IN THE LITERATURE
Advancing Ethical Neuroscience Research
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Abstract
As neuroscience research advances, researchers, clinicians, and other stakeholders will face a host of ethical challenges. The Presidential Commission for the Study of Bioethical Issues (Bioethics Commission) has published two reports that provide recommendations on how to advance research endeavors ethically. The commission addressed, among other issues, how to prioritize different types of neuroscience research and how to include research participants who have impaired consent capacity. The Bioethics Commission’s recommendations provide a foundation for ethical guidelines as neuroscience research advances and progresses.

Introduction
On April 2, 2013, President Obama announced his vision for advancing neuroscience research. Through the Brain Research through Advancing Innovative Neurotechnologies® (BRAIN) Initiative, the president committed $100 million to neuroscience-related research efforts at the National Institutes of Health, the Defense Advanced Research Projects Agency, the Food and Drug Administration, the National Science Foundation, and the Intelligence Advanced Research Projects Activity [1]. In order to maintain the “highest ethical standards,” the president charged the Presidential Commission for the Study of Bioethical Issues (Bioethics Commission) with “explor[ing] the ethical, legal, and societal implications raised by this research initiative” [2]. Given the nature of the research that the BRAIN Initiative could fund, addressing and emphasizing the ethical issues surrounding neuroscience research was—and still is—a critical component of the initiative. The commission responded to the president’s charge in two reports. The first report, Gray Matters: Integrative Approaches for Neuroscience, Ethics, and Society, focused on integrating ethics at all stages of the research process [3]. The second report, Gray Matters: Topics at the Intersection of Neuroscience, Ethics, and Society, focused on three “cauldrons of controversy”: cognitive enhancement, consent capacity, and neuroscience and the legal system [4]. In particular, the Bioethics Commission’s recommendations
regarding cognitive enhancement and consent capacity make direct and important contributions to forthcoming neuroscience research. The recommendations provide a framework that neuroscientists can use to critically evaluate the implications of their research and to ensure that future research endeavors are carried out carefully and ethically [5].

Cognitive Enhancement
The Bioethics Commission found widespread agreement about the promise that neuroscience research holds in addressing neurological diseases; beyond that, the extent to which neuroscience research can—or should—proceed was found to be a matter of debate [4]. In the second volume of *Gray Matters*, the commission focused on cognitive enhancement, defined as “expand[ing] or augment[ing] function above typical or statistically normal ranges” [6]. This area attracts opposing viewpoints, with some viewing enhancements as a means to human improvement and others as “threats to moral agency and dignity” [7]. The Bioethics Commission broadened consideration of cognitive enhancement to include anything that could be classified as “neural modification,” which includes any course of action that impacts the brain or nervous system. Neural modification need not involve any advanced technologies or procedures; for example, changes in diet and sleep can affect cognitive functions and, as such, can be a means of neural modification.

Given the new, broader definition of neural modification, the Bioethics Commission stated that “altering the brain and nervous system is not inherently ethical or unethical” [6]. The Bioethics Commission’s stance is an important contribution to an often-polarized topic [8]. The report emphasizes that, as neuroscience research progresses, assessments of the ethicality of neural modification practices must be conducted on a case-by-case basis and must include an evaluation of the risks and benefits of a particular practice and circumstance. Certain practices might be ethically acceptable in one instance and ethically problematic in another. For example, a pharmacological intervention can be ethically used to treat a diagnosed neurological disorder, but the same intervention’s use by a healthy person to augment cognitive performance might be ethically problematic. Assessments must also consider who is choosing the neural modifier, and for whom, as the assessment might vary depending on the parties involved. For example, instances in which adults with the capacity to understand and consent to neural modification choose a particular intervention for themselves might differ from instances in which adults are choosing that same intervention for a child or person who lacks consent capacity.

There are at least three goals of neural modification, according to the new taxonomy proposed by the Bioethics Commission: to maintain or improve neural health, to treat neurological disorders, and to enhance neural functioning. In its ethical analysis, the Bioethics Commission stated that research on low-technology methods to maintain or
Improve neural health and research to understand and treat neurological disorders should be prioritized over research on ways to enhance or augment human functioning, as these two goals advance individual and public beneficence, with less potential risk and possibility for irreversible change [4]. Such research can help provide necessary interventions to those who need them and who might benefit from them. After considering diverse perspectives on the future of novel neurotechnologies and the ramifications of conducting such research, the Bioethics Commission also recommended that funders support research to better understand novel neural modifiers that could enhance or augment neural function, noting that much of the data about practices used to augment cognitive functions, such as the use of prescription stimulants such as methylphenidate, were inconclusive [4]. A better understanding of these interventions is a critical prerequisite to evaluating their ethical use. However, the commission specifically urged that if interventions to augment or enhance human cognition become available, stakeholders ensure equitable access to them in line with public beneficence, justice, and fairness [4]. The research prioritization agenda put forth by the Bioethics Commission will help advance the field of neuroscience by encouraging funders to focus on research to understand and treat disease rather than high-technology cognitive enhancements based on hyped public interest and inconclusive existing data.

**Consent Capacity**

Neuroscience research focused on the etiology, pathology, and treatment options for neurological conditions cannot proceed without the involvement of study participants with those conditions. However, the nature of certain neurological conditions, such as Alzheimer’s disease, might impact a potential study participant’s ability to consent to participate in a research trial; thus the inclusion of those with impaired consent capacity in research studies raises ethical challenges. Informed consent is a widely established condition for participation in a research study [9], and, in order to provide informed consent, people must have ability to consent, which includes skills such as understanding relevant information and using that information to make an informed decision about participation [10]. Researchers and institutional review boards sometimes reach an impasse when considering whether to conduct or proceed with research that necessitates the involvement of participants whose consent capacity might be impaired [4].

The Bioethics Commission recommended the responsible inclusion of research participants with impaired consent capacity, warning that excluding such participants from research could stifle the development of preventive interventions, treatments, and cures [4]. The Bioethics Commission’s recommendation provides a critical perspective on the benefits of including participants with impaired consent capacity in a research trial and could help alleviate the perceived obstacles for conducting research that necessitate the involvement of participants with impaired consent capacity.
At the same time, the Bioethics Commission emphasized the importance of additional ethical safeguards for these participants. One safeguard that the Bioethics Commission discussed is the federal regulatory requirement for a legally authorized representative (LAR) to grant permission on behalf of a research participant who lacks consent capacity. The report notes that the definition of a LAR in most states includes people who are authorized to make health care decisions, such as a spouse or parent; however, few states have a law that specifically extends this decision-making authority to research participation [4]. This regulatory gap serves as an obstacle to conducting research with participants whose consent capacity is or could be impaired. Researchers do not want to risk running afoul of federal regulations, but the guidance regarding the inclusion of participants with impaired consent capacity is often unclear. The unethical inclusion of research participants with impaired consent capacity is a risk that many researchers did not want to take [11].

The Bioethics Commission recommended that federal regulatory bodies clarify who can serve as a LAR for research purposes. Following the publication of the second volume of *Gray Matters*, a notice of proposed rulemaking (NPRM) for alterations to the Common Rule—US federal regulations that protect research participants [12]—highlighted this regulatory gap, citing the Bioethics Commission’s work, and included a proposed change that would allow a LAR to be designated for research purposes following a common practice standard if no state or local laws are in place [11]. The NPRM noted, in line with the Bioethics Commission’s recommendation, that the current definition of a LAR—and the lack of relevant laws at the state level—could unnecessarily hinder the progress of research [11]. Should the amended definition be included in the Common Rule, an important obstacle to conducting research involving participants who have or may develop impaired consent capacity will have been removed.

Although there have been decades of proposals and inaction regarding consent capacity, the Bioethics Commission made two important contributions intended to help researchers move forward. First, the Bioethics Commission was the first national bioethics advisory board to address this issue broadly and comprehensively. Previous groups focused on research involving persons with mental disorders [13] and persons institutionalized as mentally infirm [14] but failed to recognize the spectrum of disorders and conditions that can impair consent capacity. Second, this Bioethics Commission was the first national bioethics advisory body to influence a change in federal research regulations regarding this issue. Neuroscience research will advance more rapidly, and more ethically, due to the recommendations put forth by the Bioethics Commission and the upcoming change in federal regulation that will likely result.

**Conclusion**
The Bioethics Commission’s recommendations in the second volume of *Gray Matters* made an important contribution to the current debate regarding ethical issues in
neuroscience research. These recommendations provide an important framework that stakeholders in neuroscience research can use when planning their work and evaluating its ethical implications. Although assessments of the ethicality of neuroscience research might not always be straightforward and there might not always be consensus regarding the ethical implications of future research, it will continue to remain the responsibility of researchers, clinicians, research participants, and other stakeholders to respectfully and conscientiously engage with each other to ensure that such research moves forward in an ethical manner. The Bioethics Commission’s recommendations can serve as an invaluable resource to guide researchers in this endeavor.

References

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