

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH
NATIONAL CENTER FOR COMPLEMENTARY
AND ALTERNATIVE MEDICINE**

**NATIONAL ADVISORY COUNCIL FOR COMPLEMENTARY
AND ALTERNATIVE MEDICINE
MINUTES OF THE TWENTY-SEVENTH MEETING
June 1, 2007**

NACCAM Members present

Dr. Lori Arviso Alvord, Hanover, NH
Dr. Stephen Barnes, Birmingham, AL
Dr. Carlo Calabrese, Portland, OR
Dr. Sheldon Cohen, Pittsburgh, PA
Dr. Fabio Cominelli, Charlottesville, VA
Dr. Silvia Corvera, Worcester, MA
Dr. Jeanette Ezzo, Baltimore, MD
Dr. Joan Fox, Cleveland, OH
Dr. Margery Gass, Cincinnati, OH
Dr. Ted Kaptchuk, Boston, MA
Dr. Bala Manyam, Odessa, FL
*Dr. Lawrence Murr, El Paso, TX
Dr. Joel Pickar, Davenport, IA
*Dr. Gerald Pollack, Seattle, WA
*Dr. Richard Riman, Piscataway, NJ
Dr. Danny Shen, Seattle, WA
*Dr. Herman Taylor, Jackson, MS
Dr. Frank Torti, Winston Salem, NC
Dr. Stefanie N. Vogel, Baltimore, MD
Dr. Richard Niemtzw, Clinton, MD

*Ad hoc members

NACCAM Members not present

Dr. Bruce Redman, Ann Arbor, MI
Dr. Madhulika Agarwal, Washington, DC
Mr. Michael Leavitt, Washington, DC
Dr. Elias Zerhouni, Bethesda, MD

NIH Staff Present

Mr. Mark Headings, OD/Budget
Dr. Christine Swanson, Office of Dietary Supplements
Ms. Jody Engel, Office of Dietary Supplements
Dr. Phil Tonkins, National Cancer Institute

Dr. George Chacko, Center For Scientific Review
Ms. Linda Southworth, National Cancer Institute
Ms. Andrea Collins, National Cancer Institute
Mr. Dan Xi, National Cancer Institute
Dr. Fan Ping, Center For Scientific Review
Dr. Paul Coates, Office Dietary Supplements
Ms. Jessica Pyjas, National Cancer Institute
Mr. Frank Miller, Bioethics
Dr. Dorata Zolkowska, National Institute on Drug Abuse
Mr. William Zakia, National Institute on Drug Abuse
Dr. Windy Smith, National Cancer Institute
Ms. Jenna Zhang, Office of Extramural Research

Members of the Public

Boyd Hill
Jon-Kar Zubieta
Georgia Perdue
Alexis Johnston
Erin Loomis
Shawna Andersen
Laura Honesty
Beth Clay
Mike Dyer
Sidney Coupes
Maggie Petterson
Suzanne Niemeyer
Steven Dentali
Adriane Fugh-Berman
Martha Menard
Jim Fussell
Aviad Haramati

I. Closed Session

The first portion of the 27th meeting of the National Advisory Council for Complementary and Alternative Medicine (NACCAM) was closed to the public, in accordance with the provisions set forth in Sections 552b(c)(4) and 552b(c)(6), Title 5, U.S.C., and Section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2).

A total of 314 applications were assigned to NCCAM. Of these, 268 were reviewed by NCCAM, 46 by Center for Scientific Review. Applications that were noncompetitive, unscored, or were not recommended for further consideration by the scientific review groups were not considered by Council.

Council agreed with staff recommendations on 168 applications, concurred with IRG on 2 applications and deferred on 1 application - requesting \$ 37,893,535 in total costs.

II. Open Session—Call to Order

The open session of the NACCAM meeting convened at 1:30 p.m. Dr. Martin Goldrosen, NACCAM Executive Secretary, called the meeting to order.

Minutes from the Council meeting on February 2, 2007, were unanimously approved, with no votes against and no abstentions.

Dr. Goldrosen noted that the next Council meeting is scheduled for Wednesday, September 5, 2007.

Dr. Goldrosen introduced Dr. Ruth Kirschstein, Acting Director of NCCAM.

III. Report From the Acting Director

Dr. Kirschstein led a moment of silence in honor of NCCAM's founding Director, Dr. Stephen E. Straus, who died on May 14, 2007. Dr. Kirschstein remarked on Dr. Straus's achievements as a physician, scientist, and leader during his three decades at NIH. A remembrance service will be held on June 11, 2007, at NIH.

Budget Update

Dr. Kirschstein announced that the FY 2007 joint funding resolution provides \$28.9 billion for NIH, a \$620 million increase over FY 2006. The resolution also appropriates \$483 million for the NIH Roadmap. This allows NCCAM to recover \$1.4 million originally intended for Roadmap activities and brings the Center's FY 2007 total budget authority to \$121,576,000. The President's budget would place NCCAM's total budget authority for FY 2008 at \$120,108,000. The FY 2008 budget anticipates funding 278 research project grants, up from 260 in FY 2007.

Senate Theme Hearings

Dr. Kirschstein reported that the Senate Committee on Appropriations' Subcommittee on Labor, Health and Human Services, Education, and Related Agencies, chaired by Senator Tom Harkin, is reinstating a series of theme hearings at which directors of several NIH institutes and centers report on their latest activities. NCCAM's testimony is scheduled for June 22, 2007.

NCCAM Organizational Update

The search for the new NCCAM Director is proceeding as planned.

Dr. Kirschstein noted the retirement of Dr. Shan Wong, Division of Extramural Research and Training, as well as the departure of Dr. Marc Blackman, Division of Intramural Research.

Dr. Kirschstein also noted that Dr. Patrick Mansky has been named the Director of the new Integrative Medicine Consult Service (IMCS) at the NIH Clinical Center.

FDA Draft Guidance

Dr. Kirschstein noted NCCAM's role in responding to the Food and Drug Administration (FDA) December 2006 draft document, *Guidance for Industry on Complementary and Alternative Medicine Products and Their Regulation by the Food and Drug Administration*. Dr. Jack Killen, Acting Director of NCCAM's Office of Policy, Planning, and Evaluation, led the effort to submit comments on the draft guidance on behalf of NIH.

Recognition of Retiring Members

Dr. Kirschstein presented certificates of appreciation to retiring Council members: Dr. Carlo Calabrese, Dr. Jeanette Ezzo, Dr. Bala Manyam, and Dr. Joel Pickar.

Discussion

In response to a question from Council about staffing and CAM expertise within IMCS, Dr. Kirschstein discussed Dr. Mansky's role in leveraging the Clinical Center's existing CAM services, such as acupuncture and massage therapy, and in identifying services that could be enhanced by IMCS staff and outside resources.

IV. NCCAM's Investment in Placebo Research

Dr. Kirschstein introduced Dr. Catherine Stoney, NCCAM Program Officer, Division of Extramural Research and Training. Dr. Stoney provided background information about the placebo response, its role in medical research, and NCCAM's research activities. Dr. Stoney explained that the placebo response, also called the placebo effect, consists of beneficial physiological or psychological responses associated with the use of inert medications or sham procedures, or with therapeutic encounters or symbols. NCCAM-funded researchers are exploring the potential of the placebo response to enhance the effects of conventional treatments and to elucidate mind-body connections.

Dr. Stoney noted that NCCAM's interest in the placebo response dates back to its early days as a Center. As a partner in trans-NIH mind-body research, NCCAM has funded studies of the placebo in conjunction with other institutes and centers. In 2001, NCCAM and the National Institute of Diabetes and Digestive and Kidney Diseases cosponsored "The Science of the Placebo," a conference that brought together both basic and clinical researchers to investigate the role of placebo. The conference led to the publication of a Book, *The Science of the Placebo: Toward an Interdisciplinary Research Agenda*, and to

2 NCCAM-led initiatives to study research into placebo's role in clinical practice, and mechanism of placebo.

NCCAM's current investment in placebo research includes 10 investigator-initiated research projects (R01), 6 exploratory/development grants (R21), 2 training awards (K), and a Centers award (U19). The wide-ranging topics covered by these studies include the role of patient expectation and interpersonal factors, on placebo methodological considerations, and individual variability related to placebo responding. The researchers are studying the placebo response's potential effects on pain control and conditions such as major depressive disorder, Parkinson's disease, the common cold, osteoarthritis, and irritable bowel syndrome.

V. Signal or Noise? Researching Placebo

Dr. Stoney introduced Dr. Ted Kaptchuk, Associate Professor of Medicine, Harvard Medical School.

Dr. Kaptchuk reviewed the scientific, clinical, and methodological rationale for studying placebo responses:

- Scientific—to elucidate clinical events and mechanisms of mind-body interactions
- Clinical—to harness/optimize placebo effects
- Methodological—to increase power to detect intervention-placebo differences in clinical research

Dr. Kaptchuk described several NCCAM-funded studies that his research team has conducted. One examined the ritual of the placebo intervention and the expectation of a therapeutic effect on placebo responding by comparing two placebo treatments (sham acupuncture and inert pill); another investigated the effects of placebo expectancy using sham acupuncture for pain and examined neural mechanism of placebo using fMRI; and the third examined the patient-provider interaction in a comparison of three placebo "doses" for irritable bowel syndrome. To date, results from the first two of these three studies have been published.

Among the key findings are

- Different types of placebo interventions have different impacts on pain analgesia. For instance, one study found that sham acupuncture had a greater effect on chronic arm pain than did an inert pill.
- Adverse effects associated with using a placebo (called nocebo effects) can be shaped by information provided to the patient. For example, patients receiving placebo reported side effects that mirrored those described during the informed consent process.
- Brain activity as measured by fMRI indicated that placebo-induced analgesia may occur through multiple brain pathways and mechanisms, depending on characteristics of the placebo intervention.

- Placebo responses can be “dose dependent.” For example, when sham acupuncture was administered with different levels of patient-practitioner interaction, the higher the level of interaction, the stronger the placebo response.

Dr. Kaptchuk summarized several of the clinical, biological, psychosocial, cultural, methodological, and conceptual questions about placebo that are still to be answered, and he suggested that these questions might be used to direct future research. A key area for further study is the impact of individual differences on the placebo response.

VI. Neurochemistry of Placebo and Nocebo Responses in Humans

Dr. Stoney introduced Dr. Jon-Kar Zubieta, Professor, Departments of Psychiatry and Radiology, and Research Professor, Molecular and Behavioral Neuroscience Institute, University of Michigan.

Dr. Zubieta summarized his research that focused on the role of endogenous opioids in the placebo response and on individual differences in the placebo response. He reported findings from several NCCAM funded studies. Among the findings are

- Studies using PET imaging show that neurotransmission of endogenous opioids and dopamine are increased when a placebo is expected to provide pain relief.
- The emotional characteristics of the pain experience can account for a substantial proportion of the variance in individual differences in the regional activation of endogenous opioid and dopaminergic neurotransmission.
- Genetic and sex-associated factors are also important individual differences that influence the placebo response. For example, in women, higher estrogen levels have been associated with greater placebo induced endogenous opioid release and pain relief.

Discussion

Council and NCCAM staff discussed Drs. Kaptchuk’s and Zubieta’s presentations and potential implications for clinical research and practice. The discussion focused on the state of the science and possible directions for future research. Discussion points included how factors such as personality characteristics, sociocultural context, patient-provider interaction, genetic and epigenetic factors, and endogenous hormones might affect the placebo response.

Dr. Kirschstein thanked Drs. Stoney, Kaptchuk, and Zubieta for their presentations.

VII. Public Comment Session

Dr. Goldrosen opened the floor for public comment.

Beth Clay spoke in support of more research into CAM use for children with autism.

Dr. Kirschstein thanked Ms. Clay for her comments.

Dr. Goldrosen adjourned the meeting at 3:38 p.m.

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

Martin Goldrosen, Ph.D.
Executive Secretary
National Advisory Council for
Complementary and Alternative
Medicine

Ruth L. Kirschstein, M.D.
Chairperson
National Advisory Council for
Complementary and Alternative
Medicine