CellPress

Neuron
NeuroView

The Human Brain Project: Responsible Brain Research for the Benefit of Society

Arleen Salles,[1,2,*] Jan G. Bjaalie,[3] Kathinka Evers,[1] Michele Farisco,[1,4] B. Tyr Fothergill,[5] Manuel Guerrero,[1,6,7] Hannah Maslen,[8] Jeffrey Muller,[9] Tony Prescott,[10] Bernd C. Stahl,[5] Henrik Walter,[11] Karl Zilles,[12] and Katrin Amunts[12,13,*]

[1]Centre for Research Ethics and Bioethics, Uppsala University, Uppsala, Sweden
[2]Centro de Investigaciones Filosóficas (CIF), Buenos Aires, Argentina
[3]Institute of Basic Medical Sciences, University of Oslo, Oslo, Norway
[4]Science and Society Unit, Biogem, Biology and Molecular Genetics Institute, Via Camporeale, Ariano Irpino (AV), Italy
[5]Centre for Computing and Social Responsibility, De Montfort University, Leicester, UK
[6]Division of Neurogeriatrics, Department of Neurobiology, Care Sciences and Society (NVS), Karolinska Institutet, Sweden
[7]Department of Bioethics and Medical Humanities, University of Chile, Chile
[8]The Oxford Uehiro Centre for Practical Ethics, University of Oxford, Oxford, UK
[9]Human Brain Project, École Polytechnique Fédérale de Lausanne (EPFL), Campus Biotech, Batiment B1, Chemin des Mines 9, CH-1202 Geneva, Switzerland
[10]Department of Computer Science and Sheffield Robotics, The University of Sheffield, Sheffield, UK
[11]Division of Mind and Brain Research, Department of Psychiatry and Psychotherapy CCM, Charité - Universitätsmedizin Berlin, corporate member of Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health, Berlin, Germany
[12]Institute for Neuroscience and Medicine, INM-1, Structural and Functional Organisation of the Brain, Forschungszentrum Juelich, GmbH D, 52425 Juelich, Germany
[13]Cecile und Oskar Vogt Institute for Brain Research, Heinrich Heine University Duesseldorf, University Hospital Duesseldorf, Germany
*Correspondence: arleen.salles@crb.uu.se (A.S.), k.amunts@fz-juelich.de (K.A.)
https://doi.org/10.1016/j.neuron.2019.01.005

Recognizing that its research may raise various ethical, social, and philosophical issues, the HBP has made the identification, examination, and management of those issues a top priority. The Ethics and Society subproject is part of the core research project.

Background

The Human Brain Project (HBP) is one of two European flagship projects with a 10-year horizon. It aims to contribute to an integrated understanding of the human brain by providing a European brain research infrastructure that is intended for both neuroscience and neuro-inspired research as well as intense data sharing and collaboration on one of the most demanding scientific challenges of the 21st century. The human brain is an exceptional organ—it is the basis of our cognition, emotion, ability to act, language, memory, consciousness, and self-consciousness. Furthermore, due to its complexity, knowledge of the brain requires an integrative, multimodal, and multiscale approach—from signal molecules and genes, neuronal and glial cells, and microcircuits up to large networks with numerous, interconnected brain regions. The fact that approximately 86 billion nerve cells, each with approximately 10,000 synapses, interact in a dynamic manner with each other illustrates the challenge that the project faces.

The analysis of the human brain will provide new insights into the uniqueness of each human being and into the common biological basis of humankind embedded into the evolution of our species. Such knowledge has important practical applications, for example, the development of novel diagnostic and therapeutic tools and even the prevention of brain diseases.

The human brain and human behavior have developed during evolution by mutation, selection, and adaptive introgression, and they change structurally and functionally at each of the different developmental stages—from the embryonic and fetal periods through childhood, adulthood, and old age by progressive and regressive processes. The brain has reacted and will react to constantly changing physical, social, and cultural conditions by "cultural recycling" (Dehaene and Cohen 2007), "synaptic epigenesis" (Changeux, 2017) and "bio-cultural feedback" (D'Ambrosio and Colagè, 2017). All these conditions and biological mechanisms enable us to adapt to changing environments in a globalized world and highlight the "history of the brain."

Facing the extraordinary complexity of the human brain and the various perspectives ranging from basic, natural science to ethical and philosophical questions, the HBP has set up a roadmap to combine empirical and theoretical neuroscience with brain-inspired development in computing, data science, and robotics. Simulation is considered a central strategy to test models which are constrained by experimental data and to predict features that could then be tested again in the lab. Simulation alone, however, is not capable of decoding human brain complexity, since the models and the outcomes of simulation have to be constrained, sometimes going beyond wet lab research. Therefore, the HBP supplements simulation with big-data analysis, relying on sophisticated workflows and tools of analysis including deep and machine learning methods as well as statistical tools, image analysis, and processing. This requires considerable computing resources, sometimes exceeding those available in the fastest supercomputers. Data safety and security become increasingly important when large amounts of data from healthy subjects and patients are processed. To provide and share data, to combine data from different sources, and to avoid acquiring the same data because of missing information are

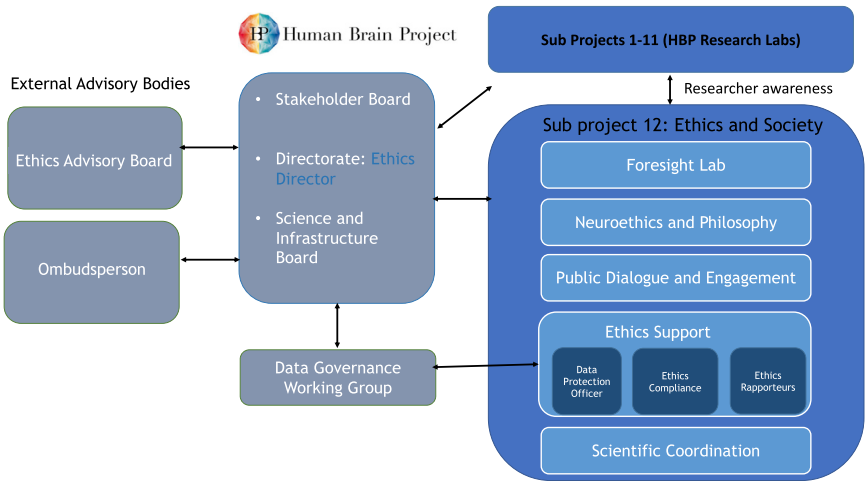

Figure 1. HBP Ethics Structures and Roles

challenges that require a dedicated infrastructure such as the HBP Joint Platform.

Ethics Structures and Roles in the HBP

The significance given to neuroethics within the HBP responds to two factors. First, from the start, the HBP has recognized that its research may raise various ethical, social, and philosophical issues. Thus, identifying, examining, and addressing them has always been a top priority. Second, the project is funded by the European Commission in the framework of the EU's Horizon2020 program, which actively promotes responsible research and innovation (RRI). RRI is generally understood as an interactive process that engages multiple stakeholders who must be mutually and jointly responsive and work toward the ethical permissibility of both research and its products. RRI calls for aligning science and technology with societal needs and for addressing the legal, ethical, and social dimensions of research and innovation by focusing not just on outcomes, but also on the examination of the values that inform the trajectory of the scientific work and that feed into the research agenda itself.

The HBP's Ethics and Society Subproject is tasked with carrying out ethical, social, and philosophical analyses and with developing, broadening, and enhancing RRI into all HBP research (https://www.humanbrainproject.eu/en/social-ethical-reflective/). The Ethics and Society Subproject is not external to the HBP but embedded in it: it is part of the core research project itself, funded with approximately 4.5% of the overall budget. It is structured around a number of interrelated activities; these range from early identification of the ethical, social, and philosophical concerns raised both by potential HBP research developments and their implications to engagement with public and private stakeholders in an attempt to strengthen public dialogue and empower those likely to be affected by HBP research via organization of citizens meetings and stakeholder dialogs (Figure 1) (http://www.tekno.dk/project/human-brain-project/?lang=en). Ethics Support carries out applied ethics research (for example, research ethics) and—together with the external Ethics Advisory Board, the Ethics Rapporteur Programme, and the Point of Registration (PORE) for ethics, regulatory and social concerns—provides the tools to ensure that the issues raised by HBP research subprojects are transparently communicated and managed and that HBP researchers comply with ethical codes and legal statutes. Lastly, the Ethics and Society Subproject includes an area devoted specifically to neuroethical and philosophical reflection and research. Within the HBP, neuroethical reflection is also intended to open up a different, productive space for carrying out theoretical analysis and to offer distinctive and possibly complementary approaches to the issues investigated by empirical science, examining key neuroscientific and philosophical notions (e.g., consciousness, or human versus artificial intelligence), thereby also contributing to the understanding of HBP research itself. The underlying idea is that, in addition to normative issues, other concerns such as the role of neuroscientific research in assessing fundamental topics (e.g., what makes us human) need to be addressed. In this respect, conceptual analysis of key scientific notions and a focus on the epistemic and ontological aspects (beliefs about knowledge and reality) embedded in the research process (e.g., in the framing of scientific questions) facilitate a more integrated picture of, and a more informed link between, neuroscientific findings and philosophical notions and questions (Salles et al., 2018).

Data Protection and Privacy

HBP's IT-based strategy to integrate neuroscientific data from around the world requires not only compliance with the relevant data protection legislation but also the design and development of mechanisms and infrastructure to manage the issues raised by each phase of data collection, storage, access, curation, retention, destruction, security, processing, and analysis. The challenges posed are partly due to a massive increase in the volume, modality, and dimensionality of data generated by novel neuroscientific instruments for imaging and activity recordings and by increased reliance on novel technical and analytical approaches to exploiting neuroscience data. In addition, data about the brain raise particularly strong concerns in many people.

The Data Protection and Privacy Opinion has shaped the project-wide approach to data governance (https://sos-ch-dk-2.exo.io/public-website-production/filer_public/42/e2/42e28dca-6d5d-4513-9771-88ab71fc3ce1/data_protection.pdf). The Opinion draws on the expertise of the researchers in the social sciences and the humanities involved in the HBP ethics and society work, including members of the Ethics Advisory Board (EAB), the Ethics Rapporteurs, and members of the Foresight Lab, the Neuroethics and Philosophy Group, Public Engagement, and Ethics Support in the Ethics and Society Subproject. This document identifies some of the main privacy-related concerns within

HBP, undertakes a conceptual and neuroethical analysis of some of the more contested notions—e.g., brain privacy—articulates the basic ethical principles that should guide examination of the issues, presents a brief overview of the public's view of privacy and the HBP, and provides a review of the history of data protection and regulation in Europe. Finally, it offers recommendations intended to minimize potential risks while securing the public benefit anticipated from HBP research.

In order to facilitate the development and implementation of responsible data governance in the HBP, interconnected structures and roles have been created. They respond to the challenges of innovative neuro-ICT research in an international, collaborative context while contributing to the open science agenda and supporting data protection (Stahl et al., 2018). The Data Protection Officer supports Data Protection Impact Assessments; for supporting legislative compliance, the Compliance Manager ensures project-wide compliance with the relevant European (Horizon 2020) ethics requirements; and internal data type experts evaluate and ensure that aspects of study documentation align with the requisite legal frameworks. Lastly, the Data Governance Working Group develops project-specific data policy, processes, and workflows and supports the development of an infrastructure for each step of the data life cycle.

In addressing the relevant concerns pragmatically, the HBP categorizes data to identify and clarify the ethical issues raised. Specific ethics review processes and controls have been developed for each type: human research data, human clinical data, non-human animal data, and model data. This is necessary both to prevent potential harm caused by the data generated, analyzed, or shared and to clearly define the conditions that apply to the use of the data.

The considerations above are balanced against the societal benefits of open science, including the need for increased credibility of published scientific literature and accelerated discovery, which requires extensive data sharing. While incentives for data sharing are not well established in neuroscience communities, the HBP's perspective is that implementing systems for data citation and contribution tracking will encourage researchers not only to publish reports but also to share data, improve study reproducibility, and increase transparency. To apply the key FAIR principles (findable, accessible, interoperable, and re-usable [https://www.go-fair.org/], the HBP developed and operates the HBP Knowledge Graph (KG), which stores curated metadata for all HBP published data. But while FAIR is generally positive, there are cases where its application must be limited to fulfil ethical and legal imperatives (e.g., anonymization of personal data). Secure analytics systems to query federated databases of human clinical and research data without access to personal information (e.g., as conceptualized for the HBP Medical Informatics Platform) are designed in part to address some privacy and data protection concerns.

In summary, the HBP attempts to manage data governance responsibly through collaborative project-wide policy development and the cultivation of key roles, groups, and dialogues at multiple project levels, reflecting the interests of stakeholders while supporting open science. Considering that the different brain initiatives have recognized the importance of data stewardship and data protection (for example, the Canberra Declaration; https://brainalliance.org.au/learn/media-releases/worlds-brain-initiatives-move-forward-together/), we expect to foster and support intensive international collaboration centering on the identification of high-priority data related issues and the development of infrastructure and the appropriate policies.

Neuroethical Themes in the HBP

In a recently published article, a group of neuroscientists, neuroethicists, and policy makers identify five key neuroethics questions and additional subquestions that can be usefully addressed across all national-level brain initiatives (Rommelfanger et al., 2018). The article is the result of the first meeting of the Global Neuroethics Summit last year in South Korea; the goal of the questions is to promote a culturally aware discussion of some of the main issues (ethical and conceptual) raised by research in the different brain projects.

There are several topics in the HBP research agenda that engage those questions. One of them (NEQN 2: what are the ethical standards of biological material and data collection, and how do local standards compare with those of global collaborators?), was discussed above. But additional fields of inquiry within the HBP are relevant to addressing the other questions identified in the article as well, particularly those about the moral significance of engineered neural circuitry; about the potential of brain interventions to affect autonomy; about the potential impact of a biological model or neuroscientific account of disease on individuals, communities, and societies; and about possible uses and misuses of neuroscience. These are outlined below.

NEQN 3: What Is the Moral Significance of Neural Systems That Are under Development in the Neuroscience Research Lab?

Consciousness Studies in the HBP

Studies on consciousness are central within the HBP efforts to describe and understand the human brain and to further enhance our knowledge of human beings. They are also central to addressing questions about moral significance (of humans, animals, and even potentially machines). Empirical, theoretical, clinical, and conceptual research is carried out by different HBP research groups, from systems and cognitive neuroscience and theoretical neuroscience to neuroethics and philosophy.

New ways to measure consciousness levels, presently being tested by empirical neuroscientists, are potentially very helpful in clinical contexts: for example, in the diagnosis and treatment of patients with disorders of consciousness such as unresponsive wakefulness syndrome and minimally conscious state. Such research might also impact how some psychiatric disorders are understood.

In collaboration with empirical scientists, philosophers from the HBP are developing a new conceptual model, i.e., intrinsic consciousness theory (Farisco et al., 2017), and investigating its clinical and ethical implications, specifically with respect to people unable to communicate verbally like infants and people with disorders of consciousness (Evers 2016). Moreover, attention is given to the impact of computer science on consciousness. The question of whether artificial systems have the potential to develop consciousness and how

this could be determined, as well as the relevance that consciousness might have for (natural or artificial) "intelligence" (topics we address next), attracts a broad audience.

On the Moral Significance of Engineered Neural Circuitry

The HBP neurorobotics platform connects spiking neural networks to virtual and real robots. It links brain research to information technology by using research data and models of cognition and behavior. While some basic types of behavior (i.e., visual-motor control) are understood in reasonable detail and their transfer to neurorobotics is increasingly within reach, the biological basis of others, including complex patterns of behavior, consciousness, and sentience is less clear. The neuroscientific notion of sentience, key for understanding the moral significance of engineered neural circuitry, is difficult to define and measure given its primarily experiential, first-person nature (the "other minds" problem). The HBP is progressing research to understand it, including the possibility of "islands of consciousness" in damaged brains (Storm et al., 2017). These islands are important with respect to sentience because they might suggest the possibility of creating consciousness, or some form of sentience, in AI or robots that embody only a partial or simplified model of the brain (Prescott 2017).

One long-standing issue is the distinction between simulation and emulation, and the question of whether and under what circumstances simulated minds could have experiential properties. Another is biocentrism, the view that all living things have inherent value by virtue of their biological nature. While biocentrism brings a greater range of organisms into the scope of moral consideration, as a result of the sufficiency of "biology" for moral value, any evidence that leads us to ascribe sentience to machines would present a challenge to the assumption that only living systems are subjects of moral consideration.

If a machine instantiated the properties sufficient for some degree of moral status, how we treat it would matter (i.e., it could be harmed and/or wronged) even if we were unable to know that it instantiated those properties. So, how should we proceed given epistemic uncertainty regarding machine sentience, sapience, or self-awareness? At what point of machine complexity would it be better to err on the side of assuming that the machine has some degree of moral status? And what degree of moral status should be presumptively ascribed to a machine under such circumstances?

NeQN 4: How Could Brain Interventions Impact or Reduce Autonomy?

Potential Impact of Brain Interventions and Manipulation on Autonomy and on What Makes Us Human

An explicit goal of the Human Brain Project is to further our understanding of what "makes us human." Additional expected consequences of brain research are the development and applications of neurotechnology to alleviate symptoms or enhance the human brain. But those neurointerventions may also change our cognitive and emotional faculties, eventually impact our freedom and autonomy, and even change our views of what human beings are. Within neuroethics, there is a lively debate on how manipulating the brain can affect and maybe threaten human autonomy and identity. In practice, expressions of fear regarding the potentially autonomy-reducing or dehumanizing aspect of brain machine interfaces, robotics, or even deep brain stimulation procedures can, at least partially, be explained by the prevalence of different, often muddled conceptions. Thus, the plausibility of the discussion itself about neuroscience's and neuro-technologies' potential impact on human agency in particular and on what makes us human in general rests on notions such as "agency," "humanity," and "identity" that require a careful conceptual examination. Taking recent neuroscientific research on cultural imprinting on brain architecture as a starting point (Changeux, 2017), philosophers in the HBP are revisiting the main questions and conceptually analyzing the relevant philosophical and scientific notions.

NeQN 5: In Which Contexts Might a Neuroscientific Technology or Innovation Be Used or Deployed?

Uses and Misuses of Neuroscience and Neurotechnology

While much HBP neuroscientific research is directed toward medical use, it can also be used for additional civilian and military applications. Dual use, a term used to address this possibility, raises conceptual, ethical, societal, and regulatory concerns. To address them, the Ethics and Society subproject has written the Opinion on Responsible Dual Use. The Opinion (https://sos-ch-dk-2.exo.io/public-website-production/filer_public/24/0e/240e2eaa-8a10-4a17-87bc-b056a3f0cc8c/opinion_on_data_protection_and_privacy_done_01.pdf) is intended to clarify operative terms (emphasizing the importance of focusing on possible domains, types, and developments of brain research that could be used for political, military, and/or warfare purposes of concern), address emerging neuroscientific research that could have dual-use capabilities, identify the ethical issues raised, examine ethical approaches employed to assess and guide dual-use brain science, and analyze international frameworks for regulating and governing both research and use of weaponizable brain science. It also develops recommendations regarding engagement, scope, and conduct of dual-use brain science that are both directly applicable to the HBP and that may serve as a basis for wider application and use within the international neuroscientific and regulatory policy communities.

In particular, the Opinion proposes that the identification of which uses are of concern be based on the applications of the principles of responsible research and innovation that allow for a distinction between responsible and irresponsible research and technological development.

Conclusion

Recognizing the important implications of HBP research, the project has given ethical, social, and philosophical reflection a key role. From its beginning, the HBP has introduced a set of structures and mechanisms intended to make sure that neuroscience, neuro-medicine, and neuro-inspired technology are carried out in a responsible way for the benefit of individuals as well as societies. For this goal to be achieved, we need a dynamic and interdisciplinary collaboration. Many of the research disciplines involved (e.g., computing, big-data analytics, simulation,

and AI) develop rapidly and pose novel challenges. We must make sure that our theoretical concepts —whether scientific, ethical, or philosophical—are informed by the rapid progress of technology and are relevant to understanding and managing its actual and potential directions. With such conceptual tools, we can proceed to identify and safeguard potential benefits as well as foresee and manage potential risks and provide a platform for societal dialogue in this field, addressing people's concerns and expectations.

ACKNOWLEDGMENTS

This research has received funding from the European Union's Horizon 2020 Framework Programme for Research and Innovation under the specific grant agreement 785907 (Human Brain Project SGA2). Special thanks to Karen Rommelfanger and the members of the Global Neuroethics Summit organizing committee for their useful comments on a previous version of this article.

DECLARATION OF INTERESTS

A.S., K.A., J.G.B., K.E., B.T.F., M.G., M.F., J.M., T.P., B.C.S., and K.Z. are researchers in the Human Brain Project. H.M. and H.W. are members of the Ethics Advisory Board.

REFERENCES

Changeux, J.P. (2017). Climbing brain levels of organisation from genes to consciousness. Trends Cogn. Sci. *21*, 168–181. Published online Feb 1, 2017.

D'Ambrosio, P., and Colagè, I. (2017). Extending epigenesis: from phenotypic plasticity to the bio-cultural feedback. Biol. Philos. *32*, 705–728.

Dehaene, S., and Cohen, L. (2007). Cultural recycling of cortical maps. Neuron *56*, 384–398.

Evers, K. (2016). Neurotechnological assessment of consciousness disorders: five ethical imperatives. Dialogues Clin. Neurosci. *18*, 155–162.

Farisco, M., Laureys, S., and Evers, K. (2017). The intrinsic activity of the brain and its relation to levels and disorders of consciousness. Mind Matter *15*, 197–219.

Prescott, J.P. (2017). Robots are not just tools. Connect. Sci. *29*, 142–149.

Rommelfanger, K.S., Jeong, S.J., Ema, A., Fukushi, T., Kasai, K., Ramos, K.M., Salles, A., and Singh, I.; Global Neuroethics Summit Delegates (2018). Neuroethics questions to guide ethical research in the international brain initiatives. Neuron *100*, 19–36.

Salles, A., Evers, K., and Farisco, M. (2018). Neuroethics and philosophy in responsible research and innovation: the case of the human brain project. Neuroethics. https://doi.org/10.1007/s12152-018-9372-9.

Stahl, B.C., Rainey, S., Harris, E., and Fothergill, B.T. (2018). The role of ethics in data governance of large neuro-ICT projects. J. Am. Med. Inform. Assoc. *25*, 1099–1107.

Storm, J.F., Boly, M., Casali, A.G., Massimini, M., Olcese, U., Pennartz, C.M.A., and Wilke, M. (2017). Consciousness regained: disentangling mechanisms, brain systems, and behavioral responses. J. Neurosci. *37*, 10882–10893.