***Brain Research Through Advancing Innovative Neurotechnologies®* (BRAIN)**
Multi-Council Working Group (MCWG) Meeting
August 29, 2023

On August 29, 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 updates from the BRAIN Neuroethics Working Group (NEWG) and other BRAIN Initiative partners. In addition, the MCWG provided feedback on a concept for a funding opportunity around non-invasive imaging.

In opening remarks, Susan Weiss, PhD, Designated Federal Official of the MCWG, welcomed all meeting participants. Dr. Weiss introduced Frank Longo, MD, PhD, as the new representative from the National Institute on Aging (NIA) for the MCWG, and thanked Elba Serrano, PhD, for her service to both the MCWG and the NEWG. Next, John Ngai, PhD, Director of the NIH BRAIN Initiative and Chair of the MCWG, welcomed new staff and summarized the BRAIN project team structure and budget. Since 2014, the BRAIN Initiative has invested more than $3 billion to fund more than 1,300 projects. In addition, the NIH BRAIN Initiative website has been refreshed to help users find content and information, including funding opportunities, more easily. Dr. Ngai then highlighted multiple recently held meetings and conferences, including the 9th Annual BRAIN Initiative Meeting and a Congressional Neuroscience Caucus Briefing on the BRAIN Initiative. Dr. Ngai described upcoming events and competitions, including the BRAIN Initiative Cell Census Network (BICCN) Enhancer Prediction Challenge (September 2023) and the Targeted Genome Editor Delivery (TARGETED) Challenge (October 5, 2023). He also presented an overview of current BRAIN programs and associated funding opportunities and notices.

Lastly, Dr. Ngai highlighted new scientific findings and developments from the BRAIN Initiative: (1) use of improved next generation genetically encoded voltage indicators (GEVIs),[1,2,3] (2) mapping of the complete adult *Drosophila* brain connectome and development of associated tools (e.g., FlyWire), (3) music reconstruction from human auditory cortex activity using nonlinear decoding models,[4] (4) a first-in-human trial successfully evaluating the safety and feasibility of combining DBS and traditional rehabilitation for late-stage post-stroke recovery of upper extremity control,[5] and (5) a wearable platform for closed-loop stimulation and recording of single-neuron and local field potential activity in freely moving humans.[6]

Following Dr. Ngai's updates, Christine Grady, RN, PhD, Chief of the NIH Department of Bioethics and Co-Chair of NEWG summarized the July 2023 NEWG workshop, which focused on understanding the ethical considerations around sharing individual-level human brain data, and considering the trade-offs of benefits and risks that come with sharing brain data. That workshop also discussed potential safeguards

---

[1] S. Wenceslao Evans et al. (2023). A positively tuned voltage indicator for extended electrical recordings in the brain. *Nature Methods, 20*(7), 1104–1113. https://doi.org/10.1038/s41592-023-01913-z
[2] Jelena Platisa et al. (2023). High-speed low-light in vivo two-photon voltage imaging of large neuronal populations. *Nature Methods, 20*(7), 1095–1103. https://doi.org/10.1038/s41592-023-01820-3
[3] He Tian et al. (2023). Video-based pooled screening yields improved far-red genetically encoded voltage indicators. *Nature Methods, 20*(7), 1082–1094. https://doi.org/10.1038/s41592-022-01743-5
[4] Ludovic Bellier et al. (2023). Music can be reconstructed from human auditory cortex activity using nonlinear decoding models. *PLOS Biology, 21*(8), e3002176, https://doi.org/10.1371/journal.pbio.3002176
[5] Kenneth B. Baker et al. (2023). Cerebellar deep brain stimulation for chronic post-stroke motor rehabilitation: A phase I trial. *Nature Medicine*, 1–9. https://doi.org/10.1038/s41591-023-02507-0
[6] Uros Topalovic et al. (2023). A wearable platform for closed-loop stimulation and recording of single-neuron and local field potential activity in freely moving humans. *Nature Neuroscience, 26*(3), 517–527, https://doi.org/10.1038/s41593-023-01260-4

to mitigate any risks arising from sharing of human brain data, including for example, improvements to informed consent. During the August 2023 NEWG meeting, as a follow-up panel from the workshop, the NEWG focused on a deep dive of informed consent, and more specifically, disclosure and participant control in the sharing of human brain data. On disclosure, NEWG discussion focused on what individuals need to understand prior to sharing their data (and in what level of detail). The NEWG also heard from speakers around different models of informed consent, towards the goal of providing information to help participants make choices around sharing their data, and to respect those choices.

Next, Floh Thiels, PhD, Program Director at the National Science Foundation (NSF) updated the group on cross-cutting and new programs supporting brain science at NSF, including BioDesign, BioFoundries, Regional Innovations Engines, Convergence Accelerator, Collaborative Research in Computational Neuroscience, the Behavioral and Neural Systems programs, Biology Integration Institutes, and Integrative Research in Biology. Other relevant NSF programs include: Human-Centered Computing, Robust Intelligence, Disability and Rehabilitation Engineering, Emerging Frontiers in Research and Innovation, Mathematical Biology, Statistics, Chemistry of Life Processes, Physics of Living Systems, and Education (EDU) Core Research.

Shumin Wang, PhD, Program Director at the National Institute of Biomedical Imaging and Bioengineering (NIBIB) presented on a concept on transformative discovery to resolve the heterogeneity of the brain through non-invasive imaging. Current non-invasive methods—including PET, MRI, ultrasound, and optical imaging—are limited by dimensionality differences, scaling differences, and tissue accessibility. To address these limitations, researchers can mine BRAIN cell census data to nominate and prioritize imaging targets. The expected outcome of this research will answer what, how, and to what extent non-invasive imaging features can identify and localize different brain cells. These approaches can potentially accelerate the development of new research paradigms, diagnoses, targeted therapies, and treatment management for the brain and beyond. Dr. Wang provided multiple publications implementing targeted approaches to non-invasive imaging.[7,8,9,10,11] For example, one research group developed a genetically targeted reporter for PET imaging of deep neuronal circuits in mouse brains.[12] There was robust discussion among MCWG members and NIH staff on this concept, including the degree to which some of the techniques are considered non-invasive, but MCWG were overall supportive of the concept and emphasized its importance in furthering our understanding of the brain. Moreover, Dr. Ngai stated that AAV techniques can help identify cell type targets and support the feasibility of non-invasively imaging these targets, allowing researchers to develop ligands for non-invasive imaging in humans.

The next MCWG meeting will be held on February 13, 2024, and a video recording will be available for live viewing and archived.

[7] Tushar Kamath et al. (2022). Single-cell genomic profiling of human dopamine neurons identifies a population that selectively degenerates in Parkinson's disease. *Nature Neuroscience, 25*(5), 588–595. https://doi.org/10.1038/s41593-022-01061-1
[8] Jonah Langlieb et al. (2023, March 13). The cell type composition of the adult mouse brain revealed by single cell and spatial genomics. *bioRxiv*. https://doi.org/10.1101/2023.03.06.531307
[9] Hyla Allouche-Arnon et al. (2022). Computationally designed dual-color MRI reporters for noninvasive imaging of transgene expression. *Nature Biotechnology, 40*(7), 1143–1149. https://doi.org/10.1038/s41587-021-01162-5
[10] Agessandro Abrahao et al. (2019). First-in-human trial of blood–brain barrier opening in amyotrophic lateral sclerosis using MR-guided focused ultrasound. *Nature Communications, 10*(1), 4373, https://doi.org/10.1038/s41467-019-12426-9
[11] Ali R. Rezai et al. (2020). Noninvasive hippocampal blood−brain barrier opening in Alzheimer's disease with focused ultrasound. *Proceedings of the National Academy of Sciences, 117*(17), 9180–82, https://doi.org/10.1073/pnas.2002571117
[12] Masafumi Shimojo et al. (2022). A genetically targeted reporter for PET imaging of deep neuronal circuits in mammalian brains. *The EMBO Journal, 40*(22), e107757, https://doi.org/10.15252/embj.2021107757