***Brain Research Through Advancing Innovative Neurotechnologies*® (BRAIN)**
Multi-Council Working Group (MCWG) Meeting
August 22, 2024

On August 22, 2024, 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 opening remarks, Susan Weiss, Ph.D., designated federal official of the MCWG, welcomed meeting participants and introduced new MCWG members: Angela Laird, Ph.D., Florida International University, representative for National Institute on Drug Abuse (NIDA); Tor Wager, Ph.D., Dartmouth College, representative for National Center for Complementary and Alternative Medicine (NCCIH); and Kathleen Zackowski, Ph.D., O.T.R., National Multiple Sclerosis Society, representative for *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD). Dr. Weiss thanked Hugo Bellen, D.V.M., Ph.D., Baylor College of Medicine; Kafui Dzirasa, M.D., Ph.D., Duke University; and Bruce Rosen, M.D., Ph.D., Havard Medical School, for their service to the MCWG.

Next, John Ngai, Ph.D., director of the NIH BRAIN Initiative and chair of the MCWG, presented BRAIN Initiative updates and events. Dr. Ngai highlighted the announcement of the 2024 Kavli Prize in Neuroscience for the discovery of a specialized system for representation of faces in human and non-human primate (NHP) neocortex, which included BRAIN contributors, Drs. Nancy Kanwisher and Doris Ying Tsao. He described celebrations for 10 years of the BRAIN Initiative, debriefs of the 10th Annual BRAIN Initiative Conference and the BRAIN Initiative Workshop on Advancing Human Neuroscience through Neural Stimulation and Recording, and the upcoming BRAIN Initiative Alliance Toolmakers Satellite Event at the 2024 Society for Neuroscience meeting. In addition, he reviewed BRAIN community engagement efforts, including the 2024 Congressional Neuroscience Caucus Briefing, the 2024 Brain Awareness Lecture Series, a tour of the Princeton Neuroscience Institute, and the upcoming American Brain Economy Summit.

Dr. Ngai then shared current funding opportunities and summarized the BRAIN project team structure and budget. Lastly, Dr. Ngai highlighted new scientific findings and developments from the BRAIN Initiative: (a) a new adeno-associated virus that mediates blood-brain barrier crossing for brain-wide delivery in humans,[1] (b) subicular neurons encoding concave and convex geometries,[2] (c) semantic encoding that occurs during language comprehension at single-cell resolution, [3] and (d) the development of an accurate and rapidly calibrating speech neuroprosthesis.[4]

NEWG Co-Chair Christine Grady, Ph.D., NIH Clinical Center, then summarized the August 21, 2024, NEWG meeting. Overall, the meeting focused on discussing the intersection of artificial intelligence

[1] Huang, Q. et al. (2024). An AAV capsid reprogrammed to bind human transferrin receptor mediates brain-wide gene delivery. *Science 384*, 1220-1227. https://doi.org/10.1126/science.adm8386
[2] Sun, Y., Nitz, D.A., Xu, X. et al. (2024). Subicular neurons encode concave and convex geometries. *Nature 627*, 821-829. https://doi.org/10.1038/s41586-024-07139-z
[3] Jamali, M., Grannan, B., Cai, J. et al. (2024). Semantic encoding during language comprehension at single-cell resolution. *Nature 631*, 610-616. https://doi.org/10.1038/s41586-024-07643-2
[4] Card, N. et al. (2024). An accurate and rapidly calibrating speech neuroprosthesis. *New England Journal of Medicine 391*, 609-618. https://doi.org/10.1056/NEJMoa2314132

(AI), neuroscience research, and ethics. To begin the meeting, several speakers provided an overview of foundational brain models implemented in neuroscience. Next, the NEWG explored two cases of intersectional AI and neuroscience research to engage discussions of ethical considerations among NEWG members. For the first case, speakers presented on AI models that implement brain data for deep phenotyping of mental health and psychiatric conditions, as well as ethical considerations for such AI models, such as informed consent, privacy and confidentiality, equity and access, and algorithmic biases. For the second case, speakers previewed a proof-of-principle generative AI model that trains on electroencephalography (EEG) datasets to predict future EEG outputs, ethical considerations for downstream applications of such AI models, and existing AI governance and ethical frameworks. Lastly, NEWG discussed next steps for developing neuroscience-specific AI ethical guidance, such as upscaling AI models as their complexity increases, mitigating algorithmic biases, and inventorying existing AI ethics work across NIH to avoid duplicative efforts. Dr. Grady also highlighted several AI neuroscience events in 2024, including a National Academies workshop on exploring the bidirectional relationship between AI and neuroscience, the upcoming BRAIN NeuroAI Workshop, and the upcoming 2025 International Neuroethics Society Annual Meeting.

Finally, Tirin Moore, Ph.D., Professor of Neurobiology at Stanford University and MCWG member, presented on how intermittent rate coding and cue-specific neuronal ensembles support working memory. Currently, two competing mechanistic models of working memory exist: the spiking model describes working memory as encoded by elevated neuronal spiking activity, and the synaptic model describes working memory as encoded by patterns of short-term plasticity. To help determine which model more accurately represents working memory, Dr. Moore's group implanted Neuropixel probes in the dorsolateral prefrontal cortex of non-human primates (NHPs) to record large-scale, high-density electrophysiology. The group then recorded neuronal response during a delayed-response task, in which NHPs were presented with a visual cue on a screen and then asked to recall the screen location of the cue. The group concluded that mnemonic information from cues does not persist in the spiking activity of neuronal populations, but instead alternates between neuronal "On" and "Off" states. "On" states are formed through novel neuronal connections during cue presentation. At the level of single neurons, "On" states are driven by increased spiking activity, while "Off" states are driven by both a loss of selectivity for memoranda and a return of neuronal firing rates to spontaneous levels. During "Off" states, mnemonic information is available in the patterns of functional connections among neuronal ensembles, supporting the synaptic model. These findings highlight opportunities for future research using Neuropixel probes for *in vivo* electrophysiology recordings.

For more on the open session of the August MCWG meeting, view the video recording. The next MCWG meeting will be held on January 31, 2025.