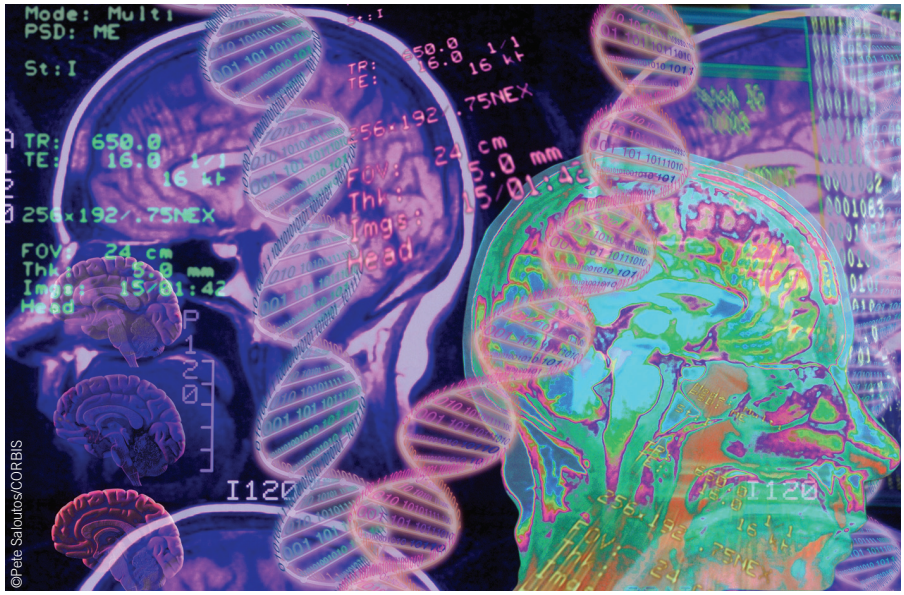
Commercializing cognitive neurotechnology—the ethical terrain

Margaret L Eaton & Judy Illes

Lack of recognition of the ethical, social and policy issues associated with the commercialization of neurotechnology could compromise new ventures in the area.

Mental illness is one of the leading causes of disability worldwide, afflicting one in five Americans and over one in four Europeans[1]. Cognitive neurotechnologies—technologies that enable the monitoring and/or modulation of the function of the brain—promise to improve the treatment of neurodegenerative and psychiatric disorders and may ultimately be applied to enhance emotional stability, cognitive clarity and sensory experiences. At the same time, they challenge existing notions of free will, identity, privacy and mental health and well-being, and pose additional social and ethical concerns when commercialized as products for both medical and nonmedical applications[2,3]. If ignored, these concerns could compromise successful application of neurotechnology products in the marketplace and increase the potential for harm. Companies must therefore anticipate and appreciate social and ethical issues so that corporate decisions can maximally promote health benefit and neurocognitive well-being, and preserve the value of the technology.



Companies cannot afford to ignore the ethical and social implications of implementing neurotechnology in both medical and nonmedical applications.

What is possible?

Like any new technology, neurotechnology promises much but also poses several ethical, social and policy problems. On the upside, it may offer new treatments for mental illness, enable enhancements of mental performance and cognitive capacity, and open up new opportunities for commerce[4]. Although the healthcare market is neurotechnology's major focus, nonmedical uses of neurotechnology assessment tools are also proliferating. Such uses concern a range of professionals—neuroscientists, bioethicists, scholars from the humanities, law and policy[2]—and include applications by judicial, government or military authorities as well as in business and sports.

Diagnosis and management of disease. The application of brain-scanning techniques, such as electrophysiology (electroencephalogram, EEG) and evoked response potential (ERP) technology, positron emission tomography (PET)/single-photon emission-computed tomography (SPECT) and functional magnetic resonance imaging (fMRI), to identify, control and predict diseases of aging, childhood disorders, addiction and anxiety disorders represents a large portion of the cognitive neurotechnology market[5,6]. The techniques variously rely on electrical signals recorded at the scalp (EEG/ERP), on changes in brain metabolic activity (PET/SPECT) and on stimulus-related changes in regional levels of blood oxygenation (fMRI). With or without brain scans, clinical workups for cognitive impairments can involve complex protocols, can take many days and, because they require the services of highly trained neurology

Margaret L. Eaton is at the Graduate School of Business, Stanford University, 518 Memorial Way, Stanford, California 94305-5615, USA, and Judy Illes is at the Stanford Center for Biomedical Ethics, Department of Pediatrics (Medical Genetics), 701 Welch Road, Building A, Suite 1105, Palo Alto, California 94304-5748, USA. e-mail: illes@stanford.edu

or psychology professionals, can cost thousands of dollars. The results are often variable due to patient and test administration differences and are subject to differences of interpretation. Physicians, parents, patients, teachers and medical insurers have long lamented the lack of certainty in diagnosis because relatively small interpretive changes can significantly alter the diagnosis for a given patient.

Neuroimaging research aims to eliminate the problems of interpretation and potentially, with streamlined technology, lower cost. Current technology allows simultaneous neuroimaging and real-time cognitive assessment. Developers expect that automated screening and assessment will soon be performed in less than one day (possibly in an hour or less) and, depending on the equipment used, cost orders of magnitude less. Some of the new technology will also require much less active participation by the clinician and the patient because detection, transmission and assessments of brain activity will be done using wireless and other automated sensing equipment. These improvements will produce more detailed brain function images and thus improved quantification and precision of brain function characterization. In addition, because some of these technologies capture brain function without relying on responses that are consciously or actively controlled by the person being tested, artifacts due to limited cooperation may be eliminated. Reminiscent of older biofeedback methods, emerging neurofeedback technologies based on cues about changing levels of blood oxygenation, for example, may afford relief to patients suffering from debilitating pain[7].

Assessment of cognitive state. Cognitive assessment tests are currently being marketed to physicians and athletic trainers to measure the effects of head injury, such as concussion[8]. With greater diagnostic precision, the tests can insure that return to pre-trauma activity is safe. Similar tests are also being tried to assess the cognitive impact of physiological states, such as hypoglycemia[9] and fatigue[10,11]. A future in which neurological or mental health screening for performance readiness is widely available is easy to anticipate, therefore, and will extend to military personnel, hospital workers, airline pilots, bus and truck drivers and others who are on extended or night shifts and whose performance affects many people. The reliability of these assessments, however, will depend on periodic baseline testing of cognitive well-being.

Affective and forensic uses. Neurotechnologies are also enabling new approaches to evaluate mental and behavioral states for social purposes. Studies include those on personality assessment, cognitive perceptions of ethnicity and race[12–14] and researchers may in the future investigate musical, verbal or athletic prowess.

Government, law enforcement, security and military uses. Nonmedical government, judicial and military applications of neurotechnology include training of personnel to subvert interrogation and cope with stressful combat situations, and for the purpose of detecting socially problematic behaviors, cognitive overload, stress and waning attention and arousal. Several startup companies working in this domain began with an initial business plan to develop medical products and services but then redirected R&D when given funding from sources, such as the US Department of Homeland Security or the US Defense Advanced Research Projects Agency (DARPA)[15].

Cognitive enhancement. Good cognitive assessment tools will create opportunities for enhancing mental function[16,17], and some such systems have already been given approval by the US Food and Drug Administration (FDA). Electrical Geodesics (Eugene, OR, USA), for example, has used its EEG technology on Tibetan monks to study the brain activity and benefits of meditation. Harnessing the inherent powers of the mind can potentially enhance behavior, memory, sexual experience, sleep, attention and confidence without the side effects of drugs that can achieve similar results.

Lie detection. Functional MRI studies have demonstrated differences between levels of oxygenation in the brains of people who are performing truthfully or lying[18–20]. This still emerging capability has led to commercial development of lie detection systems, with potential uses in crime investigations, parole and child-custody hearings, immigration screening, insurance or government security interviews, civil litigation to determine the truth of allegations and counterintelligence. There has long been a need to replace unreliable polygraph analysis, and the US National Research Council Canada (Washington DC, USA) has recommended that brain-scanning technology, such as fMRI, be developed for this purpose[21]. Given the expense of MRI scanners, it is likely that more cost-effective and portable lie-detection technologies will be developed. One technology, EEG-based brain fingerprinting, already exists and is being marketed as an improved lie detector that does not depend on any willingness of the subject to respond to questions[22].

Education. Many researchers are currently using fMRI and EEG-based tools to investigate neural networks underlying learning. Studies have shown, for example, that intensive remedial training can promote brain plasticity in children with dyslexia and generate normal responses with a concomitant improvement in reading skill[23]. These studies ensure that cognitive assessment will become widely used to screen for learning skills and disabilities, validate interventions and assess outcomes.

Consumer product marketing. Among the most controversial of the nonmedical uses of new neurotechnologies is their application to advertising. Newly emerging 'neuromarketing' firms use fMRI in consumer research to assess people's unconscious, unfiltered reactions to advertisements for consumer products[24]. These companies were formed in the wake of studies reporting brain function correlates to brand preference[25].

Issues related to neurotechnology

Although neurotechnologies clearly promise significant benefits in diverse applications, their increasing adoption is likely to prompt further reexamination of existing concepts of mental health and illness as well as pose questions concerning infringement of an individual's right to privacy, autonomy and identity.

As neurotechnologies are increasingly applied in diagnosing and treating disease, disagreements may arise concerning definitions of brain health, and acceptable thresholds and ranges of human motor and cognitive behavior. For example, imaging that can detect increasingly small differences in cognitive processing can lead to disputes about whether these variations are within the normal human range or are hallmarks of mental disease. Also, questions will probably arise whether or not use invites coercion and invasion of privacy.

For affective and forensic applications, acceptance of the tempting conclusion that cognitive assessment tools can provide an objective description of a person's brain state is generally regarded as naive. Particular emphasis has been placed on the dangers of using functional brain images to predict future behavior, such as suitability for employment or aggressive behaviors, a caution that stems from the likelihood that people may do just that. Acceptance of the notion of biological determinism—in this case, that brain activity determines who you are and how you will behave—is highly controversial.

Neurotechnology applications in the military are particularly troubling. Although alertness is essential in the armed forces, concerns exist that neurotechnology could be used to coerce

soldiers beyond the limits of normal human endurance[26–28]. As a result, at least one ethicist has advised researchers involved in developing neurotechnology to decline military funding if the potential military uses are considered objectionable[29].

Cognitive enhancement has been characterized as both advantageous for people and society and as unnatural and threatening[30]. On the one hand, it is possible that these kinds of enhancements will have the undesirable effect of increasing disparities in social and economic opportunity; on the other hand, they may result in the equally unpalatable blunting of differences among people[17].

In the context of lie detection, if it becomes possible to perform brain scans on unwilling, or even unwitting, subjects, issues about privacy, constitutional protections against self-incrimination, and the prohibitions against unlawful search and seizure are likely to become acute[31,32]. Premature use is another risk, especially until the distinction between deception and confused memory can be made reproducibly. Moreover, as the courts will be faced with scans obtained at different field strengths and visual resolutions, important differences due to such paradigmatic and other protocol variables will be difficult to appreciate by nonexperts. The increasingly powerful and visually compelling scans may tempt judges and juries, in fact, to defer good judgment and personal values to the images[33].

For consumer marketing applications of neurotechnology, it is debatable whether use of such powerful neuroimaging tools to improve sales of products, including to children, is socially positive[25]. The concept of marketing-related diseases—disorders, such as obesity, type 2 diabetes, alcohol abuse and lung disease, that might result from behaviors encouraged by ads for fast or junk food, alcohol or tobacco—and the possibility that fMRI may be used to assess political or propaganda campaigns have fueled social concerns[34].

Issues related to commercialization

Neurotechnology shares many of the same ethical and social issues that are associated with the commercial development of many other medical diagnostics and therapeutics. These issues include, for example, responsible conduct of animal and human research, maximizing product safety and efficacy, integrity of published data, intellectual property and fair advertising balance between benefits and risks. We do not discuss these here; rather, we focus on the ethical issues that are unique or especially relevant to the commercial development of neurocognitive assessment tools that have the potential to affect diagnostic and medical outcome, human identity, autonomy and decision-making. Some of the most important challenges are outlined below.

Initial validity. When marketing any innovation, commercial developers must address a fundamental question: what degree of product maturity is required to move the technology from research to commercial sale? Because brain scan data from new neurotechnologies are subject to differences in interpretation, differences in definitions of product validity and maturity will follow[35]. Another central question focuses on the point at which a brain database is sufficiently large, representative, and both medically and culturally sound to deliver valid assessments of individual cognitive function.

These readiness questions arise most acutely for neurotechnologies that can be deployed without a regulatory gatekeeper, such as the US Food and Drug Administration (FDA). Even when FDA approval is necessary before marketing a neurotechnology, the regulators' lack of experience with new technologies often means that they must rely on company expertise and advice. Companies cannot rely on the sophistication of the end-user to understand the limits of the technology; only the company knows in detail, for example, how in-house brain-function databases were compiled. Because much of the new wave of cognitive testing devices produces clinically detailed and mathematically sophisticated reports, physicians may also be tempted to accept findings and diagnostic conclusions at face value. Given the possibility of knowledge disparities, it is the duty of the company to introduce to the market only those products and services that have been fully validated and for which the safety and efficacy have been corroborated by scientific and medical consensus.

Sustained validity. The question of sustained validity arises after a technology or service has been marketed. Innovation is naturally a continuous and dynamic phenomenon, and in the case of neurotechnology, it is progressing especially fast. This makes it imperative that companies anticipate and respond to changes in knowledge and technological obsolescence. Unlike modifications to drug treatment regimens based on new knowledge that are relatively simple to implement, physician customers who are early adopters of cognitive assessment technologies may be reluctant or unable to upgrade complex and costly hardware and software. Given rapid change in this field, keeping abreast of and informing clinicians of new developments is a fundamental company responsibility. Pre-market commitment both to product upgrades and to identifying how upgrades affect prior assessments will be key to sustained validity. If a company maintains a database of patient assessment data, for example, a retrospective examination of patients who should be reevaluated in light of new technological and clinical findings may be a necessary feature of the upgrade process.

Brain privacy and confidentiality. Even with the most sophisticated protections in place, repeated access to online databases for monitoring therapeutic progress will strain mechanisms for information privacy. It is unlikely that all testing will yield only intended information or information that is only about the medical parameter in question. Information that a person would prefer to keep private—personality traits, emotions, memories and sexual preference—may be gleaned from an assessment. This capacity invites misuse of information[36–40]. Unauthorized disclosure can be especially injurious if socially problematic thinking can be detected in patients who have been able to control their associated behavior[41]. The fact that cocaine craving, for instance, can be detected in brain scans is one illustration of this possibility[42]. Studies have shown that scans revealing cognitive impairments can lead to stigma and discrimination[43]. Dilemmas of confidentiality may also surface if neural signatures predictive of diseases, such as dementia, are discovered.

What is the obligation of companies to inform physicians or patients of a finding? Disclosure may both violate promises of confidentiality and enlarge the population of the asymptomatic 'worried well' who repeatedly seek medical care and reassurance[44]. Predictive evidence of lapses of consciousness or cognitive behavior, including rage control, will also generate reporting dilemmas. Private sector neurotechnology developers attuned to these challenges, like owners of genetic databases before them[45], can thoughtfully build in safeguards to minimize privacy risks.

Conflicts of interest. Several sources of conflict of interest affect neurotechnology firms. In the context of combined assessment and post-assessment treatment services, companies face an inherent self-interest that can affect their business decisions where the frequency of diagnosis directly promotes growth in the treatment or service arm of their business. Given that mistrust of corporate motives is common, knowing that such bundled products and services can have merit is sometimes not sufficient to diminish the perception of this kind of conflict of interest. Companies can benefit substantially by curbing self-serving practices and thus mitigate negative public perception.

A second potential source of conflict of interest is related to the fact that cognitive assessment has traditionally been the purview of a relatively small number of highly specialized medical practitioners. However, many new cognitive assessment tools and services are designed for and marketed to nonspecialist physicians, thus creating a larger potential market. While the nonspecialists may see new opportunities for neurocognitive testing, an overuse of services, while financially rewarding to both the company and the physician, will not be in the best interest of patients. As with any situation that generates potential conflicts of interest, openness about associations and mindfulness that financial gain can skew decision making are strong steps to preventing negative outcome.

A third conflict-of-interest consideration involves databases that contain both baseline and post-treatment cognitive assessment measures from patients, as well as data acquired from healthy individuals. Although such large databases can improve the quality of information, if competition for data becomes the driving force for recruitment, rather than product or service improvement, practices could become aggressive or coercive. Any corporate R&D action that might undermine the rights of subjects and patients to give free and informed consent should be avoided.

Continuing end-user education. A significant benefit of the newer cognitive assessment technologies is that many will become automated and simple to use. Turnkey systems are being developed for technologies as complex as fMRI. This raises questions about quality control and training, especially with an expanding market of nonspecialists. Physicians may come to rely on automated diagnosis and statistics at the expense of other important medical information that skilled personal interaction can provide. It will therefore be necessary for nonspecialist physicians to undergo continuing education for proper patient selection, test performance, and data analysis and interpretation. Selective marketing and comprehensive user-training are vital to achieving these goals.

Therapeutic gap. The concept of 'therapeutic gap' was first introduced when genetic tests revealed a risk for disease or disorder, such as breast or ovarian cancer and Huntington disease, for which no prevention, treatment or cure existed[46]. This same gap exists for biomarkers of brain abnormalities, such as for the detection of early dementia[47–49] that are untreatable. In these still early phases of brain biomarker development, cognitive technology companies can learn from previous practices adopted by gene test companies[50–52]. Such practices include discovering how to communicate information to patients and perhaps most important, understanding how a patient being tested is likely to react to that information[53].

Experience with patients undergoing genetic tests predictive of untreatable disease has shown that they are often at risk for developing depression, anxiety and social problems related to their assumption that illness with a potentially lethal disease is inevitable. Is knowledge about brain disease risk, therefore, empowering or harmful[54]? Proactive collaboration with physicians and patients during R&D will provide neurotechnology companies with insights about when and how to market a brain biomarker, and how best to prevent or mitigate harm.

Dual and off-label uses. There is a strong tendency for neurotechnologies to be adopted for multiple purposes, some useful and some dubious. Developers and manufacturers of cognitive assessment technologies must be aware of this potential and be both forthright about and proactive in managing it. The issue can arise either in the context of sales or collaboration. In sales, for example, a company may ask whether it should sell a scanner to a memory clinic that intends to use it for purposes that have not yet been vetted in the scientific literature or that may be scientifically questionable. In business collaborations, companies may reflect on whether they should codevelop hardware and software for certain military applications. Careful investigation of the intentions of clients and potential business partners is warranted. Rejection of questionable collaborations is good business practice. If technology misuse is detected after sales have transpired or collaborations have been formed, the company bears responsibility for addressing a problem of which it has become aware. It may be appropriate to attempt to stop or otherwise influence unsound uses by alerting users and other stakeholders. Any loss of sales revenue in such a situation is more than offset by avoiding criticism that financial gain was achieved through tacit permission for medically or morally inappropriate uses of a product.

Conclusions

Reliability, validity, privacy protections and fairness in the marketing of technological promise of cognitive assessment tools are legitimate requirements before product rollout. Given the power of information about brain function and what it can reveal about people, companies in this market sector must be alert to all of the ethical and social impact of their R&D and marketing activities and be prepared to incorporate these issues into business development plans. Doing so will ultimately fulfill both business and altruistic ends by lowering barriers to acceptance and enhancing the likelihood that products and services will maximize benefit and minimize harm.

ACKNOWLEDGMENTS

Judy Illes's contribution is supported by NIH National Institutes of Neurological Disorders and Stroke no. 045831. Don DuRousseau is gratefully acknowledged for his support and comments on this manuscript.

COMPETING INTERESTS STATEMENT

The authors declare competing financial interests: details accompany the full-text HTML version of the paper at www.nature.com/naturebiotechnology.

1. http://www.europeanbraincouncil.org/ (accessed April 26, 2006).
2. Illes, J., DeVries, R., Cho, M.K. & Schraedley-Desmond, P. *Am. J. Bioeth.* **6**, 24–31 (2006).
3. Eaton, M. & Kennedy, D. in *Ethical Challenges in Medical Technology Innovation.* p. 84–93 (Johns Hopkins University Press, Baltimore, 2007).
4. Fitzgerald, M. VCs psyched over brain investments. *Venture Cap. J.*, published online 1 August 2005. <http://www.venturecapitaljournal.net/vcj/1122124806471.html>
5. Gazzaniga, M. *The Ethical Brain* (The Dana Foundation Press, New York, 2005).
6. Illes, J. & Kirschen, M.P. *AJNR Am. J. Neuroradiol.* **24**, 1932–1934 (2003).
7. deCharms, R.C. *et al. Proc. Natl. Acad. Sci. USA* **102**, 18626–18231 (2005).
8. Collie, A. & Maruff, P. *Br. J. Sports Med.* **37**, 2–3 (2003).
9. Anderson, A.W. *et al. Magn. Reson. Imaging* **24**, 693–697 (2006).
10. Caseras, X. *et al. Psychosom. Med.* **68**, 947–955 (2006).
11. Tanaka, M. *et al. BMC Neurol.* **6**, 9 (2006).
12. Canli, T. & Amin, Z. *Brain Cogn.* **50**, 414–431 (2002).
13. Canli, T. *Neuroethics: Defining the Issues in Theory, Practice and Policy.* (ed. Illes, J.) 165–183 (Oxford University Press, Oxford, 2006).
14. Phelps, E.A. *et al. J. Cogn. Neurosci.* **12**, 729–738 (2000).
15. Silberman, S. *Wired Magazine* **14**, 14 (2006).
16. Farah, M.J. *Nat. Neurosci.* **5**, 1123–1129 (2002).
17. Farah, M.J. *et al. Nat. Rev. Neurosci.* **5**, 421–425 (2004).
18. Spence, S.A. *et al. Neuroreport* **12**, 2849–2853 (2001).
19. Lee, T.M. *et al. Hum. Brain Mapp.* **15**, 157–164 (2002).
20. Kozel, F.A. *et al. Biol. Psychol.* **58**, 605–613 (2005).
21. National Research Council. *The Polygraph and Lie Detection.* (National Academies Press, Washington, DC, 2003.) <http://darwin.nap.edu/books/0309084369/html> (accessed April 26, 2006).
22. http://www.brainwavescience.com (accessed January 26, 2007).
23. Temple, E. *et al. Proc. Natl. Acad. Sci. USA* **100**, 2860–2865 (2003).
24. McClure, S.M. *et al. Neuron* **44**, 379–387 (2004).
25. http://members.forbes.com/forbes/2003/0901/062.html.
26. Anonymous. *Christ. Sci. Monit.* January, p. 17 (2003).
27. Lawton, G. *New Scientist* February, p. 18 (2006).
28. Laurence, C. *Sunday Telegraph (London)* January, p. 5 (2005).
29. Hoag, H. *Nature* **423**, 796–798 (2003).
30. President's Bioethics Council. *Better Memories: The Promise and Perils of Pharmacological Interventions.* (President's Council on Bioethics, HarperCollins, Washington, DC, 2003).
31. Illes, J. *Cerebrum* **6**, 73–80 (2004).
32. Greely, H.T. Regan lecture (Markkula Center for Applied Ethics, Santa Clara University, Santa Clara, CA, 2004).

33. Schuman, D. Comment on: J. Illes. Authenticity, bluffing and the privacy of human thought (Lecture presented at the University of Texas, Dallas, January 9, 2007).
34. http://www.nytimes.com/2004/04/20/science/20SCAN.html?pagewanted=1&ei=5007&en=20e627931944313d&ex=1397880000&partner=USERLAND
35. Quackwatch: A skeptical view of SPECT scans and Dr. Daniel Amen. http://www.quackwatch.org/06ResearchProjects/amen.html
36. Kennedy, D. in *Neuroethics: Mapping the Field*, vol. 1. (ed. Marcus, S.J.) 193–207 (The Dana Press, San Francisco, 2002).
37. Illes, J. & Racine, E. *Am. J. Bioeth.* **5**, W3–W4 (2005).
38. Illes, J., Kirschen, M.P. & Gabrieli, J.D. *Nat. Neurosci.* **6**, 205 (2003).
39. Olsen, S. *Science* **307**, 1548–1550 (2005).
40. http://www.cognitiveliberty.org/ (accessed April 26, 2006).
41. Moreno, J.D. *Nat. Rev. Neurosci.* **4**, 149–153 (2003).
42. Childress, A.R. *et al. Am. J. Psychiatry* **156**, 11–18 (1999).
43. Gray, A.J. *J. R. Soc. Med.* **95**, 72–76 (2002).
44. Illes, J. *et al. Radiology* **228**, 346–351 (2003).
45. Lin, Z., Owen, A.B. & Altman, R. *Science* **305**, 183 (2004).
46. NHGRI. Promoting safe and effective genetic testing in the United States. <http://biotech.law.lsu.edu/research/fed/tfgt> (accessed October 10, 2005).
47. Bookheimer, S.Y. *et al. N. Engl. J. Med.* **343**, 450–456 (2000).
48. Jack, C.R. *et al. Neurology* **60**, 253–260 (2003).
49. Albert, M. The Use of MRI and PET for Clinical Diagnosis of Dementia and Investigation of Cognitive Impairment. Working Report: Neuroimaging Workgroup of the Alzheimer's Association (Alzheimer's, Chicago, IL. 2005).
50. Collins, F.S. *N. Engl. J. Med.* **34**, 186–188 (1996).
51. Wadman, M. The DNA hard sell. *New York Times* Dec. 16, p. A15 (1996).
52. Saltus, R. Gene test for cancer risk is offered; some geneticists dispute its value. *Boston Globe* Oct. 25, p. QA1 (1996).
53. Illes, J., Rosen, A.C., Grecius, M. & Racine, E. Prospects for prediction: an ethics analysis of neuroimaging in Alzheimer's Disease. *Ann. NY Acad. Sci.* **1097**, 278–295 (2007).
54. Leshner, A. *Am. J. Bioeth.* **5**, 1–2 (2005).