

**Brain Research through Advancing Innovative Neurotechnologies® (BRAIN)  
Neuroethics Working Group (NEWG) Meeting  
January 30<sup>th</sup>, 2020**

On January 30, 2020, the National Institutes of Health (NIH) Brain Research through Advancing Innovative Neurotechnologies® (BRAIN) Initiative convened a meeting of the [Neuroethics Working Group \(NEWG\)](#) in Bethesda, Maryland. Meeting participants outlined broad goals for BRAIN 2.0, identified NEWG priority topics and neuroethical challenges, discussed updates on BRAIN-funded first-in-human studies, and reviewed neural device regulations.

[In opening remarks](#), Walter Koroshetz, MD, Director of the National Institute of Neurological Disorders and Stroke (NINDS) and co-leader of the NIH BRAIN Initiative, introduced John Ngai, PhD as the NIH BRAIN Initiative Director designee, who is expected to join NIH this spring. Dr. Koroshetz then emphasized how, at its halfway point, the BRAIN Initiative has led to numerous scientific and technological advancements in human research. To support this, Dr. Koroshetz summarized findings from a BRAIN-funded study, published in [Neuroimage](#), in which [David Dunson](#), PhD at Duke University and his collaborators developed a novel statistical method to analyze a large structural brain network dataset and numerous behavioral traits, such as those related to cognition and substance use. Researchers found that several traits were highly associated with specific brain connectivity patterns. This study demonstrates how innovative analysis approaches can reveal new links between brain connectivity and human behavior. Dr. Koroshetz concluded by reminding the group of the upcoming BRAIN Investigator’s meeting on June 1-3<sup>rd</sup>, 2020.

Dr. Ngai introduced himself as the BRAIN Initiative Director designee. He briefly recapped his former leadership roles at the University of California, Berkeley and involvement in the [BRAIN Initiative Cell Census Network \(BICCN\)](#). Dr. Ngai then provided an update on [BRAIN 2.0](#), the second phase of the BRAIN Initiative, and discussed his shared vision for the BRAIN Initiative and strategic goals. He also outlined operational goals, including fostering partnerships between academia, industry, and other federal agencies, and promoting ‘big idea’ projects that will broadly impact neuroscience.

Christine Grady, PhD, Chief of the NIH Department of Bioethics and NEWG co-chair, began a working group discussion by mentioning that the [BRAIN 2.0 Neuroscience](#) and [Neuroethics](#) reports were accepted by the Advisory Committee to the NIH Director (ACD) in October 2019. The group then focused on identifying priorities from the Neuroethics report that the NEWG could support. As the discussion ensued, NEWG members deliberated options for workshops focused on topics relevant to neuroethics, such as data sharing and privacy. The group also discussed the possibility of informing and linking BRAIN-funded investigators to workshops on policy-related neuroethics issues hosted by the National Academies, the International Neuroethics Society, and other organizations. Lastly, the NEWG discussed ideas for neuroethics training and engagement for neuroscientists.

Saskia Hendriks, MD, PhD, NINDS neuroethics consultant and faculty in the NIH Bioethics Department, presented findings from a review of neuroethical considerations in the BRAIN FY19 portfolio. Overall, the portfolio analysis identified 10 neuroethical themes of potential interest. For example, the group discussed posttrial responsibilities to research participants and the importance of detecting and characterizing atypical risks in human research.

The first open session concluded with roundtable updates by NEWG members. In addition, the NEWG heard a brief update by James Giordano, PhD, Chair of the [Institute of Electrical and Electronics Engineers \(IEEE\) Brain Neuroethics Subcommittee](#), who detailed the new [IEEE neuroethics framework](#).

The meeting proceeded with a closed session of the NEWG and federal staff, followed by another open session. The second open session included talks from a BRAIN-funded PI, an expert in biomedical ethics, and a center director at the FDA on first-in-human studies.

### **First-in-human Trial of an Intracortical Sensorimotor BCI**

[Jennifer Collinger](#), PhD, from the University of Pittsburgh presented results from two first-in-human (FIH) studies using sensorimotor brain computer interfaces (BCI), neural devices implanted into the motor cortex that allow paralyzed patients to control neuroprosthetic limbs. First, Dr. Collinger described a recent FIH study where her research team demonstrated the long-term safety and efficacy of a sensorimotor BCI. Next, she described her ongoing efforts to develop a somatosensory BCI, a novel device that allows patients to adjust limb movements based on sensory or tactile feedback. She described a series of successful preclinical intracortical microstimulation experiments in non-human primates. These studies showed minimal brain tissue damage from stimulation, no fine motor impairments, and allowed researchers to create and debug a closed-loop stimulation system prior to transitioning it to humans. Preliminary results in humans showed that stimulation felt ‘possibly natural’ and that somatosensory feedback via the device improved fine motor skills. Lastly, she overviewed a timeline for the informed consent, screening, and monitoring process for participants, and emphasized the importance other ethical considerations, such as disclosure of unforeseen risks, privacy, and posttrial responsibilities.

### **Ethics and FIH Clinical Trials**

[Jonathan Kimmelman](#), PhD, from McGill University shared his perspective on the ethics of first-in-human (FIH) trials. Dr. Kimmelman began his talk by describing two primary ethical considerations in FIH studies:

1. Researchers who perform FIH trials are a scarce resource and should be well utilized
2. Information gathered in FIH trials is used to make life-and-death decisions

He elaborated on the second point by suggesting that FIH research should thus be responsive to the healthcare system and generate reliable information. This requires careful FIH trial design. In doing so, Dr. Kimmelman advised that it may help to consider a ‘theoretical model’ of FIH trials, which includes interventional ensembles (*e.g.*, determining optimal doses), time of trial initiation, therapeutic value, and patient eligibility. In deciding when to begin FIH trials, sponsors and investigators often must judge the risk/ benefit balance of a FIH study. To determine an optimal risk/benefit balance, Dr. Kimmelman suggested that individuals strongly consider background knowledge (*i.e.*, the risk/ benefit balance of similar interventions) and the likelihood of preclinical success when clinical promise is both high and low.

### **A Primer on FDA Oversight of Neurological Device Early Feasibility Studies**

Carlos Peña, PhD, Director of Office of Neurological and Physical Medicine Devices at the [FDA Center for Devices and Radiological Health](#) presented an overview of FDA neurological device regulations. Dr. Peña first defined early feasibility studies (*e.g.*, <10 subjects, device in early development, etc.) and discussed current FDA review timelines for neural device applications. He also emphasized two primary considerations of neurological device research and regulations: safety and effectiveness. Dr. Peña elaborated on device safety by underscoring the importance of reporting adverse events and recognizing both short- and long-term safety. Further, he discussed informed consent requirements, including potential risks, alternative procedures, confidentiality of records, and several others. Dr. Peña also provided the group with regulatory resources, such as information on ethics consults and FDA feedback mechanisms for neural device applications. Overall, he conveyed that the FDA is open to collaborating with the NEWG to ensure that neural device researchers can easily navigate the regulatory process.

The next NEWG meeting will be held on August 20, 2020.