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NATIONAL INSTITUTE OF MENTAL HEALTH

National Advisory Mental Health Council

Minutes of the 212th Meeting

May 11-12, 2006

Minutes of the 212th Meeting of the National Advisory Mental Health Council

The National Advisory Mental Health Council (NAMHC) convened its 212th meeting in closed session for the purpose of reviewing grant applications at 8:30 a.m. on May 11, 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 5:10 p.m. and continued the open session on the following day, May 12, 2006, in Building 31C, National Institutes of Health (NIH), Bethesda, Maryland, from 8:30 a.m. until adjournment at 1:05 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.

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.

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:

A. Kathryn Power, Center for Mental Health Services (CMHS), Substance Abuse and Mental Health Services Administration (SAMHSA)

Others Present:

Bruce Altevogt, Institute of Medicine of the National Academies

Paul Brounstein, Ph.D., Center for Mental Health Services (SAMHSA)

Jaclyn Diamond, Society for Neuroscience
Cynthia Folcarelli, National Mental Health Association
Stephen Foote, None (retired)
E. Aracelis Francis, Council on Social Work Education
Sarah Hanson, Institute of Medicine of the National Academies
Alan Kraut, Association for Psychological Sciences
Pamela Moore, LRP Publications (Press)
Timothy Nanof, American Occupational Therapy Association
Michelle Rodrigues, SRI International
Beth Roy, SSS
Donna Savage, Science Writer
Angela Sharpe, Consortium of Social Science Associations
Lloyd, R. Sloan, Howard University, Department of Psychology
Karen Studwell, American Psychological Association
Timothy Tunner, National Association of Social Workers
Barbara Wanchisen, Federation of Behavioral, Psychological & Cognitive Sciences
Richard Yanes, Clinical Social Work Federation
Joan, L. Zlotnik, Institute for the Advancement of Social Work Research

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.

Open Discussion with Council on Budget Issues

Dr. Insel welcomed the members of the public in attendance at this public session and opened the session by referring to several editorials that recently appeared in the *Journal of Clinical Investigation* concerning the tightening budget at NIH and the current NIH policies and practices for managing the biomedical research enterprise. He invited Council members' comments on their interactions with the community around these issues.

Referring to the NIH Roadmap, Dr. Cohen commented that the goal of identifying and supporting major research initiatives that no single Institute alone could tackle is a positive one, but the community is voicing concerns about the NIH Roadmap cooperative agreement initiatives associated with the theme of supporting interdisciplinary research. These are seen as large and expensive enterprises and may not be the best way to support innovative science.

Dr. Freedman reinforced Dr. Cohen's comments by noting concern that the large Roadmap-support mechanisms may create a division across the country in that universities unable to compete for some of these large initiatives may also be disadvantaged in competing for other NIH Roadmap research opportunities. Dr. Insel added that a similar concern has been voiced concerning the clinical and translational science awards (CTSA) program that would replace the general clinical research centers (GCRC) program, and universities with multiple GCRCs are

concerned that being limited to one GCRC would significantly restrict available research resources.

Dr. Wagner noted that anxiety in the research community, particularly in the child area, is associated with a number of factors, including tightened pay lines for awarding investigator-initiated grants, the perception that less resources are targeted at career development awards, and the heightened sensitivity among academic institutions concerning faculty productivity. Dr. Gur agreed that the level of anxiety among investigators and experienced in other areas of science as well, including clinical and basic neuroscience, given the perception that high-scoring applications that would have been funded a few years ago are no longer fundable—a situation that can seriously impede an investigator's promotion for tenure.

Dr. Kelly echoed the level of nervousness regarding funding and added the general perception that funding for investigator-initiated studies is being diverted to large-scale Roadmap activities. He added that as established investigators experience more limited research funding for competing continuation and new research applications, this may have the unfortunate effect of decreasing support for new investigators who may have participated on these studies as co-investigators.

Dr. Insel reiterated that the NIH Roadmap currently represents about 1.2 percent of the NIH budget, and the Roadmap primarily supports R01 grants rather than the large-scale studies. He noted that NIH is funding approximately the same number of or more grants than in the past but that the success rate has decreased as the number of applications and the cost of conducting science has increased.

Dr. Hollenbeck commented that as the availability of research support tightens and competitiveness for research funding intensifies, academic institutions face uncertainties about the availability of incoming monies to support the research capacity that has developed over time, and in particular during the period of doubling of the NIH budget. Some successful investigators are being encouraged to submit multiple applications, which could result in a trend for awards to be more centralized at institutions with successful grant-competition track records, rather than more evenly distributed across the country. He noted that data is needed to support or refute that concern.

Dr. Canino commented that in the editorials referenced by Dr. Insel, Andrew Marks questioned whether the 1.2 percent of funding for the Roadmap is misleading since not all research monies fund investigator-initiated grants. If that pool were used as the denominator, he noted that the percentage of funds dedicated to the Roadmap would be significantly higher. Dr. Insel replied that the calculation is a complicated one. In any given year, about 75 percent of funding is directed to non-competing continuation grants, with the remainder available for new and competing renewal applications. Dr. Insel noted that 1.2 percent of NIMH research funds or about \$15 million will support the NIH Roadmap this fiscal year (FY). He also noted that NIMH investigators have been successful in competing for NIH Roadmap funds, including support for behavioral scientists.

Ms. Hellander referred to a comment in the editorials that more clinical studies should be supported by pharmaceutical companies, but she worried that research in areas such as child research may not receive adequate attention and support. Dr. Insel replied that NIMH supports the clinical trials that provide needed answers but that likely would not be supported if not by NIMH, such as effectiveness trials conducting head-to-head comparisons of drugs. He stressed the important function that NIH provides in supporting highly relevant, publicly needed clinical research.

Dr. Aguilar-Gaxiola relayed his experience at the University of California, Davis, in preparing a CTSA submission as a positive one that brought several departments together to look at how the health system was going to be transformed under the CTSA approach to science. He said that the prevailing attitude among his colleagues is that the mechanism provides a collaborative opportunity and is a positive step to move the science closer to and increase its relevance for the public.

Dr. Insel explained that one of the goals of the CTSA is to build an academic home for the next generation of physician scientists with a strong clinical science research background and to transform the way academic health centers work by bringing together several components currently in place in medical centers around the country—the old GCRCs, some P30s, and other cores—with training and other resources that would be in an academic health center to provide a rich environment for training clinical investigators with cutting-edge science of clinical trials, biostatistics, and all the other aspects needed for the next generation of scientists.

Dr. Gur reinforced Dr. Aguilar-Gaxiola's comments about the value of the CTSA's for promoting a new and unified approach to transforming clinical research and supported Ms. Hellander's position that NIMH has an obligation to the public to support clinical trials. She praised the efforts of staff in the Division of Adult Translational Research and Treatment Development (DATR) to bring scientists, basic scientists, physician scientists, and industry to the table to address how to blend studies and invigorate and challenge the field. She noted that the public places much trust in NIH-supported research and interactions such as these increases the credibility of research.

Dr. Insel followed up on Dr. Gur's comments by noting that expanding public/private partnerships would be a way to maximize resources and promote shared programmatic goals. He referenced the Genome Association Information Network (GAIN), an initiative to allow for whole genome association studies, as a model for collaboration with the Food and Drug Administration, the Centers for Medicare and Medicaid Services, State agencies, families, and the pharmaceutical industry, on areas of mutual interest, including biomarkers, drug development, and development of new PET ligands.

Turning to a recent workshop that brought together clinical scientists and behavioral scientists, Dr. Salovey asked for a brief report on that meeting. Dr. Ellen Stover, Director, Division of AIDS and Health and Behavior Research (DAHBR), explained that in May, DAHBR sponsored a 2-day meeting with the purpose of bringing together scientists whose work has focused on prejudice, stereotyping, discrimination, stigma, and related areas. The meeting was jointly planned and co-chaired by Drs. Jennifer Crocker, University of Michigan, Bernice Pescosolido, Indiana University, and Emeline Otey, DAHBR. Dr. Wayne Fenton, Director, DATR, continued

that there was collaboration interest on both sides, but it was evident that the cultures were very different. The clinically oriented investigators were interested in understanding, for example, stigma more deeply and how it affects individuals and their integration into the community, with a goal of designing interventions. They were looking to the social psychologists for richer theories to explain stigma as it relates to designing interventions. The social psychologists were focused on more general theoretical constructs that would apply to a range of applied problems, including mental illness. Dr. Nakamura noted that by the end of the workshop, there was useful discussion about how to apply the theories in practical ways and that it appeared that several participants were interested in collaborating on future studies.

Dr. Kelly noted a pressing need to develop a research agenda for the application of basic and social psychological science to clinical problems, rather than the more typical approach of studying university students or populations with little clinical relevance. He suggested bringing basic behavioral and social scientists together with clinical scientists to articulate a research agenda, with stigma as an obvious area of need, although many areas remain to be developed. He reiterated the importance of having training mechanisms in place to train the next generation of basic scientists. Dr. Stover noted that Council had explored this issue as reflected in its report “Translating Behavioral Science into Action.” Dr. Insel responded that “Research Teams for the Future” is a major Roadmap theme and includes an interdisciplinary research training initiative with an emphasis on translational research, behavioral/social sciences, and quantitative sciences. He continued that this initiative would work well at institutions where the infrastructure already naturally brings together those different disciplines.

Dr. Insel also described a 2004 workshop on cognitive perspectives on mental health practice that brought together researchers in the services area with basic behavioral scientists. Many of the issues surrounding dissemination, services, and organizational change relate to decision-making, the perception of risk, and how to integrate basic science with services research. Dr. Kurtzman of the Division of Neuroscience and Basic Behavioral Science (DNBBS) explained that no one NIH Institute has primary responsibility for research on medical decision-making or for basic cross-cutting social psychology research since such research spans multiple diseases and is supported in many Institutes.

Dr. Cohen noted that psychiatry residents are eager to study human behavior but may not have the opportunity for training that integrates, for example, symptoms, receptor types, and the connectivity between them. Social psychology, cognitive psychology, cognitive neuroscience, and social neuroscience are the opportunities scientifically to make those connections, but training programs generally have not oriented to that opportunity. Dr. Insel added there are many opportunities for linking clinical and neuroscience resources for trainees at their home institutions but that these opportunities are not being fully explored.

Dr. Cohen stated that training issues are of particular concern in the behavioral sciences area. Although there is a clear training path for residents interested in pursuing biological psychiatry as a career, the path is less clear for residents in psychiatry with an interest in the behavioral sciences. Dr. Gur agreed, noting that psychiatry training programs would benefit from a restructuring that expanded training opportunities in critical areas to provide links to successful investigators to increase interactions with residents.

Session Recess

Dr. Insel thanks Council members for their valuable comments and recessed the initial portion of the open session of the 212th meeting at 5:10 p.m. The Council reconvened the following morning to continue the open session on the main campus of the NIH in Bethesda, Maryland.

Call To Order and Opening Remarks

Dr. Insel called the continuation of the open session to order at 8:30 a.m. He welcomed back Ms. Kathryn Power as the Center for Mental Health Services liaison to the Council.

Approval of the Minutes from the Previous Council Meeting

The minutes of the February 2006 Council session were unanimously recommended for approval by the Council.

NIMH 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/dirreportmay06.pdf>).

Budget

Midway through the FY 2006 budget, Dr. Insel explained that NIMH is working with a 0.6 percent reduction in funding compared to funding in FY 2005. The President's budget request for FY 2007 calls for a funding decrease of 2.7 percent for the Department of Health and Human Services (DHHS), with a decrease of 0.6 percent for NIH. Dr. Insel cautioned that an important factor impacting the availability of funds for future awards is the cost of conducting biomedical research, which has risen by approximately 3.8-4 percent in the past year. Turning to the NIH Roadmap, Dr. Insel noted that Roadmap funding is currently about \$13 million, increasing to approximately \$17 million for FY 2007, representing a little more than 1 percent of the overall NIH budget.

In terms of NIMH funding for new and competing research project grants, Dr. Insel projected that the number of awards will increase in FY 2007. Since 1998, the number of competing research project grant applications increased from 1,618 to a projected 2,979 applications in FY 2007, with the greatest increase (500 new applications) in the past 2 years. An important factor driving the increase in applications was the expansion of academic health centers in terms of buildings and faculty that took place during the "period of the doubling."

While the number of new and competing grant awards increased at a modest rate—from 451 in FY 1998 to an estimated 614 in FY 2007—there has been an accompanying decline in success rates. Dr. Insel explained that in any given year, about 70 percent of NIMH’s research monies support non-competing continuation grants. Since many large commitments initially made in 2001-2002 (during the period of “doubling” of the NIH research budget) will be ending in 2006-2007, more funds should be available to support new grants in FY 2007. Also, NIMH is managing costs by typically reducing the amount of the awards for new grants. In terms of funding strategy, in general, NIMH plans to fund applications scoring up to the 10th percentile and about half of those scoring between the 10th and 20th percentiles, based on relevance to the NIMH mission, traction, and innovation.

Support for new investigators is a priority for NIMH. In FY 2005, of the 541 awarded new and competing research project grants, 155 (28.6 percent) provided support for new investigators. In an effort to reduce the average age of first-time (new) principal investigators obtaining R01 research funding, currently 42.6 years, a new funding mechanism, the “Pathway to Independence” (K99/R00), will support new investigators and accelerate an investigator’s independence by facilitating the investigator’s receipt of an R01 award earlier in his/her career. The award, which is being used across NIH, will provide up to 5 years of support consisting of an initial mentored phase that provides support for up to 2 years, while a postdoctoral scientist completes his/her mentored research work, publishes, and searches for an academic position, and a second independent phase, when 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. An important feature of the award is that non-U.S. citizens are eligible. NIMH plans to fund ten K99/R00 awards in FY 2007. Future considerations include targeting the awards to specific groups or areas of research (e.g., MD/PhDs or translational research).

Dr. Insel noted that innovation is another important emphasis at NIH as exemplified by the NIH Pioneer Award Program, a part of the NIH Roadmap. This year, five NIMH grantees received Pioneer Awards that provide 5 years of support based on a streamlined (five page) application evaluated first by NIH staff for eligibility and then by a multidisciplinary panel of experts, with the most outstanding candidates invited to NIH for an interview with a panel of outside experts. The award encourages innovation and risk taking, is highly competitive, and expands NIH’s traditional investigator-initiated grants program by providing support for highly creative and pioneering investigators rather than projects.

Innovation also was the topic of a 2-day workshop that preceded the Institute’s Interventions Research and Services Research peer review committee meetings. Co-sponsored by the Division of Services and Intervention Research (DSIR) and the Division of Extramural Activities (DEA), the workshop provided reviewers with the opportunity to discuss the meaning of innovation in mental health research, how NIMH supports innovation, and how the peer review groups can assist in fostering innovation.

The Innovation Award is another mechanism designed to support innovation. This R56 mechanism is intended to provide 1 year of support for high-risk and potentially high-yield projects that fall just outside the limits of funding. For the past 18 months, program staff members have been nominating

applications for consideration by an Innovation Committee, chaired by Dr. David Armstrong, Chief of the Review Branch in DEA. The Committee presents its funding recommendations to the NIMH Director for funding decisions. Examples of supported studies include an examination of calcium spikes and synaptic formations, the genetics of the serotonin 1A receptor and how it may relate to gene/environment interactions and susceptibility to depression, and a project on child neglect and foster care and the development of specific interventions. The majority of awardees have been successful in competing for funding following receipt of the R56 award.

Turning to personnel changes, Dr. Insel reported that several NIMH staff members had retired, including Dr. Steve Foote, Director, DNBBS; Mr. Richard Pine, NIMH Budget Officer; and Dr. Steve Moldin, Director of the NIMH Office of Genetics and Genomic Resources. Dr. Heather Ringeisen, Director of the Child and Adolescent Services Research Program in DSIR, would soon be leaving NIMH to take a position in North Carolina. Dr. Insel also noted that Dr. Susan Swedo, who had served as Director of the Division of Pediatric Translational Research and Treatment Development, returned to the Institute's Intramural Research Program (IRP) to develop a local autism research program and that she would continue to work with the extramural program as Associate Director for Pediatric Research. Searches are underway for new directors for DNBBS and DSIR and for a new Scientific Director, Clinical Director, and Chief of the Laboratory of Neuropsychology at the IRP.

Dr. Insel stated that the NIMH Press Office has been particularly busy with the flurry of press releases on the large-scale practical clinical trials [Treatment for Adolescents with Depression Study (TADS), Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE), Sequenced Treatment Alternatives to Relieve Depression (STAR*D) Study, and Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD)]. These trials included approximately 10,000 patients at 200 sites across the country and have investigated a range of questions that span adolescent depression, schizophrenia, treatment-resistant depression, and the management of bipolar disorder. All of the trials have the same basic themes: doing projects in the real world, looking at functional outcomes, and investigating long-term effectiveness to understand what helps people recover. The September 2006 Council meeting will celebrate the clinical trials program by highlighting the work of these trials and the implications of study findings for the general community.

In addition to the findings from the large trials noted above, several ancillary studies have provided additional important and useful information. For example, a study of the offspring of mothers treated for major depression in STAR*D showed that for children with a diagnosis at baseline (these children did not participate in the trial) whose mothers recovered during the trial, there was an 11 percent decrease in the rate of diagnoses at 12-14 weeks post treatment for the children compared with an 8 percent increase for children whose mothers did not recover [see Weissman, M.W., Pilowsky, D.J., Wickramaratne, P.J., Talati, A., et al. "Remissions in Maternal Depression and Child Psychopathology: A STAR*D-Child Report." *Journal of the American Medical Association* 22;295(12):1389-98, 2006]. These data demonstrate that in addition to the personal devastation associated with an illness like depression, it can have a marked impact on family members as well. However, successful treatment of a family member can have a positive effect on others around him/her.

In another STAR*D ancillary study, intramural and extramural researchers collaborated to examine gene variation among study participants to predict who will respond to treatment and who will develop adverse events, including suicidal ideation, activation, and tremor (see McMahon, F.J., Buervenich, S., Charney, D., Lipsky, R., et al. "Variation in the Genes Encoding the Serotonin 2A Receptor is Association with Outcome of Antidepressant Treatment." *American Journal of Human Genetics* 78:804-814, 2006). Of the 68 candidate genes considered, there was one in particular that was found to be highly predictive of either remission or response—it was a polymorphism in the 5HT2A receptor. This finding may have important implications for medication treatment decisions for patients with depression. Dr. Insel credited the Council for its guidance that led to the collection of DNA for the participants in these large clinical trials

Dr. Insel closed his presentation by reiterating the NIMH research vision to identify the pathophysiology of schizophrenia, bipolar disorder, autism, major depressive disorder, eating disorders, and general mood and anxiety disorders and by applying that knowledge to the identification of biomarkers to serve as targets for new treatments that attack the core pathology of these illnesses. The ultimate goal is to individualize care as done in other areas of medicine, using available technologies—molecular diagnostics, proteomics, and clinical genomics—to guide treatment choices and ultimately preempt the emergence of disease. The findings from the STAR*D trial suggest the opportunity to use genetics, in combination with personal history, family history, and neuroimaging, to determine which treatment for whom, with the expectation that science will lead beyond treatment response to cure therapeutics.

Discussion

Dr. Levitt noted that one of the most significant developments to come out of these larger studies has been the coordinated efforts to bank DNA materials and other information and make them available to the larger research community, thus driving research well beyond the initial projects. However, there is concern about timely access to the materials and the cost of access, and Dr. Levitt asked if NIMH has considered strategies to fiscally manage these resources. Dr. Insel responded that the DNAs from these clinical trials are stored at the Rutgers Cell and DNA Repository and are available without cost to researchers on NIH grants or at a cost of \$90/sample for researchers without a grant, which covers the costs of making the cell lines, shipping, and managing the resource. The phenotyping information should be available to the research community in 2007, if not sooner for CATIE.

Dr. Freedman commented that personalized treatment may be realized as we make substantial inroads into understanding the genetics of illness, and Dr. Insel replied that there is an unprecedented opportunity to explore the genetic contributions to treatment response in CATIE, STAR*D, and STEP-BD. He referenced a public/private partnership—Genome Association Information Network (GAIN)—that will be managed by The Foundation for NIH and include corporations, private foundations, advocacy groups, concerned individuals, and NIH. As noted on its Web site http://www.fnih.org/GAIN/GAIN_home.shtml, GAIN is designed to provide data to help address key questions about the complex contributions of genes to human health and disease. The Foundation has solicited applications from investigators at universities and research centers worldwide to have existing disease-specific samples from case-control (or similar) studies genotyped at no cost. Applications will be peer reviewed this summer.

Referring to the large contracted clinical trials, Dr. Kraemer stressed the importance of providing to the larger scientific community the opportunity to consider a variety of potential moderators of treatment response, including gender, ethnicity, and age. She reiterated the value of public access to this type of data, and Dr. Insel clarified that the GAIN project datasets, including genotyping and phenotyping data, are made available to the public as rapidly as possible so that investigators can conduct independent data analyses. In terms of protecting the rights to the data of the investigators who conducted the studies, Dr. Insel reported that The Foundation for NIH, through the GAIN project, is pilot-testing a policy of making the data available to everyone but allowing only the principal investigator who did the initial work to submit a paper for publication for the first year after the data are posted. Dr. Insel noted that the GAIN experience could become a model for NIMH in its efforts to make large databases widely available for a range of analyses, while protecting and recognizing the contributions of the investigators who were responsible for the collections.

Dr. Aguilar-Gaxiola stressed the importance of conveying to the public in easily accessible, understandable, and relevant terms, the important findings and their implications to the public as rapidly possible. Dr. Insel replied that the NIMH Office of Science Policy, Planning, and Communications is dedicated to effective information dissemination strategies to convey important timely information to the public that is both understandable and accurate.

Ms. Hellander suggested that NIMH press releases are an important resource to the community, but perhaps they might be expanded to include information on newly funded studies as the public wants to know what NIMH is doing now as well as the results of the studies that have been completed. Dr. Insel welcomed Ms. Hellander's suggestion and noted the potential utility of an electronic newsletter that could include, for example, information on the concepts that have been approved by Council for future research, as well as information on new grants that have been funded—in particular in new and exciting areas of research. Dr. Levitt stressed the importance of providing policy makers with research findings as well as information about where the Institute is going in terms of the research that is being funded now and why it will impact people's lives. He also noted the importance of working with professionals to frame messages in an understandable and meaningful way.

Dr. Kelly commented that providers also are another important audience that could benefit from information dissemination targeted at them and suggested that NIMH consider new strategies to strengthen the uptake of research findings in the provider community, especially as more is learned about what treatments works best for whom and under what circumstances.

“Sleep Disorders and Deprivation: An Unmet Public Health Problem”

Dr. Charles Reynolds, UPMC Professor of Geriatric Psychiatry at the University of Pittsburgh School of Medicine, began his presentation by noting that in April, the Institute of Medicine (IOM) report "Sleep Disorders and Sleep Deprivation: An Unmet Public Health Problem" was released and includes recommendations for improving public awareness and strengthening the field of

sleep medicine. The project was initiated and funded by NIH, the American Academy of Sleep Medicine, the Sleep Research Society, and the National Sleep Foundation.

In setting the context for the recommendations contained in that report, Dr. Reynolds noted that sleep medicine is truly an interdisciplinary science that has developed from many other disciplines – chronobiology, neuropharmacology, neuroanatomy, neurophysiology, psychiatry, neurology, medicine, and nursing over the past 25-30 years. He noted that sleep research is relevant to NIMH because sleep is critical to brain health, mental health, and successful aging.

In the last 10 years, there have been some exciting advances in the field, including genetic control of circadian rhythms and application of the tools of functional brain imaging to understand how functioning of the brain changes during sleep in relation to illnesses like major depression and healthy aging. Much has been learned recently about neuropsychiatric sequelae of common sleep disorders such as sleep apnea and chronic insomnia. In terms of chronic disease management strategies for people living with chronic insomnia, a better “tool box” is now available; for example, investigators have applied the strategies and principles of cognitive behavior therapy to improving the lives of people who live with chronic insomnia. Much of this work has been sponsored by NIMH and is yielding tremendous fruit scientifically and clinically.

Dr. Reynolds continued that from a public health perspective, we have the challenge of a relatively small field of sleep research coupled with a large public health burden. The IOM Committee on Sleep Medicine and Research estimated that between 50 million and 70 million Americans live with a chronic disorder of sleep/wake regulation, with the major disorders in terms of public health impact and cost being chronic insomnia and sleep apnea syndromes. One in five motor vehicle accidents is related to sleep loss or sleep deprivation. Thus, sleep loss and sleep disorders have enormous consequences for health, including mental health and well being, and people with sleep disorders require chronic disease management strategies.

The Committee found that although the field of sleep research is the paradigm of a successful interdisciplinary effort, there remain significant gaps in sleep research, education, and training. Regarding infrastructure and training, the Committee emphasized the important leadership role of the NIH National Center for Sleep Disorders Research and the need for a coordinated strategy to promote continued scientific and clinical advances. In terms of an appropriate organization of academic sleep programs to promote interdisciplinary research and the next generation of principal investigators, the committee proposed a three-tiered model of academic sleep centers where the Type I clinical interdisciplinary sleep program would provide appropriate multidisciplinary care to people living with sleep disorders and basic education to students of the health sciences such as nurses, medical students, and residents; the Type II center would go beyond providing expert clinical care to encompass an agenda in either basic or clinical research; and the Type III center would be modeled after the National Cancer Institute’s Comprehensive Cancer Center and include expert clinical care and education, basic and applied research, and the capability to serve as a regional resource for a proposed network of sleep disorders centers. The Committee also recommended establishing a network of Centers of Excellence in sleep disorders medicine around the country, thus creating the infrastructure that would enable, for example, large practical trials in sleep disorders. Dr. Reynolds concluded his comments by noting that the NIMH response to the IOM’s report on reducing suicide provides an analogy and model to considerations about sleep

disorders research. NIMH created a network of developing centers, using the P20 support mechanism, to help galvanize the field of suicide prevention research. This network provides an informative approach for what might be done to catalyze activity in the sleep disorders field.

Discussion

Ms. Power asked whether the IOM had inventoried the universities and hospitals that are currently doing sleep disorder research or running sleep clinics, from which the network could grow.

Dr. Reynolds responded that an inventory was conducted, and one of the important lessons learned from this inventory is that these centers can be profitable and serve as a strength in the field of sleep research.

Council Workgroup on MRI Research Practices: An Update

Dr. Jonathan Cohen, Director, Center for the Study of Brain, Mind, and Behavior, and Director, Program in Neuroscience, Princeton University, introduced the Workgroup's activities by noting that in recent years, much cognitive neuroscience research has been conducted in departments of psychology and other programs that are outside of traditional clinical settings, and issues began to emerge about the standards of practice where they involve situations or purposes that are not covered by current guidelines and standards of practice. For example, ethical issues have been raised in the literature about how to handle incidental findings in normal populations, especially if non-clinicians are performing the study.

Safety guidelines, Dr. Cohen continued, are available as the American College of Radiology (ACR) issued a white paper on safe magnetic resonance imaging (MRI) practices, including the training of MR technologists and procedures in the scanner suite, in 2002, with revisions in 2004. Also, the Web site www.mrisafety.com is maintained by the Institute for MR Safety Education Research and offers complimentary perspectives to the ACR report. Both of these resources are focused primarily on the use of MR in a medical setting.

To address safety issues associated with MR research, an MRI Workgroup was formed in September 2005 to examine the current situation and to discuss issues to consider in conducting research with MRIs. The group is composed of a broad representation of the community, including members of the NAMHC, neuroscientists in the field who are using MRI in a variety of developmental and adult populations, MRI experts, and representatives of the NIMH intramural program. The Workgroup continues to address questions in a variety of topic areas, including screening subjects for scanning, training personnel who operate scanners, operating procedures, emergency procedures, characteristics of the physical facilities, safety considerations, and documentation of equipment specialized to research use. Subject health and safety factors, issues specific to the nonmedical versus medical setting, and how to keep the practices and guidelines up to date have also been discussed. Dr. Cohen noted that in the rapidly emerging field of research with MRIs, it is important that these issues be monitored and that any guidelines or standards keep pace with developments in the field.

The Workgroup met initially in September 2005 and is in the process of producing its final report that will include points to consider, with the goal of encouraging the community to develop standards of practice in conducting MRI research.

Dr. Cohen thanked members of the Workgroup who generously gave their time for this effort, including Dr. Jennifer Kulynych at Johns Hopkins, Dr. Bruce Rosen at Massachusetts General Hospital, Dr. Sean Marrett in the NIMH Intramural Research Program, and Drs. David Shore and Judy Rumsey in the NIMH extramural research program.

Discussion

In response to Ms. Hellander's query about the recommendation on incidental findings, Dr. Cohen acknowledged that the Workgroup's recommendation was extensive and that the key element is informed consent—letting the subject know up front that MRI in a research setting is not a medical procedure and how to handle an incidental finding.

Council Workgroup on Services and Clinical Epidemiology: Final Report

Dr. Susan Essock, Professor and Director, Division of Health Services Research, Mount Sinai School of Medicine, presented the final report, "The Road Ahead: Research Partnerships to Transform Services," prepared by the Council Workgroup on Services and Clinical Epidemiology Research. That document is now available on the NIMH Web at <http://www.nimh.nih.gov/council/TheRoadAhead.pdf>.

Dr. Essock enumerated the three-pronged charge of the Workgroup: What services and clinical epidemiology research is NIMH currently supporting and what areas should be developed? What opportunities exist to affect policy, care, and ultimately reduce the burden of mental illness? Where does NIMH have traction to make a difference through research, including collaborative opportunities with other communities and agencies?

The Workgroup developed several crosscutting themes that served as a foundation in developing its recommendations: (1) expand partnerships in research with a range of stakeholders—consumers, payers, and providers and in coordination with other Federal and State agencies; (2) promote quality-of-care research to identify the care received in clinical settings as well as establishing and testing standards for assessing it; (3) focus on fairness in access to services for all segments of the population; (4) support research that expands the evidence base on interventions that maximize an individual's level of functioning within a community and on how to implement and sustain such interventions so that they are readily accessible and acceptable; (5) enhance communication strategies for soliciting the input of multiple stakeholders and implement dissemination strategies to transfer what is known into practice more effectively; and (6) promote ongoing evaluation to evaluate the effectiveness of and costs associated with new treatment programs and how they can be generalized to other sites and settings.

The Workgroup's recommendations fall into three areas—enhancing research responsiveness to stakeholders, capacity building, and knowledge exchange, and Dr. Essock focused her presentation on the first category—enhancing research responsiveness to multiple stakeholders.

Services research will have its greatest impact when findings are incorporated by purchasers and providers in routine clinical practice and made available to those in need. In order to achieve this goal, scientifically exciting research initiatives must be targeted at pressing clinical issues. There is a significant gap between what is known to be effective and what occurs in usual care in diverse communities. For example, psychosocial interventions to augment medications for people with schizophrenia, treatments for patients with disruptive disorders, collaborative care models within primary care settings, and critical time interventions for homeless individuals have all benefited from NIMH investments and are ready to be implemented but are not readily available in the community.

By nurturing and expanding partnerships with payers, providers, consumers, and other stakeholders—beyond convening meetings to true collaborations, allowing for active priority setting and follow-up, user-friendly public health communications, and public feedback on the NIMH services research portfolio—NIMH can ensure that research investments target stakeholder needs and thereby enhance the public health significance of the work undertaken and the likelihood that findings will be implemented and sustained in clinical care settings.

How can this new era of research be accomplished most effectively and efficiently? The standard NIH submission and review cycle may not be optimal for seizing opportunities to address emerging policy questions. Rather, NIMH must be prepared to initiate, for example, supplements for translation and implementation research, as well as contracts for needed studies. The center mechanism provides another route for encouraging researchers to create meaningful partnerships with key payers and other stakeholder groups. In addition, novel approaches may be needed to develop the capacity of the field, including the possibility of a new type of administrative supplement whereby a principal investigator can place a junior person in a mental health setting to learn the challenges faced by administrators and payers and design studies with them that address these real-world information needs. Some of these mechanisms may be high-risk initiatives that will require more ongoing oversight than typical research grants, but NIMH should have goals and benchmarks for these initiatives that are routinely assessed with any mid-course adjustments made to promote needed research.

In developing its recommendations, the Workgroup recognized that additional in-house capacity at NIMH may be needed to identify and respond to emerging policy issues, as well as investments in staff training and mentorship with stakeholders.

Dr. Essock concluded her remarks by noting that the Workgroup looks to NIMH to promote and utilize ongoing relationships that current grantees and stakeholders have with each other in building stronger partnerships and in extending communication efforts that will ultimately reduce the burden of mental illness. Many trails have been blazed, she said, and the challenge remains to make these roads well traveled.

Addressing the Workgroup's Recommendations: NIMH Activities

Dr. David Chambers, NIMH Associate Director for Dissemination and Implementation Research, reported on NIMH activities that are planned or in process to address the recommendations of the Council Workgroup on Services and Clinical Epidemiology Research.

A number of overarching principles underlie the NIMH's activities: reducing mental health disparities, improving the timeliness of dissemination and implementation of research findings, capitalizing on emerging opportunities to add components to existing initiatives, and strengthening the connection between science and service.

Turning to strategies for disseminating research findings, Dr. Chambers noted that opportunities exist within NIMH for program staff to partner with the Office of Constituency Relations and Public Liaison (OCRPL) to disseminate services research findings through a number of programs managed by OCRPL:

- The NIMH Outreach Partnership Program is a nationwide program that enlists national and State organizations in partnerships to help bridge the gap between research and clinical practice.
- The NIMH Alliance for Research Progress is a group of patient and family advocates representing national voluntary organizations that meet twice a year with the NIMH Director and staff to discuss research priorities.
- The NIMH Professional Coalition for Research Progress includes representatives of professional organizations with an interest in mental health that meet annually with the NIMH Director and staff.
- The Integrated Information Management System has a database of 680 contacts from over 460 organizations that can be used for tailoring messages to key audiences.

The NIMH Office of Science Policy, Planning, and Communications (OSPPC) is another important partner for disseminating information. Among other activities, that Office creates and implements the Institute's communication efforts, including disseminating research findings and management of the NIMH Web site. With approximate yearly public distribution of 2.6 million print copies of mental health publications and more than 25 million Web hits per year, tremendous demand exists for relevant research information. Future activities include working with 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) to explore a "Planet for Health" Web portal modeled after the Cancer Control PLANET Web portal, a collaborative effort aimed at providing access to data and resources that can help cancer control planners, health educators, program staff, and researchers design, implement, and evaluate evidence-based cancer control programs (<http://cancercontrolplanet.cancer.gov/>).

Communication is a two-way street, Dr. Chambers continued, and multiple forums are being explored through which the research needs of all relevant stakeholders can be identified and aligned with the Institute's research priorities. These include a series of science and service regional meetings, which are cosponsored by the Center for Mental Health Services (CMHS) and the

National Association of State Mental Health Program Directors (NASMHPD). NIMH and CMHS also are investigating possible Listservs to continue the dialogues begun at the regional meetings and other forums to create a community of science and service. NIMH efforts to promote community-based participatory research through workshops, conferences, and funding opportunities are increasing, and NIMH staff members are participating in a series of interagency working groups that include a focus on suicide prevention, emergency response, integration of primary care and mental health care, financing, and employment to further raise relevant questions. These groups include a range of representatives from NIH, the Department of Health and Human Services, and other Federal agencies.

As part of NIMH commitment to partnerships and in an effort to increase the relevancy of research to financing and delivery systems, efforts are underway with the Center for Medicare and Medicaid Services, State Medicaid Directors, the National Business Group on Health, which represents Fortune 500 employers, CMHS, and NASMHPD. Relatedly, through the Interventions and Practice Research Infrastructure Support Program (<http://grants.nih.gov/grants/guide/pa-files/PAR-06-441.html>) and the recently released center announcements (<http://grants.nih.gov/grants/guide/pa-files/PAR-05-144.html> and <http://grants.nih.gov/grants/guide/pa-files/PAR-05-161.html>), NIMH is emphasizing the importance of community partnerships and reducing health disparities.

NIMH is taking the lead at NIH to focus on developing the knowledge base of how best to fit effective interventions within service settings. The first trans-NIH program announcement on dissemination and implementation research is now available (<http://grants.nih.gov/grants/guide/pa-files/PAR-06-039.html>). In concert with the Agency for Healthcare Research Quality, NIMH is leading an interagency working group to identify existing and future opportunities to augment ongoing projects and initiatives with research components addressing issues of relevance to other agencies.

Dr. Chambers concluded his presentation by noting the tremendous responsibility and opportunity to impact public mental health through research and his appreciation for the Workgroup's important report.

Discussion

Several NAMHC members expressed thanks to the Council Workgroup and to its chairperson, Dr. Essock, and stressed the importance of engaging multiple partners to address the relevancy of research to stakeholder needs. Dr. Kelly suggested the importance of studying how best to disseminate information, referring to literature showing that an awareness and knowledge of new techniques are important factors influencing providers' behavior but that providers adopt innovations when they are not satisfied with the current repertoire of approaches. He challenged NIMH to take the recommendations of this Workgroup to an international level as well as a national level to find ways to influence provider behavior.

Dr. Levitt commented on the variability across States in terms of how mental health services are organized and asked how the Workgroup grappled with engaging State policymakers to help them understand how utilization of research and best practices will benefit their population.

Dr. Essock noted the importance of paving the way for new partnerships with policymakers and providers in States and the opportunities to work together to promote research that addresses questions and issues that can lead to changes in the mental health service systems.

Dr. Vogel-Scibilia noted the importance of addressing the required infrastructure to provide needed services, including increasing the pool of providers, delivering services in an equitable and fair way, and addressing funding shortages. In response, Dr. Insel referenced CMHS' Transformation Action Initiative that addresses the needed infrastructure for providing services that emulate evidence-based practices in a fair and effective way.

Approval of the Report of the Council Workgroup on Services and Clinical Epidemiology Research

After Dr. Insel called for a Council vote on the Workgroup's final report, a motion for approval was made, seconded, and unanimously approved.

The Science of Mental Illness: NIMH/NIH Middle School Curriculum

Dr. Wayne Fenton, Acting Director, DATR, NIMH, introduced a new middle school curriculum "The Science of Mental Illness." Cosponsored by NIMH and the NIH Office of Science Education (OSE), the curriculum supplement is one of 15 supplements intended to improve science literacy and to attract young people to careers in medical and behavioral science.

Dr. Fenton noted that school systems address major public health issues that affect young people, such as driving, substance abuse, and sexually transmitted diseases, but typically convey little about depression and schizophrenia. In 1999, between 83-98 percent of middle school students knew that AIDS was transmitted by sharing needles and 88-98 percent knew that AIDS could be transmitted through sexual intercourse. As a contrast, in a survey conducted in 2005, more than 50 percent of 1,600 middle school students endorsed statements that indicated they believed that:

- Mental illnesses could not be diagnosed by a doctor.
- Depression was the same as being sad.
- Family history did not increase the risk of mental illness.
- The brain controlled thinking and the heart controlled feelings.
- Treating mental illness does not change how the brain works.
- Depression was not a disease.
- No treatments exist for mental illness.

The goals of the new curriculum supplement are to teach middle students that mental illnesses are like other illnesses in that they have a biological basis and can be diagnosed and treated effectively, to increase understanding of the determinants of mental illness, and to reduce negative attitudes and misunderstandings about mental illness through education. The material includes background information for teachers, assessment tools, student pages, and take-home activities.

As part of the curriculum development process, a field test was conducted of 23 teachers in 16 geographically dispersed States; of the approximately 1,600 participating middle school students, about half were female and about 30 percent were minorities. The pre-post test evaluation showed significant increases in knowledge as well as significant reductions in stigmatizing attitudes and beliefs about mental illness.

Dr. Fenton concluded his remarks by noting that NIMH is working with OSE to disseminate these materials, including direct mailings to 60,000 teachers and school systems around the country and presentations at conferences such as the National Middle School Association, the National Association of Biology Teachers, the National Science Teacher Association, and the National Alliance for the Mentally Ill. The supplement is accessible online and available for free distribution to school systems throughout the United States at <http://science-education.nih.gov/customers.nsf/MSMental>.

Discussion

Dr. Wagner asked whether attempts would be made to obtain a national endorsement of this supplement to make it a mandatory part of the curriculum. Dr. Fenton responded that the plan is to encourage people at the local level to add this supplement to the curriculum and to generate interest through advocacy organizations.

Dr. Gur noted the importance of including adequate information about mental illness, including recognizing psychopathology in children, in the training curriculum for subsequent generations of teachers, along with making such information available to parents and current teachers.

Dr. Hollenbeck suggested that the “health classes” might be the appropriate venue for this curriculum supplement.

Dr. Canino urged NIMH to consider developing these kinds of materials for parents because it is important that parents be able to recognize a mental illness in a child.

Ms. Hellander expressed concern that the use of the term “mental illness” could alienate middle school students and suggested that rather than distinguishing the various illnesses described in the curriculum from other illnesses, they be described more generally as illnesses that afflict children. Dr. Fenton acknowledged that there is disagreement about the most appropriate terminology to use.

Ms. Power commented that many children do not understand the meaning of good mental health. She referred to SAMHSA’s Safe Schools/Healthy Students Initiative (http://www.samhsa.gov/news/newsreleases/060711_EDgov.htm) that draws on the best practices of education, juvenile justice, law enforcement, and mental health systems to provide integrated resources for prevention and early intervention services for children and youth. The curriculum is another approach to addressing mental health and mental illness.

Dr. Salovey suggested that one of the next steps might be to create a curriculum supplement for younger and older students. He stated that teacher training will be important for maximum

effectiveness of this supplement. Dr. Salovey also noted that there is a growing movement in many school districts across the country, and even mandated in some, to include K-12 social and emotional development education in the curriculum. However, finding appropriate places in the curriculum to integrate this supplement will be challenging, as most curricula are already quite full. The challenge will be to convince school boards of the value of understanding mental illness.

Dr. Kelly commented that peers are often the first to hear about problems from other students, and thus the curriculum has the potential to help students tell when other students are having ordinary problems versus when they need help. Referring to the data that Dr. Fenton presented on increasing knowledge of AIDS among middle school students in a short period of time, Dr. Kelly expressed optimism that this kind of program can have similar effects for mental illness.

Concept Clearances

Mechanisms of HIV Neuropathogenesis: Emerging Domestic and Global Issues

Dr. Jeymohan Joseph, Chief, Mechanisms of HIV Neuropathogenesis Program, and Chief, Viral and Host Genetics Program, Center for Mental Health Research on AIDS, Division of AIDS and Health and Behavior Research, explained the broad goals of the proposed research are to study the mechanisms regulating the changing phenotype of HIV-associated dementia in the era of HAART (highly active anti-retroviral therapy) and to look at viral and host genetic mechanisms regulating HIV neuropathogenesis from a global perspective.

Since the introduction of HAART, the incidence of HIV-associated dementia has declined; however, the prevalence of dementia has increased because people are living longer under treatment. AIDS has changed, and the frequency of milder and more chronic forms of the disease has been rising.

Changes have also occurred in the symptomatology. Predominant subcortical involvement was seen in pre-HAART, but currently a more cortical type of involvement is common; so the underlying pathophysiology of the disease may be altered in the HAART era. There are also confounding aspects such as aging-related issues, hyperlipidemia, vascular dementia, and involvement of hepatitis C as a co-infection. Interaction between HIV-associated dementia and Alzheimer's disease is also seen, as is amyloid deposition in HIV-infected patients. New syndromes, such as immune reconstitution syndromes, are now seen so that with the activation of the immune system inflammatory reactions to preexisting pathogens emerge. The toxicity of the treatment may bring forth neuropsychiatric effects.

Research questions for this initiative will focus on understanding the mechanisms that drive this changing pathophysiology. One goal would be to identify novel biomarkers involved with these more chronic and milder forms of the disease and to understand the mechanisms of the fluctuating patterns of central nervous system (CNS) symptomatology, the mechanisms driving hepatitis C associated neurocognitive functions, the mechanisms involving the aging-associated confounding factors, and the mechanisms driving novel forms of these diseases and mechanisms of CNS toxicities.

The second major research area is looking at viral and host mechanisms that drive neuropathogenesis, particularly viral clade differences, from a worldwide perspective. For example, some data show that subtype C clade is less neuropathogenic than subtype B, which is found in the United States. Therefore, important molecular differences that drive the disease process may exist in these viruses.

The broad questions are to understand the incidence and prevalence of HIV-associated dementia in different regions of the world where distinct HIV clades predominate, to understand the molecular motifs associated with these different viruses that contribute to HIV-associated dementia, and to understand the interactions of host genetic factors with these viral genetic differences in different regions of the world in the development of the disease.

Refining and Testing Interventions and Service Delivery Models for Youths Transitioning to Adulthood

Dr. Joel Sherrill, Chief, Psychosocial Treatment Research Program, Child and Adolescent Treatment and Preventive Intervention Research Branch, Division of Services and Intervention Research, explained that the goal of this initiative is to stimulate research on refining and testing interventions in service delivery models for youth transitioning to adulthood. Based on longitudinal studies of the rates and course of mental disorders among youth, it is known that mental health problems and related impairment during this critical period are associated with a host of negative outcomes, including chronicity and relapse, hospitalization, incarceration, homelessness, and disruptions in parental custody. However, a review of the existing literature and of the currently funded child and adolescent studies suggest limited empirical focus on the development of tailored interventions in service delivery models for use in this age range.

Developmental considerations and unique aspects of the nature and course of problems during this period have implications for how to think about developing and testing interventions and service models for youth in this age range. Developmentally, this is a period of increased expectations for self-reliance, entry into the workforce, emergence of romantic relationships, and sometimes parenting roles, and clinical care for individuals in this age range is often complicated by co-occurring problems that include substance abuse problems and disorders, suicidal behaviors, and other high-risk behaviors. In addition, this period heralds the onset of serious mental illness, including early psychotic disorders and bipolar disorders, and impairment during this time impacts future educational, vocational, and interpersonal functioning and achievement. Limitations in available interventions (i.e., “acute care” models and disorder-specific intervention approaches are often inadequate for treating and restoring functioning among multi-problem youth in this age range) and discontinuities in services (e.g., shifts in service venues, disruptions in services, and financing across youth and adult systems) further complicate care for transition-age youth.

This initiative would seek to address the gaps in available interventions and service delivery models through research employing a variety of research strategies. These efforts could address various target populations, in particular, seriously mentally ill youth, youth with multiple problems or co-occurring conditions, and youth in settings such as community mental health and residential treatment facilities, the juvenile justice system, as well as homeless youth. A goal of the effort will

be to promote the relevance and impact of the research to multiple stakeholders, including youth, families, providers, payers, and policymakers.

Discussion

Ms. Henry commented on the importance of this initiative given the experience in Delaware where children initially enter the child mental health system only to reenter the adult system a few years after they turn 18.

Dr. Essock noted that this area is an example of a high policy-relevant research where vast amounts of money are currently being spent in the publicly and private mental health systems and may be an ideal one for engaging partners to ensure the relevancy of proposed research. She also noted the importance of attaching monies to any announcement to encourage submissions.

Ms. Hellander suggested that NIMH reach out to organizations like the National Association of Therapeutic Schools and Programs, which is an organization of high-quality, innovative, therapeutic boarding schools and residential treatment centers.

Dr. Levitt noted that the knowledge base in this area of life transitions is extremely limited, from a neuroscience perspective. More activity in this area would create a natural interface between policy and science.

The Translational Research on the Relationship of Anxiety and Depression

Dr. Michael Kozak, Chief, Adult Psychopathology Research Branch, Division of Adult Translational Research and Treatment Development, explained that the background for this concept comes from several lines of evidence that indicate a relationship between anxiety and depression. For example: disorders of anxiety and depression are frequently comorbid, and the prevalence of depression has been found to be elevated among offspring with family histories of anxiety. Serotonin reuptake inhibitors are effective for both anxiety and depression, and emerging psychotherapy procedures for depression are employing exposure-like techniques that have been found effective for anxiety disorders.

Despite abundant findings demonstrating the magnitude of comorbidity, limited empirical research has examined the nature and causes of that comorbidity. This initiative is intended to stimulate increased understanding of the relationship of anxiety and depression by promoting the development and evaluation of specific hypotheses about this relationship.

Beyond an understanding of the causal relationship between anxiety and depression, there is a need to understand specific affective, biological, cognitive, and social mechanisms of the association. Elucidation of the mechanisms for the comorbidity of anxiety and depression could inform an understanding of the etiology and could suggest approaches for the refinement of assessment tools and intervention strategies. It is possible that mechanisms for comorbidity might differ for different subtypes of anxiety and depression, and research that parses these relationships might be important in understanding the nature of the comorbidity.

Developmental considerations are also important. Disorders of anxiety and depression often begin in childhood and adolescence. The onset of anxiety typically precedes that of depression and often follows a developmental sequence, with anxiety onset by middle childhood and depression onset during early to middle adolescence. With the exception of panic disorder and OCD, onset of anxiety disorder rarely follows the onset of major depression. Additionally, family studies suggest that anxiety is a precursor for depression among offspring of depressed parents. The sequential comorbidity of early anxiety and later depression is germane to understanding the development and the nature of their association.

Potential research topics include the mechanisms of co-occurring affect and cognition in anxiety and depression, integration of biological and psychological explanations of the relationship of anxiety and depression, the mechanisms of covariation in family studies of anxiety and depression, and childhood antecedents of later depression.

Committee Motion 2

Having been moved and seconded, all three concept clearances were accepted unanimously by the Council.

Public Comment

Ms. Joan Levy Zlotnik commended NIMH on the concept on youth transitioning to adulthood and for the recommendations of the Council Workgroup on Services and Clinical Epidemiology Research. She suggested that the National Governors Association and the National Conference of State Legislators might be partners in understanding how the issues of service delivery in mental illness impact policy and decision makers. In terms of implementation and barriers, it will be critically important to engage provider organizations as well as providers, including social workers, psychologists, the Veterans Administration, the Child Welfare Agency, and substance abuse agencies, as partners in future research activities.

Mr. Tim Nanof explained that he is a representative with the American Occupational Therapy Association (AOTA). AOTA gets much of its funding on general rehabilitation research through several NIH Institutes, including NIMH, as well as the Department of Education. He noted that the profession needs additional and continuing support related to the role and efficacy of occupational therapy in working with mental health treatment and rehabilitation.

The occupational therapy profession started about 100 years ago as an offshoot of the field of psychiatry. Recently, AOTA's leadership and membership have made the area of mental health a point of emphasis and an area of growth for the profession. At the AOTA annual conference in April 2006, the representative assembly approved a statement related to mental health and occupational therapy:

“Occupational therapy sees the growth of psychiatric rehabilitation as a re-emergence of a belief in the importance of meaningful activity or occupation in the lives of persons labeled with psychiatric disabilities in mental illness. The profession has been guided by

a holistic approach to therapy with an emphasis on psychosocial factors that impact human function. It brings a rehabilitation perspective to mental health treating, in keeping with increased emphasis on recovery and functionality. According to the Institute of Medicine's Quality Chasm Report on Mental Health Care and Substance Abuse Conditions, integration and collaboration among mental health practitioners is crucial to improving the mental health system. Occupational therapy is an essential part of the mental health assessment, treatment, planning, and intervention process, to improve and restore function and independence for people with mental illness. Through the use of real-life activities as therapy, occupational therapy practitioners improve functional capacity and quality of life for people with mental illness in areas of employment, education, community living, and home and personal care. AOTA sees the inclusion of occupational therapy as part of the core treatment team for people with mental illness, as an essential part of ensuring high-quality mental health treatment that is efficient and effective at delivering positive outcomes, reducing disability, and promoting recovery. Occupational therapy practitioners are already functioning as mental health professionals in many Federal settings, including Medicare, the Public Health Service, the United States Army, and the Department of Veterans Affairs. Finally, AOTA intends to continue to reach out to other associations representing mental health practitioners, as well as consumer advocacy organizations, providers, and Federal agencies and State programs, to develop a cooperative approach to including occupational therapy more frequently in mental health treatment, planning, implementation, and evaluation."

Dr. Insel suggested that AOTA consider membership in the Institute's Professional Coalition for Research Progress (see <http://www.nimh.nih.gov/outreach/index.cfm>).

Dr. Lloyd Sloan explained that he is a principal investigator at Howard University with the NIMH Career Opportunities and Research (COR) program. Speaking on behalf of the Nation's COR students, faculty, and directors, Dr. Sloan urged NIMH to sustain and expand the NIMH Undergraduate Honors Research Training Program because it is the only long-term training program that is designed to draw in underrepresented undergraduates. The predoctoral programs are valuable in accelerating the careers of these individuals, but the undergraduate program is nearly unique in being able to draw people into mental health research earlier in their careers. The COR programs have produced positive outcomes, and, without them, many of the approximately 1,000 trainees who have graduated and the hundreds of Ph.D.s would have gone elsewhere, as would most of their fellows. If the program is diminished, it will reduce this volume and the diversity that has resulted.

Dr. Sloan also explained that the participants in the COR program wanted to thank NIMH and particularly Dr. Nakamura for his efforts as a visionary champion for the COR program. For his tireless and dedicated and outstanding efforts, Dr. Sloan presented Dr. Nakamura with a book of thanks and admiration, which was signed by COR program students at the past National Convention in Atlanta in November. The book was assembled by the program's co-director at San Diego State, Dr. Theresa Cronin, and with it, Dr. Sloan continued, comes sincere thanks to Dr. Nakamura.

Dr. Nakamura responded that he looks forward with great pleasure to meeting with the students of the COR program and to see all the interested students who are eager to follow careers dedicated to helping those with mental disorders, and he thanked Dr. Sloan for his dedication to the program.

Ms. Cynthia Folcarelli said that she is with the National Mental Health Association (NMHA). She thanked NIMH for inviting members of the public to attend these meetings. She stated that NMHA is excited about the middle school curriculum presented today. It is important in terms of reducing stigma and bullying against students with mental disorders. The NMHA hopes that this curriculum supplement will encourage young people who are having symptoms of mental illness to tell someone and to seek help. Training a new generation of adults to have greater understanding of these issues is also important.

The NMHA is also pleased with the efforts of NIMH and others to translate science into service and policy. In order for that to happen successfully, findings must be translated into language that can then be used to educate consumers, providers, and the public about these issues and about the cutting-edge research findings. She also expressed concern about the reductions to Medicaid and acknowledged the support of individuals and groups who advocated for the needs of consumers with mental illness.

Turning to the findings that have been released from the CATIE and STAR*D trials, Ms. Folcarelli continued that these findings will refine the understanding of what treatments work for whom and in what circumstances. One concern is the impact of medication side effects on consumer recovery. Recovery cannot be achieved solely through symptom reduction, and side effects can have a significant negative impact on an individual's ability to recover and remain on medication. Clozapine is a case in point as providers may hesitate to prescribe it because of required monitoring for potentially serious side effects. It is important that NIMH consider the impact of findings as they translate to the real world in which people operate.

Several months ago, Ms. Folcarelli continued, a group of advocacy organizations, including NMHA, attended a meeting with NIMH and expressed concern about the misinterpretation of data that often happens in the media and that happened when the results from the first phase of the CATIE trial were published. The NIMH leadership took those concerns seriously and has been working with advocacy groups to find solutions and ways to work together to address that problem. Ms. Folcarelli expressed NMHA's thanks for NIMH's attention to this deep concern.

Ms. Folcarelli concluded her comments by announcing that David Shern, currently the Dean of the Luis de la Parte Florida Mental Health Institute at the University of South Florida, has been appointed as the new President and CEO of NMHA and will begin his official duties in June 2006.

Update: National Institute of Neurological Disorders and Stroke

Dr. Story Landis, Director, National Institute of Neurological Disorders and Stroke (NINDS), began her presentation by describing the mission of NINDS, which is to reduce the burden of neurological disease—a burden borne by every age group, every segment of society, and people

all over the world. To accomplish this goal, NINDS supports and conducts basic and clinical research on the normal and diseased nervous system including the brain, fosters the training of investigators in the basic and clinical neurosciences, and seeks better understanding, diagnosis, treatment, and prevention of neurological disorders. More than 600 diseases afflict the nervous system, and some of the more commonly known ones include stroke, epilepsy, Parkinson's disease, and autism, although many other neurological disorders are rare and known only to the patients and families affected, their doctors, and scientists who are investigating them.

NINDS shares research interests with other NIH components, including a focus with NIMH on Tourette syndrome (TS), Williams syndrome, autism, obsessive-compulsive disorder, and neurological diseases that often include psychiatric comorbidities, such as depression and epilepsy as well as depression and Parkinson's disease.

Dr. Landis described several activities that provide an opportunity for collaboration with NIMH, including a microarray consortium, a joint Request for Applications (RFA) to encourage collaborations between psychiatrists and neurologists, and the Gene Expression Nervous System Atlas (GENSAT)—a project initiated by NINDS but now with NIMH support. This project identifies and maps the spatial patterns and cellular localizations of about 12,000 genes in the mouse nervous system throughout development. An unintended result of this project has been generation of several new genetic research tools. GENSAT activities include in situ hybridization to rapidly screen approximately 1,100 genes per year to determine if, when, and where they are active in the mouse. Based on the expression patterns of some of these genes, an advisory committee that includes NIMH and NINDS program staff and investigators supported by NINDS, NIMH, NIDA, and NIAAA, selects a subset of the genes to be studied using bacterial artificial chromosomes (BAC) transgenic mice. The resulting data are placed on public Web sites, and all BAC mice are deposited in the University of California, Davis Mutant Mouse Regional Resource Center repository. One practical application of this innovative collaboration is in Parkinson's research where the discovery of completely different responses by the D1 and D2 neurons to dopamine loss is resulting in a new view of what loss of dopamine means for the striatum and is beginning to reshape approaches to therapies.

Dr. Landis explained that much has changed in the last 15 years in the field of neurology, including the availability of new treatments for diseases that did not exist in the past, such as the use of tissue plasminogen activator (tPA) for acute stroke. Twenty years ago, a stroke meant only watchful waiting to see if the patient recovered. Today, ischemic stroke patients who get to the hospital within 3 hours are treated with tPA, a clot buster; 30 percent of patients who are treated with tPA leave with no or minimal sequelae. Treatments are also now available for other illnesses, such as multiple sclerosis (copaxone and β -interferon), epilepsy (new antiepileptics), and the use of deep brain stimulation for Parkinson's disease and other disorders, including untreatable depression, dystonia, and Tourette syndrome. Recent advances in the neurosciences have dramatically altered the ways in which neurologists treat patients by providing the ability to remodel circuits in adult brains and the identification of a series of disease genes. The challenge is to harness these advances to increase the number of available therapeutics.

A decade ago, Dr. Landis continued, Parkinson's disease was believed to be almost entirely environmentally induced. Pioneering research conducted in the intramural program at the National

Human Genome Research Institute identified the first Parkinson's gene—alpha-synuclein. As a result, researchers began to explore the occurrence of Parkinson's in families, and today several genes are known to give rise to Parkinson's. The next step is to turn these genes into animal models to gain further insights into the pathogenesis of and therapeutics for Parkinson's disease.

NINDS has a commitment to support research on translating basic science findings into therapeutics, including treatments for rare diseases where there would be limited support for investigation outside of NIH. The oldest translational research at NINDS is an anticonvulsant drug screening program that has been in place for 30 years. This program is located at the University of Utah and represents a hierarchical series of *in vitro* and *in vivo* screens that are focused on epilepsy. More than 330 people have supplied compounds to this contract organization, creating a database of 25,000 compounds, structures, and their response in many different assays. Six of the eight newly approved drugs came through this system, and several are under investigation in clinical trials.

Spinal muscular atrophy (SMA) is a genetic disease that affects children and is caused by the absence of the SMN protein in motor neurons, which results in the death of those motor neurons. A second gene—SMN2—produces the same protein, although inefficiently, and the theoretical concept was to upregulate the expression from the second gene. NINDS has a contract with the goal of having one new candidate therapy ready for clinical trials by September 2007. To date, a target has been identified; medicinal chemistry has been completed; and a provisional patent has been granted on one of the BAC mice. This program is regarded by NINDS as a pilot program and may serve as a model for other rare diseases.

A new NINDS funding mechanism focuses on the steps required for therapeutic development, with the endpoint of an investigational new drug application (IND) or an investigational device exemption (IDE). Researchers can apply for this milestone-based funding if they have an assay or a candidate molecule related to any disease in the NINDS portfolio. Through this mechanism, NINDS is currently funding high throughput screens, development of animal models for screening, secondary screening in animal models from a high throughput screen, new uses for existing therapeutics, gene therapy, and stem cell therapy. A total of \$22 million has been set aside for this program.

Turning to the assessment of the cost/benefit ratio for clinical trials supported at NINDS, Dr. Landis referred to recently published results in *Lancet* (367:1319, 2006). The analysis included all Phase III trials completed before January 1, 2001, yielding a total of 28 trials at a cost of \$335 million. The projected net benefit for a 10-year period was \$15.2 billion. Dr. Landis provided three examples that were included in this analysis: tPA for stroke, indomethacin for prematurity, and external carotid/internal carotid anastomosis bypass for stenosis. In addition, Dr. Landis noted that although beta-interferon treatment for MS costs more than the gain in quality-adjusted life years, many MS patients would argue that individual MS patients derive significant benefit from its use.

Dr. Landis concluded her presentation with an overview of NINDS funding in fiscal year 2005. Approximately 72 percent of funding supported research project grants, 5 percent for centers, 5 percent for contracts, 4 percent for training, and 9 percent for research at the intramural program. She noted that 90-95 percent of grants are funded according to the payline, with uniform paylines

across the Institute clusters, adding that some high-priority applications scoring beyond the payline are funded. Program projects (P01s) are funded with no sunset provisions, and P30 core grants are funded. More than 25 F30s are funded per year, and K awards are restricted to clinicians (with the exception of diversity awards and translational research awards).

Discussion

Ms. Hellander asked whether there is a “best age” for studying a disease or for intervening when there are clear signs that it begins in childhood. Dr. Landis responded that with neurodegenerative and lysosomal storage diseases, the goal is to intervene as early as possible. For example, although Huntington’s disease is present throughout a person’s life, manifestation of neuron loss begins at a later age. Current research is studying people who are genotype positive but movement-disorder negative, and researchers are conducting psychological testing, movement-disorder testing, and imaging studies in an effort to identify Huntington’s 5 to 10 years before any movement disorder issues appear, an advance that would allow neuroprotection to start earlier. For Parkinson’s, by the time patients present in the clinic, they will have lost 60 percent of their dopamine neurons; methods are needed to identify patients when they have lost only 10 percent. Therefore, an effort is underway to conduct biomarker studies of some genetic families to attempt to identify the first thing they “lose,” for example, sense of smell or catecholamine metabolites in cerebrospinal fluid.

Dr. Levitt asked about NINDS’ philosophy about allowing access to university services or facilities that were started under the P30 program at NINDS. Dr. Landis responded that it is hoped that those facilities would be open to neuroscience investigators funded from other NIH Institutes.

Dr. Levitt also asked about what kind of initiatives in service research and implementation were being supported by NINDS and how NIMH and NINDS could work together to address the disparities in service provision for brain-based disorders. Dr. Landis acknowledged that NINDS has participated in activities to increase awareness of the availability and the need for outreach and patient/public education and that NINDS and NIMH could work together in this arena.

Adjournment

Dr. Insel adjourned the 212th meeting of the NAMHC at 1:05 p.m. on May 12, 2006.

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

Date: _____

Thomas R. Insel, M.D., Chairperson

APPENDIX A: REVIEW OF APPLICATIONS

| IRG Recommendation | | Research | Research Training | Others | Totals |
|---------------------------|----------|--------------------|--------------------------|-----------------|--------------------|
| Scored | Dollars: | \$1,021,587,410.00 | \$2,119,374.00 | \$57,115,085.00 | \$1,080,821,869.00 |
| | Number: | 761 | 245 | 81 | 1087 |
| Not Scored/NRFC | Dollars: | \$411,804,452.00 | \$0.00 | \$16,117,855.00 | \$427,922,307.00 |
| | Number: | 473 | 0 | 24 | 497 |
| TOTAL | Dollars: | \$1,433,391,862.00 | \$2,119,374.00 | \$73,232,940.00 | \$1,508,744,176.00 |
| | Number: | 1234 | 245 | 105 | 1584 |

APPENDIX B: COUNCIL ROSTER
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NATIONAL INSTITUTE OF MENTAL HEALTH
NATIONAL ADVISORY MENTAL HEALTH COUNCIL
(Terms end 9/30 of designated year)

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