Neuroscience Becomes Image Conscious as Brain Scans Raise Ethical Issues

M. J. Friedrich

Plug in the term fMRI (functional magnetic resonance imaging) to PubMed and the search engine will generate tens of thousands of relevant citations. Since this brain imaging technique first appeared in the early 1990s, its use has “simply exploded,” says Marcus Raichle, MD, professor of radiology, neurology, and anatomy and neurobiology at Washington University School of Medicine, St Louis, a pioneer in functional brain imaging.

Not only are researchers using fMRI and other neuroimaging tools to examine basic sensorimotor and cognitive processes and brain pathology, they are also using them to explore complex brain functions involved in human motivation, reasoning, and social attitudes. This new ability to explore brain mechanisms is opening an array of opportunities to advance the understanding of the brain in health and disease.

But the use of imaging techniques to peer ever more closely into the brain also has ethical implications. Neuroscience, like genetics, deals with the biological foundations of who we are, points out Martha Farah, PhD, professor of psychology and director of the Center for Cognitive Neuroscience at the University of Pennsylvania, Philadelphia.

Like genetic data, brain scan findings raise issues of privacy, says Farah. In some cases, brain imaging may yield information that is even more personally significant than that generated by genetic tests. For example, she says, “genetic tests only provide information about traits, like personality traits, whereas brain scans not only can provide information about traits, they also can give insight into states—such as if someone is afraid at the moment.”

While it is not necessarily a bad thing to obtain this sort of information from brain imaging, explains Farah, “it can be misused. We have to safeguard privacy and begin to think about how we want to control the use of that kind of information.”

Such concerns about the uses and misuses of neuroimaging data have prompted neuroscientists such as Farah to join ethicists and others to address the challenges presented by these new neuroimaging capabilities, a key area in the emerging field of neuroethics.

NEUROLITERACY

As brain imaging becomes more commonplace, both patient and physician knowledge about the technology become ever more important. Robert Klitzman, MD, professor of clinical psychiatry and codirector of the Center for Bioethics at Columbia University, New York City, says that information needs to be gathered about how physicians are ordering brain scans—for instance, who will be tested and whether scans will be used to predict the likelihood of diseases that cannot yet be cured, such as Alzheimer disease.

He also notes that there has been little to no research done on how people understand fMRI results. He lists some of the questions that need to be addressed: “How are findings from brain scans interpreted? How do doctors report results to patients? What do patients understand of what’s been said? Is any sort of counseling being provided to help the patient cope with results?”

“The public seems to be... overly ready to accept scientific claims supported by a brain picture,” says Farah. Many people, she says, have the impression that the images reveal aspects of our true selves that other forms of data do not—a sort of mind-reading the technology is not actually capable of accomplishing.

“People make this huge jump—[assuming] that because we’ve converted a mathematical change in oxygenation and blood flow to a color-coded image on an MR scan that it must...
be real, that your eyes don’t lie,” says Dennis Spencer, MD, professor of neurosurgery at Yale University, New Haven, Conn.

“Think about it—most of the technical development in fMRI is done by physicists and statisticians, not neuroscientists,” says Farah. The layers of statistical analysis interposed between scanning and the final image inevitably require making assumptions and judgments. “You must be aware of the many decisions that go into creating those neat and unambiguous-looking false color images,” says Farah. “Anyone who is not in the field working with these kinds of data will need help evaluating it.”

What is needed, says Farah, is to make a realistic assessment of what these technologies can now do and will soon be able to do and to establish guidelines for the use of that information.

IMAGE PROBLEM

Overselling the power of an image is something that concerns Judy Illes, PhD, an imaging neuroscientist and director of the program in neuroethics at the Stanford Center for Bioethics, Palo Alto, Calif. “We have to be very cautious about how we translate lab data for public consumption—to convey the promise of brain imaging as well as its limitations,” she says.

This is particularly relevant because of the increase in the marketing of imaging services such as computed tomography and MRI directly to the consumer. Consumers can undergo screening and diagnostic imaging procedures without a physician's referral. In addition to full-body scans, structural brain imaging is also being promoted, says Illes. She notes that some clinicians are even marketing functional brain imaging, primarily to adults worried about memory loss and to parents anxious about their children’s academic performance.

In a recent study, Illes and her colleagues examined this direct-to-consumer marketing trend by analyzing 40 print and broadcast advertisements from companies that produce information about imaging procedures (Illes et al. Arch Intern Med. 2004; 164:2415-2419). The researchers concluded that the ads emphasized the benefits of these scans without providing enough information about the technology’s limitations and risks.

Illes notes that most of the advertisements did not refer consumers to additional sources of information, nor did they encourage physician consultation, as pharmaceutical ads do. While direct-to-consumer advertising can enhance consumer choice, it should provide information in a balanced way that does not overestimate the value and underestimate the risks, says Illes. She recommends establishing professional guidelines and oversight for the advertising and promotion of these services.

UNEXPECTED NEWS

Anomalous results that appear during brain scans present another ethical conundrum for neuroscientists. In a recent report, Illes and her colleagues showed that asymptomatic individuals present with a variety of abnormalities, with about 2% to 8% of them having findings of varying levels of clinical significance (Illes et al. Neurology. 2004; 62:888-890).

In a survey of 74 researchers in the United States and abroad who use MRI scans, Illes’ group discovered that substantial variability exists among research groups when it comes to handling and communicating abnormalities in individuals’ brain scans (Illes et al. J Magn Reson Imaging. 2004;20:743-747).

Some groups do have well-thought-out procedures in place for handling such incidental findings. For example, Bruce Wexler, MD, professor of psychiatry at Yale University, notes that all brain images produced in his research are scanned by a clinical neuroradiologist. His group roughly categorizes each structural brain abnormality as one of 3 types: an unusual finding with no treatment implications, which is not reported to the study participant; an unusual finding thought to have no clinical significance but which might be useful for the individual and the primary caregiver to have on file; and a clinically significant finding that warrants follow-up and possibly treatment that should be handled by the person’s clinician.

Wexler adds that he discourages colleagues and laboratory personnel from volunteering to participate in research in brain imaging studies because of the difficulty in keeping the results confidential. A breach in confidentiality could cause harm, for example, if employers or insurance companies learn of a significant incidental finding to the detriment of the volunteer’s employment opportunities or health and life insurance coverage.

But other research groups—50% of those surveyed in Illes’ study—report that they have not established a formal way of addressing incidental findings.

To address the lack of guidance on this topic, Illes brought together about 50 people from various disciplines to develop guidelines for minimum standards for detecting and disclosing incidental findings on brain MRI research (accessible at http://accessible.ninds.nih.gov/news_and_events/proceedings/ifexecsummary_pr.htm).

“We concluded that incidental findings must be anticipated in the experimental design of any brain imaging experiment,” says Illes. Meeting participants agreed that it was necessary to have a professional competent to interpret a neuroimaging scan for clinically significant findings, although there was debate about whether radiologists should be involved in reading every brain scan in every study. The participants also strongly agreed that the first person to hear about a detected finding should be the research participant (or a surrogate in the case of a minor or someone without decisional capacity).

NEXT FRAME

Anomalous findings that emerge from fMRI studies will also pose an ethical challenge. As Illes points out, “Some day, perhaps we’ll have individual activation patterns for tasks such as those involving moral judgment, deception, or sexual preference from our research subjects—those that fall within norms and those that seem anomalous.”
What happens, for example, when a young healthy human participates in a study having to do with sexual arousal, asks Illes. “Say his behavioral and physiologic data are normal but he has an anomalous brain pattern when compared to other individuals in the cohort study,” she says. “When would we have enough information to determine that the finding is anomalous? How should we communicate the results? Should we even tell him?”

This situation may not be that far in the future. As University of Pennsylvania’s Farah notes, while correlations between psychological traits and brain activity are not currently considered high enough to make brain scanning a useful tool for individual screening or assessment, functional brain imaging may be closer to being able to measure individual differences than most people in the field of cognitive neuroscience realize.

A recent survey of studies using brain imaging to look at personality traits, intelligence, and psychological variables revealed that some individual scans may be distinctive enough to offer reliable information about a person, reported Farah at the annual meeting of the Cognitive Neuroscience Society in 2004. “Perhaps not enough to pinpoint a person’s exact intelligence level,” she says, “but the range can be narrowed.”

Neuroethicists need to begin exploring these sorts of questions now, says Farah. In articles (eg, Farah. Trends Cogn Sci. 2005;9:34-40) and meetings on emerging neuroethical issues over the last few years, “we’ve said all the most obvious things,” she says. “Now I think the task is for scientifically literate ethicists and ethically sensitive neuroscientists to begin to identify specific questions and problems and work on them.”

Scientists Confront Cloning Challenges

Tracy Hampton, PhD

SAN FRANCISCO—Nuclear cloning holds great promise for curing or alleviating a number of diseases and conditions. Apart from various ethical considerations, the technique has a number of technical hurdles to clear before it has a chance of making its way into the clinic.

Nuclear cloning (also called nuclear transfer) involves replacing the DNA of a donated egg with the DNA from a patient’s cell and coaxing the egg to divide and produce embryonic stem cells. These are then manipulated and introduced back into the patient. Although a group of researchers in South Korea recently succeeded in using patient DNA in nuclear cloning to derive 11 new human embryonic stem cell lines (Hwang et al. Science. 2005;308:1777-1783), many efforts remain unsuccessful, and scientists are keen to find strategies for making nuclear cloning more efficient.

The answer may lie in “genomic reprogramming,” said Rudolf Jaenisch, MD, of the Whitehead Institute for Biomedical Research, Cambridge, Mass. During the International Society for Stem Cell Research meeting held here in June, Jaenisch discussed his work to find the genes that are crucial to successful nuclear cloning.

CLUES WITHIN CELLS

Studies have shown that nuclear cloning can be quite efficient when the DNA of an egg is replaced with the DNA from embryonic cells. But when the donated DNA comes from somatic cells, such as neurons or immune cells, the resultant cells usually die before stem cells can be harvested. Jaenisch suspects that genes expressed in the nuclei of embryonic cells may hold clues to achieving efficient nuclear cloning.

Jaenisch and his research team have identified a number of “pluripotency genes” that are active in embryonic cells but inactive in somatic cells. (Pluripotent cells have the potential to develop into more than one type of differentiated cell.) The researchers examined the activity of these genes in blastocysts—embryos at an early stage of development, when embryonic stem cells can be isolated and cultured. In their studies, every blastocyst derived from fertilized eggs was found to express all tested pluripotency genes, as did every cloned blastocyst derived from embryonic cell donors.

In cloned blastocysts derived from somatic cell donors, however, the activation of these genes was shown to be faulty and random. Furthermore, em-