Department Of Health and Human Services Public Health Service National Institutes of Health National Advisory Neurological Disorders and Stroke Council

Summary of Meeting¹ May 15-16, 2024

The National Advisory Neurological Disorders and Stroke (NANDS) Council was convened for its 223rd meeting on May 15-16, 2024, in person and via Zoom. Dr. Walter Koroshetz, Director of the National Institute of Neurological Disorders and Stroke (NINDS), served as Chairperson.

In accordance with Public Law 92-463, the meeting was:

Open: May 15, 2024: 10:00 a.m. to 4:00 p.m. for the review and discussion of program development, needs, and policy; and

Closed: May 16, 2024: 10:00 a.m. to 1:15 p.m. for the consideration of individual grant applications.

Councilmembers present:	Ad Hoc Council Members:
Dr. Amy Brin	Dr. Florian Eichler
Dr. Robert Brown Jr.	Dr. Robert Gereau
Dr. Yishi Jin	Dr. Frances Jensen
Dr. Jane Larkindale	Dr. Amy McGuire
Dr. Jin-Moo Lee	Kate Nicholson
Dr. Louise McCullough	
Dr. Hank Paulson	Ex officio members present:
Dr. Gina Poe	Dr. David Brody
Dr. Ekemini Riley	Dr. Christopher Bever, Jr.
Dr. Timothy Ryan	
Dr. Sameer Sheth	

Council Roster (Attachment 1)

NINDS employees and members of the public in attendance (Attachment 2)

The meeting was held at the Neuroscience Center and virtually via Zoom.

¹For the record, it is noted that members absent themselves from the meeting when the Council is discussing applications (a) from their respective institutions or (b) in which a real or apparent conflict of interest might occur.

OPEN PORTION OF THE MEETING

I. Call to Order and Opening Remarks

Dr. Koroshetz welcomed Councilmembers, visitors, and staff to the 223rd meeting of the National Advisory Neurological Disorders and Stroke (NANDS) Council and thanked four Councilmembers, whose terms were ending, for their service.

II. Report of the Interim Director, Division of Extramural Activities, NINDS

Dr. David Owens, Acting Director, Division of Extramural Activities, NINDS

- A. Approval of Council Minutes Dr. Owens requested, and the Council voted to approve the February 14-15, 2024 Council meeting minutes.
- B. The following future Council meeting dates were confirmed:

Wednesday and Thursday, September 4-5, 2024 Wednesday and Thursday, February 12-13, 2025 Wednesday and Thursday, May 14-15, 2025 Wednesday and Thursday, September 3-4, 2025 Wednesday and Thursday, February 11-12, 2026 Wednesday and Thursday, May 20-21, 2026 Wednesday and Thursday, September 9-10, 2026

C. Other Items

Expedited Review Process — In advance of each Council meeting, a subset of Councilmembers are asked to approve a certain number of grant applications. This expedited review process focuses on applications with scores within the payline for which there are no unresolved issues. During this Council round, there were 115 applications that were eligible to be expedited. Dr. Owens thanked Councilmembers Tim Ryan, Amy Brin, and Louise McCullough for their review of these applications

Extramural Announcements – All extramural announcements were posted to the NINDS Electronic Council Book (ECB).

III. Report of the Director, NINDS

Dr. Walter Koroshetz, Director, NINDS

NIH and NINDS Leadership Changes — Dr. Koroshetz announced that Dr. Josh Gordon would be <u>stepping down</u> as NIMH Director and Dr. Shelli Avenevoli would serve as Acting Director. Dr. Kathleen Neuzil will <u>serve</u> as Director of the Fogarty International Center and NIH Associate Director for International Research. Within NINDS, Dr. Michelle Jones-London will <u>serve</u> as the first Associate Director for Programs to Enhance Neuroscience Workforce, where she will promote equity and diversity across NINDS programs.

NINDS Budget — Dr. Koroshetz reviewed the fiscal year (FY) 2024 NINDS budget and President Biden's proposed FY 2025 budget. The FY 2024 base budget remained the same as FY 2023 and was not expected to increase significantly in FY 2025. Funding for the Brain Research Through Advancing Innovative Neurotechnologies[®] (BRAIN) Initiative was reduced by 40% after NINDS did not receive additional base funding to offset the FY 2024 decrease in 21st Century Cures Act funds.

NINDS received an additional \$10 million for AD/ADRD, and \$5 million for HEAL. The Undiagnosed Disease Network (UDN) did not receive additional funds, but NINDS was still required to spend \$18 million—some of which would be funded by other NIH Institutes and the Office of the Director. The ACT for ALS program received \$75 million through the NIH Office of the Director, which prioritized expanded access grants.

Dr. Koroshetz reviewed the NINDS extramural program budget, indicating that the Institute had to reduce the regular payline to the 11th percentile. This was due to the lack of any budget increase in the face of increasing costs for science. In this austere budget setting NINDS aims to fund as many outstanding investigators as possible, protect programs for early career investigators, and maintain its commitment to basic neuroscience. NINDS will maintain an extended payline for early-stage investigators at the 22nd percentile. NINDS has supported an increasing number of individuals, both through base and special appropriations (BRAIN, HEAL, ADRD) since 1998. In addition to managing budget constraints by implementing administrative cuts to competing and non-competing grants, NINDS also adopted a new policy to help manage the rising costs of grants in order to fund as many outstanding investigators as possible. The <u>policy</u> requires applications in response to NIH Parent R01 Notices of Funding Opportunities requesting more than \$500,000 in direct costs to achieve better than half the general NINDS payline. Dr. Koroshetz briefly reviewed the NINDS intramural program budget, which has similar budget constraints.

Helping to End Addiction Long-term (HEAL) INITIATIVE® 2.0 — NINDS and the National Institute on Drug Abuse (NIDA) had assembled a working group, led by Dr. Rob Gereau and Dr. Kathleen Sluka, to develop a strategic plan for the <u>HEAL Initiative</u>, which would align with NIDA's strategic plan for addressing the opioid crisis. Dr. Koroshetz noted the high rates of opioid overuse deaths and chronic pain that occurred among Native American communities. In response to this disparity, the HEAL Initiative would embark on an <u>ambitious program</u> to directly fund 13 tribal nations to build research capacity, as well as 3 additional programs to coordinate activities and provide technical assistance.

Changes at the Center for Scientific Review (CSR) — NIH is implementing a <u>simplified framework</u> for the peer review of the majority of competing research project grant (RPG) applications, beginning with submissions with due dates of January 25, 2025. The simplified peer review framework aims to better facilitate the mission of scientific peer review – identification of the strongest, highest-impact research – by:

- 1. Enabling peer reviewers to better focus on answering the key questions necessary to assess the scientific and technical merit of proposed research projects:
 - \circ $\;$ Should the proposed research project be conducted?
 - Can the proposed research project be conducted?
- 2. Mitigating the effect of reputational bias by refocusing the evaluation of investigator/environment to within the context of the proposed research.
- 3. Reducing reviewer burden by shifting policy compliance activities to NIH staff.

NIH Research Priorities – In response to the Executive Order on <u>Advancing Women's Health</u> <u>Research and Innovation</u>, NIH issued a <u>Notice of Special Interest</u> to fund research focused on conditions that predominantly affect women. Additionally, NIH aims to establish a primary care research network to facilitate innovative research integration in clinical settings and promote engagement with communities that are underrepresented in clinical research.

NINDS News – Dr. Koroshetz announced the winners of the <u>NINDS Rigor Champions Prize</u>, which recognizes investigators who have promoted research rigor and transparency. Additionally, the NINDS Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) intramural research team held a <u>symposium</u> on May 2. Dr. Avi Nath, Dr. Brian Walitt, and their team recently published a <u>phenotyping study</u> in *Nature Communications*. Dr. Nath was also named one of *Time Magazine's* top 100 individuals to have influenced global health.

IV. Discussion of Director's Report

Several Councilmembers expressed concern about the budget. A Councilmember suggested that investigators should have the ability to revise their study aims to account for the significant amount of funds being extracted from their grants, which may be especially important for early career investigators. Another Councilmember asked about the future of new initiatives. Dr. Koroshetz answered that in a flat budget scenario NINDS would need to decrease funding to some existing programs in order to fund new programs.

A Councilmember asked whether the instruction to spend \$18 million for the UDN program impeded the ability to effectively distribute funds across the Institute. Dr. Koroshetz answered that this type of Congressional requirement for a specific amount of funding without an appropriation was not common.

A meeting participant asked about funding for long COVID. The economic impact of long Covid on the U.S. was much greater than the amount needed to conduct meaningful science. Dr. Koroshetz said that the NIH <u>RECOVER Initiative</u> received approximately \$1.5 billion and aimed to find a cure for long COVID. He acknowledged that more funding and qualified investigators will likely be needed to address this complex issue over a longer time period.

A Councilmember asked about the dollar equivalent of an percentile point and whether the new policy created more emphasis on cost in study sections. Dr. Koroshetz said that the dollar value of a percentile point has increased from \$14 million to \$20 million in the last 10 years. He stated that the emphasis at NINDS is to respect the peer review evaluation of the science rather than asking peer review to consider cost as a factor. A Councilmember suggested focusing on the cost of individual components of grants during review, rather than applying a budget policy across the board. Another Councilmember suggested revisiting the idea of steeper administrative cuts to maintain or increase paylines. Dr. Koroshetz responded that steeper administrative cuts would be difficult as our 20.5% administrative cuts are already high, but that NINDS may have to reconsider if there were further budget decreases. He emphasized the importance of communicating the value and impact of NIH research to the public. A Councilmember added that it was important for the research community to better communicate the discoveries made with taxpayer money. It may be important to build a component for communicating scientific discovery with the public into grant programs.

A Councilmember asked whether the Women's Health Initiative would address Alzheimer's disease. Dr. Koroshetz answered that NIH would consider what other Institutes and Centers were already funding in order to coordinate research priorities in the Women's Health Initiative

V. CSR's Initiatives to Strengthen Peer Review

Dr. Bruce Reed, Deputy Director, Center for Scientific Research (CSR)

Dr. Reed said that NIH had three critical components for ensuring quality peer review: 1) study sections should have a current scientific scope; 2) reviewers should have appropriate and diverse expertise; and 3) processes should be in place for promoting scientific integrity, minimizing bias, and promoting effective evaluation. These components aligned with NIH's core operating principles of transparency, data-driven decision-making, stakeholder engagement, and staff development.

<u>Evaluating Panel Quality in Review</u> (ENQUIRE) was the systematic process that CSR used to assess and update study sections. ENQUIRE was implemented in 2019 and was a multistage process for evaluating scientifically-related study section clusters. Select members of the scientific community reviewed data and sample abstracts from these study section clusters to make recommendations about which set of study sections would be best for identifying high impact research. NIH program and review leadership with broad and relevant scientific interest reviewed these recommendations, and a CSR advisory council approved and published a final set of guidelines driven by data and stakeholder input to make changes to study sections. ENQUIRE takes about 12-18 months from initiation to implementation of new or restructured study sections. To date, CSR has reviewed 14 scientific clusters, resulting in substantive study section realignments.

The <u>Simplified Review Framework</u> for NIH Research Project Grant (RPG) Applications was developed by an external working group. The Simplified Review Framework reframed review processes to focus on whether the research *should* be done (i.e., importance of research), whether it could be done *well* (i.e., rigor and feasibility), and whether it *would* be done (i.e., expertise and resources). CSR found that the implementation of the Simplified Review Framework provided an opportunity to mitigate reputational bias in peer review and instead focus on the context of the research project. Dr. Reed emphasized that all three factors of the simplified process contributed to the overall impact score and that the process would be in effect for applications with due dates of January 25, 2025. A trans-NIH committee was working to ensure these changes were implemented.

Another change was to improve the <u>review of NRSA Fellowship applications</u> to optimize the identification and training of the next generation of promising scientists. This change was in response to concern that NIH review processes favored elite institutions and well-known sponsors. Similar to the Simplified Review Framework, changes to the review process for fellowships was developed with expert review, public input, internal advisory council review, and recommendation development and approval. NIH announced the changes in April 2024, which with new review criteria which include: Candidate Preparedness and Potential; Research Training Plan; and Commitment to Candidate and a wider range of indicators for scientific potential and preparedness, rather than traditional markers of academic success. The changes would be in effect for applications due after January 25, 2025 (i.e., generally by April 8, 2025).

Dr. Reed provided an overview of a number of other initiatives to promote fairness in review. For instance, CSR held several small group interactive sessions each year to <u>orient new chairs</u> on review processes, including how to promote fairness in peer review. Since August 2021, CSR had also provided <u>Bias Awareness Training for Reviewers</u> to more than 34,000 NIH reviewers to mitigate the most common biases that occur in the peer review process. CSR's Review Integrity Training Module was updated in August 2022 and provided an interactive setting to address the integrity of the review process, such as protecting confidentiality. More than 30,000 reviewers had completed the training, over 90% of whom <u>reported</u> a substantial increase in knowledge and comfort in reporting integrity breaches. Dr. Reed highlighted that anyone could report a breach or bias to <u>reportbias@csr.nih.gov</u>. CSR reviewed each report and took action to identify and address the root causes of the issue.

CSR recognized the importance for NIH to hear diverse perspectives during peer review—including diverse scientific backgrounds, demographics, geographies, career stages, and peer review experiences. CSR had therefore focused on enhancing diversity on Special Emphasis Panels and providing tools for Scientific Review Officers to help expand the pool of qualified reviewers. As a result of these efforts, there had been an increase in women, minority, and early stage career representation in study sections. Dr. Reed invited Councilmembers to learn more about CSR's efforts to <u>address bias in peer review</u>.

Discussion

Councilmembers noted that there could be a "diversity tax" in which women and minorities might be doing more work than their peers. A Councilmember asked whether there was also a gap between the number of male applicants and reviewers. Dr. Reed said that women were overrepresented on study sections compared to number of women submitting applications, whereas the same was not true among men. CSR considered the extent of review service to ensure that reviewers did not serve excessively. Councilmembers suggested tracking the delta to ensure that it did not continue to widen.

A Councilmember asked whether budgetary aspects had been removed from review. Dr. Reed said that, although budget had been removed from the Simplified Review Framework, there was still a legal requirement to consider it. Therefore, CSR still asked reviewers to comment on budget.

A Councilmember asked how often individuals declined to act as reviewers. Dr. Reed answered that there was no formal tracking mechanism but that the number of declines could often be quite high. To help address this issue, CSR had an advisory council that considered incentives for reviewers. The Councilmember asked whether there was a tracking mechanism for outcomes among fellowship trainees. Dr. Reed said that CSR did not track outcomes; however, Dr. Owens noted that the NINDS Office of Research Training & Career Development did.

A Councilmember suggested that the simplified scoring might result in a systemic drift for the worse in average scores. Dr. Reed suggested that there might not be a shift—although investigators might score high, reviewers did not average their criterion scores. Additionally, study sections operated independently with applications competing only within that section. CSR would monitor any shifts to evaluate the impact of the new policy.

A Councilmember noted that 25% of applications did not move to CSR review and asked where those applications landed. Dr. Reed said that those applications were reviewed within the individual Institutes, as they tended to be either topics the Institute was highly invested in or focused on a more complex topic. The Councilmember noted that applicants spent a lot of time reviewing panels to choose the most appropriate for their proposals, but often did not get assigned to their selection. Dr. Reed said that the CSR policy was to identify a panel with a good fit, and that they did consider the applicant's preference.

A Councilmember suggested that more males could be declining to review than females, which might contribute to the disparity. Dr. Reed said that study sections historically had more male representation, and that CSR had enacted several changes to overcome the disparity. While he was not aware of any particular behavioral trend contributing to the higher proportion of female reviewers, there could be a number of reasons (e.g., workload) for an individual to decline serving as a reviewer. CSR had taken a number of steps to make it easier to serve as a reviewer. For instance, they held virtual or hybrid meetings to help those who had other personal or professional responsibilities that would impede in-person meetings.

Dr. Koroshetz said that there was evidence that one key aspect of becoming a successful investigator was the mentorship they were offered within their fellowship grant. He asked whether the new process evaluated mentorship. Dr. Reed answered that the new process focused on the quality of mentorship by requiring mentors to provide specific plans for meeting the junior investigator's goals. Dr. Koroshetz also asked whether the new process ensured that a fellow had adequate grant funding to succeed. Dr. Reed said that the application must show adequate funding but that it did not matter where the funds came from.

VI. ME/CFS Research Roadmap

Dr. Vicky Whittemore, Program Director, Channels, Synapses, and Circuits NINDS Dr. Lucinda Bateman, Co-Chair, Founder and Medical Director, Bateman Horne Center Dr. Maureen Hanson, Co-Chair, Cornell University, Liberty Hyde Bailey Professor

Dr. Whittemore discussed the 2019 Report of the <u>NANDS Council Working Group for ME/CFS</u> and its recommendations, which were focused more on research infrastructure needs than on research itself. In February 2023, the Working Group began developing a roadmap to provide NANDS with scientific guidance to advance research on ME/CFS. Among the individuals who participated in the Working Group were 21 individuals with lived experience, bringing their important perspectives to the discussion. The Working Group considered eight domains involved in ME/CFS, including chronic infection, immune system, nervous system, circulation, metabolism, physiology, less studied pathogens, and genetics. The Working Group developed research priorities for each domain, which were shared with the public for feedback, then revised into a final report for NANDS.

Dr. Bateman provided an overview of the prevalence, characteristics, and diagnostic criteria of ME/CFS, as well as recent research efforts to understand individual differences in post exertional malaise (PEM), causal factors, triggers, heterogeneity, comorbid conditions, and natural history. PEM is illness relapse or symptom worsening triggered by activity or stressors. PEM can be physical, cognitive, sensory, emotional, or even being in upright posture. She highlighted some of the

parallels between ME/CFS and long COVID manifestations. She also pointed out that illness severity and functional capacity distinguished ME/CFS from other types of chronic fatigue.

Dr. Hanson reviewed key points from the research priorities across the eight domains. She emphasized that approximately 75% of individuals with ME/CFS mentioned a flu-like infection or mononucleosis, indicating that there may be a role in viral infection. Therefore, research priorities should explore the viruses that may play a role in the development and reactivation of ME/CFS. There was also evidence of abundant alterations in the immune systems of individuals with ME/CFS. Some of the research priorities for the immune system domain should therefore focus on the roles of autoimmunity, antigens, and other immune-related abnormalities.

Additionally, there was evidence of neuroinflammation, reduced cerebral blood flow, neuropathy, and other neurological dysfunctions common in individuals with ME/CFS. Research priorities in the nervous system domain should investigate the role of these impairments and their impact on sleep, cognitive function, circulation, and orthostatic dysfunction. Dr. Hanson noted that the Working Groups recommended the use of neuroimaging technology to investigate neural abnormalities and the effect of interventions, biomarker development, and sleep phase studies.

Dr. Hanson briefly reviewed research priorities across the remaining domains, highlighting the need for research in metabolomics, gut microbiota, connective tissue, mast cell activation, and other conditions that impacted the reproductive, endocrine, and gastrointestinal systems. It was also important to investigate the effects of individual genetic factors, as well as genome-wide association studies, family studies, and epigenetics. The Working Group also developed overarching priorities, including the need for multidisciplinary research, collaboration with advocacy groups and people with lived experience, innovative research approaches, and an expansion of biobanks. The Working Group highlighted the urgent need for research to help individuals who had been living with ME/CFS for several years and the importance of person-centered care. Rigorous and novel research approaches were needed to better understand the impact of ME/CFS over time, across sex, and within subtypes of the disease. The Working Group recommended that clinical trials begin immediately, despite the need to further research to develop clinical biomarkers and diagnostics.

Dr. Whittemore asked Councilmembers to review and accept the research roadmap so that their recommendations could begin moving into action. The Working Group hoped to explore future consortiums and roundtables—engaging federal, nonprofit, and individuals with lived experience to build on this momentum. Dr. Whittemore invited Councilmembers to review more information on the Working Group's <u>activities</u>.

Discussion

A Councilmember asked about efforts to collect postmortem brains to better understand the biology of the disease. Dr. Whittemore said that individuals with ME/CFS had an opportunity to donate their brain to the <u>NIH NeuroBioBank</u>, although it could be a sensitive topic in the community because of the prevalence of suicide among these individuals. Dr. Hanson acknowledged that it was an important topic to discuss, considering the insights that had been gathered about long COVID from postmortem studies. Another Councilmember suggested working with medical examiners, who may be amenable to sharing information.

A Councilmember suggested collecting clinical and natural history data to better understand the variance of the disease. Dr. Bateman agreed and said that a lot of the natural history data came from pre-electronic health records, which was difficult to code. Dr. Whittemore added that NIH-funded collaborative research centers had been collecting data that were uploaded into a data portal called <u>mapMECFS</u>.

A Councilmember commented on the need for stratification across subtypes. Dr. Hanson said that clustering symptoms was one approach for developing subtypes, but that it was also important to consider subtypes in clinical trials.

A Councilmember asked whether there was an interaction between ME/CFS and dementia risk. The panelists said that they were not aware of any studies indicating an increased risk. However, the Jackson Laboratory had been investigating immune profiling of individuals at different disease stages and found significant differences between younger individuals and those over the age of 60. While there seemed to be age-related differences, there were no data specific to dementia risk.

Dr. Koroshetz noted that although COVID-19 was a recent virus, coronaviruses had existed for a very long time. He asked whether it was possible that ME/CFS was driven by these coronaviruses. Dr. Hanson said that the possibility of a coronavirus variant as a causal factor could not be ruled out. Although there had been evidence of antivirus infection in some individuals, it was not known whether post-COVID-19 cases were related to SARS-CoV-2 or an earlier variant. Dr. Koroshetz talked about data from subgroups of individuals with long COVID that was stored in clinical trial platforms and asked whether such platforms could be used to test similar subgroups of individuals with ME/CFS. Dr. Hanson suggested that individuals with ME/CFS could be an important control group for long COVID treatment, with the exception of those who received drugs targeted for SARS-CoV-2 after 2020. Dr. Bateman added that those who had lived with ME/CFS for many years and had adapted their lifestyle would not likely be excited to join a clinical trial for exercise or sleep hygiene, but would be more interested in the development of primary interventions as soon as possible. Dr. Hanson agreed and said that there was an NIH study that showed evidence for T-cell exhaustion. Individuals with ME/CFS and long COVID might therefore be interested in the higher risk drugs for T-cell exhaustion used for individuals with cancer.

Council voted to accept the new ME/CFS report.

VII. NIH BRAIN Initiative® Update

Dr. John Ngai, Director, BRAIN Initiative

Dr. Ngai provided an overview of budget shifts for the BRAIN Initiative, which received funding from two sources—base funding from 10 participating NIH Institutes and Centers and funding from the 21st Century Cures Act through FY 2026. The 10 participating Institutes and Centers had committed to supporting the BRAIN Initiative with the BRAIN base funding even after the Cures Act expired in 2026. In FY 2023, the Cures Act provided a large increase in funding, which was met with a concomitant decrease in base funding in FY 2023 from \$468 million to \$230 million with the expectation that the base would be restored in FY 2024. Although this represented a \$60 million

increase in BRAIN in 2023 the base funding was not restored in FY 2024 when the Cures Act funding decreased by \$278 million. This resulted in a 40% decrease in the overall BRAIN Initiative budget.

Dr. Ngai published a <u>blog post</u> explaining the budget changes, which included a FAQ section. Additionally, there had been a 10% cut on out-year commitments (i.e., noncompeting awards). The budget decrease also meant that the program could only fund approximately half of the new grants that would otherwise have been awarded. Any applications that were not funded this year were deferred with the hope that the budget would be restored in FY 2025. The program also had to <u>cancel</u> a number of upcoming receipt dates and funding opportunity announcements. Funding awards in this budget environment were centered on BRAIN Initiative priorities, training a diverse cohort of next generation BRAIN investigators, research not funded through other mechanisms, research gap areas, and research that promoted geographic or institutional diversity.

Dr. Ngai reviewed recent BRAIN Initiative events. For example, to celebrate 10 years of BRAIN funding, each of the 10 participating Institute and Center Directors published or will publish a Director's Blog post—including a <u>blog post</u> from Dr. Koroshetz—on how the initiative had furthered their mission. The <u>10th Annual BRAIN Initiative Conference</u> will be held from June 16 to 18, 2024, with a number of special plenary sessions and workshops. There would also be a virtual workshop on <u>Advancing Human Neuroscience through Neural Stimulation and Recording</u> from May 23 to 24, 2024.

Dr. Ngai also provided scientific updates. The BRAIN Initiative Cell Census Project began with a series of pilots that scaled into the development of the <u>BRAIN Initiative Cell Census Network</u> (BICCN), which aimed to classify and better understand brain cells. The project also led to a number of peer-reviewed publications, including a set of 27 articles on cell type diversity in the primary motor cortex in *Nature* and *Nature* sister journals in 2021, and 10 articles (9 funded directly by BRAIN) on the Whole Mouse Brain Atlas in *Nature* in 2023. The Whole Mouse Brain Atlas analyzed more than 32 million cells across the adult mouse brain to better understand organizational principles of brain cell types. In 2023, the BICCN also published draft human and non-human primate brain cell atlases as 21 articles in Science Magazine, Science Advances, and Science Translational Medicine, which have furthered the understanding of human brain evolution, developmental changes, and neurodevelopmental and neurodegenerative disorders.

BRAIN 2.0 represented the next steps in transformative neuroscience research that would continue to scale the BICCN into the <u>BRAIN Initiative Cell Atlas Network</u> (BICAN), as well as support the <u>BRAIN</u> <u>Initiative Connectivity Across Scales</u> (BRAIN CONNECTS; a program to leverage cutting edge technology to analyze brain connectivity) and the <u>Armamentarium for Precision Brain Cell Access</u> (a program to leverage information from the Cell Census Project to develop reagents to more precisely target brain cell types and test hypotheses about cell function and connectivity). Dr. Ngai invited Councilmembers to track BRAIN Initiative projects through their <u>blog</u>.

Discussion

Councilmembers commended the BRAIN Initiative accomplishments in a challenging budget environment. A Councilmember asked how they might address the interpretation of their cell research for synaptic studies. Dr. Ngai said that the physical map was necessary for understanding how signals work in the brain, but it was also noted that a significant feature cell-cell signaling is mediated by neuromodulatory pathways that are not synaptic. He hoped that their findings would pave the way for better understanding this gap.

A Councilmember suggested that there was an opportunity for NINDS to consider the many non-R1 research institutes to leverage these datasets, possibly through education and training programs. Dr. Ngai responded that the BRAIN Initiative had a dissemination program to help investigators learn how use the datasets and collaborate across resource-limited institutions. Various Institutes and Centers had started to promote these tools, and there was hope that momentum would accelerate as more investigators were brought in.

A Councilmember expressed the need to address early brain development and plasticity. Dr. Ngai said that a large number of BICAN projects focused on human development and lifespan. For example, the blood-brain barrier was a non-static structure that changed over time. Lifespan was therefore important for targeting precision and personalized treatments.

VIII. Initiatives for Concept Clearance

Dr. David Owens, Acting Director, Division of Extramural Activities, NINDS

Three new concepts were presented.

Concept 1: New—BRAIN Initiative: Promoting Equity Through Technology Dissemination Partnerships. *Lead: Dr. Natalie Trzcinski*

Concept 2: New—Towards a Better Understanding of the Neurological Effects of Post-Acute Infection Syndromes. *Lead: Dr. Will Daley*

Concept 3: New—Digital Health Technology Derived Biomarkers and Outcomes Assessments for Remote Monitoring and Endpoint Development. *Lead: Dr. Carol Taylor-Burds*

The Council voted to approve proposed concepts 1–3.

Additional Concepts:

- 4. Reissue BRAIN Initiative: Research Resource Grants for Technology Integration and Dissemination. *Lead: Natalie Trzcinski*
- 5. Reissue Research Opportunities for New and "At-Risk" Investigators to Promote Workforce Diversity. *Lead: Lauren Ullrich*
- 6. Reissue Development of Biomarkers or Multi-Component Biomarkers for Neurological and Neuromuscular Disorders (R61/R33 Clinical Trial Optional). *Lead: Carol Taylor-Burds*
- 7. Reissue Blueprint Medtech: Small Business Translator (U44 Clinical Trial Optional). *Lead: Eric Atkinson*
- 8. Reissue Blueprint MedTech Translator (UG3-UH3 Clinical Trial Optional). *Lead: Eric Atkinson*
- 9. Reissue Ultra-Rare Gene-based Therapy (URGenT) Network. Lead: Tjerignimin Silue

10. Reissue CCRP Initiative: NIH Countermeasures Against Chemical Threats (CounterACT) Therapeutics Discovery and Early-Stage Development (UG3/UH3 Clinical Trial Not Allowed) Lead: Neel Dhruv

The Council voted to approve proposed concepts 4–10.

IX. Adjournment

The open session of meeting was adjourned at 4:00 p.m. on Wednesday, May 15, 2024.

CLOSED PORTION OF THE MEETING

X. Review of Conflict of Interest, Confidentiality, and Council Consideration of Pending Applications

This portion of the meeting was closed to the public in accordance with the determination that it was concerned with matters exempt from mandatory disclosure under sections 552b(c)(4) and 552b(c)(6), Title 5 U.S.C., and section 1009(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. §§ 1001-1014).

Members absented themselves from the meeting during discussion of and voting on applications from their own institutions, or other applications in which there was a potential conflict of interest, real or apparent.

Conflict of Interest – Regulations concerning conflict of interest were reviewed. Councilmembers were reminded that materials furnished for review purposes and discussion during the closed portions of the meeting are considered privileged information. All Councilmembers present signed a statement certifying that they had not been involved in any conflict-of-interest situations during the review of grant applications.

Confidentiality – During the closed session, any information that is discussed and the outcome of any recommendation are considered privileged information. They may not be discussed outside of the closed session. If an applicant requests support for his or her application from a Councilmember, the Councilmember must respond that he/she is not permitted to discuss the application. Any inquiry should be referred to Dr. David Owens, Acting NINDS Advisory Council Executive Secretary, who then will refer the question to the appropriate staff member for response.

Research Training and Career Development Programs – The Council reviewed a total of 373 research career development and institutional training grant applications with primary assignment to NINDS, and 212 of them (57 percent) were scored in the amount of \$18 million first-year direct costs. It is anticipated that, of the research career development and institutional training grant applications competing at this Council, NINDS will be able to pay first-year direct costs of approximately \$5.7 million (74 grants).

Research Project and Center Awards – The Council reviewed a total of 1,864 research project and center applications with primary assignment to NINDS, and 1070 of them (57 percent) were

scored/percentiled in the amount of \$537.5 million first-year direct costs. It is anticipated that, of the research grants competing at this Council, NINDS will be able to pay first-year direct costs of approximately \$84.9 million (224 grants).

Senator Jacob Javits Neuroscience Investigator Awards – The Senator Jacob Javits Neuroscience Investigator Awards are made to distinguished investigators who have a record of scientific excellence and productivity, who are actively pursuing an area of research of strategic importance, and who can be expected to continue to be highly productive for a seven-year period. Candidates are nominated and selected at each Council meeting. Council approved four Javits nominations at this meeting: Abigail Person, Ph.D. (University of Colorado Denver), Vijayalakshmi Santhakumar, Ph.D. (University of California Riverside), Debra Silver, Ph.D. (Duke University), and Alexander Sobolevsky, Ph.D. (Columbia University Irving Medical Center).

Small Business Innovation Research and Small Business Technology Transfer Award Programs – The Council reviewed a total of 190 Small Business Innovation Research (SBIR) and Small Technology Transfer Award (STTR) grant applications with primary assignment to NINDS, and 102 of them (54 percent) were scored in the amount of \$49.4 million first-year direct costs. It is anticipated that, of the SBIR and STTR applications competing at this Council, NINDS will be able to pay first-year direct costs of approximately \$2.7 million (4 grants).

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

XI. Adjournment

The meeting was adjourned at 1:15 p.m. on Thursday, May 16, 2024.

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

1

David Owens, Ph.D. Acting Executive Secretary National Advisory Neurological Disorders and Stroke Council Director, Division of Extramural Activities National Institute of Neurological Disorders and Stroke

Water J. Koroshetz mi)

Walter Koroshetz, M.D. Chairperson National Advisory Neurological Disorders and Stroke Council Director National Institute of Neurological Disorders and Stroke

These minutes will be formally considered by the Council at its next meeting. Corrections or notations will be incorporated in the minutes of that meeting.

National Advisory Neurological Disorders and Stroke (NANDS) Council May 15-16, 2024, Meeting Attachment 1

Walter J. Koroshetz, M.D. (Chairperson) Director, National Institute of Neurological Disorders and Stroke National Institutes of Health Bethesda, MD 20892 (Ex Officio member)

Amy E. Brin, MSN, MA, PCNS-BC(2025) Executive Director/CEO Child Neurology Foundation Lexington, KY 40508

Robert H. Brown, Jr., M.D., D.Phil.(2025)Director Program in NeurotherapeuticsUniversity of Massachusetts Chan Medical SchoolWorcester, MA 01655

Yishi Jin, Ph.D. (2026) Distinguished Professor Co-Director, The Kavli Institute of Brain and Mind Department of Neurobiology University of California, San Diego La Jolla, CA 92093

Jane Larkindale, D.Phil. (2026) Vice President PepGen Inc. Cambridge, MA 02142

Jin-Moo Lee, M.D., Ph.D., FAHA (2026) Andrew B. & Gretchen P. Jones Professor Professor, Department of Radiology Professor, Department of Biomedical Engineering Professor, Division of Biology and Biomedical Sciences Washington University School of Medicine St. Louis, MO 63110

John H.R. Maunsell, Ph.D. (2025) Albert D. Lasker Professor Department of Neurobiology University of Chicago Chicago, IL 60637 Louise D. McCullough, M.D., Ph.D. (2025) Professor and Chair Department of Neurology McGovern Medical School University of Texas Health Science Center at Houston Houston, TX 77030

Henry L. Paulson, M.D., Ph.D. (2026) Lucile Groff Professor of Neurology Department of Neurology University of Michigan Ann Arbor, MI 48109

Gina R. Poe, Ph.D. (2024) Professor Department of Integrative Biology and Physiology University of California, Los Angeles Los Angeles, CA 90095

Ekemini Riley, Ph.D. (2024) Founder and CEO Coalition for Aligning Science, LLC Managing Director Aligning Science Across Parkinson's Disease Chevy Chase, MD 20815

Timothy A. Ryan, Ph.D. (2024) Professor Department of Biochemistry Weill Cornell Medical College New York, NY 10021

Sameer A. Sheth, M.D., Ph.D. (2024) Associate Professor and Vice Chair of Clinical Research Department of Neurosurgery Baylor College of Medicine Houston, TX 77030

Terms end July 31 of the designated year.

Ex Officio Members

Christopher T. Bever, Jr., M.D. Director, Biomedical and Laboratory Research Office of Research and Development Department of Veterans Affairs Washington, DC 20003

David L. Brody, M.D., Ph.D. Uniformed Services University of the Health Science Director, Center for Neuroscience and Regenerative Medicine Director, USU/NIH Traumatic Brain Injury Research Center Bethesda, MD 20892

Xavier Becerra Secretary Department of Health and Human Services Washington, DC 20201

Monica M. Bertagnolli, M.D. Director National Institutes of Health Bethesda, Md 20892

Executive Secretary

David Owens, Ph.D. Acting Director, Division of Extramural Activities National Institute of Neurological Disorders and Stroke National Institutes of Health Bethesda, MD 20892

Subject Matter Experts

Daniel L. Doctoroff, J.D. Founder and Board Chair Target ALS New York, NY 10023

Florian S. Eichler, M.D. Associate Professor Department of Neurology Harvard Medical School Massachusetts General Hospital Boston, MA 02114

Robert W. Gereau, IV, Ph.D. Vice-Chair for Research Director, Washington University Pain Center Dr. Seymour and Rose T. Brown Professor of Anesthesiology and Department of Neuroscience Washington University School of Medicine St. Louis, MO 63110

Frances E. Jensen, M.D. Professor and Chair Department of Neurology Perelman School of Medicine University of Pennsylvania Pennsylvania, PA 19104

Amy L. McGuire, Ph.D., J.D. Leon Jaworski Professor Center for Medical Ethics and Health Policy Baylor College of Medicine Houston, TX 77030

Kate M. Nicholson, J.D. President and Founder The National Pain Advocacy Center Boulder, CO 80302

National Advisory Neurological Disorders and Stroke (NANDS) Council May 15-16, 2024, Meeting Attachment 2

NINDS employees present for portions of the meeting included:

Sid Abeywickrama Amy Adams Deanna Adkins Mariam Afzal Ram Arudchandran Herson Astacio Eric Atkinson Taryn Aubrecht Debra Babcock Julia Bachman Farah Bader Linda Bambrick Jennifer Barnes Lucinda Batemen Janna Belser Mary (C) Bennett Kaitlyn Benson **Richard Benson** William Benzing **Clayton Bingham** Victoria Bitzer-Wales Sunil Bogisam Melissa Bojos Naomi Booker Francesca Bosetti Giulia Bova Vicki Brings Steve Britt Erin Bryant **Ryan Calabrese Roger Campbell** Scarlette Cella Denise Chatman Thomas Cheever Andrew Chen **Bo-Shiun Chen** Daofen Chen Liyun Chen David Cheng Maria Chiuchiolo Sophie Cho Molly Cluster Mary Coats

Christopher Conrad Rebekah Corlew Devon Crawford Cheryl Cudz Cheryl Cudzilo Adi Cymerblit-Sabba William Daley Sara Dauber Karen David Dana Day Vedangi Desai Neel Dhruv Alicia Diggs Dana Discenza Sara Dodson Anthony Domenichiello Jianxun Dong Adele Doperalski Argenia Doss **Kristin Dupre** Jaclyn Durkin Nancy Eaby Anahid Ebrahimi Debbie Eng Judy Fabrikant Christina Fang Carlos Faraco **Nicole Farhat Robin Felder** Cassandra Fields Monica Flemming Jessica Forbes Jane Fountain Megan Frankowski Natalie Frazin Deb Freaner Ben Free Patrick Frost Bellgowan Lina Garcia Shannon Garnett Hermon Gebrehiwet Annette Gilchrist Marie Gill

Ashley Givens Jordan Gladman Fana Goitom Senthil Gounder **Thomas Greenwell Brooks Gross Rogers Gross li** Amelie Gubitz Luis Guerra Mohamed Hachicha **Rodney Hall** Joseph Hall Maureen Hanson Kristi Hardy Brandon Hartsell Ali Hassani **Brian Haugen** Lanier Heyburn **Rebecca Hommer** Mariah Hoye Minghan Hu Eric Hudak Grace Hwang Smriti lyengar Lyn Jakeman Scott Janis Lawrence Janis Kari Johnson Lataisia Jones **Kevin Jones** Michelle Jones-London Cory Kelly Noam Keren Brenda Kibler Linda Kiefer Jenny Kim Jim Koenig Carol Kong Svetlana Kotliarova Jonathan Kreisler Christine Lam Nick Langhals Crystal Lantz

Tonya Lee Crystal Lee **Miriam Leenders** Nina Lichtenberg **Rosa Lopez** Quynh Ly **Timothy Lyden** Dina Lyon Ernie Lyons Laura Mamounas Sade Matthews-Fitch Amber Mccartney Linda Mcgavern Barbara Mcmakin Mirela Milescu **Daniel Miller** Pantea Moghimi Dp Mohapatra John Ngai Cristina Nigro **Glen Nuckolls** Michael Obodozie Joan Ohayon Ana Olariu Janet Oputa Leslie Osborne David Owens **Hyejung Park** Tatiana Pasternak Mary Pelleymounter Elio Peraza Leah Pogorzala Joanne Pomponio Linda Porter Pragya Prakash Rebecca Price **Michele Pucak** Sangeetha Pulicherla

Members of the public present: Ronald Bartek Bret Light Cheryl Lohman Samuel Keating Perry Kirkham Cj Puttaswamy Elizabeth Quartey Shamsi Raeissi Shanta Rajaram Srikanth Ranganathan Sridhar Ravva Alva Recinos Bruce Reed Katie Reichard Kavon Rezaizadeh Matthew Rice **Ryan Richardson** Sarah Robinson Schwartz Ken Ryland **Rashid Salehov** Sara Sameni Joshua Sanchez Lumy Sawaki-Adams Joel Saydoff Igbal Sayeed Alisa Schaefer **Gretchen Scott** Nilkantha Sen Mengge Shan Shalini Sharma Kelly Sheppard Frank Shewmaker Arvind Shukla Beth-Anne Sieber Shai Silberberg Adissa Silue Maryann Sofranko Rukmareddy Sripathi Harish Sriperambudur Natalia Strunnikova Abhi Subedi Tao Sun **Maripierre Surpris**

Christine Swanson-Fischer Elizabeth Sypek **Thomas Taetzsch** Edmund Talley James Taylor Anna Taylor **Carol Taylor-Burds** Anna Tayor Michael Tennekoon Pradeep Thapaliya **Christine Torburg** Natalie Trzcinski Amy Tsou Eric Tucker William Tyler Lauren Ullrich George Umanah Ursula Utz Yee Vang Andrea Varea Oleksandr Vedmid **Claudio Villalobos Dintrans** Tam Vo Laura Wandner **Rachel Weinberg** Elvse White Vicky Whittemore Shellie Wilburn Nasim Winchester Vahidi Sarah Woller Carl Wonders Ling Wong **Clinton Wright** Andrew Wright Patrick Wright **Guangying Wu** Xiling Yin Ran Zhang