

**Department of Health and Human Services  
PUBLIC HEALTH SERVICE  
NATIONAL INSTITUTES OF HEALTH  
NATIONAL INSTITUTE OF MENTAL HEALTH  
National Advisory Mental Health Council  
Minutes of the 215th Meeting  
May 10-11, 2007**

## **Minutes of the 215th Meeting of the National Advisory Mental Health Council**

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The National Advisory Mental Health Council (NAMHC) convened its 215<sup>th</sup> meeting in closed session to review grant applications at 10:30 a.m. on May 10, 2007, at the Neuroscience Center in Rockville, Maryland, and adjourned at approximately 5:00 p.m. (see Appendix A: Review of Applications). The NAMHC reconvened for an open session on the following day, May 11, 2007, in Building 31C, National Institutes of Health, Bethesda, Maryland, from 8:30 a.m. until adjournment at approximately 12:30 p.m. In accordance with Public Law 92-463, the policy session was open to the public. Thomas R. Insel, M.D., Director, National Institute of Mental Health (NIMH) chaired the meeting.

### **Council Members Present at the Open Policy Session:**

Glorisa J. Canino, Ph.D.  
Elizabeth Childs, M.D.  
Jonathan D. Cohen, M.D., Ph.D.  
Raquel E. Gur, M.D., Ph.D.  
Martha E. Hellander, J.D.  
Peter J. Hollenbeck, Ph.D.  
Dilip V. Jeste, M.D.  
Ned H. Kalin, M.D.  
Helena C. Kraemer, Ph.D.  
Pat R. Levitt, Ph.D.  
John S. March, M.D., M.P.H.  
Enola K. Proctor, Ph.D.  
Suzanne E. Vogel-Scibilia, M.D.  
Stephen T. Warren, Ph.D.

### **Ex-officio Members Present at the Open Policy Session:**

Ira R. Katz, M.D., Ph.D., Department of Veterans Affairs

### **Others Present:**

Aysha Ahktar, Physician's Committee for Responsible Medicine  
Virginia Anthony, American Academy of Child and Adolescent Psychiatry  
Ann Bettsworth, American Psychological Association  
Dara R. Blachman, Office of Behavioral Social Sciences Research  
Alan Friedman, Transcriber  
Stephen Foote, Retired  
Hope Ferdowsian, Physician's Committee for Responsible Medicine  
Reuven Ferziger, Johnson & Johnson  
E. Aracelis Francis, Council on Social Work Education  
Alan Kraut, Association for Psychological Sciences  
Mary Giliberti, National Alliance on Mental Illness  
Noel A. Mazade, NASMHPD Research Institute, Inc.  
Marilyn Massey-Ball, MasiMax Resources, Inc.  
Ann Michaels, National Foundation on Mental Health (Friends of NIMH)  
Gerald Overman, College of Psychiatric & Neurologic Pharmacists

Eldridge Proctor, Tourette Syndrome Association  
Stephanie Reed, American Association for Geriatric Psychiatry  
Darrel A. Regier, American Psychiatric Institute for Research and Education  
Michelle Rodrigues, SRI  
Barbara Wanchisen, Federation of Behavioral, Psychological & Cognitive Sciences  
Jill Wetzel, Infinity Conference Group  
Vicky Whittemore, Tuberous Sclerosis Alliance  
Barbara Wolff, Depression and Related Affective Disorders Association  
Joan Zlotnik, Institute for the Advancement of Social Work Research

## **OPEN POLICY SESSION: CALL TO ORDER AND OPENING REMARKS**

NIMH Director Dr. Thomas Insel called the meeting to order, welcoming all in attendance. He introduced Dr. Ira Katz, a former NIMH grantee and geriatric and services researcher, and welcomed him as an ex-officio member of Council representing the Department of Veterans Affairs.

## **APPROVAL OF THE MINUTES OF THE PREVIOUS COUNCIL MEETING**

Turning to the minutes of the January 2007 Council session, Dr. Insel asked if Council members had revisions or comments on the minutes. Hearing none, the minutes were unanimously approved.

## **NIMH DIRECTOR'S REPORT**

In his Director's Report, Dr. Insel updated the Council on several important activities at three levels: the Department of Health and Human Services (DHHS), the National Institutes of Health (NIH), and the NIMH (see report at <http://www.nimh.nih.gov/council/dirreportmay07.pdf>).

Dr. Insel reported that following the tragic shootings at Virginia Tech in April, he was invited by Secretary Leavitt to participate in a "listening tour" visiting several states (West Virginia, Minnesota, Utah, Colorado, Tennessee, Florida, and Texas) to identify concerns and best practices related to the issue of violence in American schools and to discuss mental health and violence. A theme that emerged was the mismatch between the supply and demand of mental health services, particularly the urgent demand for services in students. From the NIMH perspective, this discussion was an opportunity to clarify that mental illness is not involved in most acts of violence. Other issues raised included the need for assessment and treatment in schools, primary care settings, emergency rooms and criminal justice systems; continued confusion about privacy laws and sharing patient information; and the ongoing challenge of protecting privacy while ensuring public safety without increasing stigma.

Dr. Insel reported that The Combating Autism Act of 2006 assigns the Secretary of HHS responsibility for implementing several new authorities in research and services for those with autism spectrum disorders. This Act authorizes expanded activities related to autism research, prevention, and treatment through FY 2011 and establishes a new

Interagency Autism Coordinating Committee (IACC) to coordinate research across the Federal Government and private sector. As one part of its responsibility, the IACC is charged with developing a strategic plan for autism research, including proposed budgetary requirements, to be updated annually. It is anticipated that the Office of the Secretary of DHHS will delegate authority to implement the provisions of the Combating Autism Act with respect to the IACC to the NIH, as was done with the original IACC established by the Children's Health Act of 2000, and that NIMH will be designated the lead for this activity.

Dr. Insel then turned to NIH activities, beginning with a discussion of the new iteration of Roadmap, "Roadmap 1.5." There is an NIH committee, co-chaired by the Directors of NIH Institutes and Centers (ICs) and populated by nominees from interested Institutes, that is responsible for developing initiatives for Roadmap 1.5. This group's focus is to support innovative science, stimulate interdisciplinary research, and reshape clinical research to accelerate medical discovery and improve public health. The five new Roadmap initiatives under discussion are Microbiome; Epigenetics; Inflammation as a Common Mechanism of Disease; Phenotyping Services and Tools; and Protein Capture/Proteome Tools. IC Directors will be meeting in the near future to discuss these initiatives and propose specific efforts for future Roadmap activities.

Dr. Insel outlined the current NIH funding strategy, which includes targeting areas of need such as the pool of new investigators and investigators submitting applications for a first renewal. The '07 funding strategy allows for no inflationary increase for non-competing grants and mandates that Roadmap initiatives be paid through an NIH common fund. This plan, including the initiation of the NIH common fund, makes approximately \$18 million previously committed to Roadmap for 2007 available to fund other initiatives at NIMH, and these funds will be targeted to the identified areas of need. Dr. Insel stressed that the decreasing budget represents a real challenge for NIMH. He noted that tough choices need to be made, but the hope is that NIMH can keep the pool of new Principal Investigators (PIs) as robust as it has been in the past.

Dr. Insel outlined the creation of the Research Condition and Disease Categorization (RCDC) system, a single coding system being developed for use NIH-wide. This system will be used to provide information to NIH staff as well as to Congress and the advocacy community on how much research NIH is supporting on specific disorders. Currently, each IC has its own coding system and can provide this information specific to its institute, but the RCDC system will provide data NIH-wide. This federally mandated system is an enormous effort and is scheduled for reporting the fiscal year 2008 awards. Dr. Insel thanked the more than 40 staff members who contributed innumerable hours and their scientific expertise in developing "fingerprints" for each disorder, which will allow for consistent categorization and coding of research projects across NIH.

Dr. Insel noted that Congress has been increasingly interested in having public hearings featuring NIH and its institutes. The House Labor-DHHS-Education Subcommittee on Appropriations held a "theme" hearing at which the leaders of NIMH, the National Institute on Drug Abuse (NIDA), the National Institute on Alcohol Abuse and Alcoholism (NIAAA), and the Substance Abuse and Mental Health Services Administration

(SAMHSA) testified about their programs and current plans and priorities. The corresponding subcommittee in the Senate also held a hearing focusing on mind, brain, and behavior featuring testimony from NIMH, NIDA, NIAAA, the National Institute of Neurological Disorders and Stroke (NINDS), and the National Institute on Deafness and Other Communication Disorders (NIDCD). Members of this Senate subcommittee were very interested in hearing about what these institutes hope to accomplish through the science supported with appropriated funds. The same subcommittee later held a hearing specifically about autism, and included testimony from Dr. Insel representing NIH, Dr. Julie Gerberding, Director of the Centers for Disease Control and Prevention, as well as public, non-federal witnesses. In addition, the House Energy and Commerce Committee's Subcommittee on Health held a hearing on post-partum depression featuring testimony from NIMH.

Dr. Insel highlighted several exciting scientific discoveries. Two very exciting recent discoveries related to bipolar disorder have been published. First is the publication of the first genome-wide study of bipolar disorder that identified genes implicated in the etiology and treatment of bipolar disorder (published in *Molecular Psychiatry* May 2007). Second is the publication of findings regarding the efficacy of pharmacologic and psychotherapy treatments for bipolar depression based upon the multi-site Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-PD) in the *New England Journal of Medicine* (March 2007) and the *Archives of General Psychiatry* (April 2007). He also recounted recent scientific discoveries on the characterization of autism as a disorder of genetic structure (*Science* April 2007) and autism as heritable in the sense that it is based on changes in the genome (*Nature Genetics* March 2007). He also summarized a set of articles from the National Survey of American Life and the National Latino and Asian American Study. These studies will help researchers understand the prevalence of disorders, access to and utilization of mental health services, and the impact services have on the community. Together with other national surveys such as the National Comorbidity Survey, these surveys provide improved data on the mental health of racial and ethnic minorities living in the United States and serve as an excellent resource for researchers examining programs and services and addressing current health care disparities. Given time constraints, he highlighted only a few but encouraged those interested to review the May 2007 Director's Report, which provides more detailed information as well as references (see <http://www.nimh.nih.gov/council/dirreportmay07.pdf>).

Another major undertaking within NIMH is the development of a new strategic plan. NIMH has a vision, mission statement, and principle objectives established and in place. The goal of the strategic plan is to develop a framework for implementing research that will reach these objectives. This is ongoing within the Institute, and it is hoped that an update will be provided at the January Council meeting.

Turning to staff changes, Dr. Insel noted that Molly Oliveri, Ph.D. was selected as the Director of the Division of Pediatric Translational Research and Treatment Development (DPTR). Ana Velez has been named the NIMH Budget Officer. Thomas Lehner, Ph.D., M.P.H. was selected as the Chief of the Genomics Research Branch in the Division of Neuroscience and Basic Behavioral Science (DNBBS). William Fitzsimmons, NIMH Executive Officer, is retiring this summer. Patrick Shirdon, M.S., the Deputy Executive

Officer for the last 2 years, will be acting Executive Officer through the summer while a search for a permanent Executive Officer is conducted.

Dr. Insel continued by raising an area of emerging interest for NIMH. Researchers have been talking about mental disorders as developmental disorders for some time, and it appears that there is an opportunity for NIMH to encourage a new discipline that brings together the fields of developmental neurobiology, developmental psychopathology, and developmental psychology.

Dr. Levitt commented that this is an important issue for Council to address because the NIMH research portfolio is relatively thin in the integration of developmental neurobiology and behavioral development in the context of understanding psychopathological processes. The discipline is starting to emerge, and researchers from three disciplines (developmental neurobiology, developmental psychopathology, and developmental psychology) are converging, with the goal of understanding the path that the nervous system takes to psychopathology. Dr. March added that there is also the issue of workforce capacity and stressed that a cadre of researchers is needed that is capable of working at the intersection of developmental neurobiology, developmental psychopathology, and developmental psychology. There was a call for a Council workgroup to assess issues related to neurodevelopment. Council members Drs. March and Levitt volunteered to co-chair this workgroup, and several Council members offered to participate in this effort.

Dr. Jeste agreed with the importance of this area and stressed that when thinking about neurodevelopment, it is important to take a lifespan perspective, looking at aging as well as issues specific to childhood. Research provides evidence for neuroregeneration and neuroplasticity later in life, and therefore the end of the lifespan is important for inclusion in this discussion. Dr. Gur added that there is sufficient literature to suggest there are early markers that could assist in diagnosing these disorders at an early stage. Ms. Hellander stressed the importance of this workgroup and is encouraged by the fact that it is not disease-specific, but broad-based. She also suggested that NIMH capitalize on the attention this issue has gained and use it to recruit researchers from other areas of medicine.

Dr. Insel noted training as another emerging issue. NIMH will be undertaking a review of its programs due to both new NIH requirements and the need to be sure that NIMH programs are meeting workforce needs. Both the Career Opportunities in Research Education and Training (COR) program (T34) and the Minority Research Infrastructure Support Program (M-RISP) will be included.

Dr. Insel added that another emerging issue for NIMH is the issue of community violence. As a follow-up to the themes that emerged in the listening tour, NIMH is engaged in discussions to assess the scientific evidence related to an association between violence and mental illness. Ms. Hellander and Drs. Jeste and Vogel-Scibilia volunteered to assist with this work. Ms. Hellander suggested that the effort include discussions with mothers of children with emerging mental illness. Dr. Insel emphasized NIMH's ongoing interest in this area and noted that DPTR recently held a meeting on the developmental antecedents of conduct disorder and antisocial behavior.

## **UPDATE ON THE NIMH CLINICAL TRIAL NETWORKS AND “THE ROAD AHEAD” COUNCIL WORKGROUP REPORT**

Philip Wang, M.D., Dr.P.H., Director of NIMH Division of Services and Intervention Research (DSIR), provided an update on the NIMH Clinical Trials Networks as a follow-up to the presentation at January Council. The Clinical Trials Networks include the Depression Trials Network, the Schizophrenia Trials Network, and the Bipolar Disorder Trials Network. Over the last few years, the networks have implemented several large-scale clinical trials. In September 2006, Council reviewed the current status of the networks and suggested that NIMH quickly get research going on the networks. To achieve this goal, NIMH took a three-pronged approach: (1) reconvening the Council Network Workgroup to identify the priorities for research projects on the networks; (2) issuing a Request for Information (RFI) to solicit ideas from the field; and (3) gathering ideas from the advocacy community via the NIMH Alliance for Research Progress meeting.

The Council Network Workgroup met on January 10, 2007, and the group was charged with the task of identifying high-impact areas of science that might positively impact the burden of mental illness and clinical practice, as well as consider the public health importance, feasibility, size, resources and timeframes required of such studies. This meeting resulted in general recommendations for studies on all of the networks as well as several specific to each network. As general recommendations, the Workgroup advocated for the inclusion of biomarkers and pathophysiology studies, the examination of the impact of interventions on the longer-term course of illness, the inclusion of outcomes beyond symptoms reduction, patient burden, and risk of remission, and the need to address issues of morbidity, comorbidity, and mortality.

For specific network recommendations, the Workgroup suggested studies on the Bipolar Trials Network include longitudinal effectiveness of therapies; to target residual symptoms; to address early signs of relapse; to emphasize suicide prevention with this population given the high rate of suicidality; and to explore expanded strategies for the use of lithium (including low-dose maintenance, the use of lithium as an initial treatment, and switching to or augmenting other medications with lithium). The Depression Trials Network recommendations included optimizing treatment strategies and improving long-term outcomes (e.g., what it takes to achieve full remission and which treatment for which people to better guide practice). Given that the Schizophrenia Trials Network is already engaged in research projects, it was felt that the urgency to increase traffic on this network was not as strong.

NIMH issued an RFI to solicit specific study ideas for each network. This yielded a good response with approximately 10-15 responses for each network. These ideas are under discussion.

As a third action item, ideas were solicited at the January 2007 NIMH Alliance for Research Progress Meeting. Some of the themes that emerged from this meeting included optimizing and personalizing existing treatments and moving from short-term symptom reduction to longer-term outcomes and recovery.

For next steps, NIMH is exploring ways to solicit and review research proposals to be conducted on the existing networks, as well as to introduce competition into the structure and functioning of future networks. The goal is for these networks to be a resource for the field.

Dr. Wang also provided an update on how DSIR has responded to the Council Workgroup report "The Road Ahead." This is the final report of a Council workgroup charged with the task of identifying high-priority research needs and opportunities in services research and clinical epidemiology. This report recommended that NIMH services research focus on four domains: (1) enhancing research responsiveness to stakeholders; (2) capacity-building; (3) knowledge exchange; and (4) ongoing evaluation.

Dr. Wang outlined NIMH plans to enhance research responsiveness to stakeholders. NIMH is collaborating with the National Association of State Mental Health Program Directors (NASMHPD) Research Institute to create ongoing state policy laboratories. These laboratories would use states' existing data to evaluate service systems and inform policymakers. NIMH is exploring similar initiatives with other stakeholders at the Federal level as well as business coalitions. Moreover, NIMH has convened researchers and stakeholders on policy-relevant topics, including pharmacoeconomics, reduction of health disparities, and a planned summer NIMH 2007 mental health services research conference addressing the policy impact of research. NIMH has also issued three new program announcements on the topics of community-based participatory research, reducing health disparities, and trans-NIH dissemination and implementation research. NIMH has also been able to provide timely support to grants with high policy relevance and impact.

For capacity-building, DSIR has been strategically supporting mentored career grants from the most promising mental health services and clinical researchers. DSIR is conducting national searches for open positions within the Division, including branch chief and program chief positions. DSIR has established a biweekly forum to provide an opportunity for every member within DSIR to meet and have a discussion on cross-cutting issues. An Internal Analysis Team, lead by Michael Schoenbaum, Ph.D., a nationally known mental health services, economics and policy researcher, has also been developed to inform the decision making of Dr. Insel, NIH leadership, and other stakeholders who routinely make requests of the Institute. The team will work on several issues in the future, such as examining mental health burdens, unmet need for treatment, and the indirect costs of mental illness. The team also anticipates engaging key stakeholders to assess how large employers make decisions regarding mental health benefits and what factors influence payors' decisions to purchase and reimburse mental health services.

Dr. Wang described NIMH activities related to knowledge exchange, which include public forums developed jointly with the NIMH Office of Constituency Relations and Public Liaison. The purpose of these public forums is to provide public education and stakeholder feedback. This effort includes establishing a two-way communication with purchasers of mental health care services. This relationship would foster an

understanding of the important research that could be used to guide purchasing decisions. DSIR is working with the NIMH Office of Science Policy, Planning, and Communications to develop more tailored methods to communicate effectively to stakeholder audiences and identify research needs. Furthermore, targeted messages for key stakeholders and web-based systems for providing both public health practitioners and other stakeholders with information about effective interventions are being developed.

Finally, Dr. Wang outlined the activities related to ongoing evaluation. To do this, the Internal Analysis Team is exploring the methods used to determine the worth of individual research studies. The team is also examining the existing Federal Government Performance and Results Act (GPRA) goals that are the performance metrics proposed and used by NIMH to track progress and is considering the development of other quality assurance mechanisms that would assess NIMH intervention and implementation activities. The goal of this evaluation process is to ensure that NIMH research investments are beneficial.

Dr. Insel thanked Dr. Wang for the progress report and for his excellent leadership in this effort. Dr. Insel also noted Dr. Wang's active role in following up on report recommendations.

#### **Discussion:**

Dr. Jeste commented that SAMHSA has published a list of proven psychosocial interventions for serious mental illness, yet these interventions have not been disseminated or implemented in communities. This appears to be an important area of research focus. He noted these interventions are typically not targeted to minority populations. Dr. Wang encouraged a continued discussion to address why the interventions were neither targeted for diverse populations nor implemented in the community. Dr. Wang suggested the need for research proposals in this area.

Dr. Proctor detailed the need to develop a method to implement evidence-based treatments—in essence, finding an effective way to measure implementation processes and their outcomes. She urged further studies on and attention to this matter. Dr. Insel concurred, agreeing that “implementation science” is challenging and reiterated the need for a strong research base.

Dr. Levitt indicated that the concept of a state policy laboratory would provide researchers with a large set of very useful data. To support this statement, he referred to his work with the developmental disability population, where service is a critical issue, and with the criminal justice system. Dr. Wang echoed the need for these state laboratories and the difficulties researchers have in establishing relationships with the different agencies that can provide research data. State laboratories could potentially provide PIs with access to crucial data, while giving states the ability to measure how they are serving their citizens.

Dr. Katz reiterated the importance of the state policy laboratories. He cited the Veteran's Administration (VA) as one instance in which a state policy laboratory would be

particularly useful because of the decentralization of information in the VA. Dr. Katz also posed the question of incorporating genetic knowledge into service delivery systems. He argued that models must be developed using the knowledge that is currently available rather than waiting for definitive findings.

Dr. Vogel-Scibilia supported the presented ideas but contended that the larger problem is in workforce training and implementing evidence-based practices in the community. Dr. Vogel-Scibilia suggested that the NIMH might consider issuing directives for continuing education training (e.g., training on evidence-based practices like cognitive behavioral therapy) and make suggestions to state licensing boards on training topics as a method of further disseminating evidence-based practices.

Dr. Wang agreed that the lack of an adequately trained workforce may be one of the reasons that proven psychotherapies are not implemented in communities. Dr. Wang also agreed that setting higher standards for continuing education of health professionals (e.g., CME/CEU) might accelerate dissemination. Dr. Insel indicated that this situation is similar to the scenario that the diabetes research community dealt with regarding the uptake and use of glucose monitoring systems in the community. The research community went to the insurers, who developed a study that showed that the monitors were cost-effective and, therefore, had the evidence for reimbursement. He challenged researchers to consider the goal of their research, beyond getting studies funded and published in journals, and focus on getting treatments to those in need.

## **REASSESSING APPROACHES TO THE GENETICS OF MENTAL ILLNESS**

Dr. Insel introduced Stephen Warren, Ph.D., a member of the NAMHC Council and the William Patterson Timmie Professor and Chair of the Department of Human Genetics at Emory University. Dr. Warren is an internationally recognized expert in the science of human genetics and has been awarded the Allen Award from the American Society of Human Genetics for his research on Fragile X. Dr. Warren was invited to speak on the topic of genetics and mental illness.

Dr. Warren began his presentation noting that almost any disease and particularly mental disorders have a strong genetic component, but are not solely genetic diseases. However, progress in identifying predisposing genes has been somewhat slow. For example, the genetic studies of schizophrenia show 243 positive association studies and 237 negative association studies.

We know that mental disorders are very complex and researchers have not, until recently, had the resources available to do the optimal studies. With new genetic tools the resources are now available, and Dr. Warren predicts a great deal of progress will be made in the near future. The types of studies needed in the future include whole genome association studies, large-scale deep resequencing studies, phenotypic complexity studies, copy number variation studies, and epigenetic variation studies (where the environment meets the genome).

Dr. Warren summarized the reasons for conducting each of the types of studies. Whole genome association studies are important to conduct because: (1) there is a lack of knowledge on the fundamental molecular pathophysiology of complex human diseases; (2) the genetic paradigm identifies genes in the face of ignorance of the pathways involved; (3) the studies can provide an unbiased search/scan across the whole genome; and (4) association studies are (but linkage analysis are not) efficient for mapping disease genes when the underlying alleles are common (>5%). Deep resequencing studies will be increasingly important because they identify both common and rare variations in a patient's genome. With the recent advances in technology, this type of genetic analysis is much easier and faster than in the past.

Dr. Warren also cited the increasing importance of common and rare copy number variation (CNV) studies. The human genetics community had been surprised by the amount of variation in our genomes that are caused by deletions and duplications. This rich source of variations in humans had been largely ignored in genetic susceptibility studies for many diseases. He contended that without CNV analysis other approaches may be compromised given this degree of variation. Finally, Dr. Warren discussed the importance of epigenetic studies, as epigenetic variation links the environment to the genome, and nearly all psychiatric disorders show a significant non-genetic component. To come full circle, Dr. Warren ended by reiterating his initial point. We know that mental disorders are genetic disorders, but that does not appear to be the entire picture.

### **Discussion:**

Dr. Kalin noted Dr. Warren's theoretical approach, given how little we know and the vastness of the genome and epigenetic factors. Dr. Kalin wondered if a non-hypothesis-driven approach to research is the best method for these sorts of studies. Dr. Warren indicated that the examples he presented are large-scale projects and all are hypothesis-driven; for example, resequencing studies are a broad, not blind, expedition. He indicated that these types of studies will result in genetic tests, targets for therapy, and clinical descriptions of different and distinct disorders that were previously thought of as one disorder.

Dr. Gur noted that the genetic studies do not appear to be detecting major features of disorders (e.g., autism, schizophrenia), and expressed surprise at the amount of information gathered from these studies. Dr. Gur noted that in addition to diagnosis, the last three collaborative studies for schizophrenia have important clinical information, positive and negative symptom information, and consistent computerized neurocognitive batteries.

Dr. Insel noted that the next 6 months will be an historic period for this field. Large-scale whole-genome association studies will be conducted in almost every mental disorder. The studies will be a good opportunity for a variety of hypotheses to mine the genotypes and the phenotypes to redefine the disorders based on allelic variation. He predicted much change in the understanding of this topic in the upcoming year.

Dr. Cohen agreed with Dr. Insel, but asked how studies are characterizing the phenotypes separately and if there are standard symptom batteries. Dr. Insel replied that it depends on the study and noted that Dr. Warren was helpful in assisting NIMH to make the decision 5 years ago to collect good phenotyping data (genotyping will be done later). However, Dr. Insel noted that the critical piece in the process is having the data accessible in some way that allows the cross-talk. Dr. Insel outlined NIH and NIMH efforts in this regard. NIH-wide efforts include the Genetic Association Information Network and a database of Genome Wide Association Studies designed to archive and distribute data from genome-wide association studies. NIMH's own effort collecting phenotyping data is a repository at Washington University in St. Louis.

Dr. March asked Dr. Warren to comment about pharmacogenomics and the search for genes that can predict response and non-response to medication. Dr. Warren answered that genetic variation in drug response and adverse reactions may be one of the first areas of genetics that will change medical practice. Dr. Warren predicts that the genetics of adverse drug reactions may not be complex since we typically do not give a drug to an entire family and might involve very few genes with high penetrance.

Dr. Jeste noted that the presentation focused on diseases; he asked Dr. Warren if the genetics of health, including successful aging, could be characterized, even though there are no verifying criteria or phenotypes? Dr. Warren said that perhaps elderly individuals who are and have been largely disease-free could be studied and cited it as a fascinating area of study.

## **CAPITALIZING ON SCIENTIFIC OPPORTUNITIES: UPDATE FROM THE DNBBS CONTE CENTER WORKSHOP**

Dr. Insel welcomed Linda Brady, Ph.D., Director of the Division of Neuroscience and Basic Behavioral Science, to discuss the Silvio O. Conte Centers for Neuroscience Research Program. Dr. Brady provided an overview of the Conte Centers program within the Institute, which consists of an interdisciplinary behavioral science program and an exploratory or collaborative neuroscience/development program for neuroscience research. The centers programs solicit accomplished multi-disciplinary teams of scientists to conduct a set of interdisciplinary, highly integrated innovative research projects that would not be conducted as independent R01 projects. The charge of this workshop was to identify gap areas in the science and also to examine the program in terms of the review criteria and review method used within the program.

The workshop participants suggested that the number of distinct NIMH centers announcements is confusing to the field; to this end, separate neuroscience and behavioral science announcements will be combined into a single centers announcement. The group also identified several gap areas in the science such as neurodevelopment, social cognition/social neuroscience, basic and human functional genomics, physiology and behavior, integrative studies of disease models and human studies, and preclinical drug discovery to phase I. The workshop encouraged NIMH to think in terms of both vertical and horizontal levels of analysis and the translation between levels of analysis, emphasized exploratory, high-risk projects

and technology/methods development, and explored the inclusion of a research training component within the centers program.

## **CONCEPT CLEARANCES**

Andrea Beckel-Mitchener, Ph.D, Program Chief of the Functional Neurogenomics Program (DNBBS), described the concept clearance request for the proposed Mouse Models Containing Human Alleles: Novel Tools to Study Brain Function. The goal of this initiative is to develop and characterize novel mouse models that express human genes or human genetic elements; these models can aid in understanding the molecular mechanisms underlying brain function relevant to the research priorities of the NIMH. Potential topics to be supported include the creation and validation of mice expressing human gene:

- “Disease” alleles, “susceptibility” genes, or other genetic elements of interest
- Duplication outcomes or other human gene dosage anomalies
- Differential response to psychotherapeutic drugs
- Epigenetic phenomena with relevance to mental health
- Associations that may alter developmental trajectories and/or other critical phenotypes associated with brain development

Kathleen Anderson, Ph.D., Program Chief of the Neural Bases of Cognition Program (DNBBS), described the concept clearance request for the proposed Novel Methods for Examining Prefrontal Interactions with Cortical and Subcortical Systems that Support Complex Mental Function. This initiative developed from the growing recognition and set of literature that shows that the cortex is not organized in a modular fashion where specific functions and contents are mediated by individual regions. Rather, networks of regions support multiple functions and particularly complex cognitive and emotion functions. The goal of the initiative is to stimulate the application of new techniques used to investigate how regions of the prefrontal cortex interact with other cortical and subcortical systems in order to support complex mental function, including cognition, emotion and motivation. The research calls for a systems level approach (rather than investigating different regions separately) to investigate:

- Simultaneous multi-site, high density neurophysiological recordings in behaving animals
- Pharmacological and electrical stimulation and inactivation of regions in behaving animals
- Genetically-enabled cell and circuit inactivation
- Molecular and genetic tracers to map prefrontal circuits
- Pre and postnatal neurophysiological and anatomical development of prefrontal circuits
- Molecular and cellular development of prefrontal circuits

### **Discussion:**

Dr. Cohen commended this work and requested that the research include in its methods the imaging of non-primate brain. Dr. Kraemer urged that the researchers make a clear distinction between *risk factors* and *interactions* study because, otherwise, the statistical results will be uninterpretable.

The Council unanimously voted to approve both of the concepts.

### **Public Comments**

Aysha Akhtar, M.D., M.P.H., Medical Research Advisor with the Physicians Committee for Responsible Medicine (PCRM), applauded the efforts of the NIMH to understand mental illness. Dr. Akhtar reiterated that a significant portion of NIMH research is focused on using non-human primates (NHPs). This concerns PCRM because the use of NHPs in harmful and distressing studies causes significant stress to NHPs, given that they have many of the same behavioral and mental capabilities as humans, and by investing in NHP research, PCRM believes that more harm than good may result because NHPs stressful experience in studies causes hormonal, immunological, and neurological changes that confound results and may then invalidate study outcomes. Dr. Akhtar asked that NIMH make a committed effort to phase out funding for NHP studies.

Joan Zlotnik, Executive Director, Institute for the Advancement of Social Work Research, thanked NIMH for the recent meeting it sponsored with her organization on Partnerships for Implementation of Evidence-Based Treatments in Social Work Training and Research. She indicated that the meeting was important because it discussed the need for strategies in training and educating professional providers around evidence-based treatments, as well as the necessity for research on dissemination and implementation. The meeting participants discussed issues beyond training, including issues such as payment, case load, structure of the service delivery systems, and gaps in the service delivery system. She indicated that a report will be issued and sent to Council, urging Council to consider the issues of an interdisciplinary workforce and ensuring that a cadre of people is available to do services and implementation research.

Barbara Wolf from the Depression and Related Affective Disorders Association presented three ideas to Council. First, as an advocate, Ms. Wolf believes that research is the answer to stigma because from the research, education flows and with education, stigma disappears. Second, Ms. Wolf strongly encouraged NIMH to collaborate with other agencies to help educate internists and family practitioners in terms of issues of mental health. Third, Ms. Wolf stressed the importance of clinical research, citing her own participation in clinical research studies on Alzheimer's Disease.

Ginger Anthony, Executive Director, American Academy of Child and Adolescent Psychiatry (AACAP), indicated that there is one crucial gap that must be closed-the need for more researchers in child and adolescent psychiatry. The AACAP has been working closely with the American Academy of Pediatrics in recruiting pediatricians into child psychiatry research, but more efforts are needed.

Darrel Regier, M.D., M.P.H., Deputy Medical Director, American Psychiatric Association (APA), expressed appreciation for efforts to understand the etiology and pathophysiology of mental disorders, citing APA's enthusiasm for incorporating new information on genetic etiology into the next iteration of the Diagnostic and Statistical Manual (DSM). The APA has appointed a task force for the revision of the DSM-IV and will be reviewing the literature to recommend any changes to DSM criteria. Dr. Regier also expressed thanks to NIDA, NIAAA and NIMH for their support of conferences to review the research literature in this area. In addition, Dr. Regier noted a new publication in the *Journal of the American Psychiatric Association* on Medicare Part D and the difficulties inherent in serving 2 million patients with severe mental illness who have been transitioned from Medicaid. He cited the many challenges this population faces, including negotiating the new system and its many rules (e.g., pharmacy benefits). In the next year, APA will be tracking issues of homelessness and interactions with the criminal justice system.

## **ADJOURNMENT**

Dr. Insel adjourned the 215<sup>th</sup> meeting of the NAMHC at 12:33 p.m. on May 11, 2007.

I hereby certify that, to the best of my knowledge, the foregoing minutes are accurate and complete.

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Thomas R. Insel, M.D., Chairperson

## Appendix A

### REVIEW OF APPLICATIONS – MAY 2007 Council\*

Category	IRG Recommendation							Total Direct Cost \$
	Scored #	Scored Direct Cost \$	Not Scored (NRFC) #	Not Scored (NRFC) Direct Cost \$	Other #	Other Direct Cost \$	Total #	
Research	638	\$742,128,586.00	452	\$377,142,873.00	25	\$32,473,970.00	1115	\$1,151,745,429.00
Research Training	187	\$2,863,624.00	26	\$0.00	11	\$0.00	224	\$2,863,624.00
Career	73	\$52,403,700.00	22	\$14,201,720.00	4	\$3,342,414.00	99	\$69,947,834.00
Other	0	\$0.00	0	\$0.00	0	\$0.00	0	\$0.00
<b>Totals</b>	<b>898</b>	<b>\$797,395,910.00</b>	<b>500</b>	<b>\$391,344,593.00</b>	<b>40</b>	<b>\$35,816,384.00</b>	<b>1438</b>	<b>\$1,224,556,887.00</b>

\* Applications with primary assignment to NIHM

APPENDIX B

**DEPARTMENT OF HEALTH AND HUMAN SERVICES  
NATIONAL INSTITUTES OF HEALTH  
NATIONAL INSTITUTE OF MENTAL HEALTH  
NATIONAL ADVISORY MENTAL HEALTH COUNCIL**  
*(Terms end 9/30 of designated year)*

CHAIRPERSON

Thomas R. Insel, M.D.  
Director  
National Institute of Mental Health  
Bethesda, MD

EXECUTIVE SECRETARY

Jane A. Steinberg, Ph.D.  
Director  
Division of Extramural Activities  
National Institute of Mental Health  
Bethesda, MD

**MEMBERS**

Sergio A. Aguilar-Gaxiola, M.D., Ph.D. (07)  
Professor of Clinical Internal Medicine  
Director, Center for Reducing Health Disparities  
University of California, Davis School of Medicine  
Department of Internal Medicine  
Sacramento, CA

Glorisa J. Canino, Ph.D. (09)  
Director, Behavioral Sciences Research Institute  
University of Puerto Rico  
Medical Sciences Campus  
San Juan, PR

Elizabeth Childs, M.D., P.C. (10)  
Private Practice  
Brookline, MA

Jonathan D. Cohen, M.D., Ph.D. (08)  
Eugene Higgins Professor of Psychology  
Director, Center for the Study of Brain, Mind  
and Behavior  
Director, Program in Neuroscience  
Princeton University  
Princeton, NJ

Raquel E. Gur, M.D., Ph.D. (08)  
Director, Neuropsychiatry Section  
University of Pennsylvania Medical Center  
Philadelphia, PA

Martha E. Hellander, J.D. (07)  
Founder, Child and Adolescent Bipolar Foundation  
Wilmette, IL

Peter J. Hollenbeck, Ph.D. (08)  
Professor of Biological Sciences  
Department of Biological Sciences  
Purdue University  
West Lafayette, IN

Dilip V. Jeste, M.D. (10)  
Ester and Estelle Levi Chair in Aging  
Distinguished Professor of Psychiatry and Neurosciences  
University of California, San Diego  
VA San Diego Healthcare System (116A-1) (10)  
La Jolla, CA

Ned H. Kalin, M.D. (07)  
Hedberg Professor and Chairman  
Department of Psychiatry  
University of Wisconsin Medical School  
Madison, WI

Jeffrey A. Kelly, Ph.D. (08)  
Professor of Psychiatry and Behavioral Medicine  
Director, Center for AIDS Intervention Research (CAIR)  
Medical College of Wisconsin  
Milwaukee, WI

Norwood Knight-Richardson, M.D., MBA (09)  
Vice Chairman of Department of Psychiatry  
Director of the Public Psychiatry Training Program  
Director of Oregon Health and Science University  
Neuropsychiatric Institute  
Oregon Health and Science University  
Portland, OR

Helena C. Kraemer, Ph.D. (08)  
Professor, Department of Psychiatry and  
Behavioral Sciences  
Stanford University  
Stanford, CA

Pat R. Levitt, Ph.D. (09)  
Professor, Department of Pharmacology  
and Director, Vanderbilt Kennedy Center for  
Research on Human Development  
Vanderbilt University  
Nashville, TN

John S. March, M.D., MPH (10)  
Professor and Chief  
Department of Psychiatry  
Child and Adolescent Psychiatry  
Duke University Medical Center  
Durham, NC

Enola K. Proctor, Ph.D. (10)  
Frank J. Bruno Professor of Social Work Research  
Washington University in St. Louis  
St. Louis, MO

Peter Salovey, Ph.D. (07)  
Dean of Yale College  
Chris Argyris Professor of Psychology  
Yale University  
New Haven, CT

Suzanne E. Vogel-Scibilia, M.D. (08)  
Medical Director  
Beaver County Psychiatric Services  
Beaver, PA

Stephen T. Warren, Ph.D. (07)  
William Patterson Timmie Professor and Chair  
Department of Human Genetics  
Emory University School of Medicine  
Atlanta, GA

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National Institutes of Health  
Bethesda, MD

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Department of Veteran's Affairs  
Office of Mental Health Services  
Washington DC

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Director, Center for Mental Health Services  
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