

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 211th Meeting
February 2-3, 2006

Minutes of the 211th Meeting of the National Advisory Mental Health Council

The National Advisory Mental Health Council (NAMHC) convened its 211th meeting in closed session for the purpose of reviewing grant applications at 11:00 a.m. on February 2, 2006, at the Neuroscience Center in Rockville, Maryland, and adjourned at approximately 3:30 p.m. (see Appendix A: Review of Applications). The NAMHC reconvened for an open session at the same location from 4:00 p.m. to 4:45 p.m. and continued the open session on the following day, February 3, 2006, in Building 31C, National Institutes of Health, Bethesda, Maryland, from 8:30 a.m. until adjournment at 12:55 p.m. In accordance with Public Law 92-463, the open policy session was open to the public. Thomas R. Insel, M.D., Director, National Institute of Mental Health (NIMH), chaired the policy meeting.

Council Members Present at the Grant Review and/or Open Policy Sessions:

(see Appendix B: Council Roster)

Sergio A. Aguilar-Gaxiola, M.D., Ph.D.

Glorisa J. Canino, Ph.D.

Jonathan D. Cohen, M.D., Ph.D.

Susan M. Essock, Ph.D.

Raquel E. Gur, M.D., Ph.D.

Martha E. Hellander, J.D.

Renata J. Henry

Peter J. Hollenbeck, Ph.D.

Ned H. Kalin, M.D.

Jeffrey A. Kelly, Ph.D.

Norwood Knight-Richardson, M.D., M.B.A.

Helena C. Kraemer, Ph.D.

Pat R. Levitt, Ph.D.

Charles F. Reynolds, III, M.D.

Peter Salovey, Ph.D.

Suzanne E. Vogel-Scibilia, M.D.

Karen Dineen Wagner, M.D., Ph.D.

Stephen T. Warren, Ph.D.

Chairperson

Thomas R. Insel, M.D.

Executive Secretary

Jane A. Steinberg, Ph.D.

Ex-officio Members Present at the Grant Review and/or Open Policy Sessions:

Robert Freedman, M.D., Department of Veterans Affairs

Douglas A. Waldrep, M.D., FAPA, COL, MC, USA, Department of Defense

Liaison Representative Present:

Anne Mathews-Younes, Ed.D., for Ms. Kathryn Power, Center for Mental Health Services,
Substance Abuse and Mental Health Services Administration (SAMHSA)

Others Present:

Aysha Akhtar, M.D., Physicians Committee for Responsible Medicine

Jonathan Balcombe, Ph.D., Physicians Committee for Responsible Medicine

Ronald Barnett, Social and Scientific Systems, Ind.

Kevin Beverly, Social and Scientific Systems, Inc.

Paul Brounstein, Ph.D., Center for Mental Health Services, SAMHSA
Andrea Browning, Society for Research in Child Development
Douglas Bunnell, Academy for Eating disorders
Cynthia Folcarelli, National Mental Health Association
E. Aracelis Francis, Council on Social Work Education
John F. Greden, M.D., University of Michigan
Alycia Halladay, National Alliance for Autism Research/Autism Speaks
Sara Isikian, Society for Women's Health Research
Alan Kraut, Association for Psychological Sciences
John Krystal, M.D., Yale University School of Medicine
Stephanie Reed, American Association for Geriatric Psychiatry
Darrel Regier, M.D., American Psychiatric Association
Michelle Rodrigues, SRI International
Gene Russo, Research Policy Alert
Angela Sharpe, Consortium of Social Science Associations
Viviana Simon, Society for Women's Health Research
Barbara Solt, Institute for the Advancement of Social Work Research
Karen Studwell, American Psychological Association
Tim Tunner, National Association of Social Workers
Kerri Wade, Society for Neuroscience
Barb Wanchisen, Federation of Behavioral, Psychological, and Cognitive Sciences
Karen White, Children and Adults with Attention-Deficit/Hyperactivity Disorder
Richard Yanes, Clinical Social Work Federation

OPEN POLICY SESSION: CALL TO ORDER AND OPENING REMARKS

Thomas R. Insel, M.D., Director, NIMH, called the open session to order at 4:00 p.m.

COUNCIL GUIDANCE ON GRANT REVIEW AND POLICY ISSUES

Dr. Insel asked Council members for feedback on the process for soliciting Council's guidance on the activities carried out by the Institute and the policies affecting these activities.

Dr. Knight-Richardson suggested that in conducting its grant review business, it would be helpful for staff to identify prior to the Council Grant Review Sessions those applications they wish to discuss—particularly among those scoring between the 10th and 20th percentiles. Dr. Insel stated that Council's advice on the relevance of proposed work to Institute priorities would be helpful. He also encouraged Council members to identify promising research opportunities among applications scoring beyond the 20th percentile, noting that NIMH's general funding strategy is to award applications scoring at the 10th percentile or better, with remaining funds to support approximately half of the applications between the 10th and 20th percentiles.

To Dr. Levitt's query about how Council is informed of Institute priorities, Dr. Insel replied that new initiatives typically are presented to Council for consideration as concept clearances prior to issuing Requests for Applications (RFAs). Dr. Insel noted the importance of balancing new

Institute-driven priority research areas with those generated in the scientific community. He encouraged Council members to identify areas providing rich research opportunities. Dr. Freedman suggested the value of small group discussions at the Council Grant Review Session to allow more discussion time with program staff of the science under consideration each Council round. Dr. Kalin suggested that Council members might interact more with program staff around particularly difficult scientific issues in advance of the Council meeting. Dr. Cohen reinforced that members can provide another perspective on those applications that entail difficult funding decisions. Dr. Insel replied that NIMH takes that approach on a case-by-case basis but that strategies might be employed to do so more routinely. Dr. Kelly asserted some of the most innovative applications may be those scoring beyond the 10th percentile, and he urged program staff members and Council to work together to define a vision to advance our understanding of mental illness. Dr. Aguilar-Gaxiola concurred that Council members' expertise is well utilized when interacting with program staff around research questions and that maximum time should be devoted to such discussion at the Grant Review sessions. Dr. Insel reiterated the value of Council discussions for advising on individual applications as they relate to current priorities and future research directions, while fostering innovative science and supporting new investigators.

SCHIZOPHRENIA RESEARCH FORUM

Dr. Mayada Akil, Office of Science Policy, Planning, and Communications, NIMH, described the Schizophrenia Research Forum (SRF), an international online forum for researchers from around the world whose work can shed light on schizophrenia and related disorders (see <http://www.schizophreniaforum.org/>). The Web site, funded by NIMH with the National Alliance for Research on Schizophrenia and Depression (NARSAD) and the Mental Health Research Association serving as site sponsors, is independent, nonprofit, and free of charge to users. The Web site features original news stories and interviews with leading scientists in the field. Among specific forums that invite contributions from the field, "Current Hypotheses" presents theory reviews, while an "Idea Lab" posts less formal treatments. Most features of the site are interactive and solicit comment.

Launched in October 2005, the forum boasts more than 1,200 members from 51 countries and has received nearly a million hits. SRF staff has written 18 new stories on a broad spectrum of subject matter. In the December 2005 issue, *Science* listed SRF as an interesting Web site for further reading.

Discussion

Dr. Gur stated that family members have shown interest in SRF, and Dr. Levitt suggested that SRF might be useful in residency training programs. Dr. Akil noted that the SRF editorial board is compiling a group of classic papers in schizophrenia that may be useful not only for training programs but also for neuroscientists whose work becomes relevant to schizophrenia as, for example, new susceptibility genes are identified. Dr. Insel explained that like the popular Alzheimer Research Forum (ARF) that includes high-profile lectures with slides and video streaming and posts the latest scientific information (see <http://www.alzforum.org/>), SRF has enormous potential to serve family members and researchers as a resource for daily updates on the latest research information.

Dr. Hollenbeck stressed that SRF can be a valuable resource to families in providing information on schizophrenia, particularly since the information is provided under the auspices of NIH, and that the information likewise will be useful to educated laymen. Dr. Canino urged attention to presenting information in a way that is easily understood by families. Dr. Akil responded that SRF was designed to present information and stimulate discussion by researchers from multiple disciplines, perhaps from multiple countries, in addressing issues raised by other researchers and/or by physicians involved in treatment delivery. She noted that SRF tries to balance the needs of researchers, the public, and physicians. Dr. Cohen suggested collaborating with other entities with expertise in communicating to the public, such as the Dana Alliance. He noted that as SRF becomes more popular with family members, they may have an increased role at the site. Dr. Insel commented SRF and ARF share some of the same writers and editors and that the ability to make scientific language accessible and concise has been well demonstrated at ARF and during the first few months of operation of SRF.

SESSION RECESS

Dr. Insel recessed the initial session of the 211th meeting at 4:45 p.m. The Council reconvened to continue the session the following morning on the main campus of NIH in Bethesda, Maryland.

CALL TO ORDER AND OPENING REMARKS

Dr. Insel called the open policy session to order at 8:30 a.m. He welcomed new Council members Drs. Glorisa Canino, Pat Levitt, and Norwood Knight-Richardson, and introduced Dr. Anne Mathews-Younes who was representing Ms. A. Kathryn Power as the Center for Mental Health Service liaison at the session. Dr. Insel acknowledged Ms. Karen Shangraw's long-time service at NIMH and her pending retirement. Dr. Insel also congratulated Dr. Aguilar-Gaxiola on being the recipient of the Department of Health and Human Services Minority Health Community Leadership Award.

APPROVAL OF THE MINUTES FOR THE PREVIOUS COUNCIL MEETING

Turing to the minutes of the September 2005 Council session, Dr. Insel noted that the minutes should be amended to reflect that fewer new and competing awards were made in fiscal year (FY) 2005 than during FY 2004 and that even though some large non-competing projects will be ending, NIMH should be able to support approximately the same number of competing awards in FY 2006. The minutes were adopted unanimously as amended.

DIRECTOR'S REPORT

In his Director's Report, Dr. Insel updated the Council on important recent issues and activities (see <http://www.nimh.nih.gov/council/dirreportfeb06.pdf>).

Budget

Dr. Insel reported that Congress passed the FY 2006 budget in December 2005 with a 0.5 percent increase for NIH, followed by a 1 percent rescission, leaving a net budget decrease of 0.5 percent from the FY 2005 level. To address this reduction, funding for non-competing continuation grants will be reduced by 2.35 percent in remaining out-years to preserve as much funding as possible for new and competing awards. The conference language requires funding for new and competing awards to be held to FY 2005 average costs. NIMH's FY 2006 research budget of \$1.4 billion, although double the FY 1997 budget level, represents a decline of 0.6 percent from FY 2005. Dr. Insel stated that Roadmap dollars now appear in the budget and that although the community has expressed concern about increased emphasis on the Roadmap, it provides for major collaborative opportunities across NIH that are anticipated to have a large impact on medical progress. NIMH's FY 2006 contribution will be \$13 million.

Dr. Insel pointed out that although the number of new and competing awards continued to increase through FY 2004, there was a slight decrease in FY 2005 with another projected slight decrease for FY 2006. In terms of competing awards, 550 awards are projected for FY 2006, down slightly from FY 2005 because much of the budget (approximately 70 percent) is dedicated to non-competing awards. The total number of grants funded in FY 2006 represents an increase by 50 percent over the FY 1998 levels, with the associated 40-50 percent increase in grant costs significantly impacting the number of awards. NIMH plans to fund applications scoring up to the 10th percentile and about half of those scoring between the 10th to 20th percentiles as ranked on relevance, traction, and innovation.

New Principal Investigators

Turning to support for new investigators, Dr. Insel announced the Pathway to Independence Award, a new mechanism (K99/R00) to fund new investigators and facilitate an investigator's receipt of an R01 award earlier in his/her career. The current average age at receipt of first independent award for M.D.s, Ph.D.s, and M.D./Ph.D.s has risen to 42-44 years. At NIMH, only 5 percent of grantees with an independent award are under age 35.

The new K99/R00 award will provide up to 5 years of support consisting of two phases. The initial mentored phase will support, for up to 2 years, the most promising postdoctoral scientists to complete their mentored research work, publish, and search for an academic position. In the second independent phase, the candidate may request up to 3 years of support to transition as an independent scientist to an extramural sponsoring institution at which the individual has been recruited. This will allow the individual to continue working toward establishing his/her own independent research program and to prepare an application for regular research grant support (R01). Support for the R01 is contingent upon being accepted by an extramural institution and the successful NIH programmatic review of the individual's mentored postdoctoral phase of the award. The total cost per award in the first stage will be \$90,000, including 8 percent indirect costs, and \$249,000, including full indirect costs, in stage two. An important feature of the new award mechanism is that non-U.S. citizens are eligible for the award. The mental health applications will be reviewed at the Institute, and NIMH intends to fund ten K99/R00 awards in FY 2007 and more in the future.

Dr. Insel noted that the Center for Scientific Review (CSR) reviews about two-thirds of mental health applications and that with the arrival of Dr. Antonio Scarpa as Director, major changes are underway, including electronically posting summary statements within 1 month after review sections meet (rather than the typical 2-3 months) and a pilot study to cut 1½ months from the reviews of R01 applications submitted by new investigators. Resubmission deadlines will be extended to allow these new investigators to resubmit immediately if only minor revisions are necessary. The goal is to speed their transition to independence and allow for more rapid funding.

Innovation

Turning to innovation, Dr. Insel stated that NIH has several mechanisms to support the most innovative science. As part of the Roadmap effort, five NIMH grantees have been the recipient of NIH Pioneer Awards designed to promote pioneering approaches to major challenges in biomedical research. Eligibility for the award extends to applicants from all fields, a unique application form is completed, and reviews are conducted by interview in committee format. The annual award is \$500,000/year for 5 years—larger than the Nobel Prize.

Another innovation is the R56 award that provides 1 year of funding to high-risk but high-priority new applications that fall outside of the payline but offer great opportunity. An internal NIMH Innovations Committee reviews staff nominations for these awards and makes recommendations to the NIMH Director.

An evaluation of innovation is an important component of peer review of applications, and Dr. Insel referenced a recent workshop on innovation in mental health research that preceded the Interventions Research Review Committee and Services Research Review Committee review meetings where participants discussed what constitutes innovation, how it can be promoted, and how the Institute can use innovation to help meet the public need to reduce the burden of mental illness.

Dr. Insel explained that NIH's new Office of Portfolio Analysis and Strategic Initiatives (OPASI) will have a role in promoting innovation by identifying and funding cutting-edge research. OPASI's mission includes providing the methods and information necessary to improve transparency and management of portfolios across Institutes; identifying opportunities or rising public health challenges; assisting in acceleration of investments for specific areas, focusing on trans-NIH multiple Institute efforts; and improving access to the evaluation process. The NIH Roadmap is one of the major activities in OPASI, along with other cross-Institute initiatives such as the Neuroscience Blueprint and Obesity Initiative. The NIH Institutes will contribute \$340 million, representing 1.1 percent of the NIH total research budget in FY 2006, to support OPASI cross-Institute activities, and this commitment will rise to 1.7 percent in FY 2008.

New Science

Dr. Insel updated Council members on new science directions. Since the last Council meeting, NIMH studies have produced numerous breakthrough papers that have opened up new areas of research, and Dr. Insel spoke about three of them.

Turning to the gene stathmin, Dr. Insel reported that Dr. Eric Kandel and his colleagues have discovered that stathmin is essential for regulating innate and learned fear. Knocking out this gene in the mouse produces a fearless mouse, and over-expressing the gene produces increased fear (see Shumyatsky, G.P., Malleret, G., Shin, R.M., Takizawa, S., Tully, K., Tsvetkov, E., Zakharenko, S.S., Joseph, J., Vronskaya, S., Yin, D., Schubart, U.K., Kandel, E.R., and Bolshakov, V.Y. "Stathmin: A Gene Enriched in the Amygdala, Controls both Learned and Innate Fear." *Cell* 123(4):697-709, 2005). This new candidate for research was part of an area of the genome previously unexplored.

A similar finding was made for gene p11, an important protein found to serve as a chaperon for the 5-HT1B receptor. This gene is increased in rodent brains with the use of antidepressant medications or electroconvulsive therapy and decreased in brain tissue from patients with depression (see Svenningsson, P., Chergui, K., Rachleff, I., Flajolet, M., Shang, X., El, Yacoubi, M., Baugeois, J.M., Nomikos, G.G., and Greengard, P. "Alterations in 5-HT1B Receptor Function by p11 in Depression-Like States." *Science* 311 (5757):77-80, 2006).

Another example of new domains and new candidates are DISC1 and PDE4B. DISC1, a major candidate gene for schizophrenia, is now linked to PDE4B, formerly known as DUNCE and known to be involved in learning and memory in drosophila (see Millar, J.K., Pickard, B.S., Mackie, S., James, R., Christie, S., Buchanan, S.R., Malloy, M.P., Chubb, J.E., Huston, E., Baillie, G.S., Thomson, P.A., Hill, E.V., Brandon, N.J., Rain, J.C., Camargo, L.M., Whiting, P.J., Houslay, M.D., Blackwood, D.H., Muir, W.J., and Porteous, D.J. "DISC1 and PDE4B are Interacting Genetic Factors in Schizophrenia that Regulate cAMP Signaling." *Science* 310(5751):1187-1191, 2005). The finding suggests a molecular pathway that would link to cognitive deficits in schizophrenia.

With the advent of tools to explore the genome and clinical genetics, new candidates may more rapidly be identified to offer even further explanation about the etiology of anxiety, depression, and schizophrenia. Dr. Insel indicated his expectation of finding biomarkers and possibly new treatments in the process of determining the pathophysiology of these illnesses.

Noting that another important part of relieving the burden of mental illness is to move scientific discoveries into clinical practice, Dr. Insel identified several points of progress. A series of effectiveness trials that began in 1999 and have now been completed involved about 10,000 patients at 200 sites:

- The results of the first 12 weeks of the Treatment for Adolescents with Depression Study (TADS), published about a year ago, showed that fluoxetine was effective for treating adolescents with depression, and when combined with cognitive behavioral therapy, the results were even better (see <http://www.nimh.nih.gov/healthinformation/tads.cfm>).
- The Clinical Antipsychotic Trials of Intervention Effectiveness trial (CATIE) compared the results of older and newer antipsychotic drugs in patients with schizophrenia (see <http://www.nimh.nih.gov/healthinformation/catie.cfm>).

- The Sequenced Treatment Alternatives to Relieve Depression study (STAR*D) showed citalopram effective in 31 percent of patients with treatment-resistant depression, including patients in primary care settings (see <http://www.nimh.nih.gov/press/stard2.cfm>).
- The Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD) trial demonstrated that when people with bipolar disorder relapse, they relapse into depression (see <http://www.nimh.nih.gov/press/stepbd.cfm>). About 58 percent of people show recovery within 2 years with appropriate treatment, but many relapse again.

Dr. Insel indicated that this has been an extraordinary time in terms of scientific discoveries and scientific opportunities. Although the period of rapid budget growth has passed, there are considerable funds to support quality science, and he encouraged Council's guidance in keeping the focus on relevance, traction, and innovation.

Personnel Update

Dr. Insel noted that Dr. Steven Foote, Director of the Division of Neuroscience and Basic Behavioral Science, will retire in March. An active search is underway for a new director for that Division, along with a director to replace Dr. Junius Gonzales, former Acting Director of the Division of Services and Intervention Research. In addition, a search is underway for a Scientific Director to head the Institute's Intramural Research Program—a position previously held by

Dr. Robert Desimone, who now directs the McGovern Institute for Brain Research at the Massachusetts Institute of Technology.

COUNCIL WORKGROUP ACTIVITIES

Members of several Council workgroups updated Council members on their activities.

Council Workgroup on MRI Research Practices: An Update on Activities

Council member Dr. Jonathan Cohen explained that the Council Workgroup on MRI Research Practices was convened in September 2005 in response to the proliferation of neuroimaging research outside of traditional clinical settings, e.g., in psychology departments, cognitive neuroscience programs, and independent research institutes, to consider the diversity of practices regarding safety and human subjects protections, such as the handling of incidental findings.

The Workgroup's report is in preparation and will be reviewed by Workgroup members, legal counsel, and safety experts. It will present information on reasonable ways to address safety issues.

Discussion

Dr. Gur observed the need for researchers to communicate professionally, carefully, and responsibly about MRI research findings, and that she looked forward to the set of considerations to be provided by the Workgroup.

Council Workgroup Racial/Ethnic Minority Issues

Dr. Richard Nakamura, Deputy Director, NIMH, and Council member Renata Henry reported on a recent meeting with Council members Drs. Sergio Aguilar-Gaxiola and Charles Reynolds, former Council member Dr. Faye Gary, and Dr. Erich Jarvis, an Associate Professor at Duke University. Dr. Nakamura stated that goals of that meeting were to review the participation of diverse populations in NIMH-supported clinical studies, the success of diversity training mechanisms to increase diversity among the scientific population, and recent trends regarding NIMH's ability to increase diversity among staff.

Dr. Nakamura presented statistics showing that underrepresented minority populations (URP) among the Institute's extramural managerial staff rose from 7.6 percent in FY 1994 to 12.1 percent in FY 2005, non-managerial from 17.3 to 25.4 percent, and overall from 13.8 to 18.8 percent. In the intramural program, URP among managerial staff rose from 3.5 to 4.8 percent and nonmanagerial, from 18.8 to 22.3 percent, with a total change from 14.2 to 14.4 percent. In tracking URP among NIMH principal investigators, 102 competing and non-competing R01 awards were made to 89 URM investigators in FY 2005, compared to 70 awards in FY 2002. In terms of membership on NIMH standing review committees, 32 percent of reviewers are from diverse populations and 16 percent from URP. On special emphasis panels, 19 percent of reviewers are from diverse populations.

Turning to research and training, NIMH diversity supplements, which include the full range of populations other than gender, amounted to \$4.2 million in FY 2004 or about 0.5 percent of the overall research budget. NIMH support for investigator research and career development to achieve diversity has risen from \$21.4 million in FY 2000 to \$27.4 million in FY 2005.

Dr. Nakamura reported that a review of training mechanisms to increase diversity showed that a targeted mentoring program for Hispanic investigators on grantsmanship and generating scholarly papers is yielding higher funding success rates than other programs. A mentoring program for African-American scientists is experiencing similar results.

Turning to recruitment in clinical trials, for FY 2005, there was a slight majority of women participants, of whom 20 percent were African American, 7 percent Hispanic, 8.7 percent Asian, 1 percent American Indian/Alaskan Native, and 60 percent Caucasian. Program staff will carefully track overall clinical trial recruitment and work with investigators to ensure that overall targets, including the participation of minority populations, are met. In response to Dr. Wagner's question, Dr. Nakamura stated that numbers for children, adolescents, and adults have not been broken out to date, but he anticipates expanding the tracking function. Dr. Insel recognized the efforts of staff to compile this important information.

Renata Henry presented a series of recommendations generated at the meeting on racial/ethnic minority recruitment and diversity:

- Consider approaches to encourage senior scientists and MERIT awardees to enact pilot programs or special incentives to increase mentoring and training with diverse populations.

- Ensure that there is a supportive NIMH environment for minority staff recruitment and retention. Create internal mentoring or training programs.
- Given existing plans for decreasing NIMH's investment in training, ensure that NIMH does not disproportionately decrease its support for training diverse populations.
- Develop measures to assess the impact of various training support programs on the development of minority investigators.
- Consider methods to increase review committee diversity by training scientists from underrepresented populations to serve on review groups, possibly through mentoring by experienced review committee members.
- Track retention in clinical research using progress reports and electronic mechanisms.
- Include responsibility for monitoring grant progress in staff performance plans, including, where appropriate, clinical recruitment reports. Ensure that adequate internal training exists for implementing such monitoring.
- Focus more efforts on inclusion and health disparity reduction for American Indian/Alaskan Natives.
- Work to increase diversity on the Council.

Ms. Henry asserted that it is critical to NIMH's vibrancy and health to ensure that it is a diverse organization and that the science that it supports applies to reducing the burden of mental illness in all populations and, in particular, to racial/ethnic minority populations.

Discussion

Dr. Aguilar-Gaxiola recognized progress on the issue and the commitment of NIMH leadership, but he asserted that the data indicate much work remains to be done. He expressed concern about a declining trend in aggregate numbers of American Indian/Alaskan Natives and Hispanics and managerial staff. Dr. Vogel-Scibilia echoed Dr. Aguilar-Gaxiola's concerns and urged expressions of strong support from senior NIMH leadership. Dr. Salovey noted that trends might be affected by the change in reporting practices. Dr. Nakamura stated that the Institute is committed with Council to address minority issues in both its staffing and the research that it supports. Dr. Insel remarked on the importance of improved data collection strategies and business practices to track retention and recruitment.

Council Workgroup on Services and Clinical Epidemiology Research

Dr. Susan Essock, Professor and Director, Division of Health Services Research, Mount Sinai School of Medicine, and Chairperson of the Council Workgroup on Services and Clinical Epidemiology Research, explained that the Workgroup's charge was to develop a vision for NIMH's services and clinical epidemiology research that would promote more rapid translation of research findings into clinical practice and services. The Workgroup members included services researchers, advocates, public and private payers, and State mental health officials. The Workgroup was convened in October 2005, and members participated in two in-person meetings and several conference calls. The Workgroup solicited expert advice from stakeholders with an interest in mental health, who offered valuable insights into the type of research needed to inform decisions about mental health treatments and services.

The Workgroup identified several cross-cutting themes that served as the foundation in developing its recommendations: (1) partnerships with a range of groups (consumers, payers, researchers, and other Federal and State agencies); (2) quality of care and how to identify it; (3) fairness in access to services; (4) maximizing recovery; (5) communication for soliciting the input of multiple stakeholders and for transferring what is known into practice; and (6) evaluation—including evaluating the success of research efforts to impact public policy and to decrease the burden of mental illness.

Dr. Essock presented the Workgroup’s preliminary recommendations that fall into three interrelated domains:

(1) Enhancing research responsiveness to stakeholders:

- NIMH should support research on the implementation and sustainability of evidence-based interventions to determine the mechanisms underlying successful implementation of these interventions in varying service settings with culturally and geographically diverse populations.
- Interventions should be selected for study in partnership with entities currently paying for services and with other agencies and stakeholders involved in science-to-service activities. Candidates for such implementation research should be well documented as effective, yet difficult to access in community settings. Examples include Multisystemic Therapy, pharmacotherapies for ADHD, critical time interventions, and integrated mental health and substance abuse treatment for individuals with co-occurring disorders. The charge should be to develop new knowledge about how to make effective treatments available and acceptable in routine community settings.
- NIMH should create a means of identifying those policy changes and other shifts likely to have the most significant impact on mental health and seize opportunities to study their impact.
- NIMH should seek out opportunities to add research components to service projects funded by other agencies and departments to identify the organizational, financial, relational, and treatment approaches that make them successful. These entities may conduct demonstration projects, with which NIMH should be involved to learn as much as possible.
- NIMH should continue to support the development, adaptation, and validation of research tools to measure quality of care and fairness, as well as meaningful consumer and family outcomes including service need, service use, and maximizing recovery. These efforts should be made in concert with the NIH Roadmap for Research to develop clinically useful tools that can measure the quality of mental health care.

(2) Capacity Building:

- NIMH should create time-sensitive ways to bring the most rigorous methodologies possible to bear on policy initiatives to learn what works for whom and under what conditions and how to get effective interventions implemented and sustained. Traditional investigator-initiated grants and career awards will be useful, but not sufficient, mechanisms to travel this road.
- NIMH should enhance Division of Services and Intervention staff to meet the new demands.

- NIMH should work with payer, professional, provider, and advocacy groups to ensure that evidence-based treatments are integrated into the core curricula for clinical training across the mental health professions.
- The cadre of researchers trained to conduct policy-relevant research in partnership with mental health service, community, and administration settings should be increased through mentored career awards and a new type of administrative supplement.

(3) Knowledge Exchange:

- NIMH should contract for independent, disease-specific annual reviews of the current state of science in targeted areas to synthesize the evidence base, develop practice guidelines, and identify gaps in research.
- To improve communication between patients and providers, NIMH should develop information technology solutions for use across a range of mental health settings. This could include electronic decision support systems for practitioners and patients, decision aids, and tools for shared decision making.
- NIMH should periodically provide updates on the progress made on the Workgroup's recommendations so that Council and the public may advise on course corrections and on promoting successes.

Discussion

Dr. Kelly pointed to the gap between increasing scientific knowledge and the state of practice. He asserted that dissemination is often an afterthought and that changing practice behavior takes more than just creating information. A behavioral science research agenda exists for how to disseminate—to learn, for example, about effective staff training practices with feedback loops that enable service providers to discuss their experiences with researchers. Dr. Insel emphasized the opportunity to partner with the patient advocacy community. He noted that pharmaceutical companies have engaged successfully in evidence-based marketing in direct-to-consumer advertising. He noted that the Dana Alliance may be an important partner to help disseminate findings in a useful format. Dr. Salovey urged NIMH to support systematic studies by known experts of how to disseminate information. He stated that additional research on social influence, persuasion, attitude change, communication strategies, and social marketing may be needed.

Dr. Vogel-Scibilia noted the need for public dissemination of information about psychopharmacological and nonpsychopharmacological treatments. Using STAR*D as an example, Dr. Kalin commented that disseminating treatment findings to primary care providers in a variety of settings also could be extremely helpful. Dr. Essock commented on the value of increasing communication with researchers so that they would be in position to respond to calls for practical research initiatives that could be supported, for example, in partnership with other funding agencies responsible for mental health service delivery, such as SSA or the National Association of State Mental Health Program Directors.

Dr. Wagner urged that in addition to communicating treatment findings to the community, training for evidence-based modalities also must be provided broadly to individuals who practice in the community. Dr. Kelly concurred and emphasized the use of interactive technology.

Dr. Kraemer urged encouragement of researchers to report their results in ways that clinicians, consumers, and providers can understand, including a discussion of clinical significance. Dr. Knight-Richardson noted the difficulty in changing practice patterns, noting that change requires adequate time for learning new treatment approaches as well as a financial reimbursement system that would support such changes. He noted the importance of communicating with public and private payers to adopt treatment changes and provide incentives for needed change. He also identified the complex problem of how to evaluate the utility of various treatments, and Dr. Essock responded that the Workgroup considered this issue, which led to the recommendation on the development of clinically useful and economically feasible tools, such as one-page forms to track treatment that would enable supervisors to review progress.

Ms. Hellander commented that, in response to families' demand, the Child and Adolescent Bipolar Foundation created treatment guidelines, which can serve as an aid to parents when interacting with treatment providers about the care of their children. She supported the value of the consumer community in voicing research needs, and Dr. Insel noted that several mechanisms are in place for such feedback, including the Institute's Office of Constituency Relations and Public Communication, which oversees the Institute's outreach activities, including requesting and receipt of public input related to the Institute's activities, as well as the regular meetings of the NIMH Alliance for Research Progress and the Outreach Partnership Program, the Public Forums and Dialogue meetings. Ms. Hellander commented that incorporating training on the delivery of treatments for mental illness in medical schools would be an important step in ensuring adequately trained providers.

Ms. Henry urged NIMH to focus on strategic partnerships to move the recommendations forward, particularly with the Centers for Medicare and Medicaid Services (CMS), and to develop effective lines of communication with big payers to present new and easily understood information that can be implemented in new policies and procedures. She asserted the need to train a variety of treatment providers, including social workers and others. Dr. Insel referred to the Federal Action Agenda (see http://www.samhsa.gov/Federalactionagenda/NFC_preface.aspx) that was formulated in response to the recommendations contained in the President's New Freedom Commission on Mental Health. He noted that the Federal Executive Steering Committee on Mental Health recently met to push ahead implementation of those recommendations and that several agencies (SAMHSA, VA, CMS, NIMH, and others) are collaborating to transform programs and practices. Ms. Henry suggested that if Medicaid could be expanded to cover, for example, four interventions with demonstrated efficacy, amazing change could result. Dr. Insel thanked Council members for their suggestions and comments and noted that the Workgroup's full report will be submitted to Council for consideration at the May Council meeting.

REPORT FROM THE NATIONAL PSYCHIATRY TRAINING COUNCIL

Dr. Insel explained that the National Psychiatry Training Council (NPTC) was commissioned in response to a 2003 Institute of Medicine (IOM) report (see <http://www.nap.edu/catalog/10823.html>) that reviewed the current state of psychiatry research training, the obstacles to such training, and approaches for overcoming them. One of the specific

recommendations was to charter a council (NPTC) to examine those obstacles more carefully and develop a series of recommendations to enhance psychiatric residency training.

Dr. John Greden, Chairman, Department of Psychiatry, University of Michigan, and Co-Chair, NPTC, began his report by describing the problem, an acute shortage of psychiatrist investigators, particularly in the child and adolescent, addiction, geriatric, and clinical and investigational areas. Shortages are attributable to many factors, including the limited number of training programs that integrate clinical and research training and thus a limited number of potential psychiatrist investigators, regulatory obstacles, mentor shortage, inadequate retention associated with limited monies available for research training, increasing loan burdens and poor comparison to earning in other disciplines, minimal outcome data on what has worked well in terms of attracting psychiatrist investigators to the field, and the lack of a change agent to address the overall shortage.

The NPTC crafted recommendations that fall into nine areas—model programs, pipeline, regulatory revisions, mentorship, research literacy, retention, finance, outcomes, and dissemination. Dr. Greden highlighted several accomplishments, including formation of a federation of key stakeholders that successfully partnered to address research training issues during residency. Partners included NIMH, American Psychiatric Association, American Association of Chairs of Departments of Psychiatry (AACDP), IOM, Residency Review Committee (RRC), advocacy and academic groups, and other organizations. It became apparent that the RRC needed to interface with model programs to identify provisions to free time for research, enhance research training flexibility, and foster model programs in developing the criteria for psychiatric resident program accreditation. These provisions will be submitted for consideration to the American College of Graduate Medical Education. New provisions include: child training can now occur during the first year due of residency; up to 20 percent of child and adolescent experience in general residency can qualify for child and adolescent training requirements; the minimum for inpatient training was reduced to 6 months; subspecialty and research training can now be integrated. Dr. Greden noted that several model programs were drafted and approved in this process. RRC regulatory revisions include, for example, that Graduate Medical Education must include learning how to appraise relevant research and apply findings to practice; residents must be taught research literacy; and opportunities to develop research skills must be included in residencies.

Additional highlights include: Psychiatry RRC plans to invite programs that provide opportunities for integrated training in general psychiatry as well as in a subspecialty; NIMH funded a conference grant to conduct five conferences nationwide on research literacy; AACDP partnered with APA in developing a new national mentorship award; retention will be aided by NIH's new Pathway to Independence Award; the American Psychiatric Institute for Research and Education has established the Center for Workforce and General Medical Education Studies, with partners the Association of American Medical Colleges and the American Medical Association, to monitor outcomes by tracking careers of psychiatry residents with research training. Dr. Greden also reported that volunteers have been named to take the lead on new initiatives to followup on the NPTC's recommendation in the nine target areas, noting that dissemination of the principles of model programs is already underway.

Dr. Greden concluded by noting that the NPTC report incorporates hundreds of recommendations targeted to NIMH, department chairs, deans, and training directors. He urged NIMH consideration of: (1) sustaining the federation of key stakeholders by supporting annual meetings; (2) establishing mentorship training programs; (3) developing public health impact measures to incorporate into outcomes; and (4) disseminating principles of model programs, training materials, and outcome strategies to speed the development of more model programs and avoid duplication of effort.

Discussion

Dr. Knight-Richardson commented on aspects of the institutional culture that discourage psychiatry researchers, such as pressure on residents to put in extensive clinical time, financial constraints, lack of encouragement to female researchers, and asymmetrical mentoring matches for minorities. In addition, psychiatry departments struggle with stigmatization within academic centers. Dr. Nakamura observed that women constitute 36 percent of NIMH-funded researchers, but less than 20 percent of NIMH funded psychiatrists are women. He urged efforts to identify and remove barriers.

Dr. Cohen asserted, and Dr. Greden concurred, that psychiatry training programs typically fail to include programs on genetics, statistics, cognitive and social psychology, and cognitive and social neuroscience. Students are not oriented to think about how the mind works and how disturbance of the brain leads to disturbance of the mind. He urged resources and attention to redefining psychiatry's intellectual agenda.

Dr. Vogel-Scibilia encouraged retention of the huge pool of consumer psychiatrists by supporting residents with serious psychiatric illness during their training and then supporting their professional viability and the possibility of maintaining part-time as well as full-time status. Dr. Wagner expressed hope that the RRC's changes to offer research training early in the curriculum will help rekindle interest in research and noted the need for changes to the child fellowship to promote research. Dr. Greden noted that the American Academy of Child and Adolescent Psychiatry assisted in drafting the recommendations. Dr. Kraemer asserted the importance of teaching research literacy to all physicians prior to residency to enable them to think critically about research and also to improve knowledge and competitiveness of potential researchers. Dr. Gur stated the need to identify people interested in brain/mind, motivate them early, and nurture them. Dr. Kalin observed that positive reinforcers should be applied to people interested in psychiatry research, including adequate time to pursue their interest, and that there are real difficulties identifying adequate mentors for trainees. He urged NIMH to devote resources to this problem, for example, by establishing national training centers where residents or medical students could interact with the best mentors. Dr. Insel stated that the best and brightest are amongst those supported through NIMH programs, but typically through the neuroscience field, not medical schools.

Dr. Salovey stated the need to intervene earlier in the educational pipeline. Candidates for medical school typically take required coursework that provides less opportunity for creativity than the much broader educational program that reinforces creativity and independence experienced by students on course for becoming researchers. He suggested that NIMH convene

university presidents and medical school admissions officers to discuss developing programs that foster research creativity.

PROMOTING INNOVATIVE RESEARCH AT NIMH

Dr. David Armstrong, Chief of the Review Branch in the Division of Extramural Activities, NIMH, described the Institute's approach to identifying and supporting innovative research, which he described as a process requiring the identification of a problem/issue for study, a creative researcher, and a timely approach to addressing the problem-based or hypothetical-driven research. Dr. Armstrong noted that NIMH has several activities to foster innovative research, including: (1) the Pioneer Awards; (2) program flexibility in determining its recommendations for funding of applications scoring within the 10th and 20th percentiles, based on relevance, traction, and innovation; (3) an Innovation Workshop held for reviewers on the Intervention and Services Research Review Committees that was designed to raise awareness of the role/importance of innovation in the development and review of grant applications; and (4) the NIMH-staffed Innovations Committee, which recommends 1 year of support, using an R56 funding mechanism (if applicable), for highly innovative applications that score beyond the Institute's payline. These applications can be nominated by program or review staff for funding consideration, and examples of supported studies include a wide range of science stemming from developmental work using xenopus as a model system to an examination of family issues, such as child neglect and specific related interventions. Thus far, two R56-funded studies have received subsequent funding through the regular peer review and award process.

CONCEPT CLEARANCES

Mental Health Issues in Basic and Translational Social Neuroscience

Dr. Kevin Quinn, Chief, Behavioral Science and Integrative Neuroscience Research Branch, Division of Neuroscience and Basic Behavioral Science (DNBBS), NIMH, proposed a research focus in social neuroscience—the neurobiological basis of complex behavior within a social context. The planned initiative is an outgrowth of the rapid expansion in social neuroscience and will support work aimed at making the connection between basic social neuroscience research and the clinical implications of these basic research findings for psychiatric diseases. Potential activities include, for example, the development of new animal models of social behavior that will enable findings of translational significance when neuroscience methods are applied; research that will lead to potentially new endophenotypes for psychiatric disease based on discovering fundamental neural mechanisms of social behavior in the normal state that are known to be altered in disease; research that seeks to understand whether social deficits are primary or secondary consequences of psychiatric disease; and human neuroscience research to understand the time course for the development of social behaviors critical to the emergence of psychiatric disease.

Discussion

Dr. Salovey urged that language in the announcement encourage teams of investigators in the social sciences as well as neurosciences to collaborate in order to derive maximum innovation and traction. Dr. Quinn responded that is a component of the planned activity.

Implicating Noncoding RNAs in the Genetics of Mental Disorders

Dr. Steven Moldin, Director, Office of Human Genetics and Genomic Resources, DNBBBS, NIMH, explained as background that genes are important in the etiology of mental disorders. Noncoding RNAs are surprisingly prevalent in the human genome and may play a critical role in the regulation of gene expression. The potential importance of noncoding RNAs is suggested by the observation that the complexity of an organism is poorly correlated with its number of protein coding genes, yet highly correlated with its number of noncoding RNA genes, and that in the human genome only a small fraction (2–3 percent) of genetic transcripts are actually translated into proteins. A systematic analysis of transcription observed about 10 times more transcriptional activity than can be accounted for by predicted protein-coding genes. Much of this activity was subsequently shown to be regulated. Large-scale cDNA analysis and genome annotations predict thousands of noncoding RNAs and computational analyses suggests that over 20 percent of human genes are regulated by noncoding RNAs known as micro RNAs. These are believed to regulate genes expression either through messenger RNA cleavage or by translational repression. These and other findings support the notion that microRNAs have a central role in the regulation of protein translation throughout the human genome. The biological functions of most micro RNAs are unknown, but some have already been found to be of relevance to understanding the genetics of mental disorders. The focus of the proposed initiative is to understand the elements of gene expression and how that may cause alterations in nervous system function.

Treatment Response: Linking Genes with Behavioral Phenotypes of Relevance to Patients, Families, and Policymakers

Dr. Donna Mayo, Chief, Functional Assessment in Mental Disorders, Division of AIDS and Health and Behavior Research, NIMH, proposed an initiative to focus on integrating two distinct tracks of research—determining the complex genetic basis of mental disorders and creating new strategies and tools for assessing individual functioning in the real world, with the goal of characterizing the relationship between genetic risk and functional abilities. Behavioral researchers will team with psychiatric geneticists to investigate links between genetic risk and practical measures of day-to-day living. Researchers may ask questions, for example, about whether genetic variables predict functioning independent of DSM symptomatology, with the hope that characterizing the relationship will lead to practical strategies for managing, treating, and preventing mental disorders.

Concurrence

The Council agreed unanimously to approve the three concepts.

CHILDREN AS UNDERREPRESENTED POPULATION

Ms. Hellander asserted that research has established that serious mental illnesses are developmental disorders that often begin in early childhood and that their effects emerge through childhood and adolescence as the brain develops. She explained that windows of opportunity exist to intervene earlier in this process. She suggested a workgroup to look at NIMH's investment in research targeted at the earliest stages of illness. She noted that understanding the genetic components of illness will prove invaluable to parents with family histories who will want to know how to protect or treat their children early on in the disease process. Dr. Insel suggested that the Division of Pediatric Translational Research and Treatment Development is dedicated to identifying areas of need, with the ultimate goal of preventing and curing childhood psychopathology. He also noted that the Neuroscience Blueprint has named 2008 as the Year of Neurodevelopment and that the Institute's intramural research program soon will launch a study of prefrontal cortical development using nonhuman primates.

PUBLIC COMMENT

Dr. Aysha Akhtar, Physicians Committee for Responsible Medicine, expressed concern that a significant component of mental health research revolves around using animals as human surrogates. Because animals suffer pain and stress in routine laboratory procedures, she called on NIMH to divest itself of animal protocols and redirect resources into human-centered research.

Cynthia Folcarelli, National Mental Health Association (NMHA), welcomed opportunities for dialogue between consumer/patient groups and NIMH. She expressed strong support for increasing diversity among researchers and enrollees in clinical trials and services research to improve the science. She urged research on the effects of the recent policy change resulting in dramatic Medicaid reductions and the resultant reduction in funding for mental health services. She suggested that research to address such policy changes would be critical in informing policy and reimbursement systems.

Richard Yanes, Clinical Social Work Federation (CSWF), expressed support for research on developing tools to measure the effects of psychotherapy and counseling on patient outcomes. He asserted that models can be developed to close the gap in translating research results to implementation, which could increase information dissemination dramatically and ultimately impact the availability of services. He also welcomed the opportunity to make suggestions for a research agenda to the Council Workgroup on Services and Clinical Epidemiology, a process that generated much discussion among CSWF members.

Dr. Darrel Regier, American Psychiatric Association (APA), noted that the APA provided input into the Council Workgroup on Services and Clinical Epidemiology and urged emphasis in the final report on epidemiology, which is essential to understanding how to reduce the burden associated with mental disorders. Regarding Medicare Part B, APA has funding to initiate a survey of 4,000 psychiatrists treating patients to track the problems and assess the impact of the new policy. He also stressed the importance for investigators to access NIMH funds rapidly to address urgent emerging issues in the field. Dr. Regier commended NIMH for supporting the National Psychiatry Training Council's work. He noted that APA will appoint the DSM-V task

force soon and stated that he looks forward to the participation of many NIMH grantees in readdressing issues of how to use dimensional and categorical approaches to characterizing mental disorders.

ADJOURNMENT

Dr. Insel adjourned the 211th meeting of the NAMHC at 12:55 p.m. on February 3, 2006.

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

Thomas R. Insel, M.D., Chairperson



U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH • NATIONAL INSTITUTE OF MENTAL HEALTH

NIMH
National Institute
of Mental Health