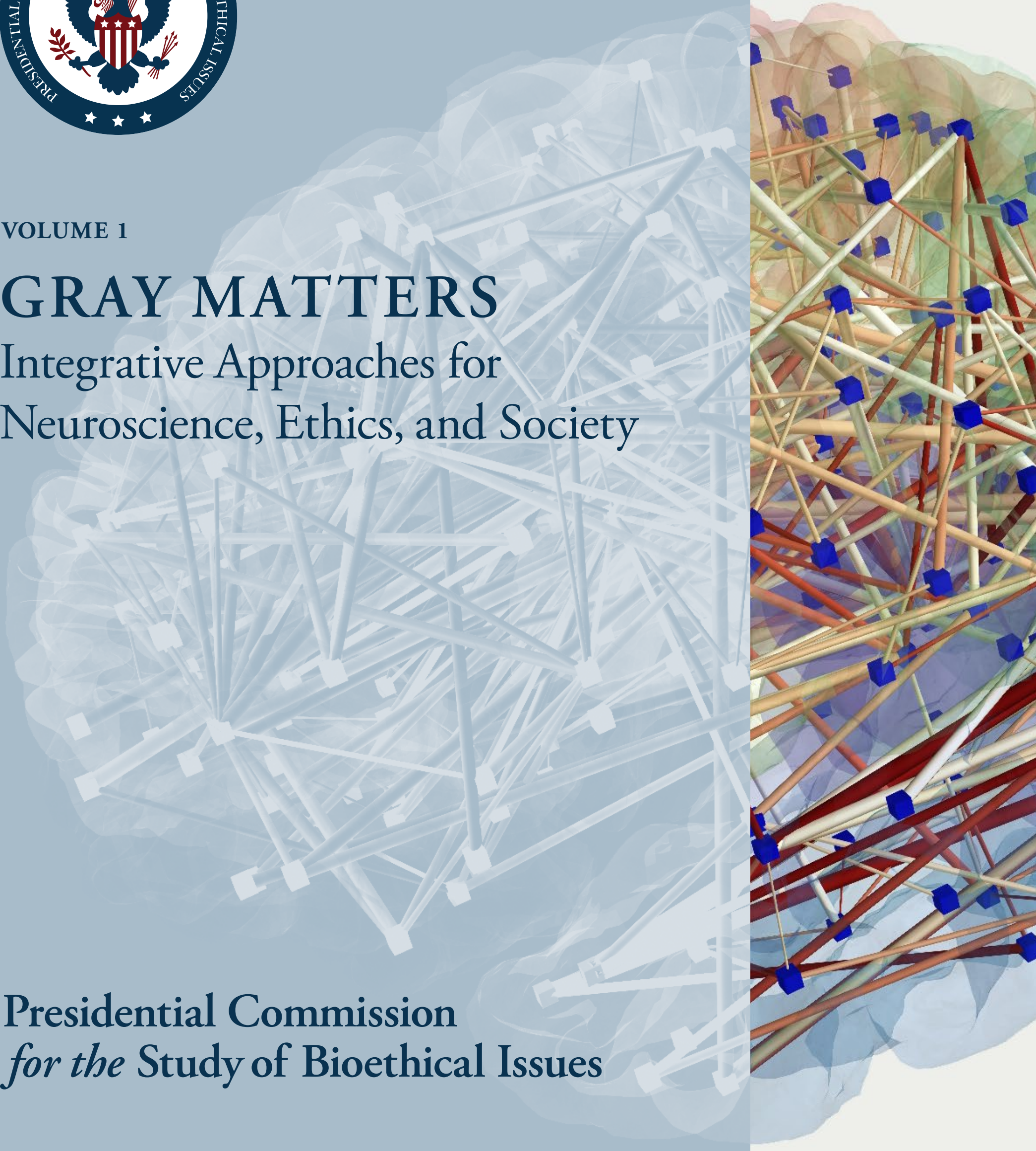
VOLUME 1

GRAY MATTERS

Integrative Approaches for Neuroscience, Ethics, and Society



Presidential Commission
***for the* Study of Bioethical Issues**

May 2014

On the cover: Image of a functional, integrated brain network – white matter fiber bundles connect gray matter regions.

Credit: Patric Hagmann & Stephan Gerhard,
Lausanne University Hospital (CHUV),
Lausanne, Switzerland

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Presidential Commission
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Washington, D.C.
May 2014

http://www.bioethics.gov

ABOUT THE PRESIDENTIAL COMMISSION FOR THE STUDY OF BIOETHICAL ISSUES

The Presidential Commission for the Study of Bioethical Issues (Bioethics Commission) is an advisory panel of the nation's leaders in medicine, science, ethics, religion, law, and engineering. The Bioethics Commission advises the President on bioethical issues arising from advances in biomedicine and related areas of science and technology. The Bioethics Commission seeks to identify and promote policies and practices that ensure scientific research, health care delivery, and technological innovation are conducted in a socially and ethically responsible manner.

For more information about the Bioethics Commission, please see http://www.bioethics.gov.

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PRESIDENTIAL COMMISSION FOR THE STUDY OF BIOETHICAL ISSUES

President Barack Obama
The White House
1600 Pennsylvania Avenue, NW
Washington, DC 20500

Dear Mr. President:

On behalf of the Presidential Commission for the Study of Bioethical Issues, we present to you *Gray Matters: Integrative Approaches for Neuroscience, Ethics, and Society*, the first part of the Bioethics Commission's response to your request of July 1, 2013. The Bioethics Commission resolved to address your charge in multiple reports to be timely and responsive in considering the rapidly emerging and evolving field of neuroscience. In this first report, the Bioethics Commission considered the need for, and various approaches to achieve, integration of ethics early and throughout neuroscience research. Explicit integration of ethics and neuroscience research will help researchers, policymakers, and the public recognize and address the ethical and societal implications of neuroscience research and its applications. The Bioethics Commission will consider the societal implications in greater detail in a later report.

Building on its past work on neuroscience and related ethical issues, which included hearing from experts at two public meetings, the Bioethics Commission held three public meetings on this topic and heard from speakers from a variety of disciplines and perspectives, including neuroscientists, philosophers, educators, ethicists, and representatives from federal agencies as well as private sector partners involved in the Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative. In addition, the Bioethics Commission solicited public comment and received many thoughtful responses.

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Contemporary neuroscience investigates the human brain and its relation to the mind, raises fundamental questions about human experiences, and has produced and could yield improved preventive, diagnostic, and therapeutic interventions for brain-related diseases that affect tens of millions of Americans. Ethical issues arise in neuroscience research, similar to other scientific fields, but are sometimes expressed in sharper relief. Ethics integration should equip scientists to recognize and address ethical issues as they arise, and ethicists to understand the science and technology with which they engage.

The Bioethics Commission concludes that ethics and neuroscience research should be integrated throughout the research endeavor and offers four recommendations to facilitate the successful integration of ethics and neuroscience research. Institutions and individuals should take steps to make explicit their plans for integrating ethics across the research endeavor, and institutions should provide sufficient resources to support integration efforts. Institutions and researchers should evaluate existing and innovative approaches to integrating ethics and neuroscience, including integration through education at all levels. In addition, professionals with experience in ethics should be included in BRAIN Initiative-related scientific advisory boards and funding review committees, particularly for the major public and private sector partners.

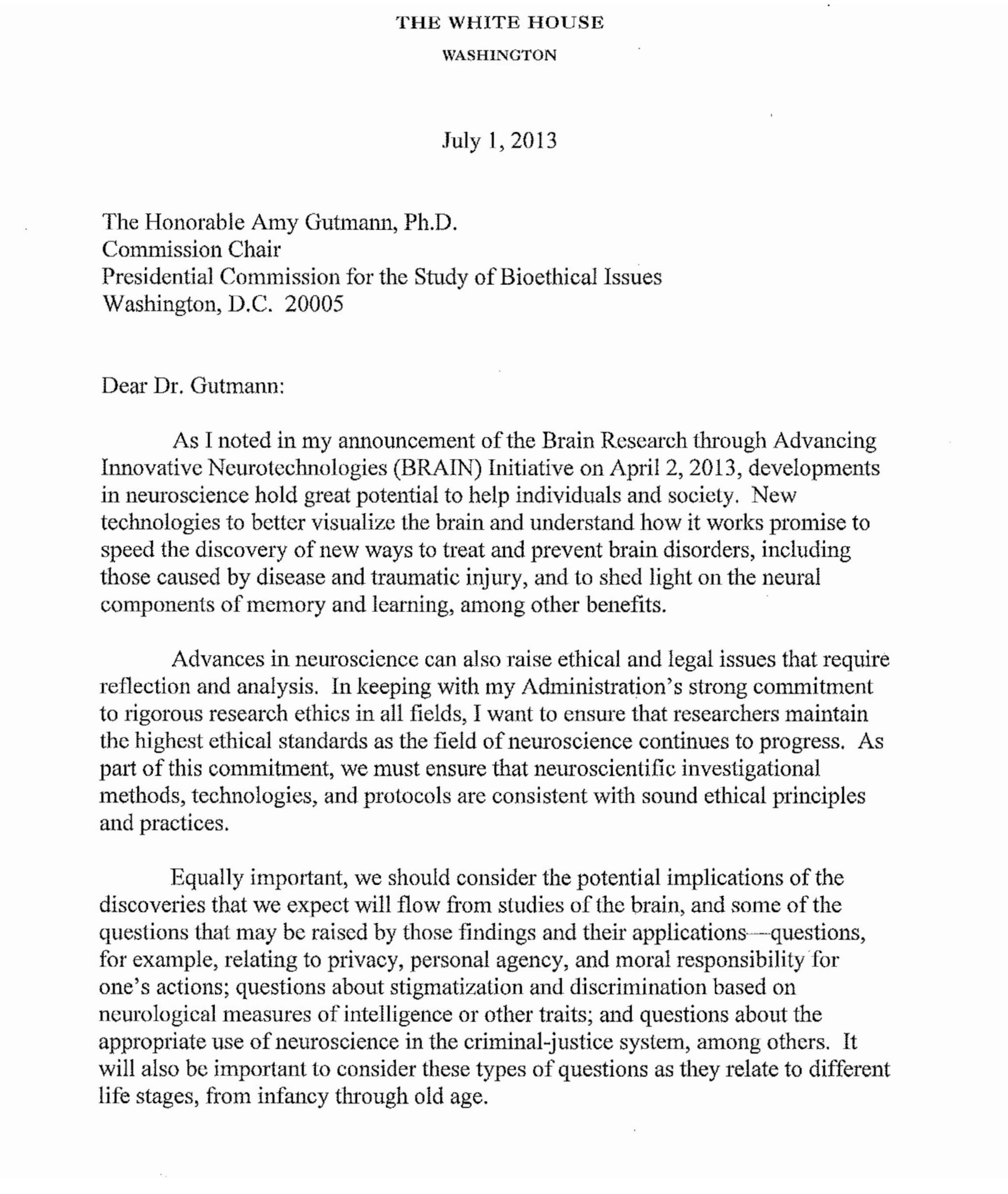
The Bioethics Commission is honored by the trust you have placed in us and we are grateful for the opportunity to serve you and the nation in this way.

Sincerely,

Amy Gutmann, Ph.D.
Chair

James W. Wagner

James W. Wagner, Ph.D.
Vice Chair



THE WHITE HOUSE
WASHINGTON

July 1, 2013

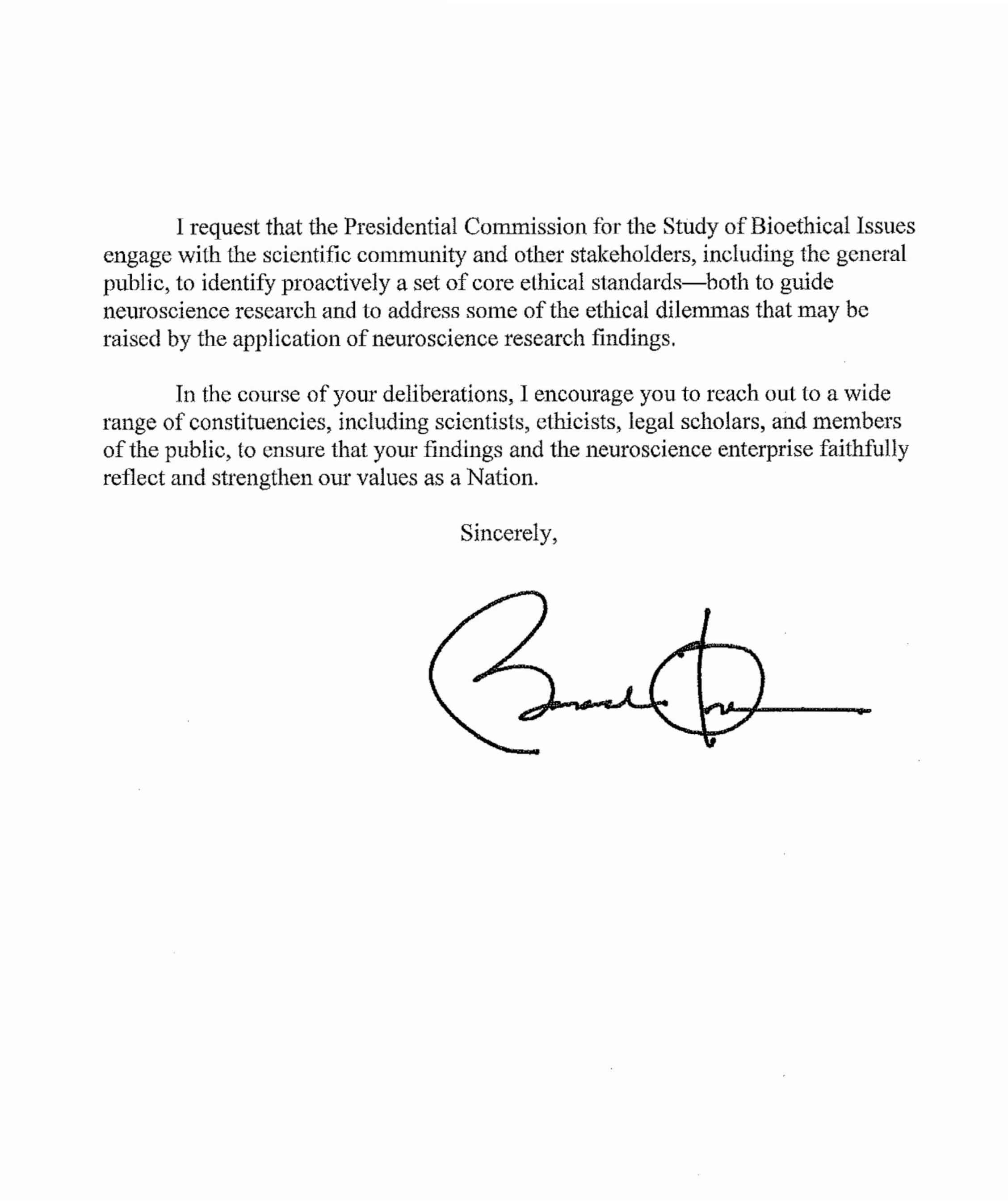
The Honorable Amy Gutmann, Ph.D.
Commission Chair
Presidential Commission for the Study of Bioethical Issues
Washington, D.C. 20005

Dear Dr. Gutmann:

As I noted in my announcement of the Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative on April 2, 2013, developments in neuroscience hold great potential to help individuals and society. New technologies to better visualize the brain and understand how it works promise to speed the discovery of new ways to treat and prevent brain disorders, including those caused by disease and traumatic injury, and to shed light on the neural components of memory and learning, among other benefits.

Advances in neuroscience can also raise ethical and legal issues that require reflection and analysis. In keeping with my Administration's strong commitment to rigorous research ethics in all fields, I want to ensure that researchers maintain the highest ethical standards as the field of neuroscience continues to progress. As part of this commitment, we must ensure that neuroscientific investigational methods, technologies, and protocols are consistent with sound ethical principles and practices.

Equally important, we should consider the potential implications of the discoveries that we expect will flow from studies of the brain, and some of the questions that may be raised by those findings and their applications—questions, for example, relating to privacy, personal agency, and moral responsibility for one's actions; questions about stigmatization and discrimination based on neurological measures of intelligence or other traits; and questions about the appropriate use of neuroscience in the criminal-justice system, among others. It will also be important to consider these types of questions as they relate to different life stages, from infancy through old age.



I request that the Presidential Commission for the Study of Bioethical Issues engage with the scientific community and other stakeholders, including the general public, to identify proactively a set of core ethical standards—both to guide neuroscience research and to address some of the ethical dilemmas that may be raised by the application of neuroscience research findings.

In the course of your deliberations, I encourage you to reach out to a wide range of constituencies, including scientists, ethicists, legal scholars, and members of the public, to ensure that your findings and the neuroscience enterprise faithfully reflect and strengthen our values as a Nation.

Sincerely,

PRESIDENTIAL COMMISSION FOR THE STUDY OF BIOETHICAL ISSUES

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ACKNOWLEDGEMENTS

The Bioethics Commission is grateful to all of those who contributed their time and expertise to this report. We would like to thank particularly the exceptional speakers who participated in public meetings, inspired thought-provoking discussions, and informed this report.

The Bioethics Commission is also grateful for its dedicated staff, which provided comprehensive research, thoughtful guidance, and unwavering support throughout its deliberations on integrating ethics and neuroscience research. The Bioethics Commission extends its special thanks to Executive Director Lisa M. Lee for her leadership on this report and on all of the Bioethics Commission's work, and to Senior Advisor Jonathan D. Moreno for his insightful contributions. The Bioethics Commission is also especially grateful to Associate Director Michelle Groman and staff lead Misti Ault Anderson for their dedication in supporting and enabling its deliberative process and engagement with this challenging topic.

REPORT AND RECOMMENDATIONS

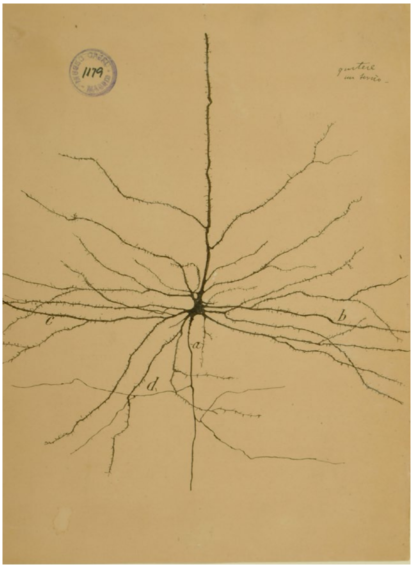
About this Report

This first report by the Presidential Commission for the Study of Bioethical Issues (Bioethics Commission), as part of the Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative, emphasizes the importance of integrating ethics into neuroscience research from the earliest planning phases. Given the promise and potential of neuroscience, we are compelled to consider carefully scientific advances that could alter our conception of the very private and autonomous nature of self. Our understanding of the mind, our private thoughts, and our volition necessitates careful reflection about the scientific, societal, and ethical aspects of neuroscience endeavors. Integrating ethics explicitly and systematically into the relatively new field of contemporary neuroscience allows us to incorporate ethical insights into the scientific process and to consider societal implications of neuroscience research from the start. Early ethics integration can prevent the need for corrective interventions resulting from ethical mishaps that erode public trust in science.

This report provides practical, conceptual, and methodological tools that can be applied directly in neuroscience research by funders, scientists, and other stakeholders. It calls for adequate resources to be allotted for successful integration of science and ethics. It also provides analysis and recommendations to guide institutions in developing necessary infrastructure for early integration of ethics into neuroscience research. In a second report, the Bioethics Commission will consider the ethical and societal implications of neuroscience research and its applications more broadly—ethical implications that a strongly integrated research and ethics infrastructure will be well equipped to address, and that myriad stakeholders, including scientists, ethicists, educators, public and private funders, advocacy organizations, and the public must be prepared to handle.

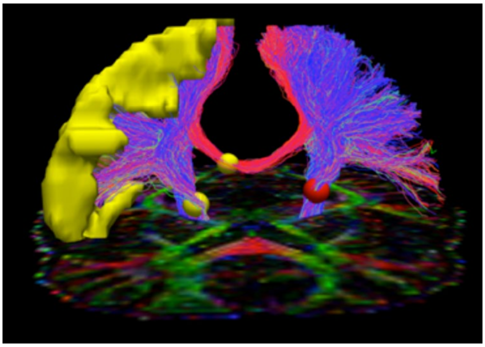
* * *

In July 2013, President Obama charged the Bioethics Commission to consider ethical and societal issues associated with advances in the field of neuroscience.[1] The Bioethics Commission is addressing the President's charge in multiple reports to be timely and responsive in the face of a rapidly emerging and evolving field. This first report reflects the Bioethics Commission's commitment to early integration of ethics and scientific research through rapid dissemination of the insights it has gained and the conclusions it has reached.[2]



Pyramidal neuron by Santiago Ramón y Cajal, 1899. From Cajal Legacy, Instituto Cajal (CSIC), Madrid.

Anatomist and Nobel laureate Santiago Ramón y Cajal wrote: "[t]he brain is a world consisting of a number of unexplored continents and great stretches of unknown territory."[3] Cajal's perspective, pronounced a century ago, remains as true today as then. The BRAIN Initiative, with its Presidential endorsement and initial investment of federal funding, represents, both practically and symbolically, an exciting investment in basic neuroscience research. Focusing on the development and application of new technologies to visualize and understand complex neural circuits, the BRAIN Initiative has the potential to make major contributions to knowledge about how the brain works. This knowledge, in turn, could inform the development of better methods for preventing and treating neurological conditions. President Obama asked the Bioethics Commission to examine the ethical considerations of not only BRAIN Initiative-related research, but neuroscience research more generally. With this broad focus, the recommendations in this report are relevant for the integration of ethics and science in neuroscience and other scientific fields.



Contemporary neuroimaging: Fiber tractography of the human motor system pathway. From Hauser, S., et al. (Eds.). (2013). *Harrison's Neurology in Clinical Medicine*, Third Edition. New York, NY: The McGraw-Hill Companies, Inc.

Ethics and Neuroscience Research

The human brain has long been a focal point of scientific and public inquiry and concern. Contemporary neuroscience—which includes molecular neuroscience, cognitive neuroscience, and clinical neuroscience, among many other subfields—has produced and could yield improved preventive, diagnostic, and therapeutic interventions for conditions that affect tens of millions of Americans and as many as a billion people worldwide.[4] Advances in neuroscience also can raise fundamental questions about central features of human experience such as conscious awareness and personal identity.

BURDEN OF NEUROLOGICAL DISORDERS IN THE UNITED STATES AND WORLDWIDE

In the United States and worldwide, the burden of neurological disorders is high and projected to "increase considerably in years to come." Neurological disorders are estimated to affect as many as one billion people globally, and millions of people in the United States. These disorders affect all age groups across geographical regions. There are many neurological illnesses with substantial health and public health impacts including dementia, epilepsy, multiple sclerosis, Parkinson's disease, schizophrenia, and traumatic brain injury, for which neuroscience research has the potential to contribute to improved interventions.

Sources: World Health Organization (WHO). (2006). *Neurological Disorders: Public Health Challenges*, Chapter 4: Conclusions and Recommendations, p. 177. Retrieved April 4, 2014 from http://www.who.int/mental_health/neurology/chapter_4_neuro_disorders_public_h_challenges.pdf; Collins, P.Y., et al. (2011). Grand challenges in global mental health. *Nature*, 475(7354), 27-30; Hirtz, D., et al. (2007). How common are the "common" neurologic disorders? *Neurology*, 68(5), 326-337; Lozano, R., et al. (2012). Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: A systematic analysis for the Global Burden of Disease Study 2010. *Lancet*, 380(9859), 2095-2128; Murray, C.J.L., et al. (2013). Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990-2010: A systematic analysis for the Global Burden of Disease Study 2010. *Lancet*, 380(9859), 2197-2223.

Many of the ethical issues raised by neuroscience research are not unique.[5] The ethical issues surrounding data privacy, informed consent, and minimization of risk, for example, are common across scientific fields. Some issues, however, such as those regarding privacy of our thoughts, threats to personal volition, or erosion of self-determination are expressed in sharper relief in neuroscience.

Advances in neuroscience highlight the relationship between theory and practice, between what we think and feel, and what we do. The complexity of the relationships among human thought, emotion, and action captures the importance of neuroscience to individuals and society. Conscious experience—communicated in many individual and cultural ways—is undoubtedly a central defining feature of human existence, and is intricately connected to human emotion and action. Advances in neuroscience excite public curiosity and challenge our self-understanding more than scientific inquiries into other bodily organ systems that lack the cultural significance of the brain as a prime locus of personal identity.[6] Grappling with complex issues that have theoretical, practical, and social dimensions suggests a need for deliberate, thoughtful, and inclusive engagement to develop responsive and nuanced guidance.

The purpose of this first report is to underscore the importance of integrating ethics and neuroscience early and throughout the research endeavor. Such integration offers a means by which researchers can recognize and respond to ethical issues that arise throughout the research process. Timely recognition of ethical issues allows one to remain responsive to the progress of research. As a starting point, this report highlights some of these ethical and societal issues that can arise through the introduction of four examples to demonstrate the need for integrating ethics throughout neuroscience research: (1) neuroimaging and brain privacy; (2) dementia, personality, and changed preferences; (3) cognitive enhancement and justice; and (4) deep brain stimulation research and the ethically difficult history of psychosurgery. While these examples bring pressing ethical issues to the fore, they will not be extensively analyzed or resolved in this report. The Bioethics Commission's second report on neuroscience and ethics will consider in greater detail the ethical and societal implications of neuroscience and the products of neuroscience research, including, for example, how neuroscience research findings are communicated.[7]

Neuroimaging and Brain Privacy. A variety of neuroimaging technologies, including computed tomography (CT), positron emission tomography (PET), electroencephalography (EEG), and functional magnetic resonance imaging (fMRI) enable us to see the brain or its activity in different ways. New insights into the brain can raise questions about privacy, particularly concerning individuals' ability to decide whether and how personal, sensitive, or intimate information is acquired and used.[8] The potential use of neuroimaging techniques for crime prevention, lie detection, or to make inferences about criminal intent raises broader concerns about the societal implications of the underlying research.[9]

The possibility of using neuroscience for such purposes is already being explored. Several laboratory studies, for example, have used fMRI to investigate questions about deception.[10] In one study, investigators asked research participants to undertake a "mock crime" by stealing either a ring or a watch. Participants were then instructed to deny stealing either of the objects, and underwent fMRI while responding to a series of questions, some of which were intended to prompt the instructed false denial. The investigators then used the fMRI data of the truthful and untruthful responses to build models to detect the deception. In the end, one model correctly predicted the veracity of responses in 90 percent of participants.[11] The investigators underscored one key limitation: "[t]his study…did not evaluate real-world scenarios or lies with severe societal, emotional, or monetary damages."[12]

This example highlights concerns about the potential—whether real or imagined—of technologies such as fMRI to observe private thoughts. As we anticipate personal and societal implications of using such technologies, ethical considerations must be further deliberated.

Dementia, Personality, and Changed Preferences. Dementia is a large and rapidly growing public health concern affecting approximately 2.4 to 5.5 million Americans and 35.6 million people worldwide.[13] It encompasses a group of cognitive disorders characterized by memory impairment and difficulty with language, motor activity, object recognition, and executive function.[14] The prevalence of dementia increases with age, affecting 5 percent of persons 71-79 years of age, 24 percent of persons 80-89 years of age, and 37 percent of persons over 90 years of age.[15]

Dementia raises ethical and societal issues with which neuroscience must engage.[16] With progress in the ability to predict future disease, growing numbers of individuals at risk might use this information to plan for their futures.[17] Future planning for disease conditions in which a person will lose the capacity to make decisions for themselves is not uncommon in health care, but it raises difficult philosophical and ethical issues.[18] Prominent among these are questions about how dementia affects notions of the self. Because the neurological changes caused by dementia can be profound, patients' wishes and preferences might change considerably as their dementia worsens and they progress from non-impaired to severely impaired states. Whereas the preferences expressed by an individual in a non-impaired state (sometimes formally expressed in an advance directive) are those of an autonomous person, the same individual with dementia might express preferences that differ from previous preferences.

Consider, for example, a man who, prior to having dementia, expressed a strong and clear preference against invasive treatments if his cancer were to return. The cancer recurs many years later after his dementia has progressed, at which time he insists on a major surgery that might extend his life, but is unlikely to markedly improve its quality. The ethical question of whether to move forward with the surgery focuses on whether his pre-dementia or post-dementia preferences should take priority and which decision best reflects his overall wishes and best interests.

Philosophers and ethicists have taken several positions in relation to cases like this one. Some have argued that respecting an individual's autonomy requires following their earlier autonomous preferences.[19] Others have argued that substantial weight should be given to the individual's current preferences, which might be markedly different from an earlier point in time.[20]

Health care professionals, caregivers, and loved ones must reconcile the ethical difficulties they encounter when pre-dementia autonomy, post-dementia autonomy, decision making capacity, and beneficence (that is, acting to ensure the wellbeing of others) appear to conflict.[21] Neuroscience, in its focus on the brain, makes engagement with these issues inevitable, as clinicians, researchers, family members, and others interact with and seek to improve the lives of those affected by neurological disorders; its discoveries also could change how we view the self of those with dementia, and our views of selfhood in general.

Cognitive Enhancement and Justice. Neuroscience advances can raise questions about justice. Humans have long had hopes and concerns about (and used) pharmacological and technological interventions meant to improve mental and physical capacities beyond normal functioning. The term "cognitive enhancement" covers a broad spectrum of methods—from nutritional supplements to brain stimulation—that improve or are thought to improve some aspect of cognitive function.[22] Coffee consumption and yoga, for example, are used by some for their cognitive effects. Certain scholars contend that some forms of cognitive enhancement are socially acceptable or possibly even desirable.[23] This example focuses primarily on prescription stimulant drugs that might be used for enhancement purposes.

Many pharmaceutical interventions associated with cognitive enhancement were developed originally for traditional clinical uses, such as the treatment of attention deficit hyperactivity disorder.[24] A considerable literature in philosophy and bioethics has explored the ethical implications of distinguishing the use of the same intervention as a treatment for a diagnosed medical condition in one case and as an enhancement of non-diseased capacity in another. Some have argued that the distinction matters ethically because while we are obliged to provide people with medical care (treatment) as a matter of justice, we are not obliged to provide people with enhancements.[25] However, beyond the distinction between treatment and enhancement, cognitive enhancement raises pressing ethical issues concerning equitable access to enhancements and their benefits, appropriate management of risks, and obligations and freedoms to enhance or not.[26]

There are anecdotal reports, media accounts, and scientific studies suggesting the use of pharmacological cognitive enhancement, particularly in educational settings such as college campuses.[27] In a web-based survey of medical students, 18 percent reported ever using stimulants, over half of which reported their first use in college.[28] Of those who reported ever using stimulants, 95 percent reported that they perceived that stimulant use could result in "some improvement in academic standing."[29] Among all survey respondents, 11 percent reported stimulant use during medical school. In a 2013 survey, about 10 percent of male and about 8 percent of female undergraduates reported using a prescription stimulant not prescribed to them in the past 12 months.[30] Additionally, in a 2005 survey, college student respondents were asked "how often, if ever, have you used any of the drugs listed below (Ritalin, Dexedrine, or Adderall)? Do not include anything you used under a doctor's orders."[31] Reported use in the past year was higher among students who were male, white, members of fraternities and sororities, had lower grade point averages, and attended more selective colleges.[32] A more recent survey indicates that "non-medical" use of Adderall is increasing, and demographic disparities remain.[33] These data could raise concerns about justice and equity, insofar as using stimulants in this way might be viewed as conferring or reinforcing advantage and exacerbating existing educational, economic, and other disparities.[34]

Deep Brain Stimulation Research and the Ethically Difficult History of Psychosurgery. The final example demonstrates how one type of ethics integration can help to further scientific advancement by addressing previous ethical controversies concerning analogous technologies. Deep brain stimulation (DBS) involves a surgical procedure to implant electrodes into specific regions of the brain for calibrated stimulation of those regions as a therapeutic treatment for symptoms of certain illnesses. The U.S. Food and Drug Administration first approved DBS in 2002 as a treatment for Parkinson's disease.[35] The relative success of DBS to manage many of the motor symptoms of Parkinson's disease, and preliminary research indicating it might be effective for several psychiatric illnesses, suggest that DBS might have a promising future for application in other disorders.[36] Careful research is required to determine whether DBS constitutes a safe and effective treatment for severe psychiatric illnesses, such as treatment-resistant depression and obsessive-compulsive disorder.

Much as the field of genetics had to contend with the history of eugenics, contemporary advances in psychosurgery, such as DBS, must contend with the widespread cultural salience of a controversial past.[37] Psychosurgery generally, and frontal lobotomy in particular, has a controversial history as early "brain science" and treatment for mental illness.[38] Implemented at a time when there were few acceptable or effective treatments for mental illness, lobotomy, at its worst, was characterized by dubious consent, crude technique, lack of scientific evidence, and major side effects.[39] With more than 40,000 procedures performed in the United States during the 1940s and 1950s, lobotomy was held in such high esteem that pioneering work in its development led to the awarding of a Nobel Prize in 1949.[40] At that time, the risks of the procedure were well known but infrequently described in the scientific literature, while its benefits were lauded in popular media. Despite eventual public and professional outcry about ethical concerns, the advent of pharmacological alternatives was likely the greatest driving force in the decline in lobotomies.[41]

A detailed history of the practice of lobotomy describes the promise it held for psychiatric professionals in terms that could now apply equally to DBS as "a ray of hope in an otherwise bleak situation for mentally ill patients."[42] Reflection on this history points out the importance of addressing ethical issues then and now, as "last-ditch medical interventions will probably always be with us. We must therefore continue to scrutinize them, not only in retrospect but as they are being conceptualized, publicized, and carried out."[43]

Because of psychosurgery's culturally and socially sensitive history, scientists and ethicists have done extensive work to safeguard the ethical conduct of current and future DBS research.[44] Proponents of DBS to treat psychiatric illness are highly invested in conducting scientifically and ethically sound research. Bioethicists, patient advocates, policymakers, psychiatrists, neurologists, and other experts met in 2007 to establish consensus regarding the standards and protections that should be in place to facilitate the ethical practice of DBS research.[45] They established a set of ethical safeguards, including the careful design of research protocols; particular attention to the vulnerabilities of participants with debilitating psychiatric illnesses; focus on adequate and fully informed consent; and careful management of expectations regarding the potential for clinical use, thereby mitigating therapeutic misconception (the mistaken conflation of the goals of research and clinical care).[46]

Integrating ethical considerations into future research protocols reduces the likelihood of ethical pitfalls and provides assurance to the public that scientific progress will not be impeded by failure to consider ethical and societal implications. Thoughtful consideration of ethical issues increases the acceptability of DBS research, and thus enhances the likelihood that DBS research will continue in a way that might result in new therapies for individuals suffering from certain psychiatric illnesses.[47]

* * *

Neuroscience is a rapidly growing, multidisciplinary field including physical and biological sciences, behavioral and social sciences, clinical research, engineering, computer science, and mathematics and statistics, each with its own ethical tradition. Integrating these various ethical traditions, elucidating a platform for ethical understanding and discussion, and allowing different ethical perspectives to be emphasized at different stages of a research project can strengthen both implementation of the study and translation of the findings to the broader public.

The many branches of neuroscience address a wide range of topics including but not limited to the evolution of the nervous system (evolutionary neuroscience), the neural mechanisms of language (neurolinguistics), and the neural mechanisms of emotion (affective neuroscience). It is unsurprising, then, that neuroscience encompasses a diversity of scientific and ethical issues.[48] Many neuroscientists explicitly wrestle with the ethical and social implications of their research and how best to address them. Others might grapple with ethical issues, even if they do not label them as such. And some scientists might not see themselves as encountering ethical issues as a part of their work at all.

> "By virtue of having a brain, you have a memory. By virtue of having a memory, you have a personal narrative. And these are the things that are devastated by Alzheimer's and we are trying to understand what goes wrong. In order to do that, we need to go to the physiology, and we need to be able to develop these new neural techniques. And that makes it a very much more challenging enterprise than helping the heart or the liver, all... important for saving lives. But somehow when you start tinkering with the brain, people get a little bit more concerned because it's really tinkering with who you are. And that's I think something that we're all grappling with."
>
> Sejnowski, T., Francis Crick Chair, Professor and Laboratory Head, Computational Neurobiology, Salk Institute for Biological Studies; Investigator, Howard Hughes Medical Institute; and Distinguished Professor, Section of Neurobiology/Neurosciences, University of California, San Diego. (2013). Presentation to the Presidential Commission for the Study of Bioethical Issues, December 18. Retrieved April 4, 2014 from http://bioethics.gov/node/3239.

It is critical that those involved in neuroscience, including researchers, research institutions and universities, public and private funders, and others, have the tools to identify and address the ethical issues they encounter. Without such tools, ethics integration is likely to be viewed by some as irrelevant or impractical, rather than as intrinsic to good science. As a first step to meaningful ethics integration, those involved in neuroscience research must identify the many areas in which ethical questions might arise in relation to their specific roles and responsibilities.

Individual scientists, for example, face ethical questions when they choose research topics, seek funding, design and conduct research, and disseminate results. There are a number of ways they might prepare to address or arrive at solutions to ethical questions, such as through professional education or discussions with experienced colleagues. Universities encounter ethical issues because they fund research; provide laboratories, equipment, and staff; and shape careers through incentive structures such as tenure. Universities can foster a community focused on responsible research through their choices about curricula and faculty, criteria for promotion, and by implementing ethics education for faculty, staff, and students. Funders require approaches that help them address ethical questions in relation to their position to influence research priorities more broadly. These approaches might include supporting research on the ethical and societal implications of a particular line of inquiry or involving those with experience in ethics on panels reviewing grant applications.

Individuals and institutions should assess their roles and influence in neuroscience research and ethical issues they are likely to encounter in order to determine which approaches to ethics integration are best suited to their context.

Approaches to Ethics Integration in Neuroscience

Ethics integration is a process by which scientists and ethicists engage with each other, and often other stakeholders, such as communities, to understand the social and ethical dimensions of their work, including the relationship between science and the societal context in which it operates. Executed well, ethics integration is an iterative and reflective process that enhances both scientific and ethical rigor. Without ethics integration, neuroscience and neuroscientists might overlook fundamental ethical and social dimensions of the complex phenomena they seek to understand. And if ethicists are not conversant in the *science* of neuroscience, they will be unable to make a meaningful contribution to the *ethics* of neuroscience. As an early bioethicist wrote, “integration can only come about by a continuing multidisciplinary discussion between people who are experts in their chosen discipline but who, in addition, have some degree of competence in fields other than their own.”[49] Without the other, ethics or neuroscience alone can offer only incomplete guidance and solutions.

Ethics is more than regulatory compliance or risk mitigation, and integration involves a deep collaboration between ethics and science such that the contributions from all disciplines are strengthened. As one presenter to the Bioethics Commission said, "bioethicists and scientists need one another," requiring both to be sufficiently knowledgeable about the others' fields.[50] This mutual understanding fosters credibility and appreciation of the technical aspects and practical exigencies of each other's work, and, for ethicists, helps to avoid overestimating or missing ethical problems.[51] Knowledge of the technical aspects of another discipline, however, does not mean that one abandons the lens of one's original field. All involved must consciously adopt and maintain a critical perspective to mitigate the danger of losing the valuable aspects of one's independent perspective or disciplinary identity.[52]

Relevant ethical considerations, and the type and intensity of integration required, will vary depending on the type of research an investigator is conducting. Developing new imaging technologies, analyzing biobank data, or conducting Phase III trials to evaluate the efficacy of a new therapy for a disease will demand a level of integration appropriate to the ethical demands of the context. Some researchers, upon reflection, might assert that they rarely confront difficult ethical issues in their daily work, while the nature of others' investigations might require more explicit, frequent, and intensive engagement with complex ethical questions. Yet relevant ethical issues take many forms based in professional ethics, research ethics, and the societal implications of the knowledge or technologies that research produces (including clinical implications). For example, laboratory researchers studying neurodegeneration in yeast models might routinely encounter questions of

ETHICS AS A LENS

In considering ethics integration, and how ethics can facilitate the work of science, the Bioethics Commission discussed the notion of ethics as a lens. Vice Chair Wagner invoked the analogy of the importance of telescope optics in the central work of astronomy.

"[A]stronomers are not physicists or optics designers, but they understand that [the] optics of a telescope is an important companion discipline that both restricts their ability to look at what they're looking at and about which they also hope it will improve."

Similarly, ethics is a necessary companion to all good science that both scientists and ethicists should aim to improve.

Source: Wagner, J.W., Vice Chair, Presidential Commission for the Study of Bioethical Issues; and President, Emory University. (2014). Research and Integration Update and Member Discussion, February 10. Retrieved April 7, 2014 from http://bioethics.gov/node/3372.

professional ethics, such as those related to analytic integrity, authorship, or mentorship of postdoctoral fellows.[53] Those conducting research with human participants have another critical set of ethical concerns with which to grapple. And all researchers must consider the potential societal implications of their research, such as how the results of a well-intended study might yield unintended applications.

FOUNDATIONAL DOMAINS OF ETHICAL CONDUCT

The foundations for ethical neuroscience research are already in place in the tenets of professional ethics and research ethics, and in early consideration of the societal implications of neuroscience advances. Integration infuses existing codes and models for ethical conduct into the research process from the outset, ensuring that those engaged with neuroscience research are aware of and draw upon these and other applicable ethics frameworks.

Professional ethics in science is derived from expectations of responsible conduct of research, codes of conduct, and the character traits that are the hallmark of good scientists. Professional ethics applies throughout the research process, from the reflective articulation of a research question to the honest and responsible communication of scientific findings.

Research ethics consists of ethical and regulatory guidelines that govern research, including those concerning research involving humans or animals. Responsible neuroscience includes recognition, interpretation, and application of existing ethical principles and regulations; assurance of compliance with regulations; and consideration of other ethical safeguards for human participants and nonhuman animals in research.

Finally, it is likely that a great deal of neuroscience research will have *societal implications*, including clinical implications, even if findings do not translate immediately into new interventions or technologies. Ethical research requires that scientists consider potential societal implications of their work from the outset.

A fundamental goal of scientific inquiry is to seek improved explanations of the world.[54] The potential of science to improve human welfare grounds a societal obligation to undertake and support scientific research generally.[55] Scientists pursue knowledge both for its own sake and for the practical problems it can help to solve. Their professional role grounds a basic duty to pursue science for the public good and to consider carefully the possible consequences of their work.[56] The duty to pursue science in the public interest derives from several ethical obligations, as well as the fact that much scientific research is directly or indirectly publicly funded.

Including ethics in science is not a new process. Value decisions implicit in science encompass practical and moral considerations, as experienced researchers appreciate. These include how to allocate limited funds to a number of possible areas of study, determine which research designs will be most beneficial and least harmful to individuals, and identify which experiments are most likely to bring about the most useful results for society at the least cost. Practical and moral considerations come into play as well in the implementation and conduct of research, from the day-to-day work of completing experiments to data analysis.

> "I think by asking the fundamental question[s]—[W]hy are you doing this? Why do you think your lab director wants to get this grant in particular? Why does your institution promote it in this way? Why did the funding agency write the solicitation in the following way?—by asking these questions you can really impact what's already there, and in the process the scientists can take ownership rather than the moral expert insisting on what the logical case is. …[I]t's a subtle move, but it allows for a co-responsible approach.… I would suggest that the word 'curiosity'… is potentially an engine for both ethical care and scientific creativity."
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> Fisher, E., Associate Director for Integration, Center for Nanotechnology in Society; Assistant Professor, School of Politics and Global Studies and the Consortium for Science, Policy and Outcomes, Arizona State University. (2014). How the Inclusion of an Ethicist on a Research Team Might Affect Change in Scientific Research. Presentation to the Presidential Commission for the Study of Bioethical Issues, February 11. Retrieved April 7, 2014 from http://bioethics.gov/node/3379.

The purpose of explicitly integrating ethics in science is to engage in ethical analysis and reflection and bring ethical decisions and assumptions inherent to the practice of science to the forefront to assess their merits, develop new standards or modify old ones, and reform practices where needed. Democratic deliberation, an approach to collaborative decision making that embraces respectful debate of opposing views and active participation by citizens, is critical to ethics integration because in an open society—and considering the societal investment in modern science—societal values need to constitute a genuine part of these decisions.[57]

Science driven by "ethics" is not always enough, however, even with public input. For example, some leading scientists, captivated by early 20th century eugenic thought, were driven by an ethical framework of perceived societal benefit.[58] They wrote at length in well-recognized journals and popular publications about the importance of making sure that science was driven by a certain ethos, one that turned out to be catastrophic both for science and for the rest of the world. Modern society can and must learn from these mistakes; this is the nature of the moral life in science and in all human experience. Ethics integration acknowledges that measures can be taken to ensure the likelihood that modern neuroscience will benefit from an awareness of the past without being paralyzed by it. With scientific and public interest in neuroscience growing, the time is especially right for a more explicit conversation about practices that facilitate ethical reflection in the research process.

The following are selected approaches to ethics integration.

Ethics Integration through Education at All Levels. Integration of ethical issues in neuroscience education is clearly demanded by the vibrant nature of the field.[59] Scholars have suggested that in order to develop an understanding and knowledge base in ethics, future research professionals should be exposed to ethics early in their education and careers.[60] This early exposure facilitates a deeper understanding of the implications of science, before students are immersed in their own work and overwhelmed by early career pressures. Integration of ethics and science through education can equip scientists to recognize and assess ethical issues in their work, and equip bioethicists to understand scientific practice.[61]

Early ethics education provides a strong foundation for students who might later pursue science as a profession, and professional and continuing ethics education builds on that foundation for more experienced scientists. Science programs, including but not limited to neuroscience, can challenge students to confront big questions, which mentors and educators should revisit periodically and seriously, such as: "What is science for? What are the values I bring to my scientific work? Why did I become a scientist and why am I one now?"[62] One desirable goal for ethics education is "transformational learning," which goes beyond cultivating cognitive learning or critical thinking to inculcate "habits of mind, attitudes, and dispositions."[63] If successful, it will become natural for scientists to have ongoing engagement with the societal dimensions of their work.[64]

> "[B]rain science is a fine place to begin to figure out how to integrate bioethics education into the preparation of scientists. Ethics education in this area will be particularly challenging, and therefore exciting to work on, because brain science requires collaboration across so many disciplines and because it will raise profound questions across all three domains: responsible conduct of research, research ethics, and the societal impact of the knowledge and technologies that emerge. Since existing bioethics education programs have focused much less on this third area of societal impact, and since brain science engages so many questions in that domain, I recommend that there be considerable attention to the ethical and social impact questions, not just to research ethics and RCR [responsible conduct of research]. It is also my hope that we will not just train or educate, but that we will commit to designing for learning, and specifically for a kind of learning that is transformational, so that we are preparing not just scientists, but citizen-scientists who are professional in the fullest meaning of the word, aware of the power science holds in society, and capable of secular moral reasoning in our highly pluralistic society."
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> Solomon, M.Z., President, The Hastings Center; and Clinical Professor of Anaesthesia, Harvard Medical School. (2013). Transformational Bioethics Learning in Brain Science. Presentation to the Presidential Commission for the Study of Bioethical Issues, December 18. Retrieved April 4, 2014 from http://bioethics.gov/sites/default/files/Solomon%20Remarks%20to%20Pres%20Commission.pdf.

Integration through education is not limited to exposing science students to ethics. Ethics programs also can require exposure to scientific methods. Students could be required to complete, for example, a laboratory science component or conduct independent scientific research to enhance their scientific literacy and understanding.

Early integration of ethics into curricula can begin before the undergraduate level, during high school or sooner. For example, in a pilot program that tested the effectiveness of a new high school bioethics curriculum, researchers found that the addition of bioethics awakened a curiosity in students about the science itself; the addition of bioethics did not fetter interest in science, rather, it encouraged it.[65] Efforts such as Brain Awareness Week, a worldwide "celebration of the brain for people of all ages," which includes events intended to educate about neuroscience as well as advocate for science funding, also offer opportunities for education at many levels including the public at large.[66]

Educational efforts can continue throughout higher education. Some colleges and universities in the United States and abroad have existing or are developing programs, courses, or teaching resources focused on ethical issues related to neuroscience. For example, Duke University's graduate program in Bioethics and Science Policy offers a neuroscience concentration and focuses on complex problems at the intersection of science, technology, and ethics.[67] The University of Pennsylvania Center for Neuroscience and Society provides a repository of high school, undergraduate, and graduate level neuroethics teaching materials.[68] And the University of Manchester Interdisciplinary Network on Teaching of Ethics for Neuroscientists developed an online neuroethics education module.[69]

Ethics integration through education can continue still further, through graduate and professional education and throughout a scientific career, for example, via continuing education programs for experienced researchers.

> "I think that science education has to be fundamentally restructured from the get-go, and that that is what is ultimately going to address these issues, and I think that scientists think the way they think because their education leads them to think that way. They're siloed because that's how they're trained. It should be no surprise that they exist within a particular world when that is how science education is organized, and I think that that is something that has to be dealt with."
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> Sankar, P., Associate Professor, Department of Medical Ethics and Health Policy; and Senior Fellow, Leonard Dan's Institute of Health Economics, University of Pennsylvania. (2014). ELSI Origins and Early History. Presentation to the Presidential Commission for the Study of Bioethical Issues, February 11. Retrieved April 4, 2014 from http://bioethics.gov/node/3379.

Ethics Integration through Institutional Infrastructure. Public and private institutions can develop structures and processes to facilitate ethics integration. For example, the Defense Advanced Research Projects Agency (DARPA), one of the federal agencies involved in the BRAIN Initiative, has integrated ethics formally into its neuroscience research efforts. DARPA has convened an independent panel of six nationally recognized bioethicists—not employed by the agency—to inform the ethical conduct of neuroscience.[70] The panel provides expert insight to DARPA program managers on ethical, legal, and social issues associated with their BRAIN Initiative projects. Each program manager consults an ethics mentor at the inception of a project to incorporate ethical considerations according to "the three Cs—character, consent, and consequence."[71] Ethics mentors provide insight on issues such as respecting autonomy through informed consent, or the individual and societal consequences of neurotechnologies.[72] Panel members also write an ethics-focused white paper about each program or project plan. In addition to the services provided by the independent panel, each program is required to set aside funds for similar consultation services or ethics-focused research, as a supplement to the panel's work. In this way, DARPA has combined several approaches to ethics integration—some of which are elaborated in the approaches discussed below.

Ethics Integration through Research about the Ethical, Legal, and Social Implications of Scientific Research. One approach for ethics integration is for funders to direct consideration of the ethical and social implications of the research they support.[73] For example, the National Institutes of Health's (NIH's) and U.S. Department of Energy's Human Genome Project Ethical, Legal, and Social Implications Program (HGP ELSI Program) was the first national model formally established in the United States for integrating ethical and social issues into a major federal science initiative. The agencies involved designated a percentage of their annual extramural budgets to programs examining the ethical, legal, and social ramifications of genetic and genomic research.[74] Setting aside a direct source of funds helped to create parallel and multidisciplinary research on ethical and social aspects of genomics. Previous efforts at science and ethics integration offer important lessons for future funders, scientists, and ethicists. The goals and approaches of the HGP ELSI Program developed over time. Formal review processes,

THE ROLE OF PROFESSIONAL SOCIETIES

Professional societies can play an important role in fostering a dialogue between the scientific and ethics communities. The Society for Neuroscience and the International Neuroethics Society hold their annual conferences together, ensuring that the location and timing are aligned. This coordination encourages scientists to engage with ethical issues, and ethicists to learn more about emerging developments in neuroscience. In addition, the Society for Neuroscience annual conference features the David Kopf Lecture on Neuroethics. Past topics have included behavioral sciences in the courtroom, the ethics of cognitive enhancement, and managing incidental findings discovered in neuroimaging.

Sources: Massachusetts General Hospital Center for Law, Brain & Behavior. (2013). News and Events: International Neuroethics Society to Meet at SfN 2013 in San Diego. Retrieved April 7, 2014 from http://clbb.mgh.harvard.edu/international-neuroethics-society-to-meet-at-sfn-2013-in-san-diego/; Society for Neuroscience. (2012). Neuroscience 2012 Featured Lectures. Retrieved May 5, 2014, from http://am2012.sfn.org/am2012/events/lectures.aspx?type=feature&print=on; Illes, J. (2006). Neuroethics, Neurochallenges: A Needs-Based Research Agenda. Retrieved April 7, 2014 from http://neuroethics.stanford.edu/documents/Illes.NeuroethicsSFN2006.pdf; Society for Neuroscience. (2013). Neuroscience 2013: Featured Lectures. Retrieved April 7, 2014 from http://www.sfn.org/annual-meeting/neuroscience-2013/abstracts-and-sessions/scientific-program/featured-lectures.

feedback from genetic scientists, and constructive critique from a growing community of interdisciplinary scholars helped inform changes in strategic vision and practical implementation of the Program's research, education, and policy components.[75]

The HGP ELSI Program is one among many ethics integration efforts associated with multinational and country-specific research initiatives (see Appendix I: *Ethics Integration in Selected International Neuroscience Research Programs*).

Ethics Integration through Research Ethics Consultation. Within research institutions, an ethics consultation service is one way to integrate ethics into the research process in neuroscience and other fields. Though not currently commonplace as an institutionalized service, there are established examples of research ethics consultation services.[76]

THE HUMAN MICROBIOME PROJECT FUNDS RESEARCH ON ITS ETHICAL, LEGAL, AND SOCIAL IMPLICATIONS

The goal of the NIH Human Microbiome Project (HMP) is to identify and characterize the community of microorganisms that live in or on the human body. The HMP currently funds six projects that study the ethical, legal, and social implications of human microbiome research. The projects cover topics such as the concept of risk and benefit in human microbiome research, the current regulatory framework for probiotic products on the market, and the implications of research on ancient and contemporary human microbiomes for the identities of indigenous people.

Sources: Peterson, J., et al. (2009). The NIH HMP. *Genome Research*, 19(12), 2317-2323; NIH HMP. (n.d.). Ethical, legal, and social implications [Webpage]. Retrieved April 11, 2014 from http://www.hmpdacc.org/ethical/ethical.php.

The NIH Clinical Center (Clinical Center) admits 10,000 new patients a year, all of whom are participants in some form of clinical research.[77] The Clinical Center provides a Bioethics Consultation Service for all NIH staff as well as Clinical Center research participants and families, intended to serve several purposes such as assisting in making decisions about research participation.[78]

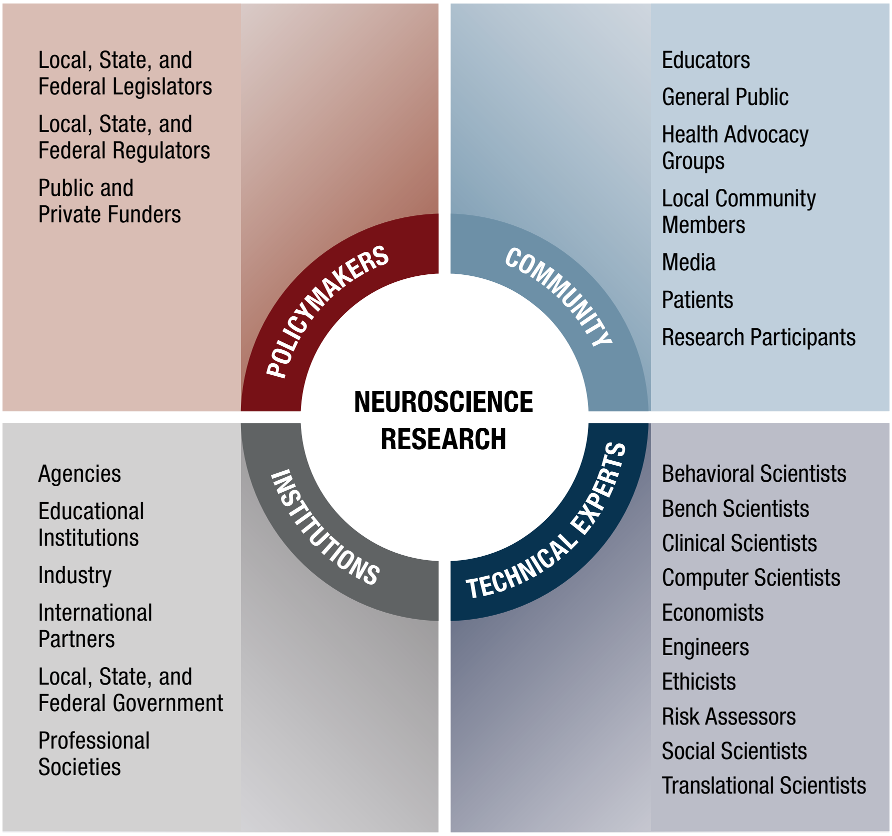
Another example of a consultation service is the Benchside Ethics Consultation Service (BECS) at Stanford University, which describes its role as making ethics advice available to bench scientists and clinical researchers "as the science unfolds," influencing study design in its early phases, and helping to ensure that research is not halted or slowed later in the process when ethical issues become more apparent or more problematic.[79] To enhance uptake and effectiveness, BECS implemented measures to increase confidentiality and set realistic expectations about the limits on confidentiality in response to researchers' concerns including "going over the heads of more senior researchers in obtaining a consultation."[80]

Consultation services formalize the longstanding practice of researchers seeking advice from colleagues on an individual basis.[81] There are several advantages to formalizing this practice. First, consultation services comprise teams of ethicists and scientists, who have a range of expertise and bring a variety of perspectives to the consultation service. This composition broadens the scope of considerations that can be brought to bear on an issue. Second, a centralized and formalized process can serve at the institutional level as well as the protocol level, allowing the consultation team to compile data on the types of ethical issues that arise, and to engage institutions, programs, and investigators in a broader conversation about implications of particular types of research. The BECS team has observed that researchers approach the ethicists at various points in the research process, before the initiation of a research project—when investigators are deciding questions of hypothesis, design, and recruitment—during the course of a study, or before or after results are published. The consultation model allows researchers ongoing access to a team of ethicists, and strives to make ethics a seamless part of the research process.[82]

Ethics Integration through Stakeholder Engagement. Another mechanism for integrating ethics and science is to engage with stakeholders, who often include members of the public, private partners, industry representatives, neuroscientists from many different subfields, patients, research participants, and community members (see Figure 1: Potential Stakeholders in Neuroscience Research). The identification and inclusion of relevant stakeholders is an important component of assessing and addressing ethical issues in specific contexts. Institutions and researchers can use stakeholder engagement strategies to better understand the perspectives and concerns of parties interested in specific research. Approaches to stakeholder engagement include public meetings; public comment; and other community engagement strategies, such as community advisory boards or community-based participatory research. Stakeholder engagement in neuroscience, as in other emerging sciences, is a process that would greatly benefit from enhanced attention by institutions engaged in the field.

Figure 1: Potential Stakeholders in Neuroscience Research*

*This list is not exhaustive. An important component of stakeholder engagement is identifying stakeholders through a variety of possible methods including literature review, referral, or community meetings.



Sources: Agency for Healthcare Research and Quality (AHRQ). (2011). *Engaging Stakeholders to Identify and Prioritize Future Research Needs*, (AHRQ Publication No. 11-EHC044-EF). Rockville, MD: AHRQ, p. 7. Retrieved April 7, 2014 from http://www.effectivehealthcare.ahrq.gov/ehc/products/200/698/MFRNGuide04--Engaging_Stakeholders--6-10-2011.pdf; UNAIDS/AVAC. (2011). *Good Participatory Practice: Guidelines for Biomedical HIV Prevention Trials*. Retrieved April 7, 2014 from http://www.avac.org/ht/a/GetDocumentAction/i/35219; MacQueen, K.M., et al. (2012). *Stakeholder Engagement Toolkit for HIV Prevention Trials*. Retrieved April 7, 2014 from http://www.fhi360.org/sites/default/files/media/documents/Stakeholder%20EngagementToolkit%20for%20HIV%20Prevention%20Trials.pdf.

One example of stakeholder engagement in ethics and science is the National Nanotechnology Initiative's process to generate a 2011 Environmental, Health, and Safety Research Strategy. A nanotechnology working group held a series of four public workshops covering topics that included an ethical, legal, and social implications capstone.[83] The working group obtained information pertinent to setting research priorities and identified gaps and obstacles to accomplishing the needed research by conducting a series of public engagement workshops and seeking public comment. The strategy was published along with a brochure intended to summarize the plan for the public and engaged stakeholders.[84]

Ethics Integration through Inclusion of an Ethics Perspective on the Research Team. Another strategy for integrating ethics and science is to include an ethicist—or a scientist with experience in ethics—directly on the research team or research protocol. This strategy incorporates social science and humanist perspectives into a research project by engaging researchers in critical examination at different decision points in the research process. This approach stimulates awareness of social considerations and incorporates them into research-process decisions (in addition to research-prioritization decisions, for example). Integrating ethical considerations into routine science decision making occurs by embedding ethicists and social scientists into the laboratory where learning is reciprocal. As one researcher who studied the effectiveness of the approach noted, "Rather than experiencing societal considerations as 'ethical speed bumps' imposed on their projects, the [researchers] indicated that such reflections broadened their decisions. They realized that they were making choices, that these choices were based on a range of considerations, and that by reflecting on them, they found that decision outputs and inputs can both vary."[85] Periodic meetings between researchers and persons with experience dealing with ethical issues can be used to discuss researchers' decisions, the relevant considerations, potential alternative choices, and possible outcomes—an approach that can be particularly responsive to the ethical issues facing individual researchers.[86]

* * *

Recognizing and confronting challenges to the integration of ethics and science is an important component of planning and implementation. Adequate funding is necessary (though not sufficient) to achieve effective integration. Inadequate funding presents practical challenges and also can be perceived to reflect a lack of political will for substantive engagement with ethical issues.

Additional potential challenges might include professional incentive structures, available expertise, and the available evidence for particular approaches to integration. First, professional reward and promotion structures, such as tenure or grants, can incentivize or disincentivize early incorporation of ethics into scientific programs.[87] For example, scientists face pressure to run their own laboratories, and are rewarded for conducting their own focused work; as a result, as one neurologist explained to the Bioethics Commission, scientists "don't go out and talk to other people because that's pro bono work.... [W]hat you need to do is advance your science. And our institutions are set up to promote that and not cross disciplinary engagements."[88] Inclusion of professional activities related to integration in professional reward structures such as tenure might encourage researchers to participate. Second, there might be an insufficient supply of available experts with relevant cross-disciplinary fluency or time.[89] The availability of trained professionals will grow with the proliferation of education programs for students and professionals. Finally, there might be gaps in knowledge or evidence about which approach or combination of approaches work best in a given context. Just as previous ethics integration efforts, such as the HGP ELSI Program, offered important lessons, increasing implementation and evaluation of various approaches to neuroscience ethics integration will advance the scholarship and body of evidence over time.[90]

It is important to acknowledge the practical, professional, and political challenges that those undertaking ethics integration sometimes face. To enhance the likelihood of success, there should be a clear vision of, and a strategic approach to, ethics integration to help identify and overcome obstacles. Funding is critical. It must be accompanied by investment in developing expertise and thoughtful articulation of criteria for success. The ethics integration approaches described here can initiate thoughtful planning that is responsive to a variety of research contexts, from basic science to clinical research. The Bioethics Commission's recommendations are intended to strengthen ethics integration infrastructure for the BRAIN Initiative and neuroscience more broadly, ensuring that this important science will continue to advance the public good.

Recommendations[91]

Ethical issues arise throughout the scientific research process. Those involved in research at all levels, including science policymakers, public and private funding institutions, and individual investigators, have a professional obligation to identify and address ethical issues encountered in their work and a broader obligation to support scientific research that furthers the public good. Fulfillment of these obligations supports scientific quality and is crucial to maintaining public trust essential for scientific progress.

Ethics integration should aid scientists in recognizing and addressing ethical issues as they arise, and ethicists in understanding the science and technology with which they engage. The goal is not to make scientists into ethicists or vice versa. It is to cultivate sufficient fluency for productive discussion and collaboration in a multidisciplinary endeavor that can include biological scientists, clinicians, historians, lawyers, philosophers, physical scientists, social scientists, and theologians, among others. Although ethics is already integrated into science in various ways—as it is in many human activities—more explicit and systematic integration serves to elucidate implicit ethical judgments and allows their merits to be assessed thoughtfully. Moreover, integration efforts can serve both to address ethical issues in particular cases as well as to cultivate an ethical sensibility beyond the bounds of the case at hand.[92]

Recommendation 1:
Integrate Ethics Early and Explicitly Throughout Research

Institutions and individuals engaged in neuroscience research should integrate ethics across the life of a research endeavor, identifying the key ethical questions associated with their research and taking immediate steps to make explicit their systems for addressing those questions. Sufficient resources should be dedicated to support ethics integration.

Existing approaches to ethics integration, as described on previous pages, include but are not limited to educational support, funding mechanisms, ethics consultation, stakeholder engagement, and incorporation of ethics expertise into research teams. Depending on their structure, research priorities, and capacity (among other things), institutions and individuals will implement different systems to integrate ethics and neuroscience research. For some, one approach to integration will be sufficient; for others, combined approaches might be necessary. Yet, in all cases, ethics integration should be explicitly acknowledged and supported to highlight the importance of robust ethical reflection and avoid formulaic approaches that might mask underlying complexity.

When planning for and conducting neuroscience research, it is important that researchers prepare for ethical issues that might arise. When responding to funding opportunities, for example, neuroscience researchers might seek funding for ethics integration. Researchers also might seek support to develop innovative approaches to ethics integration and evaluate approaches' effectiveness. Institutions, such as universities, neuroscience departments, and ethics programs, should seek to integrate ethics on a broader scale. They might develop means to integrate ethics into neuroscience research, for example, through curriculum development or broad stakeholder engagement. These institutions also might seek funding to support ethics integration and evaluation. Research funders should take action as well, such as by requiring ethical expertise as part of research teams, supporting ethics integration within neuroscience research projects, or funding innovation and evaluation of integration in practice (as discussed further in Recommendation 2).

Without dedicated resources that demonstrate commitment to addressing ethical and social issues, successful integration is impossible. Available resources must include financial resources, human capital, and expertise. Funding alone is necessary but not sufficient. Particular attention should be paid to developing and supporting a well-trained cadre of professionals. Resources allocated for integration support research; they do not compete with it. Potential funding sources include public and private institutions involved or with a stake in neuroscience research such as government agencies, private foundations, and universities. Institutions both affirm their commitment to ethics integration and enable such integration to occur through sufficient investment to assess integration needs, implement ethics integration, and make explicit existing systems of integration.

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Once implemented, systems for integrating ethics and neuroscience research should not operate in a vacuum. Institutions and individuals engaged in neuroscience research should learn from collective experience to improve existing systems and inform others about what works and what does not.

Recommendation 2:
Evaluate Existing and Innovative Approaches to Ethics Integration

Government agencies and other research funders should initiate and support research that evaluates existing as well as innovative approaches to ethics integration. Institutions and individuals engaged in neuroscience research should take into account the best available evidence for what works when implementing, modifying, or improving systems for ethics integration.

Evaluating approaches to ethics integration goes hand-in-hand with developing innovative approaches. Innovation prevents stagnation and counteracts reliance on approaches that are familiar, but potentially outdated, inefficient, or counterproductive. Evaluation informs innovation, allows for continuous improvement, and measures success. Both development and evaluation contribute to an iterative process toward better ethics integration in neuroscience research.

In evaluating their own systems and other approaches to ethics integration, funders, institutions, and researchers should look to best practices in program evaluation, such as process and outcome evaluation, that are most relevant. Key questions will include how to define criteria for success and how best to measure them. Researchers should share widely their findings and conclusions to support more robust and informed ethics integration.

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One foundational approach to integration is pairing science and ethics education at all levels of education. The Bioethics Commission is committed to doing its part to enhance bioethics education. Ethics education takes place at many stages throughout the moral development of individuals, from informal lessons from parents to professional development later in one's career. Early ethics education in academic settings is critical to prepare future scientists to integrate ethical considerations into their work—including future research in neuroscience. Professional development for experienced investigators is equally important and can serve multiple ends, contributing not only to their individual knowledge, but to the knowledge of the students and young scientists that they mentor as well. Ethics education has a better chance of informing action when it is continually reinforced and connected to practical experience.

The Bioethics Commission heard from many scientists and educators that it is essential to ensure that all scientists understand the role of ethics in good science. Graduate school is the most specialized stage of education and bioethics education should continue through all stages of a scientist's education, as ethical issues often become more complex as one advances. But graduate school is certainly not the best place to begin; foundations for ethical thinking must be laid earlier, at all levels. Moreover, these foundations should be continually reinforced—from pre-college education through continuing education for experienced scientists.

The ethical challenges that neuroscience raises are not wholly unique, and the ethics needed to ensure its progress overlap with the ethics needed to ensure progress in all science. Undergraduate liberal arts education in ethics, professional ethics, and the ethics of science—and earlier foundational education at the primary and secondary levels—will better prepare future researchers than starting foundational ethics education at the professional level. Repeated calls for graduate-level approaches are not only impractical but potentially impossible to execute effectively. It is important that ethics education take place at many points before, during, and after graduate school. Continuing professional education after graduate school will reinforce ethical perspectives, building on the strong foundation laid earlier in a scientist's education and career.

Recommendation 3:
Integrate Ethics and Science through Education at All Levels

Government agencies and other research funders should initiate and support research that develops innovative models and evaluates existing and new models for integrating ethics and science through education at all levels.

Some ethics education currently occurs at the secondary and undergraduate levels. For example, NIH offers a bioethics curriculum for high school students.[93] A pilot program testing the curriculum's effectiveness found that learning about bioethics fostered students' curiosity in the underlying science. Science fairs or pre-college competitions such as the Intel Science Talent Search or the For Inspiration and Recognition of Science and Training (FIRST) Robotics Competition could also provide opportunities for instilling the importance of ethics integration as young people contemplate a science or technology career.[94] Some continuing ethics education is occurring as well, for example, through mentoring programs for scientists at all levels, such as the Society for Neuroscience online mentoring community.[95]

While current efforts are promising, further development and evaluation of models, including curricula, for integrating ethics and science through education at all levels are needed. Innovative methods to develop critical thinking, ethical sensitivity, and moral reasoning will provide a strong foundation for students who might later pursue science as a profession, and build on that foundation for more experienced scientists. Models should be widely shared for implementation and evaluation. As with evaluating other approaches to ethics integration, researchers should look to best practices in program evaluation and should share openly their results and findings. Informed by the best available evidence, successful education models should be implemented to better prepare future scientists and engage practicing scientists—including neuroscientists—to integrate ethics into their research.

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It has been just over a year since the announcement of the BRAIN Initiative, and institutions participating in this research effort have an important opportunity to integrate ethics and science from the outset.[96] A key component of this integration is the inclusion of ethicists or scientists with experience in ethics in BRAIN Initiative-related scientific advisory boards and funding review committees, particularly for the major public and private sector partners.

Recommendation 4:
Explicitly Include Ethical Perspectives on Advisory and Review Bodies

BRAIN Initiative-related scientific advisory and funding review bodies should include substantive participation by persons with relevant expertise in the ethical and societal implications of the neuroscience research under consideration.

Major public and private sector partners might achieve this goal in different ways, aligned with their organizational structure and function. For example, DARPA's approach relies on an independent neuroscience ethics advisory panel. NIH or the National Science Foundation might choose to include ethicists on relevant scientific advisory and planning groups or study sections reviewing responses to BRAIN Initiative funding announcements. Ethical perspectives should be included appropriately on neuroscience research advisory bodies beyond the BRAIN Initiative as well.

No matter how institutions approach this aspect of ethics integration, they should ensure that scientific governance in neuroscience is imbued with an ethical perspective. For this to be successful, the mandates, structures, and processes of relevant advisory bodies should ensure that ethicists are given the opportunity to make meaningful contributions to discussions and decisions capable of influencing the research endeavor as a whole.[97]

* * *

Ethics is an important companion to science that both facilitates and enhances the scientific endeavor. Neuroscience research in general and the BRAIN Initiative in particular present important opportunities to integrate science and ethics for their mutual benefit. Successful ethics integration requires commitment, innovation, sensitivity to context, and adequate resources.

ENDNOTES

[1] Letter from President Barack Obama to Dr. Amy Gutmann, Chair, Presidential Commission for the Study of Bioethical Issues (PCSBI). (2013, July 1). Retrieved April 4, 2014 from http://bioethics.gov/sites/default/files/news/Charge%20from%20President%20Obama.pdf; Obama, B. (2013, April 2). Remarks by the President on the BRAIN Initiative and American Innovation. Retrieved April 4, 2014 from http://www.whitehouse.gov/the-press-office/2013/04/02/remarks-president-brain-initiative-and-american-innovation.

[2] Building on its past work on neuroscience and related ethical issues, including hearing from experts at two public meetings, the Bioethics Commission held three public meetings and heard from representatives from public agencies and private sector partners involved in the BRAIN Initiative, neuroscientists, philosophers, and other experts discussing the importance of and approaches to integrating ethics and science. The Bioethics Commission also published a request for public comment in the *Federal Register* and received several thoughtful and insightful responses.

[3] Ramón y Cajal, S. (1956). *Charlas de café: Pensamientos, Anécdotas, y Confidencias*, Séptima Edición [Coffee Chat: Thoughts, Anecdotes, and Confidences, Seventh Edition]. Madrid: Espasa-Calpe, S.A, p. 181. ("El cerebro humano representa un muncho donde figuran algunos continentes explorados y vastas tierras ignotas." Translated by Presidential Commission for the Study of Bioethical Issues Staff.).

[4] World Health Organization (WHO). (2006). *Neurological Disorders: Public Health Challenges*, Chapter 4: Conclusions and Recommendations, p. 177. Retrieved April 4, 2014 from http://www.who.int/mental_health/neurology/chapter_4_neuro_disorders_public_h_challenges.pdf; Hirtz, D., et al. (2007). How common are the "common" neurologic disorders? *Neurology*, 68(5), 326-337; Insel, T.R., and S.C. Landis. (2013). Twenty-five years of progress: The view from NIMH and NINDS. *Neuron*, 80(3), 561-567.

[5] See, e.g., Capron, A.M., Board Chair, Public Responsibility in Medicine and Research (PRIM&R). (2014, March 26). Comments submitted to PCSBI ("The ethics of neuroscience research is not distinct from the ethics of research in other areas of biology and medicine.").

[6] Safire, W. (2002). Visions for a new field of "neuroethics." In S.J. Marcus (Ed.). *Neuroethics: Mapping the Field* (pp. 3-9). New York, NY: The Dana Foundation.

[7] Caulfield, T., Canada Research Chair in Health Law and Policy, and Professor in the Faculty of Law and the School of Public Health, University of Alberta. (2014). Science "Hype": Sources and Solutions. Presentation to PCSBI, February 10. Retrieved April 4, 2014 from http://bioethics.gov/sites/default/files/Caulfield%20Meeting%2016%20Presentation.pdf; Neill, U., Director, Office of the President, Memorial Sloan-Kettering Cancer Center; and Editor at Large, *Journal of Clinical Investigation*. (2014). Ethics of Communication about Neuroscience Research by Scientists and Journalists. Presentation to PCSBI, February 10. Retrieved April 4, 2014 from http://bioethics.gov/sites/default/files/Neill%20Meeting%2016%20Presentation.pdf; Racine, E., Director, Neuroethics Research Unit; and Associate Research Professor, Institut de Recherches Cliniques de Montréal; Associate Research Professor, Department of Medicine, Université de Montréal; Adjunct Professor, Department of Medicine and Department of Neurology and Neurosurgery, McGill University. (2014). Neuroscientists and the Public: Perspectives and Questions from Neuroethics. Presentation to PCSBI, February 10. Retrieved April 4, 2014 from http://bioethics.gov/sites/default/files/Racine%20Meeting%2016%20Presentation.pdf; Ward, S.J.A., Professor and Director, George S. Turnbull Center, School of Journalism and Communication, University of Oregon-Portland. (2014). Journalism Ethics Amid a Media Revolution. Presentation to PCSBI, February 10. Retrieved April 4, 2014 from http://bioethics.gov/sites/default/files/Ward%20Meeting%2016%20Presentation.pdf.

[8] Dumit, J. (2004). *Picturing Personhood: Brain Scans and Biomedical Identity*. Princeton, NJ: Princeton University Press; Farah, M.J. (2005). Neuroethics: The practical and the philosophical. *Trends in Cognitive Sciences*, 9(1), 34-40; Giordano, J., Kulkarni, A., and J. Farwell. (2014). Deliver us from evil? The temptations, realities, and neuroethico-legal issues of employing assessment neurotechnologies in public safety initiatives. *Theoretical Medicine and Bioethics*, 35(1), 73-89; Santosh, P.J. (2000). Neuroimaging in child and adolescent psychiatric disorders. *Archives of Disease in Childhood*, 82(5), 412-419.

[9] Farah, M.J., et al. (2014). Functional MRI-based lie detection: Scientific and societal challenges. *Nature Reviews Neuroscience*, 15(2), 123-131; Jones, O.D., et al. (2013). Law and neuroscience. *The Journal of Neuroscience*, 33(45), 17624-17630.

[10] Farah, M.J., *supra* note 9; Wolpe, P.R., Foster, K.R., and D.D. Langleben. (2010). Emerging neurotechnologies for lie-detection: Promises and perils. *American Journal of Bioethics*, 10(10), 40-48; Langleben, D.D., et al. (2002). Brain activity during simulated deception: An event-related functional magnetic resonance study. *Neuroimage*, 15(3), 727-732; Kozel, F.A., et al. (2005). Detecting deception using functional magnetic resonance imaging. *Biological Psychiatry*, 58(8), 605-613; Langleben, D.D., et al. (2005). Telling truth from lie in individual subjects with fast event-related fMRI. *Human Brain Mapping*, 26(4), 262-272. Although some scholars believe that fMRI will replace traditional polygraph in certain settings, others caution that, "although brain imaging is a more direct index of cognition than the traditional polygraph, it is subject to many of the same caveats." Monteleone, G.T., et al. (2009). Detection of deception using fMRI: Better than chance, but well below perfection. *Social Neuroscience*, 4(6), 528-538, p. 528.

[11] Kozel, F.A., *supra* note 10.

[12] Ibid, p. 612.

[13] Moyer, V.A. (2014). Screening for cognitive impairment in older adults: U.S. Preventive Services Task Force recommendation statement. *Annals of Internal Medicine*, doi:10.7326/M14-0496. Alzheimer's disease is the most common form of dementia. WHO. (2012). Dementia [Webpage]. Retrieved April 5, 2014 from http://www.who.int/mediacentre/factsheets/fs362/en/. A recent estimate suggests that over 500,000 people over aged 75 died of Alzheimer's disease in the United States in 2010. James, B.D., et al. (2014). Contribution of Alzheimer disease to mortality in the United States. *Neurology*, 82(12), 1045-1050.

[14] Centers for Disease Control and Prevention (CDC). Dementia/Alzheimer's Disease [Webpage]. Retrieved April 9, 2014 from http://www.cdc.gov/mentalhealth/basics/mental-illness/dementia.htm.

[15] Moyer, V.A., *supra* note 13.

[16] Leuzy, A., and S. Gauthier. (2012). Ethical issues in Alzheimer's disease: An overview. *Expert Review of Neurotherapeutics*, 12(5), 557-567.

[17] Mapstone, M., et al. (2014). Plasma phospholipids identify antecedent memory impairment in older adults. *Nature Medicine*, doi:10.1038/nm.3466; Leuzy, A., and S. Gauthier, *supra* note 16; Mattsson, N., Brax, D., and H. Zetterberg. (2010). To know or not to know: Ethical issues related to early diagnosis of Alzheimer's disease. *International Journal of Alzheimer's Disease*, 2010, 1-4.

[18] Buchanan, A. (1988). Advance directives and the personal identity problem. *Philosophy & Public Affairs*, 17(4), 277-302; Dresser, R. (1986). Life, death, and incompetent patients: Conceptual infirmities and hidden values in the law. *Arizona Law Review*, 28(373), 373-405; Dresser, R.S. (1989). Advance Directives, Self-determination, and Personal Identity. In C. Hackler, R. Moseley, and D.E. Vawter (Eds.). *Advance Directives in Medicine* (pp. 155-170). New York, NY: Praeger; Dworkin, R. (1994). *Life's Dominion: An Argument About Abortion, Euthanasia, and Individual Freedom*. New York, NY: Vintage Books; Jaworska, A. (1999). Respecting the margins of agency: Alzheimer's patients and the capacity to value. *Philosophy and Public Affairs*, 28(2), 105-138.

[19] Dworkin, R., *supra* note 18, pp. 222-229.

[20] Dresser, R.S. (1989), *supra* note 18; Jaworska, A., *supra* note 18.

[21] Beauchamp, T.L., and J.F. Childress. (2012). *Principles of Biomedical Ethics*, Seventh Edition. Oxford: Oxford University Press.

[22] Dresler, M., et al. (2013). Non-pharmacological cognitive enhancement. *Neuropharmacology*, 64, 529-543.

[23] Butcher, J. (2003). Cognitive enhancement raises ethical concerns: Academics urge pre-emptive debate on neurotechnologies. *Lancet*, 362(9378), 132-133; Greely, H., et al. (2008). Towards responsible use of cognitive-enhancing drugs by the healthy. *Nature*, 456(7223), 702-705.

[24] Greely, H., et al., *supra* note 23.

[25] Daniels, N. (2008). *Just Health: Meeting Health Needs Fairly*. New York, NY: Cambridge University Press, pp. 149-155; Buchanan, A., et al. (2000). *From Chance to Choice: Genetics and Justice*. New York, NY: Cambridge University Press.

[26] Chatterjee, A. (2006). The promise and predicament of cosmetic neurology. *Journal of Medical Ethics*, 32(2), 110-113; Greely, H., et al., *supra* note 23.

[27] Dietz, P., et al. (2013). Randomized response estimates for the 12-month prevalence of cognitive-enhancing drug use in university students. *Pharmacotherapy*, 33(1), 44-50; Wilens, T. (2008). Misuse and diversion of stimulants prescribed for ADHD: A systematic review of the literature. *Journal of the American Academy of Child and Adolescent Psychiatry*, 47(1), 21-31; Teter, C.J., et al. (2006). Illicit use of specific prescription stimulants among college students: Prevalence, motives, and routes of administration. *Pharmacotherapy*, 26(10), 1501-1510; Smith, M.E., and M.J. Farah. (2011). Are prescription stimulants "smart pills"? The epidemiology and cognitive neuroscience of prescription stimulant use by normal healthy individuals. *Psychological Bulletin*, 137(5), 717-741.

[28] Emanuel, R.M., et al. (2013). Cognitive enhancement drug use among future physicians: Findings from a multi-institutional census of medical students. *Journal of General Internal Medicine*, 28(8), 1028-1034.

[29] Ibid, p. 1032.

[30] American College Health Association. (2013). *American College Health Association-National College Health Assessment II: Undergraduate Students-Reference Group Executive Summary Spring 2013*. Hanover, MD: American College Health Association.

[31] McCabe, S.E., et al. (2005). Non-medical use of prescription stimulants among US college students: Prevalence and correlates from a national survey. *Addiction*, 99(1), 96-106, p. 98.

[32] Ibid, pp. 96-106.

[33] Substance Abuse and Mental Health Services Administration, Office of Applied Studies. (2009). *The NSDUH Report: Nonmedical Use of Adderall Among Full-Time College Students*. Retrieved April 17, 2014 from http://www.samhsa.gov/data/2k9/adderall/adderall.pdf.

[34] Chatterjee, A., *supra* note 26.

[35] Collins, K.L., et al. (2010). Deep brain stimulation for movement disorders. *Neurobiology of Disease*, 38(3), 338-345. Although the benefits of using DBS to treat motor symptoms of Parkinson's disease are considerable, research has not clearly shown that DBS alters the long-term progression of non-motor symptoms of Parkinson's disease, including impaired cognition, sleep disturbances, and autonomic dysfunction. See Borgohain, R., et al. (2012). Nonmotor outcomes in Parkinson's disease: Is deep brain stimulation better than dopamine replacement therapy? *Therapeutic Advances in Neurological Disorders*, 5(1), 23-41.

[36] Clausen, J. (2010). Ethical brain stimulation—Neuroethics of deep brain stimulation in research and clinical practice. *European Journal of Neuroscience*, 32(7), 1152-1162.

[37] Johnson, J. (2009). A dark history: Memories of lobotomy in the new era of psychosurgery. *Medicine Studies*, 1(4), 367-378; National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. (1977). *Report and Recommendations: Psychosurgery*. Washington, DC: Department of Health, Education, and Welfare (DHEW).

[38] Feldman, R.P., and J.T. Goodrich. (2001). Psychosurgery: A historical overview. *Neurosurgery*, 48(3), 647-659; Rosenfeld, J.V., and J.H. Lloyd. (1999). Contemporary psychosurgery. *Journal of Clinical Neuroscience*, 6(2), 106-112.

[39] Feldman, R.P., and J.T. Goodrich, *supra* note 38; Rosenfeld, J.V., and J.H. Lloyd, *supra* note 38; Lerner, B.H. (2005). Last-ditch medical therapy—Revisiting lobotomy. *New England Journal of Medicine*, 353(2), 120-121.

[40] Feldman, R.P., and J.T. Goodrich, *supra* note 38; Rosenfeld, J.V., and J.H. Lloyd, *supra* note 38.

[41] Feldman, R.P., and J.T. Goodrich, *supra* note 38; Diefenbach, G.J., et al. (1999). Portrayal of lobotomy in the popular press: 1935-1960. *Journal of the History of Neurosciences*, 8(1), 60-69.

[42] Feldman, R.P., and J.T. Goodrich, *supra* note 38, p. 655.

[43] Lerner, B.H., *supra* note 39.

[44] Rabins, P., et al. (2009). Scientific and ethical issues related to deep brain stimulation for disorders of mood, behavior and thought. *Archives of General Psychiatry*, 66(9), 931-937; Schlaepfer, T.E., George, M.S., and H. Mayberg. (2010*).* WFSBP guidelines on brain stimulation treatments in psychiatry. *The World Journal of Biological Psychiatry*, 11(1), 2-18.

[45] Rabins, P., et al., *supra* note 44.

[46] Ibid; Presidential Commission for the Study of Bioethical Issues. (2013, December). *Anticipate and Communicate: Ethical Management of Incidental and Secondary Findings in the Clinical, Research, and Direct-to-Consumer Contexts*. Washington, DC: PCSBI, pp. 78-79.

[47] Clausen, J., *supra* note 36; Patterson, T. (2014, January 13). My brain implant saved me from depression. *The Huffington Post*. Retrieved April 7, 2014 from http://www.huffingtonpost.com/teerika-patterson/depression_b_4559861.html.

[48] Lin, J.M., et al. (2008). An analysis of the abstracts presented at the annual meetings of the Society for Neuroscience from 2001 to 2006. *PLoS ONE*, 3(4), e2052; Lemm, S., et al., (2010). Introduction to machine learning for brain imaging. *Neuroimage*, 56(2), 387-399; Deisseroth, K., and M.J. Schnitzer. (2013). Engineering approaches to illuminating brain structure and dynamics. *Neuron*, 80(3), 568-577; Amari, S. (2013). Dreaming of mathematical neuroscience for half a century. *Neural Networks*, 37, 48-51; Minati, L., et al. (2013). From brain topography to brain topology: Relevance of graph theory to functional neuroscience. *NeuroReport*, 24(10), 536-543.

[49] Potter, V.R. (1971). *Bioethics: Bridge to the Future*. Englewood Cliffs, NJ: Prentice-Hall, Inc.

[50] Solomon, M.Z., President, The Hastings Center; and Clinical Professor of Anaesthesia, Harvard Medical School. (2013). Transformational Bioethics Learning in Brain Science. Presentation to PCSBI, December 18. Retrieved April 7, 2014 from http://bioethics.gov/node/3238.

[51] Ibid.

[52] Presidential Commission for the Study of Bioethical Issues. (2014). Implementation Strategies for Ethics Integration Roundtable Discussion with Members and Presenters, February 11. Retrieved April 7, 2014 from http://bioethics.gov/node/3379.

[53] Khurana, V., and S. Lindquist. (2010). Modelling neurodegeneration in *Saccharomyces cerevisiae*: Why cook with baker's yeast? *Nature Reviews Neuroscience*, 11(6), 436-449; Steneck, N.H. (2006). Fostering integrity in research: Definitions, current knowledge, and future directions. *Science and Engineering Ethics*, 12(1), 53-74; Kovac, J. (2006). Professional ethics in science. *Boston Studies in the Philosophy of Science*, 242, 157-169.

[54] Douglas, H.E. (2009). *Science, Policy, and the Value-Free Ideal*. Pittsburgh, PA: University of Pittsburgh Press, p. 72.

[55] Harris, J. (2005). Scientific research is a moral duty. *Journal of Medical Ethics,* 31(4), 242-248.

[56] Koepsell, D. (2010). On genies and bottles: Scientists' moral responsibilities and dangerous technology R&D. *Science and Engineering Ethics*, 16(1), 119-133; Douglas, H.E., *supra* note 54, pp. i-210; Kitcher, P. (2001). *Science, Truth, and Democracy*. New York, NY: Oxford University Press, Chapter 10.

[57] Presidential Commission for the Study of Bioethical Issues. (2010, December). *New Directions: The Ethics of Synthetic Biology and Emerging Technologies*. Washington, DC: PCSBI, pp. 24-32.

[58] Lombardo, P.A. (2008). *Three Generations, No Imbeciles: Eugenics, the Supreme Court, and Buck v. Bell*. Baltimore: Johns Hopkins University Press; Kevles, D.J. (1985). *In the Name of Eugenics: Genetics and the Uses of Human Heredity*. New York, NY: Knopf.

[59] E.g., Giordano, J., Chief Neuroethics Studies Program, Center for Clinical Bioethics and Division of Integrative Physiology, Department of Biochemistry, Georgetown University Medical Center. (2014, February 5). Comments submitted to PCSBI (commenting on the importance of educating both professionals and the general public about neuroscience and neurotechnology).

[60] Eisen, A., and R.M. Berry. (2002). The absent professor: Why we don't teach research ethics and what to do about it. *American Journal of Bioethics*, 2(4), 38-49.

[61] Integration of ethics through education at all levels is especially important in light of evidence that suggests that some current models of ethics education at the graduate level are ineffective. Shorr, A.F., Hayes, R.P., and J.F. Finnerty. (1994). The effect of a class in medical ethics on first-year medical students. *Academic Medicine*, 69(12), 998-1000; Antes, A.L., et al. (2010). Evaluating the effects that existing instruction on responsible conduct of research has on ethical decision making. *Academic Medicine*, 85(3), 519-526.

[62] Wolpe, P.R., Director, Center for Ethics, Asa Griggs Candler Professor of Bioethics, Emory University. (2013). Integrating Ethics and Neuroscience through Education. Presentation to PCSBI, December 18. Retrieved April 7, 2014 from http://bioethics.gov/node/3238.

[63] Solomon, M.Z., *supra* note 50.

[64] Ibid.

[65] Solomon, M.Z., *supra* note 50; National Institutes of Health (NIH). (2009). Exploring Bioethics. Retrieved April 4, 2014 from http://science.education.nih.gov/supplements/nih9/bioethics/guide/pdf/teachers_guide.pdf.

[66] The Dana Foundation. (2014). Brain Awareness Week [Webpage]. Retrieved April 4, 2014 from http://www.dana.org/BAW/; The Dana Foundation. (2014). Brain Awareness Week Calendar of Events [Webpage]. Retrieved April 4, 2014 http://www.dana.org/baw/calendar/; Society for Neuroscience. (2014). Brain Awareness Campaign [Webpage]. Retrieved April 4, 2014 from http://www.sfn.org/public-outreach/brain-awareness-week.

[67] Duke Science & Society. (2014). Concentrations [Webpage]. Retrieved April 4, 2014 from http://scienceandsociety.duke.edu/learn/ma/curriculum/concentrations/; Duke Science & Society. (2014). FAQs [Webpage]. Retrieved April 4, 2014 from http://scienceandsociety.duke.edu/learn/ma/curriculum/faqs/.

[68] Center for Neuroscience & Society. (2013). Teaching Resources [Webpage]. Retrieved April 4, 2014 from http://neuroethics.upenn.edu/?page_id=732.

[69] Research Councils UK. (2014). Interdisciplinary Network on Teaching of Ethics for Neuroscientists [Webpage]. Retrieved April 4, 2014 from http://gtr.rcuk.ac.uk/project/8DD27A6D-FAF9-40AF-9411-A3D325990D42; The University of Manchester. (n.d.). Neuroethics Education: Interdisciplinary Network on Teaching of Ethics for Neuroscientists. Retrieved April 4, 2014 from http://www.lab.ls.manchester.ac.uk/neuroethicseducation/.

[70] Underwood, E. (2013, November 28). DARPA wants to fix broken brains, restore lost memories. *Science Insider*, Retrieved April 4, 2014 from http://news.sciencemag.org/brain-behavior/2013/11/darpa-wants-fix-broken-brains-restore-lost-memories.

[71] Casebeer, W.D., Program Manager, Defense Advanced Research Projects Agency (DARPA). (2013). Ethical Issues Associated with the BRAIN Initiative and Ongoing Work in Neuroscience. Presentation to PCSBI, August 20. Retrieved April 4, 2014 from http://bioethics.gov/node/2779.

[72] Ibid.

[73] Funders also could support foundational research in philosophy, theology, history, and social science, among others.

[74] Cook-Deegan, R.M. (1994). *The Gene Wars: Science, Politics, and the Human Genome*. New York, NY: W.W. Norton. Retrieved April 4, 2014 from http://www.genome.duke.edu/press/books/gene-wars/; ELSI Research Planning and Evaluation Group (ERPEG). (2000). *A Review and Analysis of the Ethical, Legal, and Social Implications (ELSI) Research Programs at the National Institutes of Health and the Department of Energy: Final Report of the ELSI Research Planning and Evaluation Group*. Retrieved April 7, 2014 from http://www.genome.gov/10001727.

[75] ERPEG. (2000, February 10). Review and Analysis of the ELSI Research Programs at the National Institutes of Health and the Department of Energy (ERPEG Final Report). Retrieved from http://www.genome.gov/Pages/Research/DER/ELSI/erpeg_report.pdf; National Human Genome Research Institute (NHGRI). (2002). The Role of ELSI Research and Policy Activities in the NHGRI Plan (The Role Report) [Webpage]. Retrieved April 21, 2014 from http://www.genome.gov/10005516; ELSI Research Advisors (ERA). (2005). *ELSI Research Advisors Report to the National Advisory Council for Human Genome Research*. Retrieved April 21, 2014 from http://www.genome.gov/pages/research/der/ELSI/ERA_ELSI_Report_Feb_2005.pdf; Jeungst, E.T. (1996). Self-critical federal science? The ethics experiment within the U.S. Human Genome Project. *Social Philosophy and Policy*, 13(2), 63-95; Yesley, M.S. (2008). What's ELSI got to do with it? Bioethics and the Human Genome Project. *New Genetics and Society*, 27(1), 1-6; Caulfield, T., et al. (2013). Harm, hype, and evidence: ELSI research and policy guidance. *Genome Medicine*, 5(3), 21; Lindee, M.S. (1994). The ELSI hypothesis. *Isis*, 85(2), 293-296.

[76] Cho, M.K., et al. (2008). Research ethics consultation: The Stanford experience. *IRB: Ethics & Human Research*, 30(6), 1-6.

[77] NIH Clinical Center. (2013). NIH Clinical Center: There's No Other Hospital Like It [Webpage]. Retrieved April 7, 2014 from http://clinicalcenter.nih.gov/ccc/crc/index.html.

[78] NIH Clinical Center, Department of Bioethics. (n.d.). Clinical and Research Ethics Services: Consult Service [Webpage]. Retrieved April 7, 2014 from http://www.bioethics.nih.gov/clinical/; NIH Clinical Center. (n.d.). Bioethics Consultation Service at the NIH. Retrieved April 7, 2014 from http://www.bioethics.nih.gov/clinical/brochure.pdf.

[79] Cho, M.K., et al. (2008). Strangers at the benchside: Research ethics consultation. *American Journal of Bioethics*, 8(3), 4-13, p. 4.

[80] Cho, M.K., et al., *supra* note 76, p. 2.

[81] Cho, M.K., et al., *supra* note 76; McCormick, J.B., et al. (2013). The establishment of research ethics consultation services (RECS): An emerging research resource. *Clinical and Translational Science*, 6(1), 40-44.

[82] Cho, M.K., et al. *supra* note 79; Cho, M.K., et al., *supra* note 76.

[83] National Nanotechnology Coordination Office. (2011). *National Nanotechnology Initiative: Environmental, Health, and Safety Research Strategy*, pp. 5-6. October 20. Retrieved April 7, 2014 from http://www.nano.gov/sites/default/files/pub_resource/nni_2011_ehs_research_strategy.pdf.

[84] Ibid; National Nanotechnology Coordination Office. (2011). Key Concepts in the 2011 National Nanotechnology Initiative: Environmental, Health, and Safety Research Strategy. Retrieved April 7, 2014 from http://www.nano.gov/sites/default/files/pub_resource/nni_2011_ehs_research_strategy.pdf.

[85] Schuurbiers, D., and E. Fisher. (2009). Lab-scale intervention. *European Molecular Biology Organization Reports*, 10(5), 424-427, p. 425.

[86] van Gorp, A., and S. van der Molen. (2011). Parallel, embedded or just part of the team: Ethicists cooperating within a European security research project. *Science and Engineering Ethics*, 17(1), 31-43.

[87] Kahn, J. (2011). The two (institutional) cultures: A consideration of structural barriers to interdisciplinarity. *Perspectives in Biology and Medicine*, 54(3), 399-408.

[88] Chatterjee, A., Professor of Neurology, Center for Cognitive Neuroscience and Center for Functional Neuroimaging, University of Pennsylvania School of Medicine. (2013). Roundtable Discussion. Presentation to PCSBI, August 20. Retrieved April 7, 2014 from http://bioethics.gov/node/2781.

[89] ERPEG, *supra* note 74.

[90] ERPEG, *supra* note 74; National Advisory Council for Human Genome Research (NACHGR). (2008). *ELSI Assessment Panel (EAP) Report*. Retrieved April 7, 2014 from http://www.genome.gov/Pages/About/NACHGR/EAPReportFinal.pdf.

[91] These recommendations are summarized in Appendix II: *Summary of Bioethics Commission Recommendations*.

[92] de Melo-Martín, I. (2009). Creating reflective spaces: Interactions between philosophers and biomedical scientists. *Perspectives in Biology and Medicine*, 52(1), 39-47.

[93] NIH, *supra* note 65.

[94] For Inspiration and Recognition of Science and Technology (FIRST). (n.d.). Vision and Mission [Webpage]. Retrieved April 7, 2014 from http://www.usfirst.org/aboutus/vision; Intel Science Talent Search. (n.d.). Intel STS Home [Webpage]. Retrieved April 7, 2014 from https://student.societyforscience.org/intel-sts.

[95] Society for Neuroscience. (n.d.). Mentoring and Career Advice. [Webpage]. Retrieved April 7, 2014 from http://www.sfn.org/mentoring.

[96] Obama, B. (2013, April 2), *supra* note 1.

[97] Previous efforts such as the HGP ELSI program can provide lessons about the importance and role of multidisciplinary science advisory processes. ERPEG, *supra* note 74; NACHGR, *supra* note 90, pp. 7-8. Lessons also might be drawn from institutional review board (IRB) members' experiences working with community members. Sengupta, S., and B. Lo. (2003). The roles and experiences of nonaffiliated and non-scientist members of institutional review boards. *Academic Medicine*, 78(2), 212-218.

APPENDICES

Appendix I: Ethics Integration in Selected International Neuroscience Research Programs

Note: This table was compiled using publicly available English language information. The "Examples of Ethics-related Activities" were selected because they appeared likely to address a range of different ethical, legal, or social issues, and the category of "Program" includes a variety of organizational structures.

NEUROSCIENCE RESEARCH PROGRAM TITLE	NEUROSCIENCE RESEARCH PROGRAM DESCRIPTION	EXAMPLES OF ETHICS-RELATED ACTIVITIES
Multinational		
Collaborative European Neurotrauma Effectiveness Research in Traumatic Brain Injury (CENTER-TBI)[*]	• ***Duration***: 2013-2020 • ***Structure***: Collaboration including Belgium, France, Germany, Italy, the Netherlands, Sweden, the United Kingdom, and the United States, among others • ***Purpose(s)***: Conduct traumatic brain injury (TBI) research including clinical research	• "[E]vidence translation and communication" (e.g., improved evidence-based clinical guidelines for the treatment of TBI) • Policy-related activities (e.g., information dissemination to policymakers) • Data sharing policies and procedures
Human Brain Project (HBP)[†]	• ***Duration***: 2013-2023 • ***Structure***: Collaboration including Argentina, Canada, China, France, Germany, Israel, Japan, the United Kingdom, and the United States, among others • ***Purpose(s)***: Build information and communications technology (ICT) infrastructure for neuroscience, medicine, and computing	• Ethics and Society Programme » Address social, ethical, and philosophical issues » Increase HBP scientists' ethical and social awareness » System of ethical governance
Human Connectome Project (HCP)[‡]	• ***Duration***: 2010-2015 • ***Structure***: Research consortia, investigators in Germany, Italy, the Netherlands, the United Kingdom, and the United States, among others • ***Purpose(s)***: Conduct structural and functional brain connectivity research	• External Advisory Panel ("scientific and technical advice") • Educational and outreach activities for neuroscientists • Data sharing policies and procedures

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[*] Collaborative European Neurotrauma Effectiveness Research in Traumatic Brain Injury (CENTER-TBI). (2013). Aims [Webpage]. Retrieved April 8, 2014 from https://www.center-tbi.eu/project/aims; CENTER-TBI. (2013). Project Timeline [Webpage]. Retrieved April 8, 2014 from https://www.center-tbi.eu/project/timeline; CENTER-TBI. (2013). Project Participants [Webpage]. Retrieved April 8, 2014 from https://www.center-tbi.eu/project/participants; European Commission. (n.d.) CENTER-TBI. Retrieved from http://ec.europa.eu/research/health/medical-research/brain-research/projects/center-tbi_en.html.

[†] Swiss Broadcasting Corporation. (2013). Brain Project Gets Green Light for EU Funding. Retrieved April 8, 2014 from http://www.swissinfo.ch/eng/science_technology/Brain_project_gets_green_light_for_EU_funding.html?cid=34845884; Human Brain Project (HBP). (n.d.). FAQ: Administration [Webpage]. Retrieved April 8, 2014 from https://www.humanbrainproject.eu/faq/administration; HBP. (2013). Appendix 1: Overall Vision for the Human Brain Project. Retrieved April 8, 2014 from https://www.humanbrainproject.eu/documents/10180/17646/Vision+Document/8bb75845-8b1d-41e0-bcb9-d4de69eb6603; HBP. (2013). The Human Brain Project SP12: Ethics and Society [Video file]. Retrieved April 7, 2014 from http://www.youtube.com/watch?v=0hIbt49VQCs; HBP. (2013). Administration. Retrieved April 7, 2014 from https://www.humanbrainproject.eu/faq/administration.

[‡] National Institutes of Health (NIH). (2013). Overview of the Human Connectome Project. Retrieved April 7, 2014 from http://www.humanconnectome.org/about/project/; NIH. (2010). $40 Million awarded to trace human brain's connections. Retrived from http://www.nih.gov/news/health/sep2010/nimh-15.htm; NIH. (2009). The Human Connectome Project (U54) (RFA-MH-10020). Retrieved April 7, 2014 from http://grants.nih.gov/grants/guide/rfa-files/RFA-MH-10-020.html; The NIH Human Connectome Project. (n.d.). Collaborators. Retrieved April 7, 2014 from http://www.humanconnectomeproject.org/about/collaborators/; Van Essen Lab. (2013). Van Essen Lab Wiki Home Page. Retrieved April 7, 2014 from http://brainvis.wustl.edu/wiki/index.php/Main_Page.

NEUROSCIENCE RESEARCH PROGRAM TITLE	NEUROSCIENCE RESEARCH PROGRAM DESCRIPTION	EXAMPLES OF ETHICS-RELATED ACTIVITIES
Consortium of Neuroimagers for the Noninvasive Exploration of Brain Connectivity and Tractography (Brain CONNECT)*	• ***Duration***: 2009-2012 • ***Structure***: Consortium of experts on diffusion magnetic resonance imaging (MRI) from Belgium, Denmark, France, Germany, Israel, Italy, Switzerland, the United Kingdom, and the United States • ***Purpose(s)***: Conduct brain morphology and connectivity research	• External Advisory Board • Planned report on awareness and social implications of research
International Neuroinformatics Coordinating Facility (INCF)†	• ***Duration***: 2005-present (as of 2014) • ***Structure***: Consortium of countries including Australia, India, Republic of Korea, Norway, the United Kingdom, and the United States, among others • ***Purpose(s)***: "Develops and maintains [neuroscience] database and computational infrastructure"	• Educational activities aimed predominantly at research community ("to facilitate the flow of information between researchers in academia and industry") • Data sharing policies and procedures
North American Alzheimer's Disease Neuroimaging Initiative (ADNI)‡	• ***Duration***: 2004-2017 • ***Structure***: Research centers in the United States and Canada • ***Purpose(s)***: Conduct early detection and biomarker research, support use of new diagnostics for early detection, strengthen data sharing model	• Data sharing policies and procedures • "ADNI Governance" (ensures compliance with study protocol)

[*] European Union Seventh Framework Programme. (n.d.) The Connect Consortium. Retrieved April 7, 2014 from http://cordis.europa.eu/fp7/home_en.html; European Union Seventh Framework Programme. (n.d.). Our Mission [Webpage]. Retrieved April 8, 2014 from http://www.brain-connect.eu/mission.htm; European Union Seventh Framework Programme. (n.d.). News [Webpage]. Retrieved April 7, 2014 from http://www.brain-connect.eu/news.htm; European Union Seventh Framework Programme. (n.d.). MRI and Structural Connectivity. Retrieved April 7, 2014 from http://www.brain-connect.eu/intro.htm.

[†] Belgian Federal Science Policy Office (BELSPO). (n.d.). Research Infrastructure. Retrieved April 7, 2014 from https://www.belspo.be/belspo/coordination/euCoor_Infra_en.stm#INCF; International Neuroinformatics Coordinating Facility (INCF). (2012). Who We Are [Webpage]. Retrieved April 7, 2014 from http://www.incf.org/about; INCF. (2012). Our Mission [Webpage]. Retrieved April 7, 2014 from http://www.incf.org/about/what-we-do/our-mission; INCF. (2012). INCF National Nodes [Webpage]. Retrieved April 7, 2014 from http://www.incf.org/about/who-we-are/nodes; INCF. (2012). Who We Are [Webpage]. Retrieved April 7, 2014 from http://www.incf.org/about/who-we-are; INCF. (2012). Who Funds Us? [Webpage]. Retrieved April 7, 2014 from http://www.incf.org/about/support-incf/who-funds-us; INCF. (2009). Swedish Foundation for Strategic Research (SSF) Continues INCF Funding. Retrieved April 7, 2014 from http://www.incf.org/newsroom/press-material/news/aggregator/archive/?index=effective&portal_types:list=News%20Item&archive_year:int=2009.

[‡] Alzheimer's Disease Neuroimaging Initiative (ADNI). (2013). ADNI Overview [Webpage]. Retrieved April 7, 2014 from http://www.adni-info.org/Scientists/ADNIOverview.aspx; Alzheimer's Disease Cooperative Study. (n.d.). ADNI 2 Study [Webpage]. Retrieved April 8, 2014 from http://adcs.org/studies/ImagineADNI2.aspx; Alzheimer's Association: Research Center. (n.d.). World Wide Alzheimer's Disease Neuroimaging Initiative [Webpage]. Retrieved April 8, 2014 from http://www.alz.org/research/funding/partnerships/WW-ADNI_overview.asp. There are numerous regional and country-based ADNIs. See, for example, Europe (http://www.alz.org/research/funding/partnerships/ww-adni_europe.asp); Argentina (http://www.alz.org/research/funding/partnerships/ww-adni_argentina.asp); and Japan (http://www.j-adni.org/etop.html).

NEUROSCIENCE RESEARCH PROGRAM TITLE	NEUROSCIENCE RESEARCH PROGRAM DESCRIPTION	EXAMPLES OF ETHICS-RELATED ACTIVITIES
European Brain Council (EBC)*	• ***Duration***: 2002-present (as of 2014) • ***Structure***: Council includes European neurology, neurosurgery, psychiatry, and neuroscience organizations; patient organizations; and pharmaceutical and biotechnology companies • ***Purpose(s)***: Conduct research on diagnostics and treatments; advocate for increased investment for brain disease research, education, and care; train researchers	• Activities to promote societal dialogue on "neuro-enhancement" (Neuro-Enhancement: Responsible Research and Innovation (NERRI)) • Policy related activities (e.g., information provision to European Commission)
Country-specific (Non-U.S.)		
Norwegian Brain Initiative: A Large-scale Infrastructure for 21st century Neuroscience (NORBRAIN)†	• ***Duration***: 2012-present (as of 2014) • ***Structure***: Norwegian universities • ***Purpose(s)***: Strengthen Norwegian neuroscience research infrastructure	• Educational activities (e.g., researcher education)
Brain Canada‡	• ***Duration***: 2010-present (as of 2014) (successor to the Neuroscience Canada Foundation, est. 1998) • ***Structure***: Board of Directors, Science Advisory Council, and International Science Advisory Council • ***Purpose(s)***: Facilitate research on brain disorders in Canada	• Board of Directors Committees (e.g., "Nominating and Ethics" and "Public Policy and Communications" committees) • Public education about brain disorders in Canada

[*] European Brain Council (EBC). (n.d.). About Us [Webpage]. Retrieved April 7, 2014 from http://www.europeanbraincouncil.org/about-us/; EBC. (n.d.). Aims [Webpage]. Retrieved April 7, 2014 from http://www.europeanbraincouncil.org/about-us/aims.asp; EBC. (2006). EBC Funding [Webpage]. Retrieved April 7, 2014 from http://europeanbraincouncil.org/pdfs/Publications_/EBC%20Funding%20Statement.pdf; EBC. (n.d.). Year of the Brain in Europe-2014. Retrieved April 7, 2014 from http://www.europeanbraincouncil.org/projects/eyob/indeX.asp.

[†] Norges forskningsråd. (n.d.). Infrastructure for solving challenges in neuroscience [Webpage]. Retrieved April 7, 2014 from http://www.forskningsradet.no/prognett-infrastruktur/Artikkel/Infrastructure_for_solving_challenges_in_neuroscience/1253962036478.

[‡] Brain Canada. (n.d.). Our Mission [Webpage]. Retrieved April 7, 2014 from http://braincanada.ca/en/Our_mission; Brain Canada. (n.d.). Our History [Webpage]. Retrieved April 7, 2014 from http://braincanada.ca/en/Our_history; Brain Canada. (n.d.). Brain Facts [Webpage]. Retrieved April 7, 2014 from http://braincanada.ca/files/NeuroScience_Canada_Brain_Facts.pdf; Brain Canada. (2011). Annual Report. Retrieved April 7, 2014 from http://braincanada.ca/files/brainCanadaAnnualReport2011_en.pdf; Brain Canada. (2009). Annual Report 2009. Retrieved April 7, 2014 from http://braincanada.ca/files/2009AnnualReport.pdf.

Appendix II: Summary of Bioethics Commission Recommendations

This first report by the Presidential Commission for the Study of Bioethical Issues (Bioethics Commission), as part of the Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative, emphasizes the importance of integrating ethics into neuroscience research from the earliest planning phases. In a second report, the Bioethics Commission will consider the ethical and societal implications of neuroscience research and its applications more broadly—ethical implications that a strongly integrated research and ethics infrastructure will be well equipped to address, and that myriad stakeholders, including scientists, ethicists, educators, public and private funders, advocacy organizations, and the public must be prepared to handle. In this report, the Bioethics Commission concludes that ethics and neuroscience research should be integrated throughout the research endeavor and offers four recommendations to facilitate the successful integration of ethics and neuroscience research.

* * *

Ethics integration should aid scientists in recognizing and addressing ethical issues as they arise, and ethicists in understanding the science and technology with which they engage. Although ethics is already integrated into science in various ways—as it is in many human activities—more explicit and systematic integration serves to elucidate implicit ethical judgments and allows their merits to be assessed thoughtfully.

Recommendation 1:
Integrate Ethics Early and Explicitly Throughout Research

Institutions and individuals engaged in neuroscience research should integrate ethics across the life of a research endeavor, identifying the key ethical questions associated with their research and taking immediate steps to make explicit their systems for addressing those questions. Sufficient resources should be dedicated to support ethics integration.

* * *

Once implemented, systems for integrating ethics and neuroscience research should not operate in a vacuum. Institutions and individuals engaged in neuroscience research should learn from collective experience to improve existing systems and inform others about what works and what does not.

Recommendation 2:
Evaluate Existing and Innovative Approaches to Ethics Integration

Government agencies and other research funders should initiate and support research that evaluates existing as well as innovative approaches to ethics integration. Institutions and individuals engaged in neuroscience research should take into account the best available evidence for what works when implementing, modifying, or improving systems for ethics integration.

❧

One foundational approach to integration is pairing science and ethics education at all levels of education. Early ethics education in academic settings is critical to prepare future scientists to integrate ethical considerations into their work—including future research in neuroscience. Professional development for experienced investigators is equally important and can serve multiple ends, contributing not only to their individual knowledge, but to the knowledge of the students and young scientists that they mentor as well.

Recommendation 3:
Integrate Ethics and Science through Education at All Levels

Government agencies and other research funders should initiate and support research that develops innovative models and evaluates existing and new models for integrating ethics and science through education at all levels.

❧

It has been just over a year since the announcement of the BRAIN Initiative, and institutions participating in this research effort have an important opportunity to integrate ethics and science from the outset. A key component of this integration is the inclusion of ethicists or scientists with experience in ethics in BRAIN Initiative-related scientific advisory boards and funding review committees, particularly for the major public and private sector partners.

Recommendation 4:
Explicitly Include Ethical Perspectives on Advisory and Review Bodies

BRAIN Initiative-related scientific advisory and funding review bodies should include substantive participation by persons with relevant expertise in the ethical and societal implications of the neuroscience research under consideration.

Appendix III: Guest Presenters to the Bioethics Commission Regarding Ethics and Neuroscience

William D. Casebeer, Ph.D. (U.S.A.F., Retired)
Program Manager, Defense Advanced Research Projects Agency

Timothy Caulfield, LL.M., F.R.S.C., F.C.A.H.S.
Canada Research Chair in Health Law and Policy; Professor in the Faculty of Law and the School of Public Health, University of Alberta

David Chalmers, Ph.D.
Professor of Philosophy and Co-director of the Center for Mind, Brain, and Consciousness, New York University; Distinguished Professor of Philosophy and Director of the Centre for Consciousness, Australian National University

Anjan Chatterjee, M.D., F.A.A.N.
Professor of Neurology, Center for Cognitive Neuroscience and Center for Functional Neuroimaging, University of Pennsylvania School of Medicine

Mildred Cho, Ph.D.
Associate Director; Professor of Pediatrics, Stanford Center for Biomedical Ethics, Stanford University

Miyoung Chun, Ph.D.
Executive Vice President of Science Programs, The Kavli Foundation

Martha Farah, Ph.D.
Walter H. Annenberg Professor in Natural Sciences; Professor of Psychology; Director, Center for Cognitive Neuroscience; Director, Center for Neuroscience and Society;
Senior Fellow, Center for Bioethics
University of Pennsylvania

Erik Fisher, Ph.D.
Associate Director for Integration, Center for Nanotechnology in Society; Assistant Professor, School of Politics and Global Studies and the Consortium for Science, Policy and Outcomes, Arizona State University

Hank Greely, J.D.
Deane F. and Kate Edelman Johnson Professor of Law, Stanford Law School; Professor (by courtesy) of Genetics, Stanford Medical School; Chair, Steering Committee of the Center for Biomedical Ethics; Director, Center for Law and the Biosciences; Director, Stanford Interdisciplinary Group on Neuroscience and Society and its Program in Neuroethics, Stanford Law School

Barbara Herr Harthorn, Ph.D.
Director, NSF Center for Nanotechnology in Society; Professor, Department of Anthropology, University of California, Santa Barbara

Steven E. Hyman, M.D.
Founding President, International Neuroethics Society; Director, Stanley Center for Psychiatric Research, Broad Institute of Massachusetts Institute of Technology and Harvard University

Judy Illes, Ph.D.
Professor of Neurology;
Canada Research Chair in Neuroethics;
Director, National Core for Neuroethics;
Faculty, Brain Research Centre,
University of British Columbia

Deborah G. Johnson, Ph.D., M.Phil., M.A.
Anne Shirley Carter Olsson Professor of Applied Ethics, Science, Technology, and Society Program, Department of Engineering and Society, School of Engineering and Applied Science, University of Virginia

Christof Koch, Ph.D.
Chief Scientific Officer,
Allen Institute for Brain Science

Walter J. Koroshetz, M.D.
Deputy Director, National Institute of Neurological Disorders and Stroke, National Institutes of Health

Pat Levitt, Ph.D.
Chair-Elect, Neuroscience Section, American Association for the Advancement of Science; Provost Professor, Department of Pediatrics; W.M. Keck Chair in Neurogenetics, Keck School of Medicine, University of Southern California; Director, Program in Developmental Neurogenetics, Institute for the Developing Mind, Children's Hospital Los Angeles

Bernard Lo, M.D.
Professor of Medicine;
Director, Program in Medical Ethics,
University of California, San Francisco

Peggy Mason, Ph.D.
Chair, Ethics Committee, Society for Neuroscience; Professor, Department of Neurobiology, University of Chicago

Jonathan Montgomery, LL.M.
Chair, Nuffield Council on Bioethics;
Professor of Health Care Law,
University College London

Stephen Morse, J.D., Ph.D.
Ferdinand Wakeman Hubbell Professor of Law; Professor of Psychology and Law in Psychiatry, University of Pennsylvania Law School and School of Medicine

Thomas H. Murray, Ph.D.
President Emeritus, The Hastings Center

Ushma Neill, Ph.D.
Director, Office of the President,
Memorial Sloan-Kettering Cancer Center;
Editor at Large, Journal of Clinical Investigation

John Perry, Ph.D.
Emeritus Professor of Philosophy,
Stanford University; Distinguished Professor of Philosophy,
University of California, Riverside

Eric Racine, Ph.D.
Director, Neuroethics Research Unit; Associate Research Professor, Institut de Recherches Cliniques de Montréal; Associate Research Professor, Department of Medicine, Université de Montréal; Adjunct Professor, Department of Medicine and Department of Neurology and Neurosurgery, McGill University

Nikolas Rose, Ph.D.
Member, Human Brain Project Social and Ethical Division Steering Committee; Professor of Sociology and Head of Department of Social Science, Health and Medicine, King's College London

Bruce R. Rosen, M.D., Ph.D.
Professor of Radiology, Harvard Medical School; Director, Athinoula A. Martinos Center for Biomedical Imaging, Department of Radiology, Massachusetts General Hospital

Adina Roskies, Ph.D.
Associate Professor, Department of Philosophy, Dartmouth College

Pamela Sankar, Ph.D.
Associate Professor, Department of Medical Ethics and Health Policy; Senior Fellow, Leonard Davis Institute of Health Economics, University of Pennsylvania

Marya Schechtman, Ph.D.
Professor of Philosophy,
University of Illinois at Chicago

Terrence J. Sejnowski, Ph.D.
Francis Crick Chair; Professor and Laboratory Head, Computational Neurobiology Laboratory, Salk Institute for Biological Studies; Investigator, Howard Hughes Medical Institute; Distinguished Professor, Section of Neurobiology/Neurosciences,
University of California, San Diego

Stefano Semplici, Ph.D.
Chairperson, International Bioethics Committee, United Nations Educational, Scientific, and Cultural Organization; Professor of Social Ethics,
University of Rome Tor Vergata

Mildred Z. Solomon, Ed.D.
President and CEO, The Hastings Center; Clinical Professor of Anaesthesia,
Harvard Medical School

Nicholas Steneck, Ph.D.
Director, Research Ethics and Integrity Program, Michigan Institute for Clinical and Health Research; Professor Emeritus of History, University of Michigan

Anthony Wagner, Ph.D.
Professor of Psychology and Neuroscience, Stanford University

Stephen J.A. Ward, Ph.D.
Professor; Director, George S. Turnbull Center, School of Journalism and Communication, University of Oregon-Portland

John C. Wingfield, Ph.D.
Assistant Director for the Directorate for Biological Sciences, National Science Foundation

Paul Root Wolpe, Ph.D.
Director, Center for Ethics; Asa Griggs Candler Professor of Bioethics, Emory University

David E. Wright, Ph.D.
Director, Office of Research Integrity, U.S. Department of Health and Human Services

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