Brain Research Through Advancing Innovative Neurotechnologies® (BRAIN) Neuroethics Working Group (NEWG) Meeting
August 19th, 2021

On August 19, 2021, the National Institutes of Health (NIH) *Brain Research Through Advancing Innovative Neurotechnologies®* (BRAIN) Initiative Neuroethics Working Group (NEWG) met virtually to discuss ethical considerations around the compensation of research participants, with a focused discussion on incentivization approaches to diversify donors of brain tissue.

In opening remarks, John Ngai, PhD, Director of the NIH BRAIN Initiative, introduced a new working group member, Sameer Sheth, MD, PhD (Baylor College of Medicine) and updated the group on BRAIN Initiative activities. Dr. Ngai first mentioned the reissued BRAIN neuroethics funding opportunity (RFA-MH-19-400), and pointed out a few topics relevant to the funding opportunity, including research participant engagement, special populations, social impacts, as well as data storage and sharing. He also overviewed a new neuroethics concept aimed to provide opportunities for neuroethics research spanning the National Institute on Neurological Disorders and Stroke (NINDS) portfolio, while continuing to integrate neuroethics into neuroscience research. The concept was approved by the NINDS Council in May 2021. Next, Dr. Ngai recapped the well-attended neuroethics engagement session at the virtual BRAIN Initiative Investigators meeting held in June. Lastly, he introduced several topics for NEWG discussion, including the need to diversify brain tissue samples in neuroscience research, especially as the Initiative's human brain cell census efforts commence.

Following the BRAIN Director's update, Christine Grady, RN, PhD, Chief of the NIH Department of Bioethics and NEWG co-chair, led a discussion about issues in compensation of research participants. Dr. Grady summarized the key ethical issues[1,2], including minimal guidance on compensation and confusion surrounding definitions of coercion and undue influence. She clarified that payment for research participation is not coercive, but can be an undue influence. Next, she noted common reasons behind paying research participants and summarized findings from studies on the ethics of payment[3,4]. Researchers often see payment as an incentive for participant recruitment, a way to overcome opportunity costs and motivate groups that might not otherwise participate, and as fair compensation for participants' time. Dr. Grady also noted that, apart from a few studies, there is limited evidence supporting payment as a means to overcome barriers to research study participation. Further, it's also unknown whether or not payment effectively diversifies participant pools. Lastly, she summarized three types of payment: reimbursement for reasonable expenses, compensation for time and inconvenience, and incentives for participation. Dr. Grady noted that reimbursement and compensation might be particularly important for economically disadvantaged groups and that more empirical research is needed to gain a better understanding of the ethics and impact of payment. The NEWG discussed ways to clarify the definition of undue influence and how payment affects participants' trust or personal perceptions of research studies. The group also raised concerns about inadequate compensation (i.e., What are participants' expectations and are payments too low?) and noted the need to build trust with communities.

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[1] Grady, C. (2005). Payment of clinical research subjects. *The Journal of clinical investigation*, *115*(7), 1681-1687.

[2] Gelinas, L., Largent, E. A., Cohen, I. G., Kornetsky, S., Bierer, B. E., & Fernandez Lynch, H. (2018). A framework for ethical payment to research participants.

[3] Gelinas, L., White, S. A., & Bierer, B. E. (2020). Economic vulnerability and payment for research participation. *Clinical Trials*, *17*(3), 264-272.

[4] Jennings, C. G., MacDonald, T. M., Wei, L., Brown, M. J., McConnachie, L., & Mackenzie, I. S. (2015). Does offering an incentive payment improve recruitment to clinical trials and increase the proportion of socially deprived and elderly participants?. *Trials*, *16*(1), 1-9.

Daniel Miller, PhD, Program Director at NINDS, and Jane Hettinger, PhD, Health Program Specialist at NINDS, presented an overview of possible incentives to diversify human brain tissue samples used in research supported by BRAIN. First, Dr. Hettinger summarized themes from the Tissue Quality and Pipeline for Human Brain Cell Census workshop, which included sessions on tissue preparation, inclusion/exclusion criteria, consent, and ensuring biological diversity across all demographics. She pointed out that on average, a majority of brains in brain banks are from older, White males and that most NIH NeuroBioBank donation centers are located on the coasts in urban areas. The workshop discussed possible solutions, such as increasing community outreach, raising awareness of brain donation, diversifying the scientific workforce, and others. Next, Dr. Miller highlighted two main challenges to brain banks: 1) Collecting brain tissue from healthy individuals (i.e., those who did not die from a brain-based disorder), and 2) Sampling tissue that represents our society. NeuroBioBank demographics data showed notable disparities in the race/ethnicity of brain tissue donors. Specifically, the number of Hispanic/Latino donors underrepresented this group at the U.S. population level and tissue donated by Black/African American individuals was overwhelmingly from children. Dr. Miller introduced topics for discussion, including ways to enhance community engagement at the local level and how to appropriately frame incentives.

Henry (Hank) T. Greely, JD, Director of Law and Biosciences at Stanford University and co-chair of the NEWG, led a discussion on the ethical considerations of the two preceding presentations. NEWG members considered whether or not incentives for research participation and brain donation should be offered to everyone, and if such incentives should scale to financial need. They also noted potential distinctions between living versus post-mortem brain tissue donation and healthy versus diseased tissue donation (e.g., Should living or healthy donors be paid more? What about the families of deceased donors?). The NEWG emphasized that healthy control tissue is needed to move science forward and pondered ways to boost healthy brain donations. The NEWG mentioned the need for more culturally-relevant community engagement with underrepresented populations, as well as more qualitative and quantitative data to better understand the effect of incentives on brain tissue donation. Lastly, the group proposed a possible workshop on the ethics of human brain tissue donation. The session ended with member updates.

The meeting concluded with a closed session of the NEWG and federal staff. The next NEWG meeting will be held on January 24, 2022 and a videocast will be available for live viewing and later archived.