***Brain Research Through Advancing Innovative Neurotechnologies*® (BRAIN)**
Multi-Council Working Group (MCWG) Meeting
May 24, 2023

On May 24, 2023, the National Institutes of Health (NIH) *Brain Research Through Advancing Innovative Neurotechnologies*® (BRAIN) Initiative Multi-Council Working Group (MCWG) met virtually to discuss the current state of the BRAIN Initiative and learn about research by a new MCWG member on engineering flies to study gene and protein function.

In opening remarks, Susan Weiss, PhD, Designated Federal Official of the MCWG, welcomed everyone. Next, John Ngai, PhD, director of the NIH BRAIN Initiative and chair of the MCWG, thanked David Holtzman, MD, the representative from the National Institute on Aging (NIA), for his service on the MCWG. Dr. Ngai welcomed two new employees, Joe Monaco, PhD, and Ms. Sandra Molina, to the Office of the BRAIN Director. He welcomed Susan Wright, PhD, Associate Director for Data Science at the National Institute on Drug Abuse (NIDA), as the new Team Data co-lead. Next, Dr. Ngai summarized the NIH BRAIN project team structure and provided a budget overview, noting the increase in Congressionally-appropriated funds for the BRAIN Initiative in fiscal year 2023. He also highlighted the progress over the years. Since 2014, the BRAIN Initiative has invested over $3 billion to fund over 1300 projects. Dr. Ngai recognized the recipients of the 2023 Brain Prize, Christine Holt, PhD, at Cambridge University, Erin Schuman, PhD, at Max Planck Institute, and BRAIN-funded investigator, Michael Greenberg, PhD, at Harvard University, for ground-breaking discoveries on molecular mechanisms of brain development and plasticity. He acknowledged newly elected members to the National Academy of Science (NAS) in recognition of distinguished and continuing achievements in original research. Dr. Ngai also recognized the Howard Hughes Medical Institute (HHMI) Freeman Hrabowski Scholars as outstanding early career faculty with the potential to become leaders in their fields and create diverse and inclusive environments. Among this year's HHMI Freeman Hrabowski scholars is Dr. Lucas M. Cheadle, a BRAIN K99/R00 awardee at Cold Spring Harbor Laboratory. Then, Dr. Ngai recapped the recent Brain Behavior Quantification and Synchronization (BBQS) Program Workshop: Sensor Technologies to Enhance our Understanding of Behavior, which took place on May 2-3, 2023. The goal of the hybrid workshop was to identify technologies for unraveling the biological basis of behavior and cognition. He also highlighted some upcoming events, including the 9th Annual BRAIN Initiative Meeting, which will take place on June 12-13, 2023. Dr. Ngai also noted BRAIN signed on to the Targeted Genome Editor Delivery (TARGETED) Challenge, which will include a total of $6,000,000 in prizes.

Next, Dr. Ngai presented the NIH BRAIN Initiative investigator demographic and institute geographic data for fiscal year 2022. BRAIN Investigators include 19% women, 5% underrepresented minority groups, and 1% with a disability. Other key takeaways include: 32% of investigators have engineering experience; funding rates are similar between men and women; early-, mid-, and late-career applicants have similar funding rates in fiscal year 2022; performance sites are in 42/50 states and Puerto Rico, but still favor the coasts; and BRAIN funding favors R1 institutions. He also updated the group on the Plan for Enhancing Diverse Perspectives (PEDP), emphasizing its incorporation in 130 funding opportunities across 19 NIH Institutes, Centers, and Offices since 2021. He also highlighted new and current funding opportunities for brain behavior quantification (RFA-MH-23-335; RFA-DA-23-030; RFA-MH-23-130), neural recording and stimulating techniques (RFA-DC-24-001), molecular technologies for neural circuits (RFA-MH-22-245), cell-specific and circuit-specific processes in the brain (RFA-MH-23-290), research with activities related to diversity (PAR-23-122), NIH Science Education Partnership Awards (PAR-23-137), as well as training (RFA-MH-23-110; NOT-OD-21-134) and diversity-focused (RFA-NS-21-012; RFA-MH-23-330/331; NOT-NS-22-012) programs. Lastly, Dr. Ngai discussed some recent BRAIN-funded studies focused on tracking

spontaneous behavior in mice,[1] receptors for enhanced blood-brain barrier crossing,[2] neural signatures of chronic pain,[3] and epidural stimulation of the cervical spinal cord for post-stroke upper limb paresis.[4]

Christine Grady, RN, PhD, chief of the NIH Department of Bioethics and co-chair of the Neuroethics Working Group (NEWG), updated the group on NEWG activities. Dr. Grady announced a planned NIH BRAIN NEWG Workshop on the Ethics of Sharing Individual Level Human Brain Data Collected in Biomedical Research. The workshop is planned to occur on July 17-18, 2023, as a hybrid meeting, in-person in Bethesda, Maryland, with virtual participation enabled. The goals of this workshop are to explore meaningful ways to categorize human brain data by potential risks of data sharing and any resulting differences in how to treat data and to articulate points-to-consider for researchers in disclosing the potential risks of sharing human brain data. The workshop website and registration will be available in the coming weeks. Then, Dr. Grady shared a recent NEWG consult presented by Nita Farahany, JD, PhD Professor of Law & Philosophy at Duke University and NEWG co-chair, at National Institute of Mental Health (NIMH) Council. The consult concerned the ethical considerations for open versus restricted genomic data access, as the goal of the BRAIN Initiative Cell Atlas Network (BICAN) is to build reference brain cell atlases, providing a foundational framework for the study of brain function and disorders. BICAN requires the collection of brain specimens from diverse human donors, particularly primary sequence data which is potentially re-identifiable. The consult was focused on the merits and risks of open access vs. controlled access of those genomic primary sequencing data. At NIMH Council, Dr. Farahany noted there is insufficient evidence quantifying benefits or risks of open data sharing, and without that evidence, it is difficult to determine the relative merits and risks and there should be more articulation of what the benefits are in order to justify potential risks. Experts suggested embedding additional bioethicists in BICAN projects to assist in these challenges.

The MCWG meeting continued with a scientific presentation by MCWG member, Hugo Bellen, DVM, PhD, at Baylor College of Medicine, about engineering flies to study gene and protein function and the impact on the Undiagnosed Disease Network (UDN). The UDN is a national network of clinicians and scientists who work together to diagnose rare diseases. Dr. Bellen's research team applies technological upgrades to engineer flies and efficiently tag thousands of genes in order to probe gene function rapidly and provide critical reagents to model human disease. This exciting technology has contributed to the discovery of numerous human disease-causing genes, including those involved in Charcot-Marie-Tooth disease, Leigh Syndrome, and Friedreich's ataxia, and provides tools to screen for drugs.

The next MCWG meeting will be held on August 29, 2023, and a video recording will be available for live viewing and archived.

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[1] Levy, D. R., Hunter, N., Lin, S., Robinson, E. M., Gillis, W., Conlin, E. B., Anyoha, R., Shansky, R. M., Datta, S. R. (2023). Mouse spontaneous behavior reflects individual variation rather than estrous state. *Curr. Biol. 33*(7), 1358-1364.

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[4] Powell, M. P., Verma, N., Sorenson, E., Carranza, E., Booa, A., Fields, D. P., Roy, S., Ensel, S., Barra, B., Balzer, J., Goldsmith, J., Friedlander, R. M., Wittenberg, G. F., Fisher, L. E., Krakauer, J. W., Gerszten, P. C., Pirondini, E., Weber, D. J., Capogrosso, M. (2023). Epidural stimulation of the cervical spinal cord for post-stroke upper-limb paresis. *Nat. Med. 29*, 689-699.