

**Brain Research Through Advancing Innovative Neurotechnologies® (BRAIN)
Neuroethics Working Group (NEWG) Meeting
January 24th, 2023**

On January 24, 2023, the National Institutes of Health (NIH) *Brain Research Through Advancing Innovative Neurotechnologies®* (BRAIN) Initiative [Neuroethics Working Group \(NEWG\)](#) met virtually to discuss health-related technologies that affect the brain.

[In opening remarks](#), Andrea Beckel-Mitchener, PhD, deputy director of the NIH BRAIN Initiative and Designated Federal Official of the NEWG, welcomed everyone. Next, Christine Grady, RN, PhD, chief of the NIH Department of Bioethics and NEWG co-chair, welcomed Nita Farahany, JD, PhD, as the new NEWG co-chair. Dr. John Ngai, director of the NIH BRAIN Initiative, updated the group on BRAIN Initiative neuroethics activities. First, he reminded the group of a funding supplement for integrating bioethics into current projects ([NOT-OD-23-018](#)) and recapped a [NEWG workshop](#) on continuing responsibilities for participants of neural implant trials, highlighting the need to continue discussions on this topic. Dr. Ngai summarized a recent study which showed that human cortical organoids derived from induced pluripotent stem cells can form functional connections with mouse brain tissue *in vivo*¹, and an early study that tested adaptive deep brain stimulation (DBS) of the nucleus accumbens in humans as a possible treatment for loss-of-control or binge eating disorder².

The meeting continued with two presentations on the application of health-related technologies to brain research and how the NEWG may engage in this space. Dr. Farahany highlighted a few neuroethics topics, including the potential benefits of neural modulation and how ethical considerations may vary for different types of interventions (e.g., invasive devices vs. wearable technologies). Next, Dr. Grady introduced the guest speakers. Andrew Krystal, MD, at the University of California, San Francisco, gave a presentation on closed-loop neuromodulation in an individual with treatment-resistant depression. First, Dr. Krystal overviewed the challenges of using DBS in major depressive disorder, including a lack of clarity on where to stimulate within the depression circuit, individual variability, and dose titration. Then he discussed findings from a case study in which his team developed a novel biomarker-driven closed-loop DBS approach to treat a patient with depression^{3,4}. Researchers used exploratory stimulus-response mapping to identify the amygdala and a related subcircuit as a personalized biomarker of symptoms and implemented closed-loop DBS therapy, which resulted in a rapid and sustained improvement in depression symptoms. However, more research is needed to determine if the novel approach generalizes to a broader population. The NEWG considered how closed-loop therapy may change neural circuit function over time and emphasized the need for additional rigorous testing.

Vivek Pandrangi, MD, at the Oregon Health and Science University, presented findings from a recent study on the use of virtual reality (VR) to manage post-operative pain and opioid use. In the study, Dr. Pandrangi and his team tested a VR intervention in hospitalized adults recovering from head and neck surgery. One group used the Oculus Quest console to play an immersive, active VR game (n=14) while

¹ Wilson, M. N., Thunemann, M., Liu, X., Lu, Y., Puppo, F., Adams, J. W., ... & Kuzum, D. (2022). Multimodal monitoring of human cortical organoids implanted in mice reveal functional connection with visual cortex. *Nature Communications*, 13(1), 7945.

² Shivacharan, R. S., Rolle, C. E., Barbosa, D. A., Cunningham, T. N., Feng, A., Johnson, N. D., ... & Halpern, C. H. (2022). Pilot study of responsive nucleus accumbens deep brain stimulation for loss-of-control eating. *Nature Medicine*, 28(9), 1791-1796.

³ Scangos, K. W., Khambhati, A. N., Daly, P. M., Makhoul, G. S., Sugrue, L. P., Zamanian, H., ... & Chang, E. F. (2021). Closed-loop neuromodulation in an individual with treatment-resistant depression. *Nature medicine*, 27(10), 1696-1700.

⁴ Scangos, K. W., Makhoul, G. S., Sugrue, L. P., Chang, E. F., & Krystal, A. D. (2021). State-dependent responses to intracranial brain stimulation in a patient with depression. *Nature medicine*, 27(2), 229-231.

the control group played a 2D game on a handheld smartphone (n=15). Researchers found reduced subjective pain and opioid use in the VR group compared to controls, suggesting that VR may help people manage pain and reduce reliance on opioids after surgery. The group discussed future studies on mindfulness VR, the technical challenges of implementing VR in the hospital setting, and VR misuse.

Next, the NEWG discussed the ethical implications raised by the aforementioned studies and other health-related technologies that affect the brain. Within the scope of BRAIN, they considered the importance of informed consent, reversibility of clinical interventions, understanding the biological mechanisms, and potential long-term consequences. The group also suggested developing ways to integrate neuroethics into BRAIN-funded small business projects and the need to evaluate the personalization versus generalizability of each treatment. The NEWG recognized the value of engaging with patients and people with lived experience as new therapies emerge. Further, they considered how to navigate NEWG efforts in this space; for example, participants suggested focusing on meeting researchers' needs, technologies and tools funded by BRAIN, and translational or commercialization potential. Overall, the group agreed that the NEWG can contribute to this topic. Potential next steps included revisiting findings from the "Neuroethics Roadmap" report [The BRAIN Initiative® and Neuroethics: Enabling and Enhancing Neuroscience Advances for Society](#) and convening a workshop.

Nina Hsu, PhD, Science Committee Specialist for the NEWG, moderated a roundtable update session, during which members highlighted neuroethics discussions at the [World Economic Forum Annual Meeting](#), the updated [Dana Foundation mission](#) and next-gen program, a [recent survey](#) demonstrating a desire for an increase in patient voices in research, an upcoming [brain-computer interface technology conference](#) hosted by the U.S. Department of Commerce Bureau of Industry and Security, and new [resources on rigor](#) produced by the Society for Neuroscience. The NEWG announced initial plans for an upcoming workshop on data privacy and sharing, currently planned for summer 2023.

The next NEWG meeting will be held on August 28, 2023, and a [video recording](#) will be available for live viewing and later archived.