begun on the Blueprint's FY 2006 initiatives. Staff from the 15 Blueprint ICs are shaping the following concepts for proposal: 1) the development of mouse genetic resources for the neuroscience community, which will complement the NIH Knockout Mouse Project; 2) a neuroimaging initiative that will enhance the usability and adoptability of existing tools and resources for magnetic resonance modalities by the research community, and that will increase understanding of the imaging of neural activation; 3) an initiative to promote training that bridges physics to physiology in neuroimaging, computational neuroscience, and translational research; 4) the establishment of core facilities to promote interaction among researchers funded by the 15 Blueprint ICs; 5) an initiative in neuroepidemiology to include the development of validated instruments with which to measure cognitive and emotional health.

Management Retreat and Concerns About New Investigators
The IC Directors attended a management retreat in March to discuss challenges posed by the decelerating budget. This meeting coincided with the report by the National Academy of Sciences (NAS) called *Bridges to Independence: Fostering the Independence of New Investigators in Biomedical Research,* which proposed a series of recommendations to help reverse an increase in the age of independent investigators supported by NIH. The average age for investigators receiving a first-time independent grant is now 42.6 years. Researchers under the age of 40 received just 17% of the awards in 2003. Awards to new investigators—of any age—have also declined; they received less than 4% of NIH awards in 2002. Thus, NIH asked NAS to recommend mechanisms to foster the transition to independence of post-doctoral researchers and entry-level faculty, in hopes of aiding the appropriate distribution of research resources to the most innovative and productive scientists.

NIMH Update

This has been a period of unusual change in the NIMH workforce. Several senior investigators in both intramural and extramural programs have either departed recently or have announced plans to depart in the coming weeks. There is currently a short list of possible candidates for Scientific Director and for the leadership of the Mood and Anxiety Disorders Program in the Intramural Research Program (IRP). Decisions for these positions will be delayed until the conflict of interest policy has been fully resolved.

In the extramural program, several offices have been consolidated. The Office on Neuroinformatics is now part of Division of Neuroscience and Basic Behavioral Science (DNBBS); the Office of Rural Health has been merged into the Office of Special Populations in the Office of the Director; the Office of Equal Opportunity has been consolidated with NIH programs; and the Office of Communications merged with the policy office to create a new Office of Science Policy, Planning, and Communications.

NIMH is sponsoring a dedicated research track, "From the Science of Mental Illness to Clinical Care," at this year's American Psychiatric Association (APA) annual meeting in Atlanta, Georgia, from May 21–26, 2005. Plenary lectures, symposia, and workshops will spotlight key scientific advances of interest to psychiatry. Details about the meeting are posted on the APA website at http://www.psych.org/edu/ann_mtgs/am/05/index.cfm. For more information on the NIMH track, click on "Scientific Session Search," and select "Topic 70: National Institute of Mental Health."

Below I share with you some of the recent scientific progress made by NIMH-sponsored investigators; there are also several exciting advances *in press* that merit a preview. We anticipate publication of a set of papers from the National Comorbidity Survey-Replication study, which describe the severity of specific mental disorders in the United States and the enormous impact of these conditions on the nation's public health. The study also provides information on the length of delay between onset and diagnosis and how often those with mental disorders seek and receive treatment, and from which type

of care provider they receive it. In addition, the study will provide significant new data on the impairment—such as days lost from work—caused by specific disorders, including major depression, anxiety disorders, and substance abuse disorders. This will in turn allow researchers to determine the degree of disability and the economic burden caused by mental illness.

In addition, in the next several months, results from two of our large NIMH clinical trials will be published: the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) project, comparing the effectiveness of the newer, atypical antipsychotic medications for the treatment of schizophrenia and of psychosis/agitation in Alzheimer's disease; and the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) trial, focused on providing an evidence base for the treatment of major depression, particularly in those who have proven resistant to treatment. These studies have tested various treatment options for these disorders in diverse community populations, recruiting people from heterogeneous practice settings and expanding outcome measures beyond clinical symptomatology to include functional status and economic costs, which are significant issues for consumers and policymakers.

Science of Note

Social Stimuli Produce Heightened Emotional Response in Autistic Individuals
Studies suggest that abnormal perception of faces and their social/communicative signals may contribute to the social impairment that is a core feature of autism. Related studies on brain function have also shown that the fusiform gyrus, which is strongly activated in typically developing individuals during face processing, is less activated during the same tasks in individuals with autism. Following this research path, Kim Dalton and colleagues at the University of Wisconsin recently demonstrated that in addition to under-activation of the fusiform gyrus, individuals with autism showed over-activation in the amygdala, a brain structure involved in emotional response and regulation, compared with normal subjects when engaged in facial discrimination tasks while in an MRI scanner. The activation was not specific to the emotional content of faces, but was a response to faces in general. Activation in the fusiform gyrus and the amygdala were both strongly associated with the time the individual spent studying the eye region of the stimulus face. These results indicate that the under-activation of the fusiform gyrus in individuals with autism during face processing tasks might be due to less time spent studying the stimulus face. Over-activation in the amygdala suggests heightened emotional arousal in response to face processing, with greater time studying eyes associated with greater arousal. The authors propose a model in which face processing deficits in autism arise from hyperactivation in the central circuitry of emotion, which produces heightened sensitivity to social stimuli. This in turn leads to diminished eye gazing and atypical activation in the fusiform gyrus.
Dalton KM, Brendon MN, Johnstone T, Schaefer HS, Gernsbacher MA, Goldsmith HH, Alexander AL, Davidson RJ. Gaze fixation and the neural circuitry of face processing in autism. Nat Neurosci. 2005 April;8(4):519-26.

Brain Scans Reveal How Gene May Boost Schizophrenia Risk

The interactions of the prefrontal cortex and midbrain regions are critical for motivation and working memory and have been implicated in several neuropsychiatric disorders, including schizophrenia. Using neuroimaging in humans, Andreas Meyer-Lindenberg and colleagues at NIMH and the National Human Genome Research Institute (NHGRI) shed light on the mechanism behind these interactions. They looked at the gene that regulates catechol-O-methyltransferase (COMT), an enzyme that regulates dopamine in the prefrontal cortex. The study confirmed for the first time in living humans that activity in the prefrontal cortex is regulated by dopamine production in the midbrain, which in turn, is regulated by two common gene variants of COMT. In subjects with a common substitution in the COMT gene, dopamine synthesis was reduced in the midbrain, which impaired the interaction between midbrain and the prefrontal cortex. Their findings suggest that the interaction between midbrain and prefrontal cortex can be "tuned" in the prefrontal cortex through the dopaminergic system. Such results have implications for studying individual differences in working memory function and performance, as well as furthering the understanding of schizophrenia and other neuropsychiatric disorders affected by a variation in COMT activity.

Meyer-Lindenberg A, Kohn PD, Kolachana B, Kippenhan S, McInerney-Leo A, Nussbaum R, Weinberger DR, Berman KF. Midbrain dopamine and prefrontal function in humans: interaction and modulation by COMT genotype. Nat Neurosci. 2005 May;8(5):594-596.

Brain's Executive Hub Quells Alarm Center if Stressed

Lack of control over stressful life experiences has been implicated in mood and anxiety disorders, and current treatments are thought to work, in part, by helping patients gain control. A new study led by Steven Maier at the University of Colorado provides insight into the role of the medial prefrontal cortex (mPFC) in mediating the stress response. The mPFC is a seat of higher order functions such as problem-solving and learning from experience. By examining rats with this brain area chemically inactivated, the researchers observed the same brainstem activation and eventually, the same behaviors characteristic of depression (failure to learn to escape) and anxiety (exaggerated fear conditioning) when the animals were exposed to an external stressor. These responses were similar to rats exposed to an uncontrollable stressor. The researchers also found that when it deems a stressor controllable, the medial prefrontal cortex quells an alarm center deep in the brainstem, preventing the adverse behavioral and physiological effects of uncontrollable stress. Such results imply that mood and anxiety disorders may be more about the ability to identify controllable stressors and inhibit the fear response, rather than a neural cascade responding to a learned uncontrollable stressor.

Amat J, Baratta MV, Paul E, Bland ST, Watkins LR, Maier SF. Medial prefrontal cortex determines how stressor controllability affects behavior and dorsal raphe nucleus. Nat Neurosci. 2005 Mar;8(3):365-71.

Prefrontal Brain Deficits May Predict Development of Schizophrenia

Past research indicates that patients with schizophrenia exhibit functional deficits in the prefrontal areas of the brain. It is not certain, however, whether prefrontal deficits are specific to schizophrenia, or if they exist before medication is given. A recent study led by Angus MacDonald at the University of Minnesota addressed these questions by applying cognitive tests and brain imaging techniques to observe prefrontal brain

functions in people experiencing their first episode of mental illness, before medications were administered. Never-medicated first episode patients with schizophrenia, but not first-episode patients with mood disorders, showed a specific physiological deficit in the dorsolateral prefrontal cortex under conditions of increased cognitive processing demands. The diagnostic specificity of this finding suggests that the cognitive task used in this investigation may have promise for predicting which at-risk patients will go on to develop schizophrenia versus other forms of psychiatric disturbance. Because of these promising results, the investigators are now applying similar cognitive tests and brain imaging methods to individuals who meet criteria for the earliest non-psychotic stages of schizophrenia (the prodromal phase), with the goal of combining clinical, cognitive, brain imaging, and genetic analyses to enhance risk prediction in help-seeking individuals who are at risk for serious mental illness.

MacDonald AW 3rd, Carter CS, Kerns JG, Ursu S, Barch DM, Holmes AJ, Stenger VA, Cohen JD. Specificity of prefrontal dysfunction and context processing deficits to schizophrenia in never-medicated patients with first-episode psychosis. Am J Psychiatry. 2005 Mar;162(3):475-84.

Gene May Interact with Teenage Marijuana Use to Increase Psychosis Risk

Individuals inherit two copies (one from each parent) of the gene for the COMT enzyme, which chemically breaks down dopamine. It comes in two versions, *met* and *val*, the latter being associated with slightly higher risk for schizophrenia. Clues about how *val* may increase risk are emerging from a study by Terrie Moffitt, Avshalom Caspi, and colleagues at the University of Wisconsin. The researchers have been following more than 800 New Zealanders from birth into adulthood to identify risk factors for mental disorders. Results from the study show that, by itself, *val* did not increase risk for psychosis in the study population, nor did adult marijuana use. The most significant correlation emerged when an individual carried two copies of *val* and began smoking marijuana as a teen—although such teenage-onset cannabis use also emerged as an independent risk factor. Carrying two copies of the *met* variant posed no increased risk for psychosis. The results suggest that for some people, adolescence may be a "sensitive period of neurobiological vulnerability to cannabis," but cannabis use, even in combination with the *val* variant, does not constitute a major cause of schizophrenia. People with two copies of *val* who used the drug accounted for only one-fifth of those who developed psychotic disorders, which likely stemmed from multiple causes. However, the researchers point out that unless such potential gene-environment interactions are factored into studies, a gene's connection to a disorder may remain undetected.

Caspi A, Moffitt TE, Cannon M, McClay J, Murray R, Harrington H, Taylor A, Arseneault L, Williams B, Braithwaite A, Poulton R, Craig IW. Moderation of the effect of adolescent-onset cannabis use on adult psychosis by a functional polymorphism in the catechol-o-methyltransferase gene: longitudinal evidence of a gene X environment interaction. Biol Psychiatry. 2005 Mar 22; [Epub ahead of print].

Study Reveals Fragile Process of Memory Making

Evidence suggests that as rats learn and remember, their brains adapt behavior to changes in the environment by strengthening certain connections between neurons, or synapses. To discover how this works, Roberto Malinow and colleagues at Cold Spring Harbor Laboratory genetically engineered ways to observe and interfere with the activity of glutamate receptor subtypes, called AMPA receptors, in the lateral amygdala, a fear-

processing area. Their studies revealed that AMPA receptors moved into synapses in rats conditioned to fear a tone paired with a shock, but not in rats exposed to unpaired tones and shocks. Only the rats in the paired group froze when they heard the tone hours later, indicating that they had established the memory; this suggests that receptor movement was central to learning the fear response. The researchers then blocked AMPA receptor movement, resulting in dramatic reductions in learning. By fine tuning their receptor blocking, the scientists were able to determine that disabling receptor movement in as few as 20% of lateral amygdala neurons was enough to disrupt learning. Since each learning session used about a third of lateral amygdala neurons, and many memories can be stored, one neuron may participate in many memories. The researchers suggest that memory formation may require many such coordinated changes across synapses, so disrupting just a few may corrupt this integrated function.

Rumpel S, LeDoux J, Zador A, Malinow R. Postsynaptic receptor trafficking underlying a form of associative learning. Science. 2005 Apr 1;308(5718):83-8.

Actor-Patients' Requests for Medications Boost Prescribing for Depression

Direct-to-consumer (DTC) advertising of prescription drugs in the United States is both ubiquitous and controversial. Critics charge that it leads to overprescribing, while proponents counter that it reduces underuse of effective treatments, especially for conditions that are poorly recognized or stigmatized. To ascertain the effects of DTC-related requests on physicians' initial treatment decisions, Richard Kravitz and colleagues at the University of California, Davis, conducted a randomized trial, using actors portraying patients with symptoms of major depression or adjustment disorder. People with major depression manifest several symptoms that, in combination, interfere with the ability to work, study, sleep, eat, and enjoy once pleasurable activities. Adjustment disorder is an abnormal and excessive reaction to a life stressor, such as starting school, getting divorced, or grief. The actor-patients were also randomly assigned a type of medication request. Some made brand-specific requests, others made general medication requests (not a specific brand), and actor-patients assigned "none" made no medication request. In major depression, rates of antidepressant prescribing were 53% for those making brand-specific requests, 76% for those making general medication requests, and 31% for those making no medication requests. In adjustment disorder, antidepressant prescribing rates were 55% for those making brand specific requests, 39% for those making general medication requests, and 10% for those making no medication request. For both disorder scenarios, making any medication request significantly increased the likelihood of the individual receiving minimally acceptable treatment, defined as any combination of an antidepressant, mental health referral, or follow-up within two weeks. In addition, physicians were much more likely to consider and record a mental health diagnosis if the actor-patient requested medication than if no request was made.

Kravitz RL, Epstein R, Feldman MD, Franz CE, Azari R, Wilkes MS, Hinton L, Franks P. Influence of patients' requests for direct-to-consumer advertised antidepressants: a randomized controlled trial. JAMA. 2005; 293(16):1995-2002.

Genetic Variation Yields Differences in Brain Anatomy and Emotion Regulation

Using neuroimaging, intramural researchers Lukas Pezawas, Andreas Meyer-Lindenberg, and colleagues recently discovered a genetic trait associated with reduced gray matter

volume in emotion-processing brain regions, as well as increased anxiety-related temperamental traits and elevated risk of depression. Previous studies have highlighted the role of a gene that encodes for 5-HTT, a "transporter" for the neurotransmitter serotonin, which is involved in depression and anxiety disorders and is the target of most current medication therapies (i.e., SSRIs) for those disorders. The researchers in the current study focused on 5-HTTLPR, a specific region on the gene that influences protein formation and the availability of 5-HTT. The researchers found that individuals with a short version of 5-HTTLPR had significantly less cortical volume in the limbic regions (specifically the perigenual anterior cingulated cortex and amygdala), which are involved in emotion regulation. Functional analyses of the brain showed carriers of the short 5-HTTLPR version also had deficits in the feedback circuit involved in abating negative affects following fearful stimuli. According to the researchers, these results point toward a developmental, systems-related mechanism underlying normal emotional reactivity and genetic susceptibility for depression.

Pezawas L, Meyer-Lindenberg A, Drabant EM, Verchinski BA, Munoz KE, Kolachana BS, Egan MF, Mattay VS, Hariri AR, Weinberger DR. 5-HTTLPR polymorphism impacts human cingulated-amygdala interactions: a genetic susceptibility mechanism for depression. Nat Neurosci. 2005 May 8; [Epub ahead of print].

Surgical Therapy Reverses Symptoms of Treatment-Resistant Depression

Major depression is the most common psychiatric disorder, and up to 20% of patients have no response to conventional treatments. To address the needs of this severely disabled population, Helen Mayberg and colleagues at Emory University studied the effects of deep brain stimulation, a surgical therapy that has shown marked clinical benefits in patients with Parkinson's disease. In six individuals with treatment-resistant depression, the researchers specifically targeted the subgenual cingulate region, a brain area that in previous studies has consistently shown involvement in acute sadness and response to antidepressant treatments (medications, electroconvulsive therapy, etc.). Through chronic stimulation of this region, four of the six participants demonstrated significant and sustained remission of depressive symptoms. The researchers concluded that deep brain stimulation appears to be an effective and novel intervention for severely disabled patients suffering from treatment-resistant depression.

Mayberg HS, Lozano AM, Voon V, McNeely HE, Seminowicz D, Hamani C, Schwalb JM, Kennedy SH. Deep brain stimulation for treatment-resistant depression. Neuron. 2005 Mar 3;45(5):651-60.

HIV/AIDS

Blood-Brain Barrier Integrity Plays Key Role in Regulating HIV Entry

An important area of AIDS research relates to understanding the mechanisms regulating viral entry into the nervous system. A key pathway for HIV-1 entry into the brain is through migration of infected monocytes (a type of precursor immune system cell) through the blood-brain barrier. Two papers published by NIMH grantee Michal Toborek and colleagues at the University of Kentucky examine the complex interactions between viral proteins and the blood-brain barrier and the resultant changes in integrity of the barrier. Specifically, the authors studied the impact of the HIV protein Tat on the expression of blood-brain barrier tight junction proteins, ZO-1 and claudin-5. HIV-1 Tat down-regulates the expression of ZO-1 and claudin-5, which could result in decreased

blood-brain barrier integrity and increased migration of HIV-1 infected cells into the central nervous system. The signal transduction pathways involved in the regulation of the expression of tight junction proteins by HIV-1 Tat were also studied. Multiple signal transduction pathways were involved in the regulation of ZO-1 and claudins. These findings add critical knowledge not only to understanding the pathways of HIV entry into the brain but also the regulatory mechanisms that are pivotal to the maintenance of blood-brain barrier integrity. Such knowledge could inform studies in other diseases relevant to mental health such as Alzheimer's disease, where the blood-brain barrier plays a key role in pathophysiology.

Pu H, Tian J, Andras IE, Hayashi K, Flora G, Hennig B, Toborek M. HIV-1 Tat protein-induced alterations of ZO-1 expression are mediated by redox-regulated ERK1/2 activation. J Cereb Blood Flow Metab, 2005 Apr 13; [Epub ahead of print].

Andras IE, Pu H, Tian J, Deli MA, Nath A, Hennig B, Toborek M. Signaling mechanisms of HIV-1 Tat-induced alterations of claudin-5 expression in brain endothelial cells. J Cereb Blood Flow Metab. 2005 Mar 30; [Epub ahead of print].

Antibiotic May Be Effective in Treating HIV-Related CNS Disease

Despite the availability of antiretroviral therapy, few interventions are available to treat HIV central nervous system disease, a frequent cause of serious illness and death in HIV-positive individuals. To help fill this gap, M. Christine Zink and colleagues at Johns Hopkins University examined the ability of minocycline, an antibiotic with strong anti-inflammatory and neuroprotective properties, to protect against simian immunodeficiency virus (SIV)-associated encephalitis (brain inflammation) and neurodegeneration in a pigtailed macaque model of HIV infection. Twelve macaques were infected with SIV and then treated with minocycline 21 days post-infection. Minocycline significantly decreased moderate and severe encephalitis in SIV treated animals and protected against axonal degeneration. Furthermore, minocyline suppressed HIV and SIV replication *in vitro*. These findings suggest the minocycline may be a readily available, cost efficient therapeutic agent to add to the anti-HIV armamentarium.

Zink MC, Uhrlaub J, DeWitt J, Voelker T, Bullock B, Mankowski J, Tarwater P, Clements J, Barber S. Neuroprotective and anti-human immunodeficiency virus activity of minocycline. JAMA. 2005 Apr 27;293(16):2003-11.

Motivational Prevention Counseling Reduces HIV Transmission Risk Behaviors

Seth Kalichman and colleagues at the University of Connecticut report the results of a study of HIV prevention that elucidates the most essential elements of an intervention based on the information-motivation-behavioral skills (IMB) model that was delivered to men and women receiving clinic services for sexually transmitted infections (STI). Following baseline assessments, participants were randomly assigned to one of four 90-minute risk-reduction counseling sessions that deconstructed the IMB model. Participants were followed for nine months, with STI diagnoses monitored over 12 months. Men who received the full IMB session evidenced relatively greater use of risk-reduction behavioral skills and relatively lower rates of unprotected intercourse over six months' follow-up and had fewer new STIs. For women, however, the motivational counseling demonstrated the most positive outcomes. Results suggest that brief single-exposure HIV prevention counseling can reduce HIV transmission risks.

Kalichman SC, Cain D, Weinhardt L, Benotsch E, Presser K, Zweben A, Bjodstrup B, Swain GR. Experimental components analysis of brief theory-based HIV/AIDS risk-reduction counseling for sexually transmitted infection patients. Health Psychol. 2005 Mar;24(2):198-208.

Progress on NIMH Initiatives

Schizophrenia Research Forum Website

In an effort to hasten the development of better treatments, preventative measures, and eventual cures for schizophrenia, the National Alliance for Research in Schizophrenia and Depression (NARSAD) will launch a new online scientific forum for schizophrenia researchers, in conjunction with a team of consultants who have pioneered a similar site for Alzheimer's disease researchers. NIMH, recognizing the timeliness and value of this project, is providing initial support to launch the new site. This online community is designed to foster ideas and collaboration and will be known as the Schizophrenia Research Forum (SRF). The intent is to create a knowledge management website that will present current news on schizophrenia and provide a forum for discussing research and exchanging new ideas. The site will also maintain databases, directories, research tools, and links to online resources. With most laboratories tending to work in isolation, this site will bring instant communication to the more than 8,000 researchers currently working towards the same goal. The SRF will be independent, nonprofit, and free of charge to users. Though dedicated to researchers, most features of the site will be open to patients, families, the media, and others interested in schizophrenia research. The site will be evaluated regularly in terms of effectiveness for number of hits, number of members, and actual pages accessed by users. Additionally, a Scientific Advisory Committee will provide feedback and oversight, with plans to include evaluations by an outside specialist in biomedical information technology.

Neuroimaging Informatics Technology Initiative (NIfTI): Update on common format for fMRI data

In April, the National Institute of Biomedical Imaging and Bioengineering (NIBIB) joined NIMH and National Institute of Neurological Disorders and Stroke (NINDS) as joint sponsors of the Neuroimaging Informatics Technology Initiative (NIfTI), which seeks to enhance informatics for neuroimaging research. A new, common file format for fMRI data exchange called NIfTI-1 is approaching implementation, and a significantly updated web site was launched May 6 with formal specifications. Five major fMRI software packages from around the world are implementing full support for NIfTI-1.1, with one already completed and the others planned for the end of the year. Other support packages are also being developed. In addition, the NIfTI working committee is progressing on a variety of more advanced data exchange issues, collectively dubbed NIfTI-2. These include possible use and incorporation of other evolving formats, development of taxonomies for describing and exchanging experimental designs, and testing the interoperability of results from different data analysis packages. As a major NIfTI-2 initiative, a geometry subcommittee has been formed to develop a format for representing and exchanging brain surfaces.

Collaborative RFAs

HIV and Psychiatric Comorbidity Research Project

NIMH and NIDA invited applications addressing the cellular, molecular, and genetic factors underlying the high comorbidity between HIV-1 infection and psychiatric disorders. Applications were encouraged to focus on: 1) the genetic and biological underpinnings of comorbid HIV-1 infection and psychiatric illnesses; 2) the mechanisms by which psychiatric illness or HIV-1 infection influences the comorbid disease course and contributes to inter-individual variability in disease progression; 3) the vulnerable brain structures, neurocircuitry systems, or other substrates involved in comorbid disease progression; 4) the effect of HIV on the developing brain and the mature brain as it pertains to elucidating vulnerable gene-environment or other interactions and immune profiles most likely to influence psychiatric conditions; 5) effective pharmacological agents that negatively impact the ability of HIV to infect cells or replicate and also alleviate the symptoms of depression, anxiety, or other psychiatric disorders; and 6) the role of drugs of abuse in modulating these parameters in HIV+ individuals with psychiatric disturbances.

Release Date: February 18, 2005; Expiration Date: April 27, 2005

http://grants.nih.gov/grants/guide/rfa-files/RFA-MH-05-010.html

Scientific Program Director: Kathy L. Kopnisky, PhD, Division of AIDS, Health and Behavior Research (DAHBR), National Institute of Mental Health

Course Development in the Neurobiology of Disease

On behalf of the Neuroscience Blueprint (http://neuroscienceblueprint.nih.gov), NIMH is seeking applications focusing on the development of new academic courses on the basic neurobiology of disease as well as the substantial expansion of existing courses. The primary goal is to foster course development at institutions where such an offering does not exist. For institutions developing a course on the neurobiology of disease *de novo*, it is expected that a course syllabus will be fully developed in year 1 and the course will be offered in year 2 of the award. A secondary goal is to enhance existing courses on the neurobiology of disease by expanding them beyond the current course offerings.

Release Date: March 23, 2005; Expiration Date: May 26, 2005

http://grants1.nih.gov/grants/guide/rfa-files/RFA-MH-05-011.html

Scientific Program Director: Nancy L. Desmond, PhD, DNBBS, National Institute of Mental Health

Units for HIV/AIDS Clinical Trials Networks

NIMH and six other NIH Institutes are seeking Clinical Trials Units (CTUs) to implement the clinical research plans of one or more of the HIV/AIDS Clinical Trials Networks. Each CTU will be comprised of an Administrative Component and one or more Clinical Research Sites, led by a principal investigator, and optimally configured to conduct clinical research by recruiting, screening, enrolling, and following research participants from the populations most affected and/or endangered by the HIV/AIDS epidemic.

Release Date: February 10, 2005; Expiration Date: July 12, 2005

http://grants.nih.gov/grants/guide/rfa-files/RFA-AI-05-002.html

Scientific Program Director: Office of the Director, Division of AIDS, National Institute of Allergy and Infectious Diseases

NIMH Public Outreach

First Coalition for Research Progress Meeting

NIMH is committed to maintaining open dialogue with its stakeholders and to developing a research agenda that is responsive to the needs of its constituents. Thus, the Institute convened its first meeting of professional organizations—the Coalition for Research Progress—in March 2005 in Washington, DC. The meeting had two primary goals: to share the latest developments at NIMH with professional constituent organizations and to foster dialogue on the future path and directions of NIMH funded research. The meeting began with a description of new directions for the Institute as well as its two biggest concerns in the current climate of slow budgetary growth: mentoring new investigators and promoting innovative research. Presentations on the Neuroscience Blueprint and the NIH Roadmap followed. After networking breaks, each of the NIMH division directors described the initiatives, plans, and priorities of their divisions under the new reorganization.

Sixth Annual Meeting of the NIMH Outreach Partners Program

The NIMH Outreach Partnership Program—a nationwide initiative that brings together national and state organizations to help bridge the gap between research and clinical practice—held the annual meeting of its 51 outreach partners (from every state and Washington, DC) in early April in Omaha, Nebraska. The Program receives support from NIDA and also works in cooperation with SAMHSA's Center for Mental Health Services (CMHS). NAMHC member Renata Henry joined staff from NIMH, NIDA, the National Library of Medicine (NLM), and SAMHSA, as well as grantees and state and local health experts to present updates on: 1) NIMH research highlights; 2) effective mental health and substance abuse treatments for children and adults; 3) science and the media; 4) community engagement in research and outreach to minority populations; 5) overview of ClinicalTrials.gov; 6) evidence based treatments and real world practice; 7) administering evidence based practices in New York; 8) implementing the President's New Freedom Commission recommendations; and 9) an application of NIMH's *Real Men, Real Depression* campaign in Peoria, Illinois. Additional information on the NIMH Outreach Partnership Program is available at http://www.nimh.nih.gov/outreach/partners/index.cfm.

Research Conferences and Workshops

State-of-the-Science Conference on Management of Menopause-Related Symptoms

The NIH Consensus Development Program held this conference in March, which was co-sponsored by NIMH and several other Institutes. Peter Schmidt from the NIMH intramural program and Lee Cohen, an NIMH grantee from Massachusetts General Hospital, presented on depression during perimenopause. For the draft statement resulting from this conference visit: http://consensus.nih.gov/ta/025/025MenopauseINTROpostconf.htm.

Knockout Mouse Project (KOMP) Workshop

NIMH is participating in a trans-NIH effort known as the Knockout Mouse Project, which recognizes the value of null mutants in research and is striving to develop a shared

resource for these valuable experimental models. On March 24–25, an NIH-sponsored workshop was held to gather information on the feasibility and promise of providing a collection of embryonic stem cells containing targeted null alleles for genes of interest. Workshop attendees suggested that NIH should focus its effort to provide a more comprehensive resource in coordination with current, large-scale, international efforts. The participants also strongly recommended that NIH-funded laboratories be required to release mutants created with public funds to specific repositories where they would be available as frozen embryos. Furthermore, NIH was urged to work on depositing existing strains in public repositories to be made available as frozen embryos to the research community. *For more information, please contact Andrea Beckel-Mitchener at ab595p@nih.gov.*

Neuroendocrine Signaling in Adolescence: Relevance to Mental Health
On January 31, NIMH sponsored this workshop for basic neuroscientists and clinical researchers involved in studies of brain development, neuroendocrinology, and behavioral plasticity in adolescence. Several research opportunities were identified in basic neurodevelopment, neuroendocrinology, technology development, and clinical science aimed at identifying environmental and hormonal triggers for mental disorders during adolescence. A PA is planned to strengthen the NIMH portfolio in this important, under-represented area that bridges DNBBS and the Division of Pediatric Translational Research and Treatment Development (DPTR). *For more information, please contact Lois Winsky at lwinsky@mail.nih.gov.*

3rd Annual "Baby Siblings" Autism Workshop
In March, NIMH participated in a workshop that convened a National Institute of Child Health and Human Development (NICHD)/National Alliance for Autism Research (NAAR) consortium of researchers focused on studying younger siblings of children diagnosed with autism, and other at-risk populations for autism. The meeting allowed researchers to share methodology, recent findings, and ideas for possible collaborations. Pooling of data would allow questions to be answered that cannot be sufficiently studied in single geographic locations, due to limited numbers of participants. The group is already working together to replicate recent findings of enlarged head circumference in autism. NIMH staff chaired an ethics panel, which included discussion of clinical interpretation of risk and referral in very young children who show signs of autism or related delays. *For more information, please contact Audrey Thurm at athurm@mail.nih.gov.*

Early Recognition of Eating Disorders in Children and Adolescents
NIMH convened this workshop on January 28 to identify approaches and opportunities applicable to research in the early recognition of eating disorders in the pediatric population. Experts in eating disorder research discussed critical topics associated with assessment and neurobiology of child and adolescent eating disorders. The meeting was attended by representatives from NICHD, the National Institute of Diabetes & Digestive & Kidney Diseases (NIDDK), and the Food and Drug Administration (FDA) to discuss research priorities for eating disorders in children and adolescents. *For more information, please contact Regina S. James at rjames@mail.nih.gov*

Institute of Medicine Forum on Drug Discovery, Development, and Translation
The Institute of Medicine convened this forum, at the request of the FDA, with a focus on four priority areas in drug discovery, development, and translation. These areas include: 1) scientific challenges that require a coordinated response; 2) public communication and engagement in clinical research; 3) the role of the public and private sector in drug development; and 4) alternatives to the current business model. The forum aims to bring together leaders from the private sector, federal agencies, the academic community, consumers, and federal and private health plans, and will conduct workshops to enhance mutual understanding of the drug discovery, development, and translation process among the scientific community and the general public, and provide a mechanism to foster partnership among the different sectors. The first meeting, held on March 24–25 in Washington, DC, focused on the following topics: public understanding of the value of pharmaceuticals; evaluative science; the drug discovery and development process; accelerating the development process; and post–marketing surveillance. Two workgroups will be formed to address the challenges raised at the meeting and to focus on accelerating and improving efficiency of drug development, public education, and engagement in drug development. *For more information, please contact Linda Brady at lbrady@mail.nih.gov.*

Action Planning Conference for Re-Establishing Mental Health Services and Research Programs in Iraq
A five-day meeting held in Amman, Jordan, brought together more than 25 mental health professionals and leaders in the Iraqi Government, with 20 international mental health experts from the United States, England, and the World Health Organization (WHO). The purpose of the conference was to refine action plans for mental health services and research developed by the Iraqi mental health advisor in the Ministry of Health. NIMH staff from the Office for Global Mental Health and the Traumatic Stress Disorders Research Program (Division of Adult Translational Research and Treatment Development (DATR) attended and participated in discussions focused on revitalizing university and hospital–based mental health research and training programs. The outcome of the conference was establishment of a clear set of goals, priorities, action steps, and parties responsible for developing the human resources, policies, and procedures needed to provide mental health care to the people of Iraq and to enhance the capacity for training scientists and conducting high quality mental health research. The meeting was co-sponsored by the DHHS Office of Global Health, SAMHSA, and the West Kent National Health Service and Social Care Trust in the U.K. A conference report is forthcoming. *For more information, please contact Karen Babich at kbabich@mail.nih.gov.*

Meeting-based Publications

Perinatal Depression
The NIMH cofunded an Agency for Healthcare Research and Quality evidence-based report, *Perinatal Depression: Prevalence, Screening Accuracy and Screening Outcome*, in partnership with other members of the Federal Safe Motherhood Working Group. This report emphasizes that depression in pregnancy is an under-recognized phenomenon and that health care workers should screen for depression during pregnancy as well as during

the postpartum period. The report also describes the lack of adequate data on perinatal depression in racial and ethnic minorities, and suggests that more well-controlled studies are needed on the treatment of depression during pregnancy and the postpartum period.
For more information please contact Cathy Roca at rocac@irp.nimh.nih.gov.

Cognition in Schizophrenia
A lack of scientific consensus regarding appropriate clinical trial methodology to test the efficacy of cognitive enhancing agents in schizophrenia has been one major barrier to progress in this area. A report of the **2004 FDA-NIMH-MATRICS Workshop on Clinical Trial Design for Cognition in Schizophrenia** presents consensus guidelines for the evaluation of co-therapies and broad–spectrum agents targeting cognition in this disorder. The proceedings were published as the first article in the newly privatized *Schizophrenia Bulletin*.
Buchanan RW, Davis M, Goff, D, Green MF, Keefe RSE, Leon AC, Nuechterline KH, Laughren T, Levin R, Stover E, Fenton WS, Marder SR. A summary of the FDA-NIMH-MATRICS workshop on clinical trial design for neurocognitive drugs in schizophrenia. Schizophrenia Bulletin. 2005; 31:5-20.

Consortium Emphasizes Relevance of Avian Research
The international Avian Brain Nomenclature Consortium announced new terminology to identify brain structures in birds and found that the brains of birds appear to be more similar than previously thought to those of mammals. This landmark change, the first such shift in a century, reflects new evidence about the function and evolution of the vertebrate brain, mapping out similarities between structures and cognitive abilities in avian brains and the brains of mammals. Recent findings over the years have even shown that birds possess neural capacities beyond those of some small mammal species. Providing new taxonomy erases misnomers and allows neuroscientists studying non-avian brains to understand the relevance of findings in bird research. The Consortium comprises a team of 28 neuroscientists—international specialists in avian, mammalian, reptilian, and fish neurobiology—led by Duke University neurobiologist Erich Jarvis. The project was funded through the NSF and several NIH Institutes: NIMH, NINDS, National Institute on Deafness and Other Communication Disorders (NIDCD), and NIDA.
Jarvis ED, Gunturkun O, Bruce L, Csillag A, Karten H, Kuenzel W, Medina L, Paxinos G, Perkel DJ, Shimizu T, Striedter G, Wild JM, Ball GF, Dugas-Ford J, Durand SE, Hough GE, Husband S, Kubikova L, Lee DW, Mello CV, Powers A, Siang C, Smulders TV, Wada K, White SA, Yamamoto K, Yu J, Reiner A, Butler AB; Avian Brain Nomenclature Consortium. Avian brains and a new understanding of vertebrate brain evolution. Nat Rev Neurosci. 2005 Feb;6(2):151-9. Review.

Budget

FY 2006 President's Budget Request

The FY 2006 President's Budget Request for NIH was submitted to Congress on February 7, 2005. If approved, this request would provide a total NIH program level of $28,845 million, an increase of $196 million or 0.7% over the FY 2005 Appropriation (see Attachment 1). Highlights of the total NIH request include:

NIH Research Project Grants (RPGs):
The FY 2006 President's Budget would support an estimated 9,463 competing RPGs at the NIH, an increase of 247 RPGs over FY 2005. The President's Budget Request proposes to hold the average cost of competing RPGs at the FY 2005 level while also allowing no inflationary increases for direct, recurring costs in noncompeting continuation RPGs.

NIH Research Training:
Postdoctoral recipients will receive stipend increases from 0% to 4%, depending on level of experience, and postdoctoral fellows will receive a $500 increase for health benefits. These increases will be financed by reducing the number of training positions in FY 2006.

NIH Roadmap for Medical Research:
In FY 2006, NIH will direct $333 million toward Roadmap initiatives, an increase of $97.5 million over the FY 2005 Appropriation. Of this amount, $83 million will be provided by the NIH Director's Discretionary Fund and the remaining $250 million will be provided by the ICs. The IC contribution of support for these trans-NIH research goals is estimated to be 0.9% of each individual IC's total request for FY 2006.

NIH Blueprint for Neuroscience Research:
Spending for NIH Blueprint initiatives will increase from $7 million in FY 2005 to $26 million in FY 2006, including $12 million from Dr. Zerhouni's Discretionary Fund and an additional $14 million from the 15 participating ICs.

The FY 2006 President's Budget Request provides no additional funding toward completion of the John Edward Porter Neuroscience Research Center on the NIH campus.

NIMH Funding:
The FY 2006 request of $1,418 million for the NIMH is an increase of $6 million or 0.4% over FY 2005. At the FY 2006 President's Budget level, the NIMH would support an estimated 2,215 total RPGs compared to 2,228 total RPGs in FY 2005. Approximately 600 of the 2,215 grants to be funded in FY 2006 will be competing awards, either new or renewal. This compares to an estimated 559 in FY 2005 and 630 in FY 2004. The NIMH success rate for RPGs in FY 2006 would be about 22% compared to an NIH average of about 21%. The budget will support an estimated 1,474 full-time equivalent research trainees, a decrease of 13 trainees from FY 2005.

NIMH actual expenditures by budget mechanism for FY 2004 and estimates for FY 2005 and 2006 are displayed on Attachment 2.

Major NIMH Staff Awards

DHHS Secretary's Award
In recognition of their efforts on their successful public education campaign, the **NIMH Real Men Real Depression Communications Group** will be one of four NIH teams receiving the prestigious 2005 Secretary's Honor Award for Distinguished Service from

DHHS Secretary Mike Leavitt. The ceremony is scheduled for May 25, 2005 with a reception immediately following. NIMH is also expanding the reach of this program, with production of new public service announcements and informational materials underway, which feature two Native American men from the Lakota Sioux in South Dakota, and Spanish-language materials. Outreach efforts will begin over the summer.

NIH Director's Awards

Linda Brady, PhD, was selected as one of the recipients for the 2005 NIH Director's Merit Award for Roadmap Activity in Outstanding Leadership of the Molecular Libraries Initiative, along with Christopher Austin, MD, from NHGRI. Dr. Brady played a pivotal role in moving this Roadmap project forward quickly, despite its size and complexity, in large part because of her persistence, energy, and creativity. She was integral in devising solutions on intellectual property issues, public-private partnerships, and resource sharing. Her contributions were completed in addition to her regular duties as a branch chief, demonstrating her outstanding leadership and imagination.

A group NIH Director's Merit Award was bestowed upon Linda Brady, PhD, Wayne Fenton, MD, and Ellen Stover, PhD, from NIMH, and Tom Laughren, MD (FDA), for exceptional leadership in developing medications for cognition and schizophrenia through public-private collaborations in connection with the **Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS)** project.

In recognition of their scientific and programmatic contributions to research on autism in connection with the **Studies to Advance Autism Research and Treatment (STAART)** Program, Audrey Thurm, PhD, Ann Wagner, PhD, and Molly Oliveri, PhD, of NIMH, along with Judith Cooper, PhD (NIDCD), Deborah Hirtz, MD (NINDS), Alice Kau, PhD (NICHD), and Cindy Lawler, MD, National Institute of Environmental Health Sciences (NIEHS), were presented with a group NIH Director's Merit Award.

Karen F. Berman, MD, Chief of the Unit on Integrative Neuroimaging in the Clinical Brain Disorders Branch, IRP, will receive the NIH Director's Merit Award in July for her pioneering work on William's syndrome. Her work provides a framework for examining genetic contributions at the neurobiological level to cognition in normal human subjects and offers an important guide for unraveling how cognitive symptoms emerge from molecular mistakes. Dr. Berman's work in this area has been described in *Neuron* as "fulfilling the promise of the cognitive neurosciences." Dr. Berman was also recently awarded tenure and will continue her outstanding work in IRP.

Ellen Leibenluft, MD, Chief of the Unit on Affective Disorders in the Pediatric and Developmental Neuropsychiatry Branch, IRP, will receive the 2005 NIH Director's Award for Mentoring in recognition of her exemplary dedication to the education and professional development of her fellows as part of the Fellowship Training Program. In the past nine years, Dr. Leibenluft has mentored more than 20 new investigators who have worked with her as Intramural Research Training Award and Clinical Fellows. Her scientists-in-training have published cutting-edge studies in first-class scientific journals

and have accepted faculty positions in prestigious research and academic institutions nationwide.

Neuroscience/Neuropsychiatry Award

Judith L. Rapoport, MD, Chief of the Child Psychiatry Branch, IRP, was this year's winner of the McGovern Institute's **Edward M. Scolnick Prize in Neuroscience**, an annual award recognizing an outstanding discovery or significant advance in the field of neuroscience. Dr. Rapoport was selected for her groundbreaking studies of attention deficit hyperactivity disorder (ADHD), obsessive-compulsive disorder (OCD), and childhood onset schizophrenia, according to Robert Desimone, PhD, director of the McGovern Institute for Brain Research at MIT, which established the award in 2003. In addition, Dr. Rapoport will receive the 2005 **Pasarow Medical Research Neuropsychiatry Award** from the Robert J. and Claire Pasarow Foundation, which awards three prizes annually in recognition of notable research accomplishments in cancer, cardiovascular disease, and neuropsychiatry. Dr. Rapoport pioneered the fields of neuroanatomy and neurochemistry ADHD studies, was the first to document that the symptoms of OCD in children and adolescents are similar to those seen in adults, and was the first to use structural magnetic resonance imaging to examine developmental changes in brain size and structure in children with schizophrenia.

Cognitive Neuroscience Society Award

Leslie Ungerleider, PhD, Chief of the Laboratory of Brain and Cognition in the IRP, was awarded the 2005 George A. Miller Prize in Cognitive Neuroscience by the Cognitive Neuroscience Society. This award was established in 1995 to honor the nominee whose career is characterized by distinguished and sustained scholarship and research at the cutting-edge of cognitive neuroscience. Extraordinary innovation and high impact on international scientific thinking are the hallmarks of the recipient's work.

Major Awards for NIMH Grantees

National Medal of Science

Solomon H. Snyder, MD, DSc, DPhil, a longtime NIMH grantee and director of the Department of Neuroscience at Johns Hopkins University, was awarded the National Medal of Science by President Bush at a White House ceremony on March 14. Dr. Snyder, whose distinguished research career has defined much of the current understanding on neurotransmitters and neuropharmacology, was among eight recipients selected by the NSF to receive the Nation's highest science honor.

National Academy of Sciences

Axel T. Brünger, PhD, investigator at Howard Hughes Medical Institute and Professor in the Department of Molecular and Cellular Physiology at Stanford University, and **Nancy G. Kanwisher, PhD,** Professor in the Department of Brain and Cognitive Sciences at MIT, were recently elected as new members of the National Academy of Sciences (NAS). The NAS is a private organization of scientists and engineers dedicated to promoting and advancing science, and acts, upon request, as an official adviser to the federal government in any matter of science or technology. Election to membership in the

Academy is considered one of the highest honors that can be given to a U.S. scientist or engineer.

Staff Changes

Arriving:

German Cavelier, PhD, joined the Office of Interdisciplinary Research and Scientific Technology, DNBBS, as the Chief of Informatics Research and Development. Dr. Cavelier received his doctorate from Johns Hopkins University and most recently was a senior research scientist on the faculty of Columbia University. His background in bioengineering, electrical engineering, and computational biology will provide expertise for the many bioengineering and informatics grants and program initiatives in which the Office is involved.

Serena Chu, PhD, joined the Extramural Review Branch, Division of Extramural Activities, in April and will serve as a Scientific Review Administrator. Prior to joining NIMH, Dr. Chu was a Health Scientist Specialist with the Department of Veterans Affairs where she managed the Equity and Special Populations research portfolio for Health Services Research and Development. Her projects focused on HIV/AIDS, Hepatitis C, rural health, homelessness, ethnic minorities, health literacy and communication, health disparities, complementary and alternative medicine, mental health, substance abuse, post-traumatic stress disorder, homelessness, and physical disability.

Yasmin Cypel, PhD, joined the Office of Interdisciplinary Research and Scientific Technology, DNBBS, as a Health Scientist Administrator. Dr. Cypel received her doctorate from the University of Maryland, and most recently was a senior researcher with the American College of Radiology. Her expertise in statistics and survey research will be drawn upon in coordinating program activities across many NIMH, multi-Institute, and trans-NIH efforts, including the Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) Programs, Biomedical Information Science and Technology Initiative Consortium (BISTIC), Bioengineering Consortium (BECON), Neuroimaging Informatics Technology Initiative, Human Brain Project, Neuroscience Blueprint, and NIH Roadmap initiatives.

George Niederehe, PhD, has been appointed Acting Chief of the Geriatrics Research Branch, DATR, where he also oversees the Geriatric Translational Behavioral Science and Geriatric Psychosocial Intervention Research programs.

Samia Noursi, PhD, joined the Division of Services and Intervention Research (DSIR) team as a Social Science Analyst and will be working on multiple projects including inter-agency initiatives such as Science and Service, the research conference grant program, and initiatives for innovation. Prior to joining NIMH, Dr. Noursi was the research director for the National Child Welfare Resource Center on Legal and Judicial

Issues at the American Bar Association Center on Children and the Law, funded by the Children's Bureau.

Mary Lou Prince joined the DATR and DAHBR Divisions as a Program Specialist. She will serve as the staff person responsible for planning, managing, and evaluating the research and research training grants/portfolios for both Divisions.

James Raber, DVM, PhD, joined the IRP as the new Animal Program Director and Chief of the Veterinary Medicine Resources Branch, in a joint position with the National Eye Institute (NEI). Dr. Raber has been Animal Program Director at NEI since 1988, and has served as the lead veterinarian for the Building 49 shared animal facility. He will retain both positions with NEI in addition to managing the NIMH animal program.

William Riley, PhD, joined DAHBR in the Health and Behavior Research Branch, and will serve as Behavior Change Program Chief. The Behavior Change program supports research in health behavior interventions among those with mental disorders. Prior to joining NIMH, Dr. Riley was Director of Research at PICS, a health behavior research firm in Reston, VA, which utilized SBIR funding to apply computer technologies to health behavior problems such as smoking, diet, exercise, sleep, and behavioral monitoring.

Valerie Sanders joined DATR as an Assistant Administrative Office in January. She previously served at the National Cancer Institute for the Laboratory of Cell Regulation and Carcinogenesis.

Timothy Tosten, MPA, joined the IRP as the new Associate Director for Administration and Branch Chief of the Administrative Services Branch. Mr. Tosten oversees all administrative operations of the IRP, including contracts, budget, facility management and renovations, and administrative services. He also serves as liaison between the IRP and NIMH headquarters, and the NIH, responding to questions regarding the administrative activities of the IRP. He was previously the Director of the Division of Employee Services in the Office of Research Services at NIH.

Departing:

Joan G. Abell, Associate Director of the Outreach Partnership Program, whose leadership, knowledge, and expertise in communications and outreach greatly advanced the mission of NIMH, retired from her position at the Office of Constituency Relations and Public Liaison (OCRPL) on March 1. She began her career in mental health in 1968 at the National Clearinghouse for Mental Health Information, which was part of the NIMH Office of Communications (OC). She worked her way up to Acting Deputy Director of the OC and Chief of the Information Resources and Inquiries Branch, the latter a position she held for more than 25 years. In November 2003, Joan moved to OCPRL to be Deputy Director of the Outreach Partnership Program. During her long career, Joan was detailed to the White House Special Office of Drug Abuse Education and Prevention and to the President's Commission on Mental Health. She also worked on

many of the Institute's campaigns including drug abuse prevention efforts in the early 1970s, the Anxiety Disorders Campaign, and the Real Men Real Depression campaign. Over the course of her career, Joan received many awards and recognition for her exceptional work.

Michael Brownstein, PhD, has retired as Chief of the Laboratory of Genetics and accepted a position with the J. Craig Venter Institute, a not-for-profit research institute dedicated to the advancement of the science of genomics; the understanding of its implications for society; and the communication of those results to the scientific community, the public, and policymakers.

Barry D. Lebowitz, PhD, Chief of the Geriatrics Research Branch in DATR, left NIMH after more than 25 years of service to the Institute. Barry has accepted a position as Professor of Psychiatry and Deputy Director of the Sam and Rose Stein Institute for Research in Aging at the University of California, San Diego.

Bruce Smith has retired as Chief of the Research Services Branch, which provides for the instrumentation, networking and computer needs of the IRP, after more than 32 years at NIH.

Transferring:

Kelly Linthicum, who served as a Program Analyst in DATR, moved to DNBBS. She will serve as the staff person responsible for planning, managing, and evaluating the research and research training grants/portfolios for the Division.

In Memoriam:

Anne Rosenfeld, Special Assistant to Dr. Ellen Stover, passed away on February 10, 2005 from leukemia. Anne first joined NIMH in April 1978 as a Public Affairs Specialist in the NIMH Office of the Director. During her long career at NIMH, she worked in nearly every corner of the Institute and for a number of Institute Directors. Anne was a superb writer with outstanding communication and collaborative skills. She played music, was an avid photographer, and a great listener. She will be missed by all who knew her.