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Neuroethics and the NIH BRAIN Initiative

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Abstract

The Brain Research through Advancing Innovative Neurotechnologies® (BRAIN) Initiative is focused on developing new tools and neurotechnologies to revolutionize our understanding of how the brain functions in health and disease, in large part to address the growing societal impact of neurological, mental health, and substance abuse disorders. Recent advances in neurotechnology are delivering unprecedented ways to interrogate and modulate brain function, and the BRAIN Initiative is focused on translation for human medical uses over the next decade. Since its inception, the NIH component of the BRAIN Initiative has utilized an iterative model of integrating ethics into the scientific trajectory of the Initiative, most recently with the creation of a Neuroethics Division of the NIH BRAIN Initiative Multi-Council Working Group. The Division serves as a resource of expertise, to help the BRAIN Initiative navigate issues involving ethics. Here we discuss the BRAIN Initiative, and its implications and aspirations for neuroethics. We also discuss new opportunities for collaboration and for integrating stakeholder voices.

Keywords

BRAIN Initiative; neuroethics; neural circuits; neuromodulation; neuropsychiatric disorders

The Brain Research through Advancing Innovative Neurotechnologies® (BRAIN) Initiative is focused on developing new tools and neurotechnologies to revolutionize our understanding of how the brain functions in health and disease, in large part to address the growing societal impact of neurological, mental health, and substance abuse disorders.

These tools and technologies will inevitably have ethical and societal consequences. Here we discuss the BRAIN Initiative, and its implications and aspirations for neuroethics. We also discuss new opportunities for collaboration and for integrating stakeholder voices.

1. Background of the BRAIN Initiative

The drive to understand how the brain works stems both from curiosity about the organ that is central to our ‘humanness’ and from a desire to alleviate the suffering of those afflicted with disorders of the nervous system. These disorders, including neurological, mental health, and substance abuse disorders, arise from brain circuit dysfunction. Our current inability to monitor brain circuit function is a major limitation to developing effective treatments for these disorders. Tools are now available, or under development, to collect the types of data necessary to understand the neural circuit activity underlying behavior in model organisms such as zebra fish, fruit fly, and mouse (for examples, see Yang et al. 2016; Randlett et al. 2015; Vardy et al. 2015; Yao et al. 2015). Nevertheless, the tremendous complexity of the human brain and poor access to the source signals remain imposing barriers.

Globally, the burden of disease has shifted from communicable to non-communicable diseases, which tend to leave a lengthy legacy of disability. Nervous system disorders comprise about one-seventh of this toll. In a 2010 assessment of disability-adjusted life years, mental and behavioral disorders comprised 7.4 percent of the global burden of disease, stroke comprised 4.1 percent, and neurological disorders another 3 percent (Murray et al. 2012; Bloom et al. 2011). These disorders cause immense human suffering, and are also incredibly costly. Based on 2002 data, the National Comorbidity Study Replication estimated that serious mental illness accounted for \$193 billion in lost earnings (Kessler et al. 2008). In an accompanying commentary, the former director of the National Institute of Mental Health, Dr. Thomas Insel, estimated that when factoring in \$100 billion per year in direct health care costs and another \$24 billion in disability benefits, the total cost of serious mental illness in the U.S. in 2002 exceeded \$317 billion (Insel 2008). In the last 15 years, that cost has only grown.

In an effort to meet these needs, many nations worldwide (see Brose 2016) are increasing investments in neuroscience research, through national brain projects such as the European Union’s Human Brain Project, the China Brain Project, and the United States BRAIN Initiative. The BRAIN Initiative aspires to accelerate the development and application of innovative neurotechnologies to revolutionize the understanding of human brain circuits. Launched by President Obama in April 2013, it currently includes five federal agencies: the National Institutes of Health (NIH), the National Science Foundation, the Defense Advanced Research Projects Agency, the Intelligence Advanced Research Projects Activity, and the Food and Drug Administration. This federal effort is joined by private firms, universities and research institutes, research foundations, patient advocacy groups, and more, as well as governmental and private partners from Canada, Australia, and Denmark. The recently formed BRAIN Initiative Alliance, whose mission is to coordinate and facilitate communications from its members related to the BRAIN Initiative, maintains a website at <http://www.braininitiative.org>, which serves as a central source of information about scientific successes, resources, and opportunities related to the Initiative across all partners.

The NIH component of the Initiative is guided by *BRAIN 2025: A Scientific Vision* (BRAIN Working Group, 2014), a roadmap prepared by an expert external working group of the Advisory Committee to the NIH Director (<http://acd.od.nih.gov/brain.htm>). *BRAIN 2025* was written with broad input from the U.S. scientific community, patient advocates, and the general public. It outlines a plan for accelerating technology development for neuroscience, with the intention of developing and using new tools to acquire fundamental new insights about how the nervous system functions in health and disease. Table 1 outlines how NIH currently organizes scientific programming for the BRAIN Initiative.

As research efforts like the BRAIN Initiative accelerate and advance our understanding of the brain, the things we learn can raise deep questions about human identity, agency, and function, with potential points of conflict around commonly held societal and personal values. For example, causally linking biological processes with mental states and functions may not easily square with widely held notions of personal identity and volition or notions of free will. Neuroethics, a multidisciplinary field that provides critical tools and evaluative frameworks to grapple with these issues, has emerged as a key partner for neuroscience as we channel newfound knowledge to understand and intervene on human brain function.

2. Neuroethics efforts within the NIH BRAIN Initiative

BRAIN 2025 emphasizes that a key principle for maximizing the value of the BRAIN Initiative is to consider ethical implications of neuroscience research. The report includes four explicit goals for the ethics component of the Initiative:

- (1) Joint neuroscience/ethics training programs and meetings to consider the unique issues raised by human neuroscience research, and to establish a shared vision for the ethical conduct of such research;
- (2) Resources for collecting and disseminating best practices in the conduct of ethical scientific research, particularly for the conduct of clinical research;
- (3) Support for data-driven research to inform ethical issues arising from BRAIN Initiative research, ideally with integrated activities between ethicists and neuroscientists; and
- (4) Opportunities for outreach activities focused on engaging government leaders, corporate leaders, journalists, patients and their advocates, educators, and legal practitioners in discussion of the social and ethical implications of neuroscience research.

How is ethics woven into the BRAIN Initiative in practice? The BRAIN Multi-Council Working Group (MCWG) provides ongoing oversight of the long-term scientific vision of the Initiative at NIH (<http://braininitiative.nih.gov/about/mcwg.htm>). The BRAIN MCWG comprises distinguished neuroscientists, with additional at-large members appointed to supplement the group's expertise as appropriate. The MCWG's Neuroethics Division serves as a resource to help navigate ethical issues associated with BRAIN research; the Division draws on *BRAIN 2025* for guidance, along with material from the two-volume report *Gray Matters*, published by President Obama's Presidential Commission for the Study of

Bioethical Issues (2014 and 2015). Further, the Neuroethics Division's deliberations and activity are grounded in the science itself – that is, the existing portfolio of BRAIN research supported by the NIH, and the trajectory of the Initiative as described in *BRAIN 2025*. The Division provides input to MCWG and the NIH about ethical issues associated with BRAIN research, consultations as needed on particular research projects, perspectives on areas where the BRAIN Initiative may want to support neuroethics research, and general information to investigators on resources available for identifying and addressing ethical issues. The members of the Division also collaborate on producing timely workshops exploring the ethical, legal, and social issues the BRAIN Initiative raises. In a recent publication, greely et al. (2016) describe the key role of neuroethics in the BRAIN Initiative, and in the Human Brain Project.

NIH has hosted three meetings in Bethesda, bringing together scientists and ethicists to discuss key issues in neuroethics¹. Most recently, the NIH BRAIN Initiative released a funding opportunity in neuroethics, to support efforts addressing core ethical issues associated with research focused on the human brain and resulting from emerging technologies and advancements supported by the BRAIN Initiative. We therefore characterize efforts to integrate ethics into the NIH BRAIN Initiative as an iterative model. We see this as a way to enable – and even to accelerate – research and innovation in neuroscience, by addressing potential problems early on.

3. The BRAIN Initiative: implications and aspirations for neuroethics

Both general neuroscience research and the BRAIN Initiative – with its focus on development of new research tools and technologies with increasing precision to record and modulate brain function – generate many important ethical questions related to the conduct and use of neuroscience research. Neurotechnologies that enable measuring and modulating brain function are already, and likely increasingly will be, used for non-medical purposes, but NIH focuses solely on biomedical applications. Thus we recognize that NIH's neuroethics efforts are only a piece of a broader landscape of inquiry and scholarship, which exists thanks to many experts who have written about various neuroethical issues (a small sampling: Bell et al. 2016; Farah 2015; Fins et al. 2011; Illes & Bird 2006).

What neuroethical issues does the BRAIN Initiative prompt? Some are familiar bioethical issues pertaining to studies with humans, such as questions around acceptable degrees of risk for human patients, necessary levels of antecedent evidence before human trials, consent capacity, data sharing, privacy and confidentiality, and concepts of agency, identity, and normality. Often the context of neurotechnology research, development, and widespread application brings these familiar issues into sharper relief.

In other cases, new ethical issues arise because the brain is the organ of the mind. Novel neural circuit monitoring technologies may be able to record brain activity underlying thoughts and moods, which will pose ethical, legal, and societal questions. Some of those

¹Proceedings from these meetings, held in November 2014, February 2016, and August 2016, can be found on the NIH BRAIN Initiative website <http://braininitiative.nih.gov/about/neuroethics.htm>

issues may arise even before the technologies can be applied to living humans. Small scale circuit function can be studied in brain tissue that can be kept alive for days after removal from surgical patients. At what point do we worry about decoding a person's memories stored in the tissue?

Relatedly, the BRAIN Initiative aims to deliver innovative neurotechnologies that enable precise intervention on brain circuit function to treat brain disorders. This includes invasive approaches, such as deep brain stimulation or brain-computer interfaces. What are the long-term obligations of researchers to patients with implanted devices beyond the end of the experimental trial? Explantation may not be desirable for all participants, and implantation requires long-term maintenance for devices that may be eventually discontinued.

From the medical perspective, memory is one core aspect of brain function that may be beneficial to modulate – for instance, altering specific traumatic memories to alleviate post-traumatic stress disorder. But is it a violation of one's autonomous and continuous sense of self to alter specific memories? Does it impinge on the authenticity of personal identity?

Non-invasive approaches to neuromodulation, such as transcranial magnetic stimulation, direct current stimulation, or focused ultrasound, could increase availability to patients, but they also pave the way for non-medical use for enhancement purposes. How might society wish to manage neurotechnologies commercialized for non-medical, public use? Will the boundaries for “appropriate use” differ across cultures? In thinking about commercialization of neurotechnologies, what are the necessary standards for ensuring safety and privacy? While the NIH BRAIN Initiative will focus on neuroethical issues that fall within the medical domain, ethical issues around non-medical applications are inevitable.

The Neuroethics Division of the MCWG, working in concert with NIH staff and members of the extramural community, will address many of these issues. The NIH BRAIN Initiative aims to provide leadership in this space through modeling and emphasizing the value of integrating ethics into any neuroscience research program, continuing to highlight neuroethics as a research priority within BRAIN, funding neuroethics research, and encouraging and enabling academic discourse between ethicists and researchers regarding advances in neuroscience and neurotechnology. We hope the neuroethics efforts supported by the NIH BRAIN Initiative will both complement and integrate with the transformative, breakthrough discoveries supported by the Initiative. This will allow for thoughtful guidance of the funded research, and may also influence the relatively young field of neuroethics by providing an institutional home for neuroethics within the biomedical research community anchored by the NIH.

4. New opportunities for collaboration and for integrating stakeholder voices

Widespread interest in the brain and neuroscience research has helped launch national brain projects in countries around the world, including the U.S., the European Union (EU), China, Japan, Korea, and more. At the same time, efforts to build coordination and collaboration among these projects have grown (Brose 2016; Grillner et al. 2016; Huang & Luo 2015). As

the profile of neuroethics within these projects continues to rise, there is movement towards international coordination and collaboration on neuroethics. For example, in September 2016, the Organisation for Economic Co-Operation and Development held an international workshop on *Neurotechnology and Society: Strengthening Responsible Innovation in Brain Science*. Attended by public and private sector neuroscience research stakeholders from around the world, the workshop provided an opportunity to discuss efforts aimed at addressing ethical, legal, social, and economic impacts of novel neurotechnologies, as well as models of regulation and governance. Continued opportunities to promote international coordination and collaboration around neuroethics are important. For instance, in November 2016 at its tenth annual meeting, the International Neuroethics Society launched an International Ambassador Program, to bring together representatives of national brain research programs and their neuroethics components.

In our highly interconnected world, we see value in such opportunities to build bridges between focused neuroethics efforts around the globe, to share insights, challenges, and best practices. Importantly, the relocation of a number of prominent scientific enterprises from the West to East Asia has made it abundantly clear that bridging cross-cultural differences in the ethics and values informing research is essential to realizing the power of engaging science as a collaborative global enterprise (Chattopadhyay & De Vries 2008). Some of the ethical questions we ask about how brain changes impact issues from identity to brain death would be answered differently across cultures (Yang & Miller 2015; Asai et al. 2012).

Engagement and education are two pillars that will be key to successfully integrating neuroethics into neuroscience research programs (Sahakian & Morein-Zamir 2009). Engagement refers to enabling interaction among the public, scientists, bioethicists, policy makers, and members of congress, regarding neuroscience research and its associated ethical, legal, and social implications. This ideally allows research programs to move forward in a way that is responsive to the interests and needs of a diverse set of stakeholders.

One model comes from the U.S. National Nanotechnology Initiative (NNI), begun under President Clinton and sustained by the Federal government through the present. NNI has supported development of an ‘anticipatory governance’ framework, an approach that emphasizes public engagement in consideration of the research trajectory to help inform development of policy and governance (Guston 2014). Additionally, NNI funds a Center for Nanotechnology in Society at Arizona State University and another at the University of California, Santa Barbara. These centers serve as hubs for researchers and educators interested in societal issues associated with nanotechnologies. In the EU, the concept of responsible research and innovation (RRI) was developed in response to innovation and commercialization in nanotechnology (for a historical overview, see Owen et al. 2012). RRI emphasizes bringing together societal stakeholders (researchers, citizens, policy makers, etc.) throughout the research and development (R&D) process, in order to align R&D and technological outcomes with the values, needs, and expectations of society. It is a notion that figures prominently in *Horizon 2020*, the current EU research and innovation funding initiative². There may be lessons learned here that would be helpful to neurotechnology research and development.

Education goes hand-in-hand with engagement. A populace well-educated about neurotechnology and neuroscience is critically aware of and protected against neurohype, and can more readily engage with scientists, policy-makers, and funding agencies. Ethicists who understand the scientific questions that neuroscience researchers are pursuing are better positioned to help responsibly guide research. And scientists who are well-educated about the implications of their work can be good stewards of their own research. All of these partners working together give us the best chance of delivering on the promise of scientific advances to treat, and perhaps even cure or prevent, diseases and disorders of the brain.

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²Information on RRI in *Horizon 2020* is available at <https://ec.europa.eu/programmes/horizon2020/en/h2020-section/responsible-research-innovation>

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Table 1:

The scientific landscape of the NIH BRAIN Initiative

Scientific focus	Description
Cell census	Identify and provide experimental access to the different brain cell types to determine their roles in health and disease. Integrate information on molecular identity and gene expression with connectivity, morphology, location, and physiology.
Circuit technologies	Develop tools and technologies for circuit mapping and functional, specifically-targeted manipulation of circuit activity.
Neural recording and modulation	Record and manipulate neural activity with cellular resolution, at multiple depths and locations across the brain.
Human imaging and non-invasive neuromodulation	Develop next-generation imaging technologies, and advance understanding of the relationship between imaging signals and the underlying brain circuits and cellular activity. Promote the development, implementation, and integration of innovative new technologies for human neuroscience research.
Understanding circuit function	Understand the circuits and patterns of neural activity that give rise to mental experience and behavior.
Training and dissemination	Disseminate new neurotechnologies and tools to a wide scientific user base, along with the knowledge required to use them well.
Neuroethics	Support neuroethics efforts that can both guide BRAIN Initiative research and address ethical dilemmas raised through advancements in neuroscience.