



Emerging Ethical Challenges in Advanced Neuroimaging Research: Review,
Recommendations and Research Agenda

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EMERGING ETHICAL CHALLENGES IN ADVANCED NEUROIMAGING RESEARCH: REVIEW, RECOMMENDATIONS AND RESEARCH AGENDA

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ABSTRACT: The dynamic and ever-evolving nature of neuroimaging research creates important ethical challenges. New domains of neuroscience research and improving technological capabilities in neuroimaging have expanded the scope of studies that probe the biology of the social and ethical brain, the range of eligible volunteers for research, and the extent of academic-industry relationships. Accordingly, challenges in informed consent and subject protection are surfacing. In this context, we provide an overview of the current landscape for neuroimaging and discuss specific research ethics topics arising from it. We suggest preliminary approaches to tackle current issues, and identify areas for further collaboration between neuroimagers and institutional review boards (research ethics committee).

KEY WORDS: Neuroimaging, neuroethics, bioethics, institutional review board, neuroscience, functional Magnetic Resonance Imaging

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IN THE LAST THREE DECADES, neuroscience research has made significant leaps forward (Popp & Moore, 1994) and the research and ethics community has followed the state of the art closely with specific attention emerging in neurogenetic research (MacKay, 1984), brain banking procedures (Riis, 1993), and neuroclinical trials (Young, 2002). Imaging technologies at the frontier of neuroscience today have brought advances in the understanding of brain morphology and brain function in the healthy and the diseased brain. Faster, higher resolution and noninvasive capabilities have expanded the scope of research and the range of suitable pools of volunteers (Rosen, Bodke, Pearl *et al.*, 2002). It has also stimulated private-sector

relationships (Cho, 2002). This evolving context creates challenges for informed consent and human subject protection including the management of incidental neuroimaging findings of anomalies in research (Illes, Kirschen, Edwards *et al.*, 2006; Kumra, Ashtari, Anderson *et al.*, 2006); protection of confidentiality in large neuroimaging databases and the promotion of public neuroscience literacy based on a balanced assessment of the risks and benefits of neuroimaging (Wolpe, Foster, & Langleben, 2005).

Here we provide an overview of the current landscape of neuroimaging, and we discuss specific ethical topics arising from it based on the literature and our research experience in ethics and neuroscience. We offer preliminary approaches to tackle current issues in consideration of the momentum of neuroimaging and the need to explicitly address some important emerging ethical challenges. We identify areas for further research regarding ethics in neuroimaging research.

A New Landscape for Neuroimaging

The landscape for neuroimaging involves functional imaging modalities such as Electroencephalography (EEG), Positron Emission Tomography (PET), magnetoencephalography (MEG), functional Magnetic Resonance Imaging (fMRI), magnetic resonance spectroscopy (MRS), and lately functional Near-infrared Spectroscopy (fNIR or optical imaging). *Functional* imaging modalities enable researchers to study brain activation during task performance and complement modalities that provide images of brain structure (*structural* imaging). Combined-modality imaging, such as fMRI which has good spatial resolution with MEG that has superior temporal resolution augments the power of the imaging data (Mathiak & Fallgatter, 2005).

Imaging modalities each have unique features (please see Maziotta (2000) and Illes and Racine (2005) for more details on specific imaging modalities). PET is sensitive to the decay of radioactive substances associated principally with brain metabolism and activation. Neuroimaging using fMRI monitors blood oxygenation correlates of behavior in discrete, stimulus-response

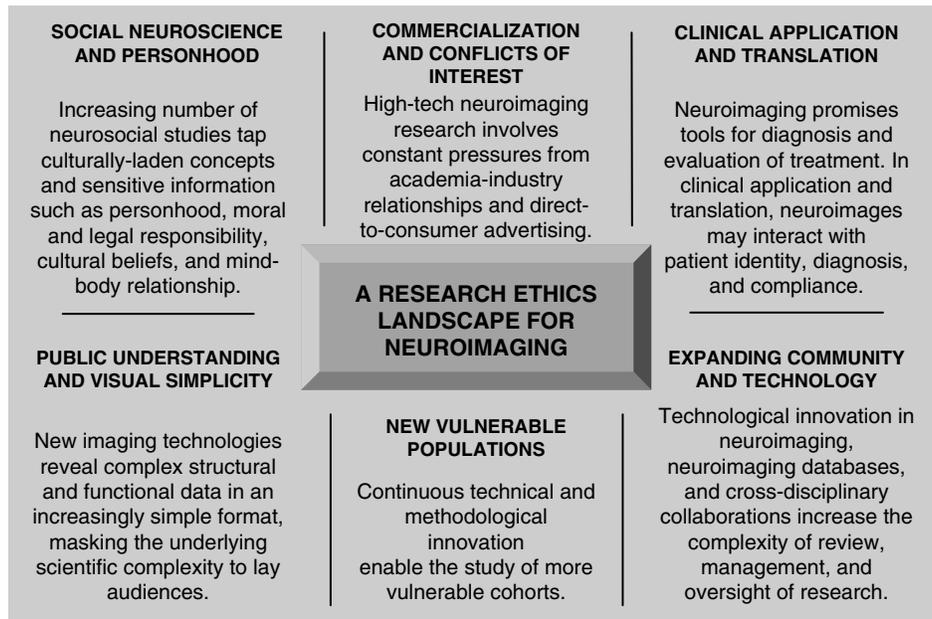


FIG. 1. A research ethics landscape for neuroimaging

paradigms. Advances in fMRI research have yielded insights into the neurobiological correlates of behaviors such as cooperation (Decety, Jackson, Somerville *et al.*, 2004), love (Bartels & Zeki, 2004), deception (Langleben, Schroeder, Maldjian, *et al.*, 2002), and moral reasoning (Greene, Somerville, Nystrom *et al.*, 2001). Practices informed by these results such as lie detection (Wolpe, Foster, & Langleben, 2005) or education interventions (Gura, 2005) are surfacing, despite important challenges in terms of external validity and varying approaches to data analysis and interpretation in functional neuroimaging (Anonymous, 2006; Gura, 2005; Illes & Racine, 2005; Wolpe, Foster, & Langleben, 2005). Neuroimaging, in combination with genetic testing, is being used to refine diagnosis in neurological and psychiatric disorders, with the goal of achieving diagnosis prior to the overt manifestation of disease, or confirming clinical diagnosis or assessing disease susceptibility such as in Alzheimer's disease (Rosen *et al.*, 2002), Huntington's disease (Rosas, Feigin, & Hersch, 2004), and depression (Pezawas, Meyer-Lindenberg, Drabant *et al.*, 2005). Neuroimaging services are being marketed directly to consumers for early detection of stroke and brain tumors (Illes, Racine, & Kirschen, 2006). The constant technological innovation has also expanded the pool of possible research volunteers, especially with the minimal invasiveness of MRI in comparison to PET for example (PET requires administration of radioactive

contrast agents by injection). Accordingly, fMRI has changed the risk-benefit ratio, justifying the participation of volunteers with more extensive disabilities than PET (Rosen *et al.*, 2002). The neuroimaging community is also growing in size (Illes, Kirschen, & Gabrieli, 2003). In Figure 1, we illustrate how these interacting areas of activity form a backdrop against which the new ethical challenges for neuroimaging research stand out.

1. Incidental Findings and Informed Consent

Neuroimaging—like all medical imaging procedures—reveals valuable information that is otherwise clinically inaccessible. Medical applications of imaging modalities such as confirmation of cerebral hemorrhage with Computed Tomography (CT) or detection of cerebral tumors with MRI are prime examples of the use of neuroimaging in diagnosis and monitoring of health interventions. However, these powerful properties of neuroimaging create challenges in the context of research when anomalies of potential clinical significance such as tumors or vascular malformations, called *incidental findings*, are detected in subjects.

Early studies of such incidental findings in neuroimaging research showed a prevalence of 2-8% (Illes, Desmond, Huang *et al.*, 2002; Katzman, Dagher, Azar *et al.*, 1999; Kim, Illes, Kaplan *et al.*, 2002; Kumra *et al.*,

2006) in adult and pediatric research populations. Although these data reflect higher rates than other population studies of brain tumors (3-6 cases per 100,000 depending on gender and geographic pool (Central Brain Tumor Registry of the United States, 2004)) and vascular disease (0.5%) (Weber & Knopf, 2006), these data suggest the need for explicit plans for managing incidental findings in imaging protocols and informed consent forms (Illes *et al.*, 2006). Pathways for handling incidental findings may recognize a range of solutions that are ethically acceptable depending upon the experimental goals, the professional training of the investigators, and the nature of the imaging site (e.g., medical or non-medical). Both the benefits and consequences of detecting and disclosing incidental findings, including false positives, must be taken into account when making decisions about how to manage them.

The potential impact of an incidental finding in research is well exemplified by the case of a Stanford medical student who volunteered for an fMRI study on verbal working memory, and in whom an arteriovenous malformation (AVM) was identified fortuitously. The student in question has written and spoken eloquently about how this was both an unexpected and life-changing personal experience (Hilgenberg, 2005) (see <http://neuroethics.stanford.edu>; at that website, go to The Case of SH). By contrast, an anonymous correspondent to *Nature* who participated in a colleague's study, shared how an incidentally detected brain tumor dramatically changed his life trajectory and adversely affected his medical insurability (Anonymous, 2005). Management of incidental findings also challenges the role of researchers, especially of those without a medical background and clear professional *prima facie* deontological obligations to patients (Philips, 2005).

2. Privacy

Ethical issues related to confidentiality and privacy are common to all research that can reveal potentially sensitive information. In neuroimaging, privacy challenges are now amplified by two factors: the growth of neuroimaging databases and the emergence of groundbreaking studies on the social and ethical brain.

In some cases of large federally sponsored research today, data sharing is required, and neuroimaging consortia (e.g., Human Brain Project, International Consortium for Brain Mapping, BrainMap, LONI-UCLA) are actively engaged in the creation of neuroimaging databases. As neuroscience is "scaling up to the leagues of big science" (Narasimhan, 2004), concerns raised for the protection of confidentiality are

reminiscent of those associated with the creation of gene banks. Indeed, based on some features of neuroimages, individual faces can be reconstructed under certain conditions, thereby providing material for the re-identification of volunteers (Canli & Amin, 2002; Toga, 2002).

Further challenges bearing on confidentiality and privacy build on the distinctively intimate nature of some of the data acquired during neuroimaging. There is an expanding pool of neurosocial studies that yield brain activation profiles associated with personal and private thought, i.e., brain signatures for personality traits that could be targeted in testing and screening procedures (Illes & Racine, 2005). For example, some leading neuroimagers have revealed neural correlates for cooperation (Decety *et al.*, 2004), judgments about race (Eberhardt, 2005; Lieberman, Hariri, Jarcho *et al.*, 2005), love (Bartels & Zeki, 2004), deception (Langleben *et al.*, 2002), economic decision-making and consumer preferences (McClure, Laibson, Loewenstein *et al.*, 2004; McClure, Tomlin, Cypert, *et al.*, 2004), and moral reasoning (Greene *et al.*, 2001). These studies explore intimate and personal processes that could impact current views on data confidentiality and "thought privacy." In addition, thoughts and attitudes could be reified based on certain unsupported interpretations. Precedents for this exist such as the use of IQ measures and lie detection tests used to support some simplified views on intelligence and cognition. The limitations of current tools and methods need to be understood and acknowledged to support good practices in matters of recruitment, informed consent and fair assessment of promises of benefits, especially when results are communicated broadly.

Other leading research has identified regional brain activation patterns that are associated with disease, including potential biomarkers for Alzheimer's disease at subclinical levels, tests that could reveal presence of a disease process in absence of overt symptoms (Rosen *et al.* 2002) or predict developmental outcomes in premature infants (Woodward, Anderson, Austin *et al.*, 2006). In addition, some innovative neuroimaging protocols have linked specific genes with differential brain morphology and brain activation patterns in depression (Pezawas *et al.*, 2005). This example demonstrates the power of combining genetic susceptibility information with neuroimaging in order to assess a person's risk to develop disease, as well as highlighting the need to define good practices of counseling in neuroimaging based on probabilistic data and still misunderstood pathological processes (Illes, Rosen, Greicius, *et al.*, 2007). The large-scale storage of neuroimages could be

used to perform second-generation studies. As we see from examples of current research, the information could in some cases be used to generate individual neuroprofiles, perhaps on data that provide material to re-identify the volunteer.

Sharing of neuroimages through neuroinformatic platforms is an emerging phenomenon for neuroimagers. Some approaches to data banking have been framed for gene and tissue banks (Austin, Harding, & McElroy, 2003; Beskow, Burke, Merz *et al.*, 2001). However, in the absence of specific examination of neuroimaging data banking, these approaches may not be revisited and updated (e.g., anonymization procedures; sharing of imaging samples through web-based platforms). Coordinators of large samples and neuroimaging data banks need to decide when access to data is legitimate and should be allowed, limited or denied.

3. Justice in Recruitment and Cohort Selection, Coercion, and Confidentiality

Neuroscience research frequently relies on the recruitment of colleagues or students. Despite cautions about recruiting volunteers from trust relationships that involve employees and their employers, this is a common practice in neuroimaging. Many neuroimagers perform their research at night or during weekends to gain access to scanners heavily booked for clinical purposes during the day and to take advantage of reduced night scanning rates to contain costs. Given the legacy of college student conscription into psychology studies and other methods of volunteer recruitment, explicit protections may be needed to ensure that students do not feel coerced to participate (either at night or during the day) and to mitigate embarrassing situations if they do. Consider, for example, the discovery of incidental findings, of previously unknown claustrophobic tendencies in the tight scanner environment, or of unusual brain responses to stimuli of emotional or sexual content in a colleague volunteering for an imaging study. This type of situation highlights the need for cautious recruitment practices. This requirement is not unique to neuroimaging, but the sheer fascination of seeing the structure of one's own brain "in action" and the tradition of recruiting students and peers may detract from the full assessment of risk.

4. Decisional Capacity and Vulnerable Populations, Stigma and Discrimination

Pediatric studies: The non-invasiveness of MRI has allowed for a growth of pediatric, neonatal and even fetal neuroimaging, although the use for sedation still

positions many pediatric studies for full research ethics committee (REC) review (Downie & Marshall, 2007). Beyond issues of safety, proxy consent is a key consideration, and carefully determining the acceptable balance of risks and benefits for a child is challenging (Illes & Raffin, 2005). Establishing the child's best interest, and also understanding how the child views his own participation in a neuroimaging study can bring contrasting views: a parent may find the prospect of participating in a neuroscience experiment fascinating, while the child may find it terrifying (Hinton, 2002).

In the search of securing assent of a child, some centers have developed innovative approaches such as using coloring books describing the MRI experience in ways that are intelligible to the child (Hinton, 2002). Preliminary data of the Cognitive Neuroscience Laboratory at Stanford University supports efforts to reach out to children volunteers: children can find the fMRI experience valuable but the reasons they give for participating are quite different than the ones provided by adults (Thompson, 2004). Still, more research is needed to generate evidence-based pediatric informed consent practices.

Adult studies: While former constraints of invasiveness and task burden on neuroimaging have limited enrolment in studies to patients with only mild to moderate neurological and psychiatric conditions, it is now feasible to scan patients with far greater ranges of cognitive disability (Rosen *et al.* 2002). While this yields greater and ever more refined understanding of disease, it also creates new challenges to existing informed consent procedures and current approaches to mitigating stigma and discrimination (Kulynych, 2002).

The specific issue of stigma of vulnerable populations has not been extensively discussed in the context of neuroimaging research (Owens, 1997) even if it is pervasive in the broader context of psychiatry and neurology (Gray, 2002; Phelan, 2002). There are now sufficient grounds to suggest that this conversation is needed. For example, in the popular press, neuroimaging tends to be simplified and results over-interpreted, especially when results are portrayed as revealing our essence based solely on characteristics of our brain (Racine, Bar-Ilan, & Illes, 2005; 2006). Neuroimaging results could therefore be uncritically understood as indicating the differential superiority or inferiority of the brains of one group over another. Pessimistic media depiction of brain damage in so-called crack babies (antenatal exposure to cocaine) or Romanian orphans in the 1980s serve here as a reminder of the possible impact of neuroscience on stigma and over-deterministic conclusions (DiPietro, 2000). Will potential deviations in brain

activation based on population averages communicated to the public—that do not in any case necessarily apply to a specific individual—be understood by the general public as an indication of abnormality and a ground to ostracize and promote beliefs in a fatalistic biological determinism? The questions raised here are akin to those of population genetic studies in matters of proper interpretation of research data and prevention of stigma on communities (Foster & Carter, 1998; Juengst, 1998; Weijer & Emmanuel, 1999). In addition, certain publicized interpretations suggesting that neuroimaging reveals our essence (neuro-essentialism) or provides a direct measure of brain activity (neuro-realism) complicate the fair and balanced assessment of the potential risks and benefits of neuroimaging for researchers, REC members as well as the general public (Racine, Bar-Ilan, & Illes, 2005).

5. Scientific Value; Conflict of Interest; Transfer of Knowledge

It is the mandate of REC review to assess the relative risks and benefits of any protocol in order to avoid unscientific and therefore ethically unjustifiable research (Emmanuel, Wendler, & Grady, 2000). This mandate is clear across the *Helsinki Declaration* and the *Common Rule* of the Code of Federal Regulations. Generally speaking, neuroimaging is widely accepted by the scientific community as a legitimate research tool but there are dissenting voices that equate neuroimaging with a new phrenology given the important and sometimes unacknowledged epistemological assumptions implicit in the construction of neuroimages (Uttal, 2001). Consequently, some scholars have remarked that neuroimaging is “a field in which the technological capacity to generate brain images far exceeds scientists’ current ability to interpret what imaging data reveal about the mind and the brain” (Kulynych, 2002). In fact, debate is growing about the limits of neuroimaging both in the peer-reviewed literature and in popular science press. In addition to being indirect measures of brain activation, as we noted earlier, the meaning of functional neuroimaging results, especially those that bear on higher-order phenomena and social behaviors, are tied to conceptual issues involving religious beliefs and cultural input in research design (Illes & Racine, 2005; Reilly, 1991). Publicized claims that functional neuroimaging can readily assess personality traits or provide literally “a window into the brain” need to be mitigated and clarified by researchers as they approach research subjects. Other challenges to the integrity of knowledge and research come from conflicts of interest (Cho, 2002), marketing of neuroimaging

services to consumers (Illes, Kann, & Karetsky *et al.*, 2004; Racine, Van der Loos, & Illes, 2007) and over-represented benefits in print media.

Recommendations for Good Practice

Based on an analysis of the literature, Table 1 captures some initial recommendations for good practices relative to the emerging issues discussed in this review paper. For many of these issues, empirical research has not yet documented current practices. Hence, only initial and tentative recommendations can be made as indicated in the table.

One area which has been further investigated concerns the management of incidental findings. For example, the Working Group on Incidental Findings in Brain Imaging Research has presented approaches for the management of incidental findings in structural imaging. The majority of the members of that working group (about 50 experts in imaging, bioethics, policy, law, and other relevant fields) felt as ethically desirable that research protocols should provide for disclosure of incidental findings (Illes *et al.*, 2006). That view was supported by both the respect of researcher obligations to subjects’ autonomy and interests as well as evidence that research subjects vastly prefer disclosure over non-disclosure (Kirschen, Jaworska, & Illes, 2006). However, this view was held as unwise by a minority of the working group members given factors such as the harmful consequences of potential false-positives. Various options for follow-up were considered by the working group (PI, primary care physician of the subject, referral physician) and a minority of the working group also found it not ethical to leave all the responsibility for follow-up to subjects. This makes it likely that the management of incidental findings will depend on choices made by PIs and RECs as well as available resources (e.g., access to neuroradiologists) and the nature of the protocol and research team (e.g., led by an M.D. or a Ph.D.). It is important to note that the working group felt that it was overall premature to apply its conclusions to functional imaging.

What follows in Box 1, is an example of informed consent language proposed at Stanford University (Lucas Center for Magnetic Resonance Spectroscopy and Imaging) acknowledging the possibility of incidental findings and describing a procedure for their management. The limitations of research neuroimaging are identified to dispel any expectations of clinical benefits. Also, the language mentions who will contact the subject, therefore helping to clarify the responsibilities of the PI and the subject in the case of a finding meriting further investigation (e.g., contacting the subject and his or her primary care physician in this case by the PI).

TABLE 1. Initial Recommendations Regarding Emerging Issues in Advanced Neuroimaging Research

Ethical topics	Context (from Figure 1)	Initial recommendations
Incidental findings and informed consent	Neuroimaging research can reveal unexpected anomalies of potential clinical significance. Expanding neuroimaging community and technology create challenges for standardization of practice and shared approaches to informed consent forms (ICFs).	<ul style="list-style-type: none"> • Transparency in research protocol and ICFs for approach to handling of incidental findings (IFs). • Collaboration between RECs and neuroimaging groups in construction of ethical approaches for IFs respectful of subjects, research goals and institutional mandates.
Privacy, especially of thought	Expanding pool of neurosocial studies may lead to applications that yield neuroprofiles of personal and private thought. Privacy challenges are amplified by growth of neuroimaging databases and consortia.	<ul style="list-style-type: none"> • Transparency about banking procedures and secondary uses in ICFs. • Proactive handling of thought-privacy concerns, and cultural and conceptual issues in design of neurosocial studies.
Recruitment practices and confidentiality	Neuroimaging research frequently relies on the recruitment of colleagues or students and challenges confidentiality and consent.	<ul style="list-style-type: none"> • Clarification of institutional recruitment practices, and student participation in neuroimaging research. • Ongoing research neuroethics education to ensure confidentiality and uncoerced participation.
Decisional capacity and vulnerable populations	Non-invasive neuroimaging procedures are expanding the pool of prospective volunteers. More vulnerable populations can now be imaged, challenging existing informed consent procedures and current approaches to mitigating stigma and discrimination.	<ul style="list-style-type: none"> • Refined communication procedures sensitive to new levels of decisional capacity, especially for children, pregnant women, and patients with severely impaired decisional capacity. • Clarity of language that proactively prevents misunderstanding of results.
Stigma and discrimination		
Scientific value	Scientific evaluation of neuroimaging is complicated by the diversity of research methods. Public understanding of research intermingles with emerging direct-to-consumer advertising of brain imaging products and academic/private sector relationships as well as current public understanding supporting expectations for early clinical applications.	<ul style="list-style-type: none"> • Evaluation of protocols taking into account diversity of research paradigms, and risk-benefit ratio. • Clarity about academic/private sector strategies and acceptability of its societal implications. • Review of strategies for dissemination of research results, and claims for technological promise.
Conflict of interest		
Transfer of knowledge		

BOX 1. Sample Language for the Management of Incidental Findings in MRI Research

"The scans performed in this study are for specific research purposes and are not optimized to find medical abnormalities. The investigators for this project may not be trained to perform medical diagnosis. The investigators and Stanford are not responsible for failure to find existing abnormalities with these MRI scans. However, on occasion the investigator may notice a finding on an MRI scan that seems abnormal. When this occurs, a physician will be consulted as to whether the findings merits further investigation, in which case the investigator will contact you and your primary care physician and inform you of the finding. The decision as to whether to proceed with further examination or treatment lies solely with you and your physician. The investigators, the consulting physician, and Stanford are not responsible for any examination or treatment that you undertake based on these findings. Because the images collected in this study may not comprise a proper clinical MRI scan, these images will not be made available for diagnostic purposes."

(Stanford University, Last update April 9, 2007, available at: <http://humansubjects.stanford.edu/consents/SUSampCons.doc>)

This excerpt exemplifies how some issues can be clarified based on specific choices regarding disclosure and referral. Ultimately, however, language used in the informed consent form will depend on the specific options approved by local RECs.

Research Agenda

In the past years, progress has been made in bridging neuroimaging and ethics. Interdisciplinary meetings and publications have led to meaningful engagement, mutual learning and important practice changes. Pathways for the management of incidental findings have been identified as well as subject's expectations toward neuroimaging research better understood. However there are still crucial gaps in our understanding of concrete challenges researchers and RECs face in the review of neuroimaging research. We highlight here some topics that need to be further researched.

Surveying actual REC practices. There are still many unknowns about how RECs are dealing with the emerging challenges of neuroimaging research. Stronger magnets are being used in fMRI research, social neuroscience is gaining momentum, and more vulnerable populations are now candidates for neuroimaging procedures. These features and others are changing the neuroimaging landscape. Specific practices that need to be documented include recruitments of students in the Academia, evaluation of risk/benefit ratios, especially for vulnerable patients (e.g., aging and pediatric) and REC assessment of scientific value of protocols, in particular those relying on a combination of imaging technologies. By surveying actual practices, different models and approaches to handle emerging issues could be identified and pave the way for comprehensive approaches to remedy identified gaps.

Further bottom-up identification of local and international challenges. The ethics of neuroimaging research is one of the topics developed in the current neuroethics literature. In spite of the considerable work already accomplished, additional research is needed to extend perspectives to local research and REC communities as well as the ethical challenges inherent to large international neuroimaging initiatives. Better clarifying the needs of different national research and REC communities through comparative analysis could help researchers fulfill their local national requirements while maintaining their participation to international initiatives.

Evaluating implemented change. In some areas such as the management of incidental findings changes have occurred in imaging research and REC review. Different models and approaches are being developed to take into account local needs and the emerging ethics

discussion. The impact of these changes needs to be assessed and their effectiveness evaluated. This crucial extra step is required to guide future collaborations between neuroimagers, RECs and bioethicists toward the smoothest and most proactive implementation of ethics-related change in neuroimaging.

Identifying research ethics challenges that fall beyond the scope of REC review. The REC process is the recognized mechanism for the evaluation of ethical, legal, and social issues in research. This being said, there are some understandable limitations to the mandate of RECs and RECs may not be the suitable forum to address all ethical issues related to neuroimaging research. For example, oversight of translational research and issues related to the commercialization of imaging procedures cannot all be fully addressed by RECs once the research evolves outside the mandate of a single REC. Public understanding and the impact of the interpretation of neuroimaging research in the media can also impact subject's expectations without this being under the control of RECs. Although the REC process is well suited to identify and address some crucial research ethics issues, others will fall beyond the scope and mandate of RECs. The identification of these issues will help acknowledge the strengths of RECs and identify approaches that complement REC mandates.

Educational Implications

The continuous ethical use of neuroimaging as well as adjustments needed to keep pace with the evolution of the science will need to rely on extensive collaborations between investigators and RECs. The positive role of education cannot be overstated to avoid ethics pitfalls as well as over-regulation of research. At the very basic level, safety training needs to be supported as well as sufficient understanding of neuroimaging principles by trainees. This is important to avoid, for example, possible incidents with the strong magnetic fields of MRI. Updated ethics training also needs to continue for neuroimagers, especially to take into account the emerging issues. Neuroimaging centers and labs are most likely best placed to identify how and when on-going training should be provided to trainees. Such training could be an ideal opportunity to cultivate quality communication and collaboration between RECs and neuroimaging. Indeed, given the emerging issues, neuroimagers and RECs need to work together in ways that reflect sensibly their institutional contexts and needs. Where discussion has not yet yielded recommendations or approaches, we can emphasize that interdisciplinary workshops on specific ethical topics have proved to be a manageable and fruitful approach to

produce initial recommendations. Overall, the challenges we have highlighted and the early stages of related discussion support the need for expanded collaboration and mutual education among neuroimagers, RECs and scholars from the biomedical ethics community.

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Judy Illes is the Director of the Neuroethics Imaging Program and Associate Professor at the Department of Pediatrics, Division of Medical Genetics, Stanford University. Her current research interests are the ethical, social and legal challenges presented by advanced functional imaging capabilities, the emergence of cognitive enhancement technologies and pharmacology, the commercialization of cognitive neuroscience, and clinical findings detected incidentally in research.

References

- ANONYMOUS. (2005). How volunteering for an MRI scan changed my life. *Nature*, 434(7029), 17.
- ANONYMOUS. (2006). Neuroethics needed. *Nature*, 441(7096), 907.
- AUSTIN, M. A., HARDING, S., & MCELROY, C. (2003). Genebanks: A comparison of eight proposed international genetic databases. *Community Genetics*, 6(1), 37-45.
- BARTELS, A., ZEKI, S. (2004). The neural correlates of maternal and romantic love. *NeuroImage*, 21(3), 1155-1166.
- BESKOW, L. M., BURKE, W., MERZ, J.F., BARR, P.A., TERRY, S., PENCHASZADEH, V.B., et al. (2001). Informed consent for population-based research involving genetics. *Journal of the American Medical Association*, 286(18), 2315-2321.
- CANLI, T., & AMIN, Z. (2002). Neuroimaging of emotion and personality: Scientific evidence and ethical considerations. *Brain & Cognition*, 50(3), 414-431.
- CENTRAL BRAIN TUMOR REGISTRY OF THE UNITED STATES. (2004). *Statistical Report: Primary Brain Tumors in the United States, 1997-2001*. Hinsdale, IL: Central Brain Tumor Registry of the United States.
- CHO, M. K. (2002). Conflicts of interest in magnetic resonance imaging: Issues in clinical practice and research. *Topics in Magnetic Resonance Imaging*, 13(2), 73-78.
- DECETY, J., JACKSON, P. L., SOMMERVILLE, J. A., CHAMINADE, T., & MELTZOFF, A. N. (2004). The neural bases of cooperation and competition: An fMRI investigation. *NeuroImage*, 23(2), 744-751.
- DIPIETRO, J. A. (2000). Baby and the brain: Advances in child development. *Annual Review of Public Health*, 21, 455-471.
- DOWNIE, J., MARSHALL, J. (2007). Paediatric neuroimaging ethics. *Cambridge Quarterly of Healthcare Ethics* 16(2), 147-160.
- EBERHARDT, J. L. (2005). Imaging race. *American Psychologist*, 60(2), 181-190.
- EMMANUEL, E. J., WENDLER, D., & GRADY, C. (2000). What makes clinical research ethical? *Journal of the American Medical Association*, 283(20), 2701-2710.
- FOSTER M. W., & CARTER T. H. (1998). A model agreement for genetic research in socially identifiable populations. *American Journal of Human Genetics*, 63(3), 696-702.
- GRAY, A. J. (2002). Stigma in psychiatry. *Journal of the Royal Society of Medicine*, 95(2), 72-76.
- GREENE, J. D., SOMMERVILLE, R. B., NYSTROM, L. E., DARLEY, J. M., & COHEN, J. D. (2001). An fMRI investigation of emotional engagement in moral judgment. *Science*, 293(5537), 2105-2108.
- GURA, T. (2005). Educational research: Big plans for little brains. *Nature*, 435(7046), 1156-1158.
- HILGENBERG, S. (2005). Formation, malformation, and transformation: My experience as medical student and patient. *Stanford Medical Student Clinical Journal*, 9(1), 22-25.
- HINTON, V. J. (2002). Ethics of neuroimaging in pediatric development. *Brain & Cognition*, 50(3), 455-468.

- ILLES, J., DESMOND, J. E., HUANG, L. F., RAFFIN, T. A., & ATLAS, S. W. (2002). Ethical and practical considerations in managing incidental findings in functional magnetic resonance imaging. *Brain & Cognition*, 50(3), 358-365.
- ILLES, J., KANN, D., KARETSKY, K., LETOURNEAU, P., RAFFIN, T. A., SCHRAEDLEY-DESMOND, P., *et al.* (2004). Advertising, patient decision making, and self-referral for computed tomographic and magnetic resonance imaging. *Archives of Internal Medicine*, 164(22), 2415-2419.
- ILLES, J., KIRSCHEN, M. P., EDWARDS, E., STANFORD, L. R., BANDETTINI, P., CHO, M. K., *et al.* (2006). Incidental findings in brain imaging research. *Science*, 311(5762), 783-784.
- ILLES, J., KIRSCHEN, M. P., & GABRIELI, J. D. (2003). From neuroimaging to neuroethics. *Nature Neuroscience*, 6(3), 205.
- ILLES, J., RACINE, E., & KIRSCHEN, M. (2006). A picture is worth a thousand words, but which one thousand? In J. Illes (Ed.), *Neuroethics: Defining the Issues in Research, Practice and Policy* (pp. 149-168). Oxford: Oxford University Press.
- ILLES, J., & RACINE, E. (2005). Imaging or imagining? A neuroethics challenge informed by genetics. *American Journal of Bioethics*, 5(2), 5-18.
- ILLES, J., & RAFFIN, T. A. (2005). No child left without a brain scan? Toward a pediatric neuroethics. *Cerebrum*, 7(3), 33-46.
- ILLES, J., ROSEN, A., GREICIUS, M., & RACINE, E. (2007). Prospects for prediction: Ethics analysis of neuroimaging in Alzheimer's disease. *Annals of the New York Academy of Science*, 1097, 278-295.
- ILLES, J., ROSEN, A. C., HUANG, L., GOLDSTEIN, R. A., RAFFIN, T. A., SWAN, G., *et al.* (2004). Ethical consideration of incidental findings on adult brain MRI in research. *Neurology*, 62(6), 888-890.
- JUENGST, E. T. (1998). Groups as gatekeepers to genomic research: Conceptually confusing, morally hazardous, and practically useless. *Kennedy Institute of Ethics Journal*, 8(2), 183-200.
- KATZMAN, G. L., DAGHER, A. P., & PATRONAS, N. J. (1999). Incidental findings on brain magnetic resonance imaging from 1000 asymptomatic volunteers. *Journal of the American Medical Association*, 281(1), 36-39.
- KIM, B. S., ILLES, J., KAPLAN, R. T., REISS, A., & ATLAS, S. W. (2002). Incidental findings on pediatric MR images of the brain. *American Journal of Neuroradiology*, 23(10), 1674-1677.
- KIRSCHEN, M. P., JAWORSKA, A., & ILLES, J. (2006). Subjects' expectations in neuroimaging research. *Journal of Magnetic Resonance Imaging*, 23(2), 205-209.
- KULYNYCH, J. (2002). Legal and ethical issues in neuroimaging research: Human subjects protection, medical privacy, and the public communication of research results. *Brain & Cognition*, 50(3), 345-357.
- KUMRA, S., ASHTARI, M., ANDERSON, B., CERVELLIONE, K. L., & KAN, L. (2006). Ethical and practical considerations in the management of incidental findings in pediatric MRI studies. *Journal of the American Academy of Child and Adolescent Psychiatry*, 45(8), 1000-1006.
- LANGLEBEN D. D., SCHROEDER, L., MALDIJIAN, J. A., GUR, R. C., McDONALD, S., RAGLAND, J. D., *et al.* (2002). Brain activity during simulated deception: An event-related functional magnetic resonance study. *NeuroImage*, 15(3), 727-732.
- LIEBERMAN, M. D., HARIRI, A., JARCHO, J. M., EISENBERGER, N. I., & BOOKHEIMER, S.Y. (2005). An fMRI investigation of race-related amygdala activity in African-American and Caucasian-American individuals. *Nature Neuroscience*, 8(6), 720-722.
- MACKAY, C. R. (1984). Ethical issues in research design and conduct: Developing a test to detect carriers of Huntington's disease. *IRB: Ethics & Human Research*, 6(4), 1-5.
- MATHIAK, K., & FALLGATTER, A. J. (2005). Combining magnetoencephalography and functional magnetic resonance imaging. *International Review of Neurobiology*, 68, 121-148.
- MAZZIOTTA, J. C. (2000). Window on the brain. *Archives of Neurology*, 57(10), 1413-1421.
- MCCLURE, S., LAIBSON, D. I., LOEWENSTEIN, G., & COHEN, J. D. (2004). Separate neural systems value immediate and delayed monetary rewards. *Science*, 306(5695), 503-507.
- MCCLURE, S. M., LI, J., TOMLIN, D., CYPERT, K.S., MONTAGUE, L.M., & MONTAGUE, P.R. (2004). Neural correlates of behavioral preference for culturally familiar drinks. *Neuron*, 44(2), 379-387.
- NARASIMHAN, K. (2004). Scaling up neuroscience. *Nature Neuroscience*, 7(5), 425.
- OWENS, D. G. (1997). Ethical aspects of research on brain morphology in psychiatric patients. *Annali dell'Istituto superiore di sanità*, 33(4), 489-496.
- PEZAWAS, L., MEYER-LINDENBERG, A., DRABANT, E. M., VERCHINSKI, B. A., MUNOZ, K. E., KOLACHANA, B. S., *et al.* (2005). 5-HTTLPR polymorphism impacts human cingulate-amygdala interactions: A genetic susceptibility mechanism for depression. *Nature Neuroscience*, 8(6), 828-834.
- PHELAN, J. C. (2002). Genetic bases of mental illness—a cure for stigma? *Trends in Neurosciences*, 25(6), 430-431.
- PHILIPS, M. (2005). Coping with unsuspected findings in volunteers. *Nature*, 434(7029), 17.
- POPP, J. A., & MOORE, D. L. (1994). Institutional review board evaluation of neuroscience protocols involving human subjects. *Surgical Neurology*, 41(2), 162-167.
- RACINE, E., BAR-ILAN, O., & ILLES, J. (2005). fMRI in the public eye. *Nature Reviews Neuroscience*, 6(2), 159-164.
- RACINE, E., BAR-ILAN, O., & ILLES, J. (2006). Brain imaging: A decade of coverage in the print media. *Science Communication*, 28(1), 122-143.

- RACINE, E., VAN DER LOOS, H. Z. A., & ILLES, J. (2007). Internet marketing of neuroproducts: New practices and healthcare policy challenges. *Cambridge Quarterly of Healthcare Ethics* 16(2), 181-194.
- REILLY, P. R. (1991). Reviewing proposals to study biological correlates of criminality. *IRB: Ethics & Human Research*, 13(6), 8-9.
- RIIS, P. (1993). The Danish Brain Collection and its important potentials for future research. *IRB: Ethics & Human Research*, 15(6), 5-6.
- ROSAS, H. D., FEIGIN, A. S., & HERSCH, S. M. (2004). Using advances in neuroimaging to detect, understand, and monitor disease progression in Huntington's disease. *NeuroRx*, 1(2), 263-272.
- ROSEN, A. C., BODKE, A. L.W., PEARL, A., & YESAVAGE, J. A. (2002). Ethical, and practical issues in applying functional imaging to the clinical management of Alzheimer's disease. *Brain & Cognition*, 50(3), 498-519.
- THOMPSON, M. (2004). The subjective experience of participating in neuroimaging research studies: Illuminating differences between children and adults. Mini-symposium: Ethical dimensions in neuroscience. Stanford University, Palo Alto, CA.
- TOGA, A. W. (2002). Imaging databases and neuroscience. *The Neuroscientist*, 8(5), 423-436.
- UTTAL, W. R. (2001). *The New Phrenology*. Cambridge, MA: MIT Press.
- WEBER, F., & KNOPE, H. (2006). Incidental findings in magnetic resonance imaging of the brains of healthy young men. *Journal of the Neurological Sciences*, 210(1-2), 81-84.
- WEIJER, C., J. & EMANUEL, E. (1999). Protecting communities in biomedical research. *Science*, 289(5482), 1142-1144.
- WOLPE, P. R., FOSTER, K. R., & LANGLEBEN, D. D. (2005). Emerging neurotechnologies for lie-detection: Promises and perils. *American Journal of Bioethics*, 5(2), 39-49.
- WOODWARD, L. J., ANDERSON, P. J., AUSTIN, N. C., HOWARD, K., & INDER, T. E. (2006). Neonatal MRI to predict neurodevelopmental outcomes in preterm infants. *New England Journal of Medicine*, 355(7), 685-694.
- YOUNG, S. N. (2002). The ethics of placebo in clinical psychopharmacology: The urgent need for consistent regulation. *Journal of Psychiatry and Neuroscience*, 27(5), 319-321.