DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH
NATIONAL CENTER FOR COMPLEMENTARY
AND INTEGRATIVE HEALTH

NATIONAL ADVISORY COUNCIL FOR COMPLEMENTARY AND INTEGRATIVE HEALTH MINUTES OF THE FIFTY-SEVENTH MEETING

October 2, 2015

NACCIH Members Present
Dr. Martin Blaser, New York, NY
Dr. David Borsook, Waltham, MA
Dr. Donald Brater, Indianapolis, IN
Dr. Alice Clark, University, MS
Dr. Stephen Ezeji-Okoye, Palo Alto, CA
Dr. Christine Goertz, Davenport, IA
Dr. Jane Guiltinan, Seattle, WA
Dr. Scott Haldeman, Santa Ana, CA
Dr. Bin He, Minneapolis, MN[2]
Dr. Frances Henderson, Jackson, MS[1]
Dr. Steven Hersch, Charleston, MA
Dr. Janice Kiecolt-Glaser, Columbus, OH
Dr. Helene Langevin, Boston, MA[1]
Dr. Lynda Powell, Chicago, IL[1]
Dr. Eric Schoomaker, Bethesda, MD
Dr. Reed Tuckson, Sandy Springs, GA
Dr. Chenchen Wang, Boston, MA

[1]Telephone
[2]Ad-hoc

SPEAKER
Dr. Thomas R. Insel, Bethesda, MD
Dr. Lawrence Tabak, Bethesda, MD

NACCIH Members Not Present
Dr. Tracy Gaudet, Washington, DC
Dr. Deborah Powell, Minneapolis, MN
Dr. Richard Niemtzow, Alexandria, VA

Members of the Public
Joe Anderson
Breanne Van Nostrand
Kennita Carter

I. Closed Session

The first portion of the fifty-seventh meeting of the National Advisory Council for Complementary and Integrative Health (NACCIH) 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 108 applications were assigned to NCCIH. Of these, 34 were reviewed by NCCIH, 74 by Center for Scientific Review. Applications that were noncompetitive, not discussed, or were not recommended for further consideration by the scientific review groups were not considered by Council.

Council agreed with staff recommendations on 50 applications, requesting $16,026,824 total costs.

II. Open Session—Call to Order

The open session convened at 9:30 a.m. Dr. Martin Goldrosen, NACCIH Executive Secretary, called the meeting to order. The minutes of the NACCIH June 2015 meeting and August 2015 teleconference were approved unanimously.

III. NCCIH Director's Welcome and Report to Council

NCCIH Director Dr. Josephine Briggs acknowledged retiring Council members Drs. Guiltinan, Haldeman, Henderson, Licciardone, and Lynda Powell. In legislative news, Congress passed a Continuing Resolution to fund the Government from October 1 to December 11, 2015, and both the Senate and the House have advanced funding bills out of appropriations committees. NCCIH's budget has decreased since the 2013 sequester; for Fiscal Year 2016, it is about $124 million in the President's budget and $127.5 million in the proposed budget before Congress. Dr. Briggs discussed the budget mechanism table.

Dr. Briggs provided examples of positive trends in news coverage of NCCIH. In staffing news, among new staff at the Center are Dr. Robin Boineau as Medical Officer in the Office of Clinical and Regulatory Affairs, four postdoctoral or post-baccalaureate fellows or trainees in the Division of Intramural Research, and Drs. Lanay Mudd and Julia Berzhanaskaya as Program Director and Program Analyst, respectively, in the Division of Extramural Research. In staffing changes across the National Institutes of Health (NIH), Dr. Thomas Insel is leaving the directorship of the National Institute of Mental Health, and Dr. Michael Lauer has been appointed NIH Deputy Director for Extramural Research.

Dr. John Williamson, NCCIH's Branch Chief for Basic and Mechanistic Research in Complementary and Integrative Health, represented the Center on a scientific panel at a Federal Trade Commission workshop on homeopathic medicine and advertising.

Dr. Briggs has accepted the interim directorship of the Precision Medicine Initiative® (PMI) Cohort Program, held concurrently with the directorship of NCCIH. She gave background on the PMI, launched by President Obama in January 2015, and summarized the convening and activities of the PMI Working Group of the Advisory Committee to the NIH Director (ACD), which has released a report of its recommendations. She also provided a brief overview of the Cohort Program, including its rationale. The Program will build a large research cohort of at least one million Americans to provide a platform

for expanding knowledge of precision medicine approaches and benefit the health of the Nation in multiple ways over many years. Dr. Briggs noted that precision medicine is highly relevant to issues around pain management, where the existing approaches are inadequate.

There are multiple scientific opportunities in the planned research enterprise, from discovery of new biomarkers that could contribute to the prediction of future disease risk to facilitation of NIH's ability to enroll specific targeted populations in clinical research. Examples of areas for emphasis include, at all stages of the process, truly reflecting the diversity of the United States and being inclusive and engaged with patient advocates, patients' rights groups, the research community, and cohort volunteers. Additional topics discussed included the program budget, possible data sources for the cohort, an initial core data set, and data flow between the coordinating center and participant sites. An immediate challenge is the enrollment of direct volunteers, Federally Qualified Health Centers, and large health care provider organizations. Initially, direct-volunteer adults will be enrolled, and then, after work on proper consent and ethical considerations, family members—who could include children. Dr. Briggs commented that she is honored to lead the Program, and that NCCIH has had past successes in running this type of collaborative trans-NIH project, such as the NIH Health Care Systems Research Collaboratory.

Discussion. Dr. Blaser asked about enrollment of children in the program. Dr. Briggs responded that direct volunteers will be asked if they wish to extend their participation by telling about their family members. Confidential information from adolescents is a problematic area. A group is being convened to address pertinent ethical constraints and consent issues, and it is hoped that an approach will emerge. Other activity in this area will include reshaping of lessons learned from the National Children's Study, particularly on how to capture longitudinal information. The ACD has directed inclusion of all stages of life, but how to quantify and target this is not yet solved. Dr. Briggs said these questions are of known importance to the planners of the effort, and she will do her best to ensure that input is invited when the ideas are ready for public comment. Dr. Blaser added that, rather than having just cross-sectional research, linking children and parents would offer much power.

Dr. Goertz asked about the minimum data set for those who want to participate as individuals. Dr. Briggs said that this is under deliberation. She has been impressed in the Collaboratory by how good direct-from-participant information is compared with information from electronic health records, for example. She was optimistic that direct-from-participant information can provide a viable data set—and for specific studies there will be re-contact with participants, enabling even richer data sets. She anticipated that the core data set will include elements like a simple physical exam; simple measurements such as blood pressure, height, and weight; and information that participants can provide such as major areas of health concern, medications, and lifestyle factors. This may provide enough information for a deeper dive.

Dr. Schoomaker noted that both the Veterans Health Administration and the Department of Defense are engaged in very large longitudinal studies, constituting a very large database of a diverse group all over the country. Dr. Briggs responded that the hope is that there can be interoperability within a few years with PMI data. She added that she recently met with Dr. Kathy Hudson, NIH Deputy Director for Science, Outreach, and Policy; Dr. Michael Gaziano, who leads the Million Veteran Program; and representatives of the Department of Defense's Millennium Cohort Study to discuss developing highly integrated crosswalks across these efforts. Dr. Hersch asked about the genetic information that will be collected, in terms of approaches to genetic privacy and giving aggregate information back to

participants; he saw this as a major issue and moving target, and the Program offers an opportunity to do it experimentally. Dr. Briggs agreed that this is a highly challenging aspect but noted that all these problems do not have to be solved right away. She agreed that the data security issues are sizeable but thinks a very secure data environment can be created, although building trust in that is very difficult. The White House has convened a group of security experts who are developing approaches to protect PMI data security.

Dr. Guiltinan asked whether the program will partner with other entities doing similar projects. Dr. Briggs answered that the ACD discussed and researched this possibility, but except for two large Federal cohorts, decided not to attempt at the beginning stage to integrate other existing cohorts. The Program's cohort will be new, not a synthetic cohort of existing cohorts. It is hoped that the created data structures will have the capacity for replication or extension for analytics with other cohort populations.

IV. Developing the NIH-Wide Strategic Plan

Dr. Lawrence Tabak, NCCIH Principal Deputy Director, presented on NIH's upcoming strategic plan. The plan is mandated by the appropriations CR Omnibus, H.R. 83-346, and the pending 21st Century Cures Act, Section 1021, is also pertinent. The plan is to be delivered to Congress by mid-December 2015.

Dr. Tabak described major goals for the plan. He described the plan as a living document, able to respond to rapid changes in science and designed to complement but not replace the strategic plans of the individual Institutes and Centers (ICs). The plan is aligned with the Department of Health and Human Services (HHS) strategic plan. The roles of NIH senior leadership, a working group of representatives from each NIH Institute/Center/Office, and the ACD were described.

Dr. Tabak provided a graphic representing the draft framework for the plan, consisting of an overview; areas of opportunity across all biomedicine (including a complex relationship among fundamental science, health promotion/disease prevention, and treatments/cures); setting priorities; and enhancing stewardship. The importance of serendipity in scientific discovery, how technology catalyzes advancement, the importance of studying health (not just pathophysiology), and enhancing partnerships were among his major themes. Channels for outreach and feedback include a Web page, a Request For Information (RFI), and webinars.

Discussion. Dr. Tucker lauded the theme of diversity in this plan and the PMI, and suggested also using the Federally Qualified Health Centers' network of minority-serving academic and research institutions and their patient bases. Dr. Tabak agreed with taking advantage of such opportunities. Dr. Blaser asked what Dr. Tabak meant by the phrase "permanently ending a pandemic." Dr. Tabak responded with the example of smallpox, which effectively has been ended; some people might think that NIH spends "disproportionately" too much to end a certain disease or condition over time, but if it is indeed ended, the cost-benefit ratio becomes favorable.

Dr. Goertz asked how NCCIH's strategic plan will fit with the NIH plan. Dr. Tabak responded that NIH's plan will link to ICs' plans, and as those plans come up for refreshing, the ICs will be asked to link back to relevant parts of NIH's plan, which in turn links back to the HHS plan. Part of the approach will consist of linking and pointing out intersections, and part of it harmonizing across agencies. Dr. Schoomaker cited the importance of NIH formulating its strategy, although mandated, as certain key

areas could be eroded too far without a strategy and it can help with elimination when needed of lower priority items. He also commented that there is so much focus on pathology that there is not enough on how the healing process operates, a topic of major interest to NCCIH. Dr. Tabak commented that this plan will allow things to be codified that have been done informally for many years, including deciding what is and isn't important as part of optimizing informed funding decisions. Cross-cutting topics across agencies will be emphasized to support leveraging resources. To Dr. Schoomaker's mention of healing, Dr. Tabak added resilience, which he said also resonates with patients and patient groups.

Dr. Borsook was intrigued with partnerships and asked whether there is an approach to bring in different disciplines and ways of thinking to difficult problems. Dr. Tabak responded that NIH is getting better at this and has been studying how other entities do it. As NIH begins to tackle the diseases and conditions that are clearly most intractable, the typical team will not be enough, so it must engage a much larger group, as has been done in the Accelerating Medicines Partnership program. Dr. Haldeman commented that he is working with medical anthropologists looking at traditional/local healers around the world and has been impressed by how many Americans go to these kinds of healers—does NIH have the means to capture the full scope of healing? Dr. Tabak responded that he recently met with an American Indian and Alaska Native group to consult with NIH on research and research training, and there was much interest in this topic, which he anticipated will be a sub-element in NIH's plan.

V. NIH and the BRAIN Initiative

Dr. Thomas Insel, Director of the National Institute of Mental Health, presented an update on the first two years at NIH of the Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative, launched by President Obama in April 2013. BRAIN is a public/private effort that builds on recent progress to create tools to accelerate discovery and build the necessary foundation to reduce the burden of brain disorders. It is the type of cross-cutting activity that NIH is trying to do more of, Dr. Insel noted. Brain disorders are the leading source of disease burden and cost burden in the United States. For example, they cause more disability before age 50 than all other illnesses combined, and the prevalence of Alzheimer's disease is expected to double by 2050. Currently, we do not know enough about the brain to meet these kinds of challenges.

Dr. Insel provided examples of major findings obtained during this initial period and discussed the formation of an NIH BRAIN Neuroethics Workgroup. A budget summary was provided, and Dr. Insel explained that the money for BRAIN is not taken from R01 grants but rather is decided by Congress. Dr. Bin He is NCCIH's representative to the BRAIN Multi-Council Working Group and is providing very useful feedback, Dr. Insel said. As much of the effort targets convergence across scales and disciplines, not only neuroscientists but physicists, engineers, nanotechnologists, and materials scientists are being funded, as other fields have excellent tools that can be applied in BRAIN. Dr. Insel closed by commenting that he is excited about the progress so far. While much of the work was under way before BRAIN funding was added, he thinks that over 10 years this initiative will truly change the landscape.

Discussion. Dr. Blaser asked whether there are mathematicians working on BRAIN, and whether the initiative will gradually increase funding for programs related to human neuroscience. Dr. Insel responded that yes, mathematicians are among those involved in BRAIN, and that funding for research in humans has been something of a tension—most of the existing evidence is in mice and we need to figure out how to scale up, which could take a decade. However, some new initiatives were released shortly before this meeting that should help the effort. Dr. Insel commented that the direction in which

we are going is toward building human neuroscience, which is what will have the greatest impact. Dr. Tuckson praised the strategic model, including because NIH cannot pursue every possibility. Dr. Insel agreed that NIH cannot do everything and saw the gap as "tool development on a meso scale."

Dr. Lauren Atlas of the NCCIH Division of Intramural Research asked whether behavioral scientists are involved in the planning for BRAIN and the PMI. Dr. Insel answered that behavioral science will have to be a part of BRAIN. Development of behavioral assays will be critical for understanding what is wanted, and funding has been toward people who tend to build tools (such as engineers) or are expert in, for example, miniaturization. In phase 2 at the application stage, there may be more involvement of behavioral scientists. Dr. Briggs spoke to the PMI piece, describing BRAIN as more reductionist and PMI as an integrated function, or an attempt to look at real-world function, and anticipated that behavioral and social science questions will be central in PMI.

VI. Concept Clearance: NCCIH Clinical Trials Initiative

Dr. Wendy Weber, Branch Chief of the Clinical Research in Complementary and Integrative Health Branch, presented a concept on a proposed NCCIH clinical trials initiative. She opened with background on related work over the past year, starting with the "Framework for Research on Developing and Testing Mind and Body Interventions" first brought to Council in February 2014. It reflects, she said, the importance of doing the early-stage research to truly define, develop, and improve interventions before moving into larger-scale efficacy, effectiveness, and comparative effectiveness types of studies. Dr. Weber also discussed relevant initiatives released so far in 2015.

The present concept clearance has three purposes: (1) To develop research initiatives to support efficacy and effectiveness trials of complementary or integrative health interventions where preliminary evidence justifies the trial; (2) to focus on previously defined high-priority topics identified in early-stage clinical study initiatives for natural products and mind and body interventions; and (3) to use the phased cooperative agreement mechanism to allow for NCCIH involvement and oversight. Dr. Weber discussed the three mechanisms by which NIH can fund research and discussed some challenges that NCCIH and NIH have encountered with clinical trials.

Discussion. Dr. Lynda Powell emphasized the importance of using a U01 cooperative agreement because many unpredictable things can happen when doing clinical trials—researchers need all the help they can get with unanticipated problems, and more perspectives when addressing a problem make the answers better. Dr. Briggs noted that often conversions of studies to cooperative agreements have been largely driven by the price tag and the need for greater staff involvement. A motion to approve the concept was made and seconded, and it passed with 14 affirmative votes.

VII. NCCIH Strategic Plan Update

Dr. Karin Lohman, Director of NCCIH's Office of Policy, Planning, and Evaluation, reported on NCCIH's strategic planning activities since the last Council meeting. The timeline for the Center's strategic plan has been extended so that its framework will align with that being developed for the NIH strategic plan. The new end date to present the finalized plan to Council is the June 2016 meeting.

Dr. Lohman gave updates on the five NCCIH working groups exploring special areas of scientific interest and potential NCCIH-funded research opportunities. This effort may or may not result in

research initiatives downstream. First, the Network Pharmacology and Natural Products Working Group, chaired by Dr. Craig Hopp, Program Director, has as its goal exploration of moving beyond the "one drug, one target" paradigm to a network analysis/multi-level view. The group will hold a webinar on December 2 featuring guest scientists and chaired by Dr. Guido Pauli, University of Illinois at Chicago. Second, the goal of the Probiotics and Microbiome Working Group, chaired by Dr. Linda Duffy, Program Director, is to target the structural and functional properties of probiotic and prebiotic modulation of gut microbiota especially as they pertain to the gut-brain axis. The group has worked on several funding opportunities released in 2015 on this topic, and applications have been received but not yet peer reviewed. The group will reconvene to discuss research gaps and opportunities, and looks forward to a lecture on October 6 by renowned probiotics researcher Dr. John Cryan, University College Cork, in NCCIH's Integrative Medicine Research Lecture Series.

Third, the Workplace- and Community-Delivered Wellness Programs Working Group, chaired by Dr. Weber, seeks to scan the state of the science and investigate where and how NCCIH could make an impact to advance the body of science in the field. This group plans to convene a special working group of Council. Dr. Eve Reider, Program Director, chairs the fourth working group, on Collaborative Efforts to Address Pain and Symptom Management in U.S. Military Personnel and Veterans. Its goal is to develop a large-scale collaborative initiative focused on mind and body approaches to address pain and symptom management in this population. The group has engaged relevant stakeholders to determine mutual interests in implementing a joint initiative involving NIH, the Department of Defense, and the Veterans Health Administration. A Government Steering Committee has been formed and will first meet in December 2015. Various other ICs have expressed interest in this joint effort.

The fifth group, the Science Communications Working Group, chaired by Ms. Alyssa Cotler, Director of the Office of Communications and Public Liaison, and Ms. Shawn Stout, Science Writer, has as its goal to plan and implement a collaborative effort to educate consumers about biomedical research so they may make informed, evidence-based decisions about their health. This group has been engaging with some others at NIH interested in this topic, including the NIH Communications Director, and has developed a short list of important topics that consumers should know about. It is exploring potential partnerships for developing this campaign and will be pilot testing one or two topics.

Dr. Lohman then discussed the analysis in process of responses to NCCIH's RFI soliciting input for its strategic plan, which ran in the *NIH Guide* in spring 2015. Other outreach efforts are being conducted as well. One of the recurrent themes in feedback to date has been NCCIH's training and career development programs, and Dr. Lohman selected this topic to discuss in detail, including historical perspective on NCCIH's relevant activities from Fiscal Years 1999–2014. NCCIH is establishing a Council working group to advise Dr. Briggs on research training priorities for strengthening the workforce to conduct rigorous research on complementary and integrative approaches.

Discussion. Dr. Ezeji-Okoye asked for a working definition of "evidence-informed practice," expressing concern that this term could become a way for any approach (even based on observation only) to be included in practice. Dr. Briggs said that she is aware of a literature on the definition of "evidence-based," but not "evidence-informed." Dr. Haldeman commented that, having sat on numerous guideline committees, he has found that the definition increasingly is a middle ground of the best available evidence; experts review that evidence and meet to work out how, in light of it, the best clinical decisions can be made. Dr. Brater asked whether there should be an NCCIH effort directed at the issue of supplement variability. Dr. Briggs responded that this is a topic worthy of more discussion, and Drs.

Williamson and Hopp have recently brought rigorous methodology to the natural products portfolio. If a grant on the topic was submitted, NCCIH would probably be the IC that funds it, but she does not see it as the Center's mission to take on the regulatory process of checking what is for sale in the marketplace; it is not a scientific research question. She invited Council's continued input on how NCCIH should position itself in this complex arena. Dr. Clark agreed with Dr. Briggs's comments and suggested the question could be as follows: in the context of the strategic plan for workforce and community delivered wellness programs, how can NCCIH prepare people to understand the science behind regulatory decisions without NCCIH getting into or advising on the regulatory decisions? Dr. Briggs commented that Dr. Robert Califf, the Food and Drug Administration's Deputy Commissioner for Medical Products and Tobacco, regularly requests her and NCCIH's input, and she thought that this topic deserved more expansion in the Center's strategic plan.

Dr. Ezeji-Okoye asked how to approach situations with existing strong beliefs—almost faith based, he said—with respect to biomedical research, accompanied by low regard for what the science says. An example is vaccines. Dr. Briggs said that this is an important question on which she has considered inviting an Integrative Medicine Lecture Series speaker and forming a panel. Dr. Blaser said that the communications issue is important—faith versus reason is historically an old issue, and the effort would face a plethora of communications devoted to questionable techniques. NCCIH would have to be very strategic since the topic is so large. Dr. Briggs commented that the Science Communications Working Group has developed some interesting ideas for topics and materials that would have targeted impact. She added Dr. Deborah Powell's previous suggestion of materials that could be used to educate health care providers, such as a short video on causation versus correlation; this could also be useful with other audiences as well, such as the media. Dr. Briggs invited Council volunteers for the five groups.

VIII. Pain Prevalence and Severity in U.S. Adults—2012 National Health Interview Survey

Dr. Richard Nahin presented findings from his recently published epidemiologic analysis on pain prevalence and severity in U.S. adults (Nahin RL. Estimates of pain prevalence and severity in adults: United States, 2012. *The Journal of Pain*. 2015;16(8):769-780) using data from the 2012 National Health Interview Survey (NHIS). The NHIS is America's preeminent health survey, in which tens of thousands of civilian, noninstitutionalized U.S. adults are interviewed by the Centers for Disease Control and Prevention (CDC) about their health- and illness-related experiences. The 2011 Institute of Medicine (IOM) report *Relieving Pain in America* identified a need for more national data looking at individuals' pain experiences, not just whether people have a given pain condition. In 2012, the NHIS contained questions relevant to the IOM's concerns on pain experiences and conditions related to pain. Dr. Nahin listed the 17 painful conditions assessed in that survey.

Dr. Nahin explained a measure he used to categorize pain, as developed by Drs. Kristen Miller and Mitchell Loeb of the CDC along with the Washington Group on Disability Statistics; he later confirmed his findings with a cut-point analysis. He presented his findings on frequency and intensity of pain in all adults and pain severity as related to number of health conditions and underlying health status. Other new information that he reported included self-reported pain severity across several demographic variables including race, ethnicity, preferred language, sex, and age (age is one of the potential confounders in pain research). Dr. Nahin closed with some ongoing unpublished work on combined data from the 2010 to 2013 years of the NHIS on pain in military veterans.

Discussion. Dr. Ezeji-Okoye asked whether Dr. Nahin examined differences by gender in veterans. Dr. Nahin responded that he did, but there were very few women in comparison to men, which affected the ability of the variances to be meaningful. Dr. Tuckson asked about a potential confounder: the underlying anxiety and stress experienced by patients of color when they feel they must prove to the health care delivery system that they truly are a human being in pain rather than, for example, a drug addict. Dr. Nahin said that he did not look at this, but it is a good idea and he will do so. Dr. Tuckson suggested sickle cell anemia as a case study. Dr. Borsook suggested that the Getting Better Syndrome in veterans and nonveterans could be something for NIH to consider. Dr. Blaser asked whether any roughly comparable studies have been done in other countries. Dr. Nahin gave as an example the United Nations initiative to develop Common Core measures of disabilities, which might be used to obtain comparable data worldwide not only on disabilities but on pain. Dr. Briggs added that she was not aware of a systematic attempt to study these pain questions in different populations.

Dr. Schoomaker commented that there have been some differences between demographic groups in the tendency to answer the question "Did you serve?" compared with "Are you a veteran?" Many younger members of the military population are heavily injured, and he is interested in a functional analog scale for pain that would include interference from loss of function or interruption of one's life. Dr. Nahin said that the NHIS has no question on whether a disability or loss of function was specifically due to pain, but Miller and Loeb's scale was based on disability and an interview process to differentiate four pain groups. Dr. Wang identified as a gap how many of the population take prescription and over-the-counter (OTC) medications, what they take, what medical conditions they have, etc. Dr. Nahin said that his team is doing that analysis, which will link 2012 NHIS data to the Medical Expenditures Panel Survey for 2013; the latter includes prescription and OTC drug information.

IX. Pain Imaging and NCCIH: Helping Close the Gap

Dr. Borsook presented on findings from his work and suggested some domains in which he thought NCCIH could best use its imaging portfolio to help structure answers to important questions. His laboratory has conducted a broad spectrum of studies related to pain, and this informed a complex, wide-ranging talk. The first domain he suggested to Council was **The Emotional Brain.** His take-home messages for the domain included (1) emotional targeting and therapeutic manipulation; (2) psychiatry as missing in the equation; (3) better understanding of specific brain targets such as the accumbens and habenula; (4) how best to bring together emotional therapeutics (e-Rx) and biologicals such as drugs; and (5) the challenges in maintaining a behavioral therapeutic effect—placebo may be a good example.

The second suggested domain was **When Drugs Do and Don't Work.** Take-home messages included (1) using functional magnetic resonance imaging to answer questions about the effects of medications, including natural products and botanicals; (2) understanding medications' targets and functional effects over time; (3) the sum is greater than the parts (adding bio-psychosocial processes); and (4) trials need to have Good Imaging Practice.

The third domain was **Integrative Processes: Teasing Them Out**. Take-home messages included (1) defining the most salient processes and their long-term effects; (2) sex matters; (3) when pain gets stuck, "explosives" are needed; and (4) the importance of integrating allostasis and allostatic load into how a disease can be treated.

The fourth domain was **Over Time: Longitudinal Studies**. Take-home messages included (1) understanding long-term effects on the brain; (2) understanding the benefits of the "Package Delivery Process" approach in targeting and modulating brain processes; (3) lingering processes being detrimental to the patient and society; and (4) precision medicine.

Discussion. Dr. Blaser asked about Dr. Borsook's early study on phantom touch after amputation: since there was no limb present, where did the signals come from, and how did they get there? Dr. Borsook responded that when a limb is amputated the cortex changes; there is a shift to other parts of the cortex that reflect a developmental profile of cortical input, and that process involves both signal-to-noise and regression to a primordial state. Dr. Briggs commented that she found this study an interesting example of neuroplasticity after amputation and relevant to the question of which patients develop phantom limb sensation and how. Dr. Wang asked about early intervention studies for children that could prevent future damage to the brain. Dr. Borsook responded that this is the theme of "Save the Child's Brain" at The Center for Pain and the Brain, Boston Children's Hospital.

X. Public Comment and Adjournment

No public comments were offered.

The meeting was adjourned at 3:00 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 Integrative
Health

Josephine Briggs, M.D.
Chairperson
National Advisory Council for
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