Seventh Annual Research Roundtable
June 10, 2003 Washington, DC

Organized by the National Institute of Mental Health (NIMH) Office of Constituent Relations and Public Liaison. Gemma Weiblinger, Director. 301-443-3673. For comments or questions, e-mail Alison Bennett: OCRPL@mail.nih.gov

AGENDA | **ROSTER** | **DIRECTOR'S REPORT** |

The NIMH held its Seventh Annual Research Roundtable Tuesday, June 10, 2003, at the National Press Club in Washington, DC.

The Roundtable is integral to NIMH's priority-setting process by providing a critical forum for the Institute to exchange information with interested organizations and groups. Equally important, it enables NIMH to learn the views and concerns of those constituents who are most interested in helping it to build a carefully planned research program. The purpose of the Roundtable is to bring together the NIMH Director and staff with consumers, providers of mental health services, family members, research scientists, representatives from advocacy and professional organizations, and others with an interest in mental health.

NIMH Director Thomas R. Insel, M.D., opened this year's meeting with a welcome and discussion of the "State of the NIMH." This year's Roundtable was privileged to hear presentations from these distinguished NIMH researchers:

- Ellen Frank, Ph.D., Director of the NIMH Mental Health Intervention Research Center, Department of Psychiatry, Western Psychiatric Institute and Clinic, University of Pittsburgh Medical Center, told participants about her research on individualizing psychotherapeutic treatments for depression;
- Charles B. Nemeroff, M.D., Ph.D., Reunette W. Harris Professor and Chairman of the Department of Psychiatry and Behavioral Sciences at Emory University School of Medicine in Atlanta, Georgia, presented depression as a disease of the whole body;
- Nina R. Schooler, Ph.D., Director of Psychiatry Research at the Zucker Hillside Hospital, North Shore Long Island Jewish Health System, discussed the early course of schizophrenia and implications of treatment; and
- Dennis S. Charney, M.D., Chief of the NIMH's Intramural Mood and Anxiety Disorders Program, shed light on the psychobiological mechanisms of resilience and vulnerability.

Following a break that gave Roundtable partners and speakers an opportunity to interact with each other and with NIMH staff, the meeting reconvened and NIMH staff presented updates:

- Jane L. Pearson, Ph.D., Associate Director for Preventive Interventions in the NIMH Adult and Geriatric Treatment and Preventive Intervention Research Branch of the Division of Services and

Intervention Research, told the Roundtable partners about NIMH research efforts to reduce suicidality; and

- Wayne Fenton, M.D., NIMH Associate Director for Clinical Affairs and Deputy Director for Clinical Affairs of the Division of Mental Disorders, Behavioral Research, and AIDS informed the group about the new Measurement and Treatment Research to Improve Cognition in Schizophrenia program (MATRICS).

The last hour of the meeting was devoted to open discussion.

Thomas R. Insel, M.D., NIMH Director, talks to participants at the 2003 Research Roundtable.

CHAIRING THE "SQUARE" TABLE

Dr. Insel told the Roundtable members he was looking forward to the meeting with great anticipation. (Director's Report) He said participants would hear from real stars of NIMH's research community and get an excellent sampling of the Institute's exciting research endeavors. He reminded them that a most important goal for the meeting was to hear from them.

Dr. Insel thanked Dr. Nakamura for his dedication and hard work in leading NIMH as Acting Director, and said he took over with the spirit of furthering what Drs. Hyman and Nakamura had spearheaded.

CORPORATE NIH

Next, Dr. Insel told the Roundtable about changes at NIH under the new directorship of Dr. Elias Zerhouni. All the major brain institutes have (or will soon have) new directors. Dr. Zerhouni appointed Nora D. Volkow, M.D., as the new director of the NIH's National Institute on Drug Abuse and Ting-Kai Li, M.D., heads the National Institute on Alcohol Abuse and Alcoholism. [Since the meeting, Story C. Landis, Ph.D., was selected as the Director of the National Institute of Neurological Disorders and Stroke.]

Dr. Insel said he believes in alliance building, and he's confident these institutes can work better together. It helps that all of the new directors have similar interests, background, and visions. He also indicated that Dr. Zerhouni has been making changes at NIH, particularly in the area of corporate management. Rather than strategic planning, Dr. Zerhouni has conceived "road mapping" as a way to lead and encourage trans-NIH research. There are 15 different planning committees. A benefit of the planning, Dr. Insel said, has been that Institute/Center Directors and staff have learned much about each other's work, particularly in the fields of (1) technology development; (2) training the next generation of clinical investigators; and (3) reengineering the clinical research enterprise.

Over the five years, there has been significant growth in the NIH budget, which has doubled since 1998. While the NIMH budget has not doubled, it has achieved an 80% increase that has allowed the Institute to try out new ideas. The NIMH budget is $1.35 billion in FY 2003. (For more about NIMH history, see http://www.nimh.nih.gov/about/history.cfm.) However, since increases around 3% are expected over the next few years, it will be necessary to look for ways to prolong good investments and opportunities.

PROMISING AREAS FOR FUTURE RESEARCH

Dr. Insel told the group about three areas that will continue to be emphasized under his leadership:

- Translational research
- New therapeutics
- Services research

Translational Research. Dr. Insel expressed satisfaction that NIMH is beginning to take findings from neuroscience and bring them into clinical science. But the most compelling scientific development has been the announcement on April 14, 2003, of the completion of the sequencing of the human genome under budget and on schedule. It is certain that most mental illness is the result of multiple genes interacting with the environment. There are approximately 30,000 genes, half of which are expressed in the brain. The most important genes are yet to be identified. "It is a little like embarking on a discovery of a new continent with Lewis and Clark, where only 5% of the continent is mapped," Dr. Insel remarked.

While we are finding vulnerability genes, what genomics will be about is understanding variations and how they play out in behavior. New research is demonstrating that there is a continuous vulnerability, and that environmental factors and genetics are multipliers, which, when combined may collectively take a susceptible person into illness. The science of mental illness is maturing in many ways. Genome sequencing and spectacular discoveries in animal studies have yielded insights that can be applied in humans. Also, remarkable progress is being made in the development of tools such as neuroimaging that make the brain more visible — it is no longer a black box. In Dr. Insel's words, "We have the alphabet — the book needs to be written."

Development of Therapeutics. Although we don't always understand their exact mechanisms of action, we are blessed by the availability of medications that work. People get well, but we don't talk about cure. Dr. Insel suggested that perhaps we need to become more ambitious in talking about developing cures or interventions that are more effective. Dr. Insel believes we need to have a have a vision that reaches all the way to curing mental illnesses.

Services Research. Services research is a vital component of the NIMH mission. Dr. Insel observed it is critical that information we gain through research be used as quickly as possible. Unfortunately, in many ways care delivered today is of poorer quality than that of 20 years ago. A major problem is that care remains outside of traditional health care systems — too many people suffering from mental illness are lost in prisons, nursing homes, and schools. Access to mental health care is a tremendous problem. There are 140 million rural Americans who have little access to services.

Dr. Insel emphasized that he greatly values his partnerships with the Roundtable members; they are vital to him as director. He said, "You need us to help you with the latest research findings, the epidemiology, and clinical successes. We need you just as much to get our findings out into the communities. We understand where our energy needs to go. Your input is crucial." Dr. Insel stressed that "I am a public servant who wants to hear your ideas about how we are to accomplish our mission."

DISCUSSION

Thomas R. Insel, Director, NIMH, and Richard K. Nakamura, Ph.D., Deputy Director, NIMH.

Mary Guardino, Executive Director of Freedom From Fear, asked Dr. Insel what NIMH thought about the crisis in Medicaid. Dr. Insel said that NIMH is focusing on how to get medications that work to people, but noted that it is a difficult challenge.

We have better medications than ever, but they can be prohibitively expensive for the state and local providers. He then said that NIMH and advocates — together — can collaborate with the pharmaceutical industry to harness a tremendous energy to work toward common goals.

Dr. Insel noted that orphan indications need support, yet at the present time, the industry does not seem to be interested in new indications for old drugs. But there is activity and progress. NIMH is working with industry to develop drugs for cognitive deficits for schizophrenia.

Dr. Fenton discussed this in greater detail later in the day. NIMH has been working with the Food and Drug Administration (FDA) to convince them that cognition is a worthy and testable endpoint for medication. Ms. Guardino said that the medication issue is a looming crisis, a catastrophe. Dr. Insel encouraged the Roundtable members to continue to lobby on behalf of their constituencies using the data and evidence that NIMH can provide.

Marilyn Benoit, M.D., President of the American Academy of Child and Adolescent Psychiatry (AACAP), also spoke in support of NIMH services research. She asked that increased attention be placed on disseminating research findings. In her view, the community needs to know what works, what is described as “science to service and service back to science” in cooperation with SAMHSA.

Dr. Insel agreed that this is critical. The Institute is looking forward to the final report of the President’s New Freedom Commission on Mental Health. The Commission conducted a comprehensive study of the United States mental health services delivery system. Its report will advise the President on implementable, evidence-based methods that can be put into action by all facets of the public and private mental health service sectors to improve coordination and quality of services.

Members were also concerned about the importance of alternate settings for care. They wanted to know if NIMH was funding research in this area and if it is a priority of the Institute. Dr. Insel told the group that NIMH’s services research portfolio has been growing in this area. He asked for their views about service settings where recipients of care are experiencing good outcomes and what works. Determining what is successful in these settings is not easy. Recently an NIMH grantee, Dr. John Rush reported preliminary results from the STAR*D trial, showing that SSRI “effectiveness” in a primary care environment may not be as great as the “efficacy” reported in academic settings.

SPEAKERS

Ellen Frank, Ph.D. "Individualizing Psychotherapeutic Treatment for Depression"

Ellen Frank, Ph.D., is Director of the NIMH Mental Health Intervention Research Center, Department of Psychiatry, Western Psychiatric Institute and Clinic, University of Pittsburgh Medical Center.

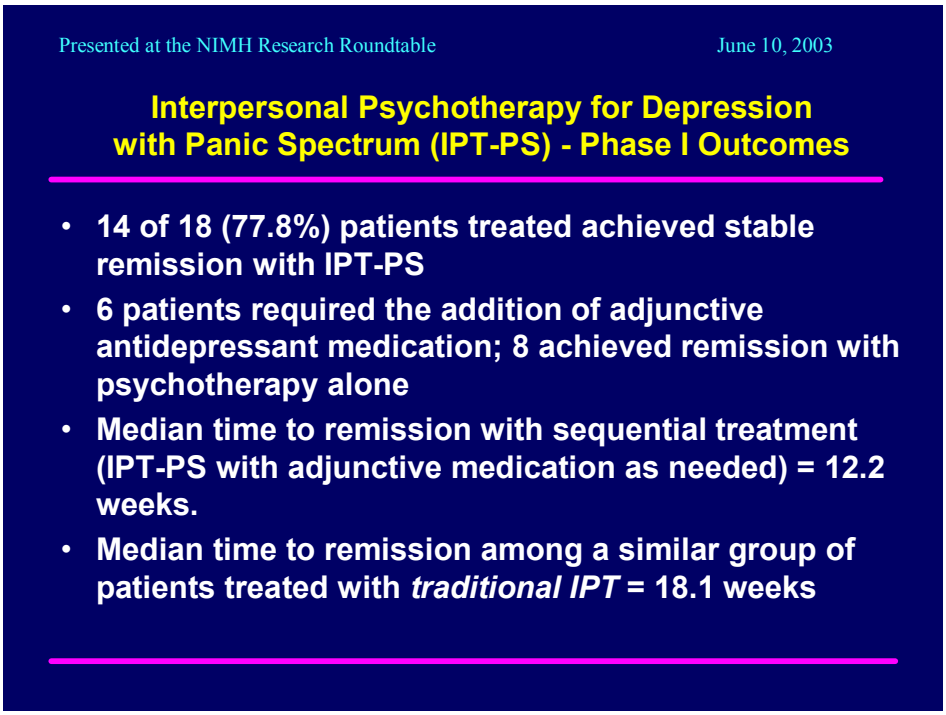

Dr. Frank addresses the NIMH Roundtable.

Dr. Frank told the Roundtable members about some of the "ways we are hacking away at Dr. Insel's goal of a cure." When looking for "cures," researchers are keenly aware that people come in many shapes and sizes. Her team is looking at what will lead to full remission of symptoms and foster a full return of functioning. The problem is many patients get better but not well.

Dr. Frank said the NIMH Strategic Plan for Depression states that "we need to learn what to do when the first treatment applied is not efficacious, as is generally the case in 35% to 55% of patients." With this goal in mind, her group has developed a way to think about depression that takes a dimensional approach, seeing it as a spectrum disorder. Many depressed patients have a presentation that includes multiple symptoms of anxiety with fears, avoidant coping, and panic attacks. Often it has been possible to diagnose these patients with comorbid disorders, but Dr. Frank's group has determined that subsyndromal manifestations of disorders may also be important. People with these symptoms are unlikely to be adequately treated by antidepressants or interpersonal therapy (IPT) alone. Such patients may never have had a panic attack but would not want to wear a turtleneck or use a seatbelt, or might feel frightened when they do not have a clear view of the horizon, for example. These panic and agoraphobic symptoms need to be targeted, as well as the depressive symptoms. When the panic-like symptoms are treated, patients have clear-cut, sustained remission and improved enjoyment in their lives.

Next, Dr. Frank presented results from a study in which treatment modifications were made to engage and retain the most challenging patients. She discussed results of an NIMH K award to Holly Swartz, M.D., for "Treating Depressed Mothers in a Community Clinic," where the focus is on adapting interpersonal psychotherapy to the needs of depressed mothers of children with mental disorders. For this study Dr. Swartz developed a specific course of brief IPT that is achieving good results. The study involves eight weekly sessions that focus on one resolvable problem, using the finite amount of time in treatment as leverage. Not only does this brief form of IPT seem to be associated with a reduction of depressive symptoms, the patients' symptoms were still under control six months after treatment. Dr. Frank said that they are making plans for a larger multisite trial.

Dr. Alan Kraut, Executive Director of the American Psychological Society, asked Dr. Frank if she knew the "active ingredient" of IPT. Dr. Frank said the insistent focus on the present and the future is key. The emphasis is such that the depressed person has little time to worry about the past or to ruminate. The therapy concentrates on their current interpersonal relationships. For patients with depression and panic-like symptoms, there is also a strong somatic focus; they are taught that all emotional arousal is not panic and that a person can survive arousal.



Results from a trial that modified standard interpersonal therapy (IPT) to address symptoms of panic syndrome (PS). [Shown by Ellen Frank at the NIMH Research Roundtable, June 2003.]

As an introduction for the next speaker, Dr. Insel reminded the Roundtable that depression, in reality, is much more complicated than textbooks tell us. It is a delicate interplay between body and brain.

Charles B. Nemeroff, M.D., Ph.D. "Depression is a Disease of the Whole Body"

Dr. Nemeroff is the Reunette W. Harris Professor and Chairman of the Department of Psychiatry and Behavioral Sciences at Emory University School of Medicine in Atlanta, Georgia.


Dr. Charles B. Nemeroff

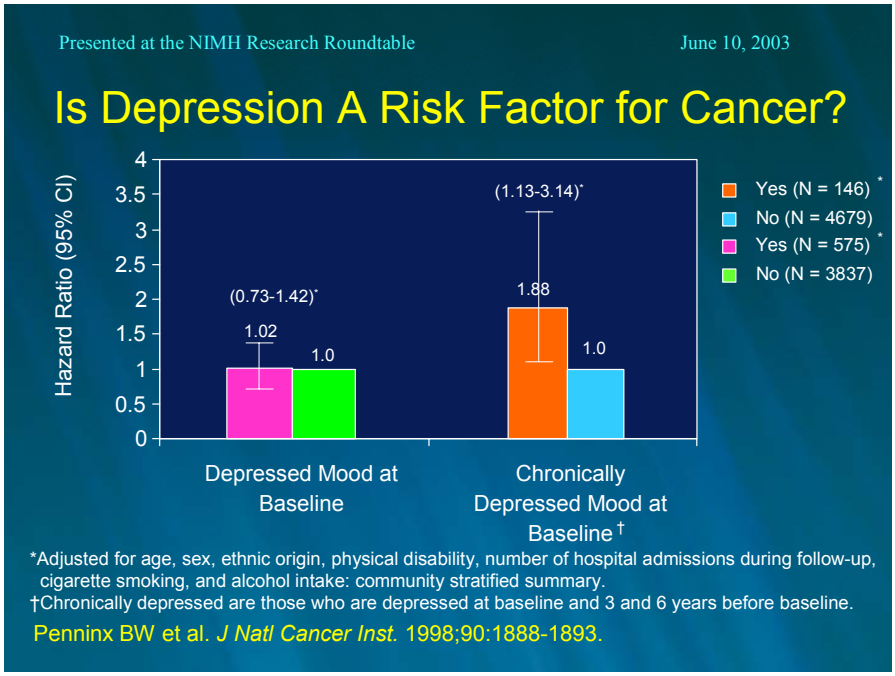
Dr. Nemeroff began his talk by telling the story of an OB-GYN patient with cancer he had at the beginning of his medical school career whom he treated for depression against his supervisor's orders. His supervisor did not see the need to treat the depression. Dr. Nemeroff said this was a galvanizing point for him in his decision to become a psychiatrist.

He said rates of depression vary with the type of comorbid disorders: 9-27% of diabetes patients are depressed, 22-50% of stroke patients are depressed, and 18-39% of cancer patients are depressed. This varies further by type of cancer: people with pancreatic cancers have higher rates of depression (50%) and patients with leukemia are rarely depressed, while 50% of Parkinson's patients have major depression.

Among people who have suffered heart attacks, 15-25% are depressed. People with depression die more often after having heart attacks. Even when two people have equal medical morbidity, a depressed person is more likely to die; the finding appears to be related to the severity of depression. This is also

true for people with congestive heart failure. Depression is a risk factor as significant as smoking for the development of cardiovascular illness.

Dr. Nemeroff described evidence that depression might be partially the result of sticky platelets contributing to clotting. Using results from a trial with paroxetine, he showed that before treatment, a measure of platelet activation in patients with major depression was significantly increased compared with normal controls. After six weeks of paroxetine treatment, platelet activation was reduced and not significantly greater than in normal controls. This effect seems specific to the selective serotonin reuptake inhibitor (SSRI) antidepressants. There is evolving evidence that alterations in cellular and humoral immune mechanisms may play a role in promoting inflammatory processes involved in heart disease and these processes may also contribute to increased risk for patients with depression.



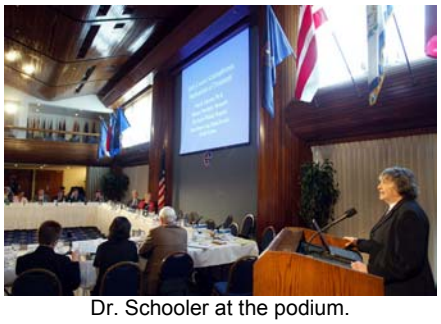
Is Depression a Risk Factor for Cancer? [Shown at the NIMH Research Roundtable, June 2003].

To date, studies have demonstrated that antidepressants are effective in treating comorbid depression. However, much more study is needed because there have been few placebo-controlled trials with a limited number of patients and poor methodology.

High rates of major and minor depression were also found in stroke patients. If a patient was depressed post-stroke, he or she was less likely to survive treatment. Predictors of post-stroke depression include disability, depressive symptom severity, history of mood disorder, stroke severity, pathological crying, and stressful life events. Like heart disease, stroke is often preceded by depression.

Dr. Nemeroff suggested that in view of the risk of heart disease in depressed patients, mental health professionals need to ask if patients have had chest pain, an EKG, or a stress test. Depression must be treated as a risk factor.

Nina Schooler, Ph.D. "Early Course of Schizophrenia: Implications of Treatment"


Dr. Schooler at the podium.

Dr. Schooler is the Director of Psychiatry Research at the Zucker Hillside Hospital, North Shore Long Island Jewish Health System.

The Zucker Hillside Hospital is a psychiatric hospital that has pioneered clinical trials for schizophrenia and the study of long-term course of early phases of the illness. For Dr. Schooler, schizophrenia has been a lifetime calling. She said it represents the essence of the problem we face with mental illnesses. The neurocognitive deficits are striking and 20% of patients are not responsive to treatment. Relapse and poor social functioning are common. Many patients quit taking their medications, which puts them at a very high risk for relapse. She showed evidence of the importance of continuing to take medication after the resolution of a first episode of schizophrenia. In a study of 28 patients, none of the people taking antipsychotic medication relapsed, while seven on placebo did.

Further, even "recovery" is not cure. Only 14% of people had full recovery after five years. Knowledge about characterization of the early course of schizophrenia has expanded remarkably in the last 20 years. What characteristics predict recovery? Good cognition, greater structural brain asymmetry (which characterizes normal brain structure), and a shorter duration of psychotic symptoms before beginning treatment are predictors.

Dr. Schooler next told the Roundtable members that there are a large number of "high risk" studies — over 30 years worth of research studying people at high genetic risk for schizophrenia. More recently, attention has turned to studies of adolescents at high clinical risk. One of these studies at the Zucker Hospital is the Recognition and Prevention (RAP) program, a clinical program for adolescents that includes research participation for consenting patients and families. The research goals of the RAP are to identify neurocognitive and clinical predictors of schizophrenia in at-risk adolescents, and to develop and evaluate pharmacological and psychosocial interventions. Data show social withdrawal and social isolation are prominent symptoms, suggesting the value of psychosocial interventions. Patients most amenable to interventions are those whose cognitive impairments are less global than individuals who have already developed the disorder. Dr. Schooler stated that much progress has been made in understanding the early course of schizophrenia, and characterization of the disease's early stages may lead to improved treatment and eventually to prevention.

Presented at the NIMH Research Roundtable June 10, 2003

Recovery in First Episode Schizophrenia (N = 118)

Year in Study	Sustained Symptom Remission (%)	Sustained Social/Vocational Recovery (%)	Full Recovery (%)
3	25	16	10
4	32	21	12
5	47	26	14

Robinson et al. *American Journal of Psychiatry*, in press.

Recovery in First Episode Schizophrenia. [Shown at the NIMH Roundtable June 2003.]

Dennis Charney, M.D. "Psychobiological Mechanisms of Resilience and Vulnerability"

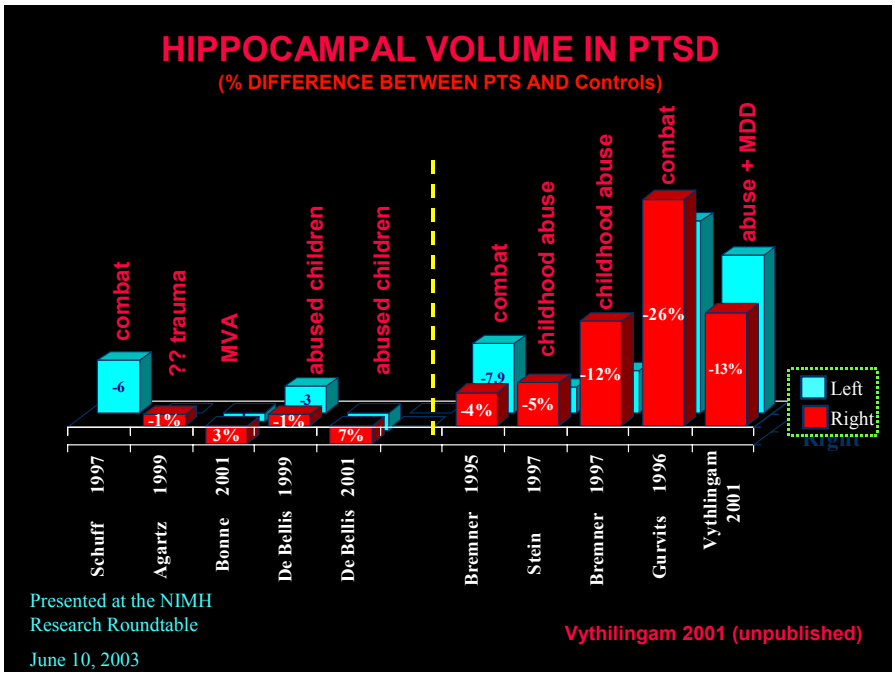
Dr. Charney is Chief of the Mood & Anxiety Disorders Program in the NIMH Intramural Research Program.

Dr. Dennis Charney

Dr. Charney told the Roundtable about individual traits, like optimism, altruism, and an active coping style, that seem to facilitate resilience or protection from depression or other mental illnesses. He talked about several historical figures, such as Theodore Roosevelt, who exemplified resilience. He said there were a number of factors that undoubtedly combine to produce individual resiliency in the face of psychological and physical trauma, including genetics, physiology, and psychology, and there were particular efforts underway looking for resilience genes.

He told about his research with Survival, Evasion, Resistance and Escape (SERE) — the brutal program of survival training in the military, during which Special Forces candidates undergo weeks of grueling emotional and physical stress, including sleep deprivation and excruciating physical demands to prepare them for capture and interrogation by the enemy. "Stress inoculation" and operant conditioning are key principles of SERE training. Cortisol, corticotrophin-releasing hormone (CRH), and dehydroepiandrosterone (DHEA) responses were measured in troops before, during, and after SERE training; the higher the DHEA/cortisol rates, the higher the SERE trainees were rated on performance by instructors. Acute stress caused changes in hormonal patterns, and the *patterns* are key. Hormones are thought to play key roles in mental illnesses. For example, CRH is elevated in people with post-traumatic stress disorder (PTSD), so hormones could be effective treatments. Several drug companies are interested in CRH antagonist as a new class of treatment and NIMH is doing pre-toxicology studies for a CRH antagonist. In the amygdala, neuropeptide Y is associated with reduced stress-induced anxiety and depression. Galanin is also a new target of investigation for the same reason. A beta-blocker that gets in the brain, propranolal blocks the effects of arousal on memory and can block effects of adrenaline to keep PTSD from ensuing.

Dr. Charney posed the question whether stress can alter the structure and function of the brain, then described how stress alters neuronal structure and impairs neurogenesis. In experiments with rats, CRH administration early in life resulted in long-term progressive hippocampal neuronal loss. In humans, smaller hippocampal volume predicts pathologic vulnerability to psychological trauma and is a risk factor for PTSD. Research has shown that antidepressants can reverse or prevent stress effects on the hippocampus, yet many unanswered questions remain.



Hippocampal Volume in PTSD, % Difference Between Patients and Controls. [Presented at the NIMH Research Roundtable June 2003.]

Jane L. Pearson, Ph.D. "Update on NIMH Update on Reducing Suicidality"

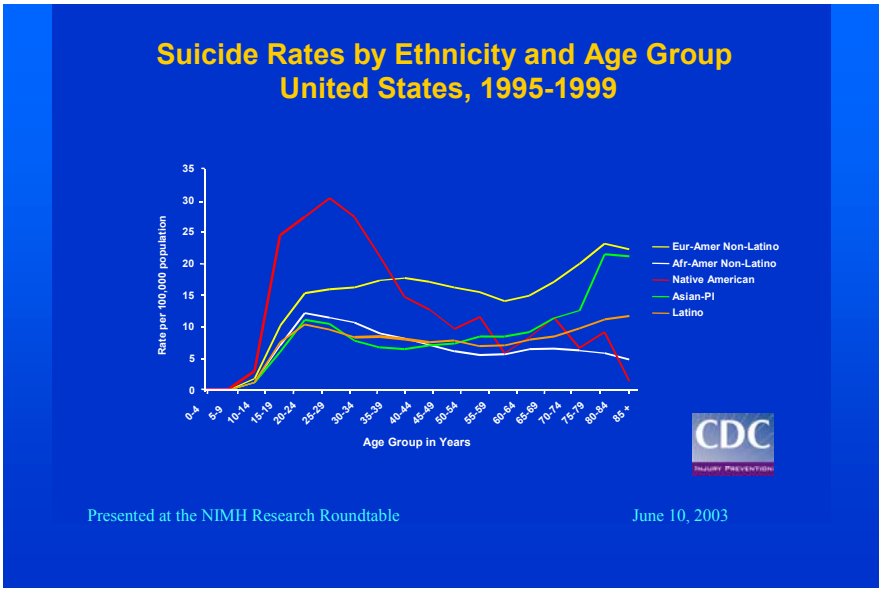
Dr. Pearson is the Associate Director for Preventive Interventions in the Division of Services and Intervention Research, NIMH.

NIMH Associate Director Dr. Jane Pearson talks about suicide.

Dr. Pearson gave a brief update about what is unique at NIMH about research on suicide, highlighting that suicide accounts for 50% of all violence-related deaths globally and, in the United States, suicides outnumber homicides five to three. She went on to explain that data indicate there are also many suicide attempts that cause significant suffering to individuals and families. An interesting slide showed how suicide rates vary with age and ethnicity: the highest rates for young people occur among Native Americans; highest rates at the end of life occur in European Americans and Asians; and African Americans, particularly women, have significantly lower rates of suicide. Science needs to study this resilience.

Dr. Pearson showed the Roundtable several examples of NIMH research on suicide, saying that the good news is that we can do trials safely and fairly, and our large contract and cooperative agreement trials, such as STEP-BD, STAR*D, and CATIE, are working to include suicidal patients. Researchers, with some NIH coordination, are sharing their measures, data, and findings. Other NIMH efforts are examining the feasibility of following up early prevention trials for suicide, accidental and homicide deaths, culture and suicide, and safe and effective approaches to public service messages on suicide. Workshops have been held on the effects of suicide on significant others and NIMH is funding developing centers on suicide prevention and intervention with the National Institute on Drug Abuse and the National Institute on Alcohol Abuse and Alcoholism for 2004. Dr. Pearson also cited promising findings from outside of NIMH, such as Air Force community-based prevention efforts that yielded a significant reduction in suicide and accidental deaths.

She concluded with future challenges that included the need for more researchers and new ways to measure progress.



Suicide rates by ethnicity and age group in the United States from 1995-1999. [Shown at the NIMH Research Roundtable June 2003.]

Valerie Porr, President of the TARA National Association for Personality Disorder, wanted to draw attention to the costs of suicide to the surviving family members. She also recommended collaborations with the pain field.

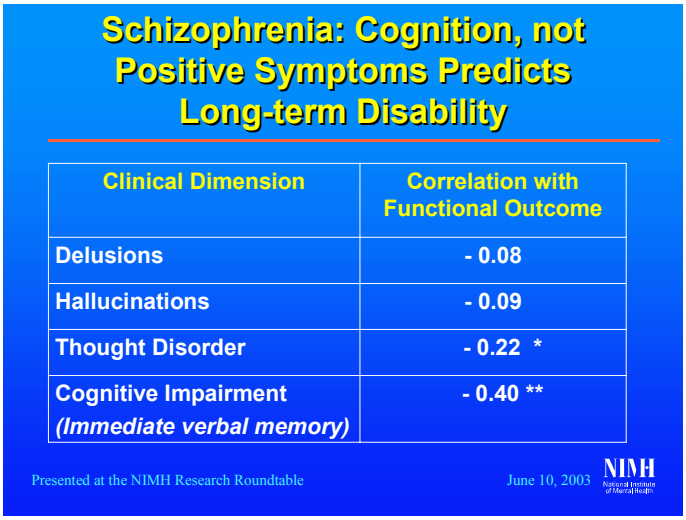
Mary Guardino said that suicide is very complicated and indicated that 70% of suicide victims had seen their primary care doctor shortly before their suicide.

Gerald H. Weyrauch, M.B.A., Executive Director, Suicide Prevention Action Network USA, Inc., thanked Dr. Pearson for being on the agenda at the Roundtable and Dr. Nakamura for his willingness over the years to discuss suicide in his own family.

Wayne S. Fenton, M.D. "Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS)"

Wayne S. Fenton, M.D., is the Deputy Director for Clinical Affairs in the Division of Mental Disorders, Behavioral Research and AIDS, as well as the Associate Director for Clinical Affairs of the NIMH.

Dr. Insel introduced Dr. Fenton, noting that Dr. Fenton has picked up where Dr. Schooler left off. Despite a decade of development of new drugs for schizophrenia, our treatments are limited. Currently, only one in five persons with schizophrenia sufficiently recovers to work and approximately 90% with a first episode will relapse. All current medications were developed to target positive symptoms, but research over the last decade has indicated that cognition, not positive symptoms, predicts long-term disability. Dr. Fenton asked, "Have we reached a ceiling with available drugs?"



Cognition, not positive symptoms, predicts long-term disability in schizophrenia. [Shown at the Research Roundtable June 2003.]

Dr. Fenton told the Roundtable that NIMH is only a small player in pharmacological treatment development, yet the Institute can make a significant contribution. Unique roles for the public sector can include discovery of new molecular targets, defining new clinical targets and promoting consensus regarding new clinical endpoints for treatment. NIMH can complement industry efforts by initiating convening activities that bring together a broad range of academic, industry, and government experts to address methodological and measurement issues that must be overcome to develop new treatments. One important target for new treatments is cognitive impairment. NIMH is developing a standardized instrument to measure cognition in schizophrenia as an endpoint in clinical trials and working with FDA to define methodological issues that must be overcome to demonstrate efficacy for a cognitive agent in schizophrenia. These efforts should provide a blueprint to facilitate pharmaceutical company efforts to bring new compounds to market.

NIMH has two initiatives on cognition in schizophrenia: MATRICS (Measurement and Treatment Research to Improve Cognition in Schizophrenia) and TURNS (Treatment Units for Research on Neurocognition and Schizophrenia). One award under the MATRICS contract will promote development of novel compounds to enhance cognition in schizophrenia, catalyze regulatory acceptance of cognition in

schizophrenia as target for drug registration, and focus economic research power of industry on this neglected clinical target. Dr. Fenton told the group that TURNS will create a network to identify, obtain, and test efficacy of new agents targeting cognition in schizophrenia; develop and validate clinical trial methodology; and conduct two NIMH-supported trials. The goal is for four sites to be awarded in September 2004 to become national resources that are autonomous — funded by federal grants, foundations or independent support. Dr. Fenton said it is possible that the psychopharmacology of the future will see disorders listed in the Diagnostic and Statistical Manual of Mental Disorders (DSM) dissected into dimensions so new clinical targets are more proximate to pathophysiology. New molecular targets will be sought with clinical effect on currently untreated dimensions of psychopathology.

Dr. Insel said these initiatives are very focused and targeted, using the contract mechanism and will certainly further our work toward the common goal of reducing the burden of illness. This is an example of an area where the Institute is being more directive, yet working in partnership. It is a specific opportunity to develop public/private partnerships.

Ms. Porr said this should be the model for every disorder. There first needs to be a national conference to take stock, next an assessment of needs, and then the development of a strategic plan. She asked if the Institute had plans to look at cognition in children, saying there are subtle predictive signs in the first decade of life that we currently are unable to measure. It may be possible to predict at age 10 who will develop mental illnesses.

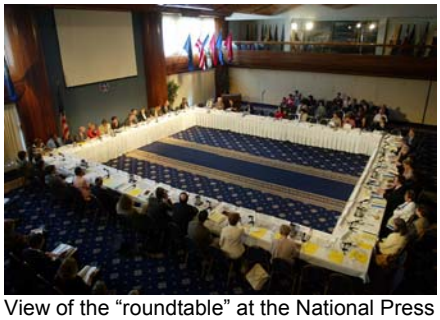
Dr. Insel replied there are several problems standing in the way of our being able to predict future mental illnesses. NIMH is looking at illnesses retrospectively and also conducting normative studies, but more need to be completed. Predictive models need to be refines and one way to do this is through genetic high-risk studies of offspring and siblings.

Mary Guardino suggested NIMH should go beyond medications; psychosocial methods should be developed using MATRICS methodology. For example, exercises on computers can be help build cognitive capacity and help people adapt to limitations.

A Roundtable member asked Dr. Fenton if the MATRICS-developed cognition measures could be used for attention deficit/hyperactivity disorder or autism. He said the specific cognitive defects are different across these various disorders. Behavioral and cognitive approaches would need to be adapted for the specific mental illness.

Anne Carpenter, Vice President of the Autism National Committee, said too much has been made of communication problems in people with autism. She said cognitive abilities of people with autism are being underestimated.

AROUND THE TABLE



View of the “roundtable” at the National Press Club. After focusing on the specific topics presented by the morning speakers, Dr. Insel asked each attendee for feedback.

Joel Streim of the University of Pennsylvania, representing the AAGP, suggested that aging research has elucidated concepts and models that inform mental illness research. For example, the dysfunction in multiple systems, highlighted by Dr. Nemeroff, has been a subject of research on aging and comorbidity for some time. Similarly, the concepts of "frailty" and "failure to thrive," that continue to emerge from aging research, may support the model of allostatic load as an important mechanism of illness, declining function, and disability, as described by Dr. Charney. These concepts and models should serve as a foundation for integration of aging and mental health research within NIMH and across Institutes.

Dr. Marilyn Benoit of the AACAP said there is a major need to focus on infants, children, and adolescents. Understanding developmental psychopathology is critical, particularly in special populations, such as abused and neglected children, gay, lesbian, and trans-gendered youths, and different ethnic groups. She asked that this be a topic on next year's agenda.

James S. Bernstein, Director, Government and Public Affairs, American Society for Pharmacology and Experimental Therapeutics, brought up the importance of training for research. Training integrative scientists is important; molecular biologists have been emphasized while training of scientists who can study the whole animal or do whole organ work has been neglected. He said that full organ biology needs strengthening. Industrial partners need these types of thinkers as well. Existing mechanisms for developing such researchers need to be exploited.

Dr. Insel said this type of research was a call to physiology and that as a discipline it seems to have disappeared. NIMH spends a great deal of its budget on training – its training budget is the second highest among NIH institutes. NIMH has focused on molecules and genes; a return to studying whole organs, as well as behavior, is crucial. Dr. Insel asked for the Roundtable partners' help in emphasizing to other institutes the critical importance of behavior research with whole organ models.

Paul S. Appelbaum, M.D., from the University of Massachusetts Medical School, representing the American Psychiatric Association as its Immediate Past President, said the current economic squeeze in academia has made recruitment difficult, with a significant impact on research training. Academic departments bear considerable costs associated with training awards such as K awards or T32s. He suggested NIMH be more creative in funding training. He pointed to the reality of the world outside of academic medicine and said the service system is being taken apart piece by piece. He noted that data is inadequate mainly due to time lags. There is a need for rapid analysis mechanisms, not just more services research. A grant may take five years and the services system changes significantly in that time. Finally, we need grant opportunities to look at changes in the service sector.

Dr. Insel commented that this brought to mind the situation with AIDS a few years ago when by the time something was published, it was old news. NIMH does have rapid mechanisms that may be used in certain situations — most recently awards were made following the terrorist attacks on September 11, 2001. RAPID grants have abbreviated review and are used to collect data in emergency situations.

Another new program that is helping to strengthen training at NIH is the loan repayment program. NIMH is hoping to fund 100 of these awards to physicians or Ph.D.s. The program offers $50,000 per year to an individual, but unfortunately, demand for these funds far exceeds the supply and NIMH cannot fix problems in the training sector alone. However, there are more things the Institute can do to make research careers easier, such as forming partnerships with the Roundtable members to make training better.

Jerilyn Ross, M.A., L.I.C.S.W., President and Chief Executive Officer of the Anxiety Disorders Association of America, offered thanks for a stimulating morning. Then she brought up accessibility to and affordability of government-funded behavioral/psychosocial treatments, such as manuals. The researchers who have the data and develop the treatment manuals control the access; treatment becomes prohibitively expensive. There are great cognitive behavioral treatments that could be more widely delivered.

Dr. Insel said he was not aware of this issue. While government contributions to medication development have been much discussed, proprietary control of behavioral treatments has not been highlighted. NIH has had a genetic data-sharing policy for some time. Treatments for HIV have been manualized on CD-ROM and passed on. NIMH has developed a specific list of treatments with sufficient evidence and is cooperating with SAMHSA on how best to train mental health care workers and to disseminate these treatments.

Anne Carpenter, Vice President of the Autism National Committee (ANC), said Dr. Insel's use of the word "cure" is problematic. She said the members of the ANC do not see themselves in need of a cure. She

remarked that autism is a spectrum of disorders that causes people with these symptoms to behave in challenging ways. She said she doesn't want to be cured, as she would lose creativity. Normal is neutral. She pointed to Temple Grandin as an example of an extremely talented autistic person whose ideas have made great contributions to understanding livestock behavior and the design of facilities for humane slaughter. Ms. Carpenter said autism causes movement and regulatory disorders; treatment should be more like that for cerebral palsy. She hoped NIMH could discover more positive ways of working with people with autism, and pointed out that autistic people need to be protected.

Dr. Insel said NIMH has taken the lead at NIH for autism, leading the NIH Autism Coordinating Committee as well as the federal Interagency Autism Coordinating Committee. Recently, NIMH has committed to funding eight comprehensive research centers, called the STAART (Studies to Advance Autism Research and Treatment) Centers Program, as called for in the Children's Health Act of 2000. Dr. Insel, who has conducted research about autism, called it "interesting and mysterious." He said NIH funding for autism research has tripled over the last two years. He put forward that there is great potential in understanding Temple Grandin's way of thinking and in getting a clearer picture of how the brain develops.

Sue Bergeson, Vice President of the Depression and Bipolar Support Alliance, said her organization really values its relationships with NIMH and its staff, but there "may be richer ways that we could get patients to the table." She told Dr. Insel she has been recruited to serve on many oversight boards for research but has not received one piece of paper or phone call asking for her input. This was very surprising to the Director, who asked her for more specific information following the meeting. Then Ms. Bergeson said we must begin to see past wellness as a cessation of symptoms. New tools are allowing us to think in bigger ways, such as peer-to-peer support. She said that currently not enough is being done to integrate this tool into other NIMH research.

Stuart Cox, Public Policy Manager for the Child and Adolescent Bipolar Foundation, said it is important to keep a focus on children and adolescents, particularly for prevention and early identification. There are not sufficient medications trials for children and there are many more indications for which trials could be mounted. NIMH could be a leader, helping with FDA, as it is in schizophrenia cognition as described during this meeting. Another important roadblock to progress is the lack of child and adolescent psychiatrists. He said that the AACAP was developing a workforce shortage bill to be introduced in Congress. Finally, he said that stigma is a prevailing problem and to end it, we must convey the concept that the brain is a part of the body.

Ms. Guardino, Executive Director of Freedom From Fear, said the goal of treatment should be to get people back to healthy productive lives. We need to understand why people fear medication and why they resist treatment. She echoed Ms. Ross, saying that NIMH-developed treatments should not be privatized just as we shouldn't allow medication developed by federal grants to be taken exclusively for profit.

Barbara E. Solt, Ph.D., LICSW, ACSW, Senior Program Associate of the Institute for Advancement of Social Work Research, discussed the importance of a training track for social workers and nurses. It would be advantageous to begin research training earlier than at the doctoral level, because it enables them to be exposed to NIMH research in their practice training and to be advised of the latest findings, while encouraging further careers at the practitioner-researcher at the PhD level.

Unfortunately, Dr. Insel was compelled to warn that NIMH expects the level of increases in its next budget (FY 2004) to be substantially lower than those of the last five years. It will not be possible to fund all of the worthy ideas it receives.

Paul Seifert, Director, Federal Relations, International Association of Psychosocial Rehabilitation Services, told Dr. Insel that the field of services research has grown considerably. There is great demand for evidenced-based practices and the lack of established treatments is causing difficulties. Effective treatments are out there, but the research portfolio lags behind. The information discussed here, about the connections between mental health and physical health, is extremely important and policy makers need to be informed about these connections.

Lynn Nielsen-Bohlman, Ph.D., Study Director of the National Academies of Science, Institute of Medicine (IOM), highlighted the importance of how consumers view risk and that when implementing behavioral approaches, all age groups and minority groups need to be covered. She said we may find that patients have different reasons for not seeking treatment.

Marcela Gaitán, M.P.H., M.A., Senior Policy Advisor for the National Alliance for Hispanic Health, regretted the difficulty of getting data broken down among ethnic groups. She also reminded Dr. Insel of the need for research on first- and second-generation immigrants and their differences in health outcomes.

Mr. Steve Doochin, Executive Director of the National Alliance for Research on Schizophrenia and Depression, was impressed by this group's power but he thought the advocates were very polite and that wasn't a good thing. NIMH can play an important proactive role, as convener and consensus builder. He said the MATRICS program sounded very impressive. He encouraged future research to harness the use of the Internet for treatment of depression. He also congratulated the Director on the "Real Men, Real Depression" campaign.

Melissa Plotkin, M.L.S. representing the National Association of Anorexia Nervosa and Associated Disorders noted the mention of an initiative on anorexia nervosa in the Director's written message, but wanted to reiterate that all eating disorders are devastating to those affected by them. Furthermore, the boundaries between these disorders are not firm and sufferers cycle among them. She also said the recognition of physical and mental interactions are extremely important and may lead to a better understanding of all eating disorders.

Kathleen McCann, R.N., D.N.S.C., Director of Clinical Services of the National Association of Psychiatric Health Systems, called attention to the problem of shrinking resources, in particular that there are few resources for adolescents in crisis after 10 o'clock at night.

Dr. Insel said these are serious problems across the country. "The house is burning down," as states are able to provide less and less. The President's Commission intends to have a plan to transform care – this is very timely indeed.

Cynthia Folcarelli, Executive Vice President of the National Mental Health Association, thanked Dr. Insel and said she looked forward to using the information she heard at the Roundtable to strengthen advocacy efforts. However, she noted that because of the budget situation in states and localities, the systems that provide mental health care are being torn apart. She pointed out that if service systems are destroyed and most people can't access mental health services, it will be difficult to maintain public support for funding mental health research, because most Americans won't see the value of that investment. To avoid this scenario, she urged NIMH and other leaders in the research community to step forward and join other mental health stakeholders in educating policymakers and the public about the importance of access to quality mental health services. She added that it's possible to advocate for improvements in the service system without engaging in partisan politics, and that now is a time when the entire mental health community—including researchers—must work together to protect and improve service systems.

Sherry A. Marts, Ph.D., Scientific Director of the Society for Women's Health Research, said she looks forward to the day when mental and physical health are not treated differently. This practice has done a particular disservice to women. She thanked NIMH for integrative and interdisciplinary research, particularly because it is always easier to break down proposals into the smallest researchable unit – but it is crucial to integrate.

Mr. Weyrauch, of the Suicide Prevention Action Network USA, Inc., said, "We want to know what works to prevent suicide." He asked for rigorous, scientific evaluation of all suicide prevention programs, saying, "We want to partner with you." There are three areas where he called for action: (1) a doubling of the investment in suicide research, (2) gathering all information and creating a business plan for effective suicide prevention research, and (3) recognition that suicide is an international problem. He called for NIMH to reach out to the world about suicide.

Dr. Insel said the timing for this couldn't be better since the release of the new IOM report, *Reducing Suicide: A National Imperative,* edited by Goldsmith, Pelmar, Kleinman, and Bunney, from the Committee on Pathophysiology and Prevention of Adolescent and Adult Suicide, Board of Neuroscience and Behavioral Health.

Ms. Porr, President of the TARA National Association for Personality Disorder, said she was "awestruck" by the number and caliber of the groups at the Roundtable. She said it is clear, though, that money doesn't seem to solve problems, but it would be a "tremendous force if we can work together." She said training needs are desperate.

Sue Levi-Pearl, Vice President, Medical and Scientific Programs of the Tourette Syndrome Association, Inc., endorsed the mind and body paradigm discussed at the Roundtable and said the study of Tourette Syndrome will enlighten our understanding of other disorders. She said NIMH had "seeded" the field with both clinical and basic research and she endorsed the new ideas for contracts, such as with MATRICS. Her organization would like to work with NIMH in partnerships for review and to develop new protocols. She reiterated the "frightening" prospects of taking care of our sickest people, who are having a great deal of difficulty finding specialists. She didn't know how NIMH could help except to call attention to this dire need and the problems in academic medicine.

Carol Embrey, of the TARA National Association for Personality Disorder Borderline Personality, cited the need for education for consumers, families, and friends. She complained that NIMH materials on borderline disorder were only one page. She requested more materials on a layperson's level.

Faye A. Gary, Ed.D., R.N., F.A.A.N., Program Consultant, Ethnic Minority Fellowship Program with the American Nurses Association, received an NIMH grant for one year of training. She works in a rural area and appreciated the "brilliance of the presentations" at the Roundtable. She shared that there are cultural lags between research and what people understand to be true. Together, scientists, government, and advocates need to address some serious issues. Fifty percent of youths in detention are on antipsychotics and when they leave incarceration they no longer receive treatment. She requested a partnership with community providers, organizations, etc., to increase health literacy – "people don't know how to take care of themselves." We must also must grapple with poverty. It is a variable that influences everything about people's lives. People must choose between seeing a doctor and eating. How can we integrate treatment with people's lives? She also said she wanted to see how to make the Roundtable more ethnically diverse next year and suggested the event be videotaped and perhaps distributed on CD-ROM in order to reach more people.

Photos below are interactions among participants and NIMH staff at the Seventh Annual Research Roundtable, June 2003, at the National Press Club.

Virginia Anthony and Valerie Porr


Sherry Marts and Thomas Insel


Marilyn Benoit & Anne Carpenter


Paul Seifert, Dennis Charney, Faye Gary, & Joel **Streim**

Clarissa Wittenberg, Grayson Norquist & Steve Foote


Karen Graham & Jane Nevins

Richard Nakamura, Cynthia Folcarelli, Jerilyn Ross, Dennis Charney, Robert Desimone, & Alies Muskin

Jerilyn Ross, Richard Levison, Alan Kraut

Steve Doochin, Marcela Gaitán, Lynn Nielsen-Bohlman, Paul Siefert, Barbara Solt, Margot Aronson, Mary Guardino

Sue Bergeson, Karen Graham, Stuart Cox, Angela Sharpe

Toby Weismiller & William Northey, Jr

Gemma Weiblinger, Marjorie Vanderbilt, Richard Nakamura & Joel Streim

Angela Sharpe & Jean Shin

Catherine Roca & Faye Gary

Ronnie Wilkins, Jerry Weyrauch, Sue Burgeson, Annetha Hall, Jennifer Lewey

Grayson Norquist & Anne Kearney Cooke