EMBO *reports*

science & society

Empirical neuroethics

Can brain imaging visualize human thought? Why is neuroethics interested in such a possibility?

Judy Illes

Neuroethics is a modern field at the intersection of bioethics and neuroscience, which, both independently and when conjoined, have philosophical and scientific roots that date as far back as the ancient philosophers, as well as eighteenth-century and nineteenth-century neurologists and physiologists such as Jean-Martin Charcot, Franz Joseph Gall, Paul Broca and Joseph Jules Dejerine (Marshall & Fink, 2003). More recently, neuroethics has drawn on the works of contemporary neuroscientists, philosophers, bioethicists, and other scholars in the humanities and natural sciences, including legal and policy experts (Changeux & Ricoeur, 2000; Churchland, 2006; Moreno, 2003; McGinn, 1991; Greely, 2006; Morse, 2006).

> **…although imaging does not visualize human thought *per se*, it does provide correlates of the cognitive functions that humans harness to create thought**

However, as the field itself is still in flux, it is difficult to pin down what exactly neuroethics is, and, therefore, what neuroethicists are, or should be, doing. Some recent definitions include: "The ethics of neuroscience; the neuroscience of ethics" (Roskies, 2002); "…the examination of what is right and wrong and good and bad about the treatment of, perfection of, or unwelcome invasion of and worrisome manipulation of the human brain" as proposed by William Safire (Marcus, 2002); and "…the examination of how we want to deal with the social issues of disease, normality, mortality, lifestyle, and the philosophy of living informed by our understanding of underlying brain mechanisms" as proposed by Michael Gazzaniga (Gazzaniga, 2005). A newer definition, which I presented at the 2006 annual meeting of the Society for Neuroscience (Illes, 2006) and that borrows from Van Rensellear Potter as cited in *The Birth of Bioethics* (Jonsen, 1998), is as follows: a discipline that aligns the exploration and discovery of neurobiological knowledge with human value systems.

Here, I discuss one arm of this field, empirical neuroethics, which has defined new territory through an approach and methodology based on experimental work. I focus on imaging methods, which represent state-of-the-art capabilities for neuroscience to visualize brain processes, in order to tackle three key issues: does imaging visualize human thought, why is neuroethics interested in thought visualization and how does neuroethics interact with this question? I conclude by making some predictions about what the neurosciences at the intersection with society—in particular using imaging methods—might expect to come next.

Imaging includes a range of technologies that have enjoyed a surge in both technical capability and application (Illes *et al*, 2003). Its roots lie in the visualization of anatomical structures combined with the intellectual and clinical pursuit of regional brain structures that underlie specific behaviours—that is, "cerebral localization" (Marshall & Fink, 2003) or, as Steven Rose might say, "cerebroscopy" (Rose, 2005). Regardless of modality, the ability of neuroscience to correlate structure and function underlies the four main pillars of modern neuroethics. Initially identified at a 2002 meeting in San Francisco (CA, USA) called 'Neuroethics: Mapping the Field' (Marcus, 2002), these keystones are the implications of neuroscience for the individual self, for social policy, for clinical neuroscience and for the dissemination of research findings.

> **The challenges presented by new diagnostic methods and their predictive potential are also shared between genetics and neuroscience…**

One of the most popular technologies is functional magnetic resonance imaging (fMRI), which measures brain function by visualizing changes in regional blood oxygenation when the brain is subjected to various stimuli (Moseley & Glover, 1995). It is important to note that these measures are made by subtracting experimental findings from control findings and are the result of highly processed averages over groups of people. They are therefore correlates, rather than direct measures, of behaviour. Research using fMRI was first published in 1991 (Belliveau *et al*, 1991). My colleagues and I found a significant increase in the number of original research studies—and the journals publishing them—from 1991 to 2002 (Illes *et al*, 2006c). At the latest count, approximately 8,700 studies had been published, with the number of publications in 2004 and 2005 alone equal to the number published from 1991 to 2001 (Fig 1; Illes, 2006).

Many of these published works began as validation studies using sensorimotor stimuli. Over time, and once their validity was established, they expanded to investigate memory and language. Since 1998, many

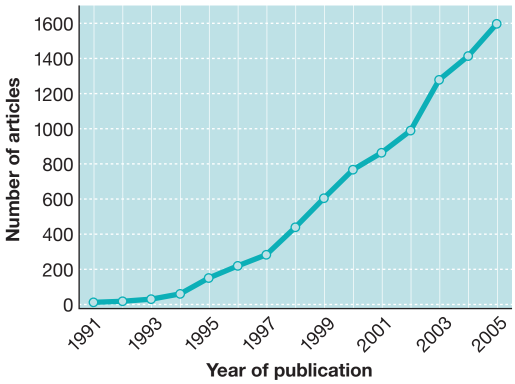


Fig 1 | Increasing number of functional magnetic-resonance imaging studies of the central nervous system over time.

studies have gone beyond these traditional topics to test for highly integrated and complex phenomena such as personality, moral decision-making, race judgements and economic decisions. In parallel to the rise in the number of such studies, coverage by the international press, which is not always as cautious as one might like, is also increasing (Racine *et al*, 2005). It is therefore no surprise that in a study I conducted with my colleagues in 2003, neuroimagers, bioethicists, policy-makers and scholars identified the nonclinical applications of imaging technology as their greatest concern. One neuroscientist said: "Eventually we'll be able to know a lot more about people through understanding more about how their brains work […] This is a domain that offers enough that's novel in the area of information about one's own persona, that we ought to be thinking very seriously about it" (Illes *et al*, 2006a).

The combination of genetics and imaging, through 'imaging genomics', might be one of the most powerful new tools of this decade

In the clinical domain, the applications are also profound. Consider, for example, studies on consciousness in patients who are in a persistent vegetative, or minimally conscious, state, in which the authors have drawn conclusions such as: "These results confirm that, despite fulfilling the clinical criteria for a diagnosis of vegetative state, this patient retained the ability to understand spoken commands and to respond to them through her brain activity, rather than through speech or movement. Moreover, her decision to cooperate with the authors by imagining particular tasks when asked to do so represents a clear act of intention…" (Owen *et al*, 2006).

By what means, and to what end, should physicians, clinical ethicists and families embody such information? More multimodal longitudinal studies are necessary, and there is an obligation on the part of investigators to assert the greatest possible caution when disseminating results of such a highly sensitive nature. At the other end of the spectrum of life, huge efforts are underway to develop fMRI for imaging fetuses, with a focus on pregnancies with complications (Bangert, 2001). Could such technology be adopted to select fetuses for predicted musical or athletic brain development? In an even more futuristic domain, could assistive machines for rehabilitation based on brain–computer interfaces ultimately be driven by mere thought?

These issues bring us to my central question: can imaging visualize human thought? The answer is certainly not. Thought is a composite of cognitive functions involving information processing, individual dispositions to information, and individual methods of integrating information into an internal schema and responding to it. However, although imaging does not visualize human thought *per se*, it does provide correlates of the cognitive functions that humans harness to create thought.

Herein lies one of the reasons for the uptake of this technology and for my second question: why is neuroethics interested in the question of thought visualization? In the inaugural lecture on neuroethics at the 2003 annual meeting of the Society for Neuroscience, Donald Kennedy, Editor-in-Chief of *Science*, provided an answer: "Far more than our genomes, our brains are us, collectively defining us as human, and individually marking out the special character of our personal capacities, emotions and convictions" (Kennedy, 2003).

To explore this statement, we must learn from the similarities and differences between neuroscience and genetics. Similarly to neuroscience, genetics provides us with a range of topics that require ethical investigation; issues of discrimination and stigma, coercion, challenges to medical privacy, secondary and extended uses of data, distributive justice, commercial potential and public perception have been well studied. The challenges presented by new diagnostic methods and their predictive potential are also shared between genetics and neuroscience, as are questions such as how to deal with incidental clinical findings in research, and the risks of false positives and negatives (Illes *et al*, 2006b).

…neuroethicists must keep up with the pulse of neuroscience, and pursue an ethically coherent agenda based on the needs of the neuroscience community and its interface with society

But imaging the brain also presents unique challenges in terms of both its promise and its limitations (Illes & Racine, 2005). First, there is physiological variability that is influenced by gender and even time of day. Second, there is paradigmatic variability owing to design issues such as protocols for data acquisition or statistics for data interpretation. Third, there is variability in interpreting data given the intrinsic nature of experimental design, the methods used for data analysis, and investigator–subject bias, values and culture. Unlike genetics, neuroscience truly bridges technique and technology. The combination of genetics and imaging, through 'imaging genomics', might be one of the most powerful new tools of this decade (Hariri & Weinberger, 2003; Canli, 2006).

Other divergences are more philosophical than technical. With some inevitable circularity, the brain is both the seat of ethical decision-making and the target of ethics discovery (Leshner, 2005). Beyond that is the question of experience. As humans, we experience brain health and brain disease differently from the way we experience health and disease in other organ systems. As an avid skier, I value the integrity of my knees; I also value the integrity of my brain, and it is best when the two work well together. But if I had to give up the integrity of one over the other, it would have to be the knees. Without my brain, it would be impossible to coordinate the function of my knees or appreciate their eventual coordination. In this context, scholars have begun to think about chimaeras—physiological mixtures of animals and humans—as they involve the central nervous system, and brain in particular, tissue engineering, questions about personhood and identity in humans, and the remote possibility of non-humans acquiring cognitive functions (Greely *et al*, 2007; Greene *et al*, 2005; Illes & Murphy, 2007).

This leads to my third and final question: how does neuroethics interact with the question of thought visualization through imaging? There is no clear-cut answer, no one set of rules. Neuroethicists have approached this question in different ways. The approach of my group has been primarily an empirical one.

Our goal has been to identify pragmatic starting points and alternatives to resolve difficult ethical challenges presented by the brain sciences through a negotiated scientific social process. Philosophically, we seek to empower the scientific process through proactive thinking. We have identified high-impact areas, such as incidental findings, biomarkers, commercialization of neurotechnology, scientific literacy and regenerative medicine, and identified funding for the research to pursue them. We then take them systematically through a process of issue identification or pre-discovery and discovery, ethics analysis and development of tools—reference, resources and research—and finally into a phase of evaluation and refinement (Fig 2).

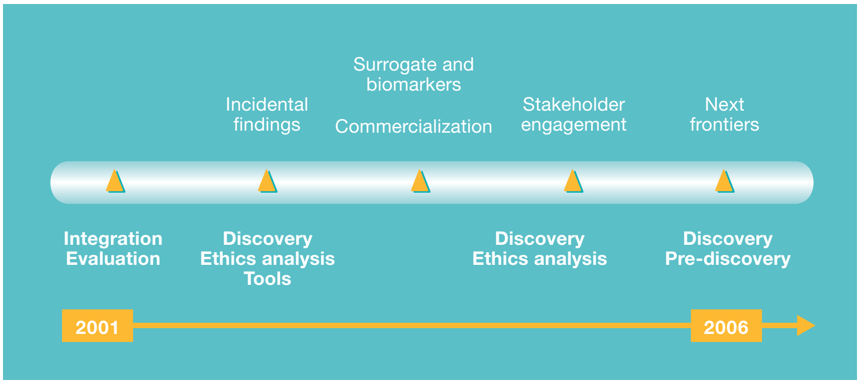


Fig 2 | Empirical approach to enquiry in modern neuroethics.

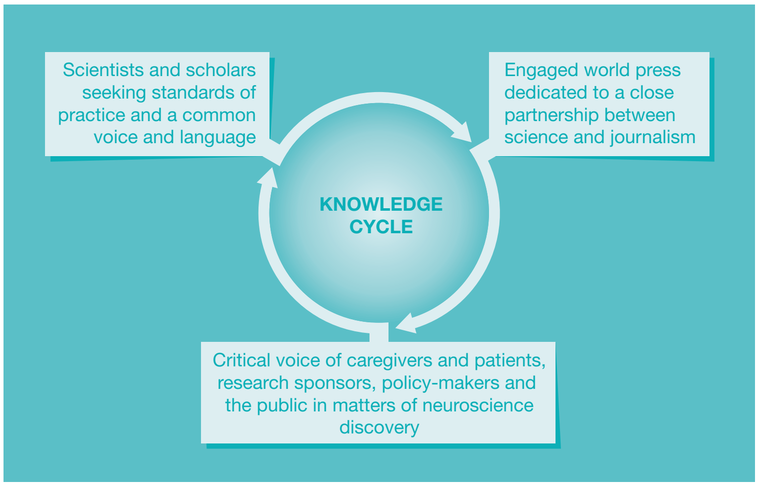


Fig 3 | Model for a dynamic and interactive cycle of knowledge among the scientific community, journalists, and stakeholders from the public, government and research sponsors.

The process is dynamic and iterative. We have also used our goal of improving science literacy to promote the proactive engagement and deliberation of multiple stakeholders at various junctures in the research development and translational process. Guided by the effort to achieve a cycle of knowledge (Fig 3), we work to enable scientists and scholars to find standards of practice and a common voice and language, to achieve a truly dedicated and close partnership between science and journalism, to involve government agencies and research sponsors in dialogue about funding priorities and policy, and to provide a platform for the critical voices of caregivers, stakeholders and the public in matters of neuroscience. In partnership with the International Network on Neuroethics—an arm of the Neuroethics Society—our vision is for a global initiative that will open up the world of neuroethics from issues spanning consent—individual, communal or tribal—to multicultural and multidimensional perceptions of, and interventions for, neurological and psychiatric disease.

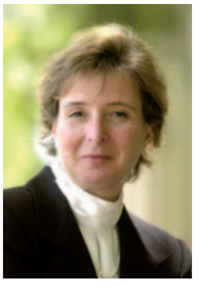
There are compelling reasons for anticipating neuroethical issues at the laboratory bench, at the bedside and in the public domain. These will require the involvement of neuroscientists and highlight a duty of care that extends beyond the laboratory. These motives further call for democratic and civic involvement to promote a better understanding both of the potential and the limitations of brain science, and of the prospective responsibility for managing real and imagined uses of technology for the brain (Illes *et al*, 2006c).

The new breed of so-called neuroethicists must lead the way in drawing from bioethics, genetics and other disciplines to meet the unique challenges that are raised by the opportunity to study and probe the brain. To succeed, neuroethicists must keep up with the pulse of neuroscience, and pursue an ethically coherent agenda based on the needs of the neuroscience community and its interface with society. Hence, they can effectively bridge cultural, linguistic and disciplinary barriers, develop capacity on an internationally relevant scale, and develop tools in the forms of resources and references that are flexible, practical and useful.

All told, careful attention to, and analysis of, the ethics of advanced science and its intersection with society are needed. A disciplinary home with its own name, such as 'neuroethics', is viewed by some as necessary, by others as a matter of organizational convenience, and by still others as a source of annoyance as it adds another layer of complexity to the already complicated disciplines of bioethics, sociology, neuroscience, STS (science, technology and society) and the law, on which neuroethics draws. Only history will tell which perspective is most visionary. In the meantime, the professional community has moved beyond accepting a *laissez faire* attitude to ethics in neuroscience. Action, anticipation and interdisciplinary efforts are now leading the way.

REFERENCES

Bangert BA (2001) Magnetic resonance techniques in the evaluation of the fetal and neonatal brain. *Semin Pediatr Neurol* **8:** 74–88
Belliveau JW, Kennedy DN Jr, McKinstry RC, Buchbinder BR, Weisskoff RM, Cohen MS, Vevea JM, Brady TJ, Rosen BR (1991) Functional mapping of the human visual cortex by magnetic resonance imaging. *Science* **254:** 716–719
Canli T (2006) When genes and brains unite: ethical implications of genomic neuroimaging. In Illes J (ed), *Neuroethics: Defining the Issues in Theory, Practice and Policy*, pp 169–184. Oxford, UK: Oxford University Press
Changeux JP, Ricoeur P (2000) *Ce Qui Nous fait Penser: la Nature et la Règle*. Paris, France: O. Jacob
Churchland PS (2006) Moral decision-making and the brain. In Illes J (ed), *Neuroethics: Defining the Issues in Theory, Practice and Policy*, pp 3–16. Oxford, UK: Oxford University Press
Gazzaniga MS (2005) *The Ethical Brain*. New York, NY, USA: Dana Press
Greely HT (2006) The social effects of advances in neuroscience: legal problems, legal perspectives. In Illes J (ed), *Neuroethics: Defining the Issues in Theory, Practice and Policy*, pp 245–264. Oxford, UK: Oxford University Press
Greely HT, Cho MK, Hogle LF, Satz DM (2007) Thinking about the human neuron mouse. *Am J Bioeth* **7:** 27–40
Greene M *et al* (2005) Ethics: moral issues of human–non-human primate neural grafting. *Science* **309:** 385–386
Hariri AR, Weinberger DR (2003) Imaging genomics. *Br Med Bull* **65:** 259–270
Illes J (2006) *Neuroethics, Neurochallenges: A Needs-Based Research Agenda*. David Kopf Annual Lecture on Neuroethics, Society for Neuroscience (Atlanta, GA, USA), 16 Oct. Washington, DC, USA: Society for Neuroscience
Illes J, Murphy ER (2007) Chimeras of nurture. *Am J Bioeth Neurosci* **7:** 1–2
Illes J, Racine E (2005) Imaging or imagining? A neuroethics challenge informed by genetics. *Am J Bioeth* **5:** 5–18
Illes J, Kirschen MP, Gabrieli JD (2003) From neuroimaging to neuroethics. *Nat Neurosci* **6:** 205
Illes J, De Vries R, Cho MK, Schraedley-Desmond P (2006a) ELSI priorities for brain imaging. *Am J Bioeth* **6:** W24–W31
Illes J *et al* (2006b) Ethics. Incidental findings in brain imaging research. *Science* **311:** 783–784
Illes J, Racine E, Kirschen MP (2006c) A picture is worth 1000 words, but which 1000? In Illes J (ed), *Neuroethics: Defining the Issues in Theory, Practice and Policy*, pp 149–168. Oxford, UK: Oxford University Press
Jonsen AR (1998) *The Birth of Bioethics*. New York, NY, USA: Oxford University Press
Kennedy D (2003) *Neuroethics: An Uncertain Future*. Annual Meeting of the Society for Neuroscience (New Orleans, LO, USA), 10 Nov. Washington, DC, USA: Society for Neuroscience
Leshner AI (2005) It's time to go public with neuroethics. *Am J Bioeth* **5:** 1–2
Marcus SJ (ed; 2002) *Neuroethics: Mapping The Field*. New York, NY, USA: Dana Press
Marshall JC, Fink GR (2003) Cerebral localization, then and now. *Neuroimage* **20 (Suppl 1):** S2–S7
McGinn RE (1991) *Science, Technology, and Society*. Englewood Cliffs, NJ, USA: Prentice Hall
Moreno JD (2003) Neuroethics: an agenda for neuroscience and society. *Nat Rev Neurosci* **4:** 149–153
Morse SJ (2006) Moral and legal responsibility and the new neuroscience. In Illes J (ed), *Neuroethics: Defining the Issues in Theory, Practice and Policy*, pp 33–50. Oxford, UK: Oxford University Press
Moseley ME, Glover GH (1995) Functional MR imaging. Capabilities and limitations. *Neuroimaging Clin N Am* **5:** 161–191
Owen AM, Coleman MR, Boly M, Davis MH, Laureys S, Pickard JD (2006) Detecting awareness in the vegetative state. *Science* **313:** 1402
Racine E, Bar-Ilan O, Illes J (2005) fMRI in the public eye. *Nat Rev Neurosci* **6:** 159–164
Rose SP (2005) Human agency in the neurocentric age. *EMBO Rep* **6:** 1001–1005
Roskies A (2002) Neuroethics for the new millenium. *Neuron* **35:** 21–23



Judy Illes is Director of the Program in Neuroethics at the Stanford Center for Biomedical Ethics, and Associate Professor of Pediatrics (Medical Genetics) at Stanford University, CA, USA. On 1 August 2007, she will become Professor of Neurology, Canada Research Chair in Neuroethics and Director of the National Core for Integrated Neuroethics at the University of British Columbia in Vancouver, Canada.
E-mail: illes@stanford.edu

doi:10.1038/sj.embor.7401007