COMMENTARY

Grey Matter – The Problems of Incidental Findings in Neuroimaging Research

Nicholas Murphy and Charles Weijer

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Neuroimaging of healthy volunteers can reveal findings unrelated to the research question that are nonetheless medically relevant to participants.[1] Incidental findings commonly arise in research involving magnetic resonance imaging, computerized tomography, and positron emission tomography. Findings range from those of clear medical relevance (e.g., aneurysm) to those of unknown relevance (e.g., Chiari I malformation) to those of negligible relevance (e.g., mastoid fluid). Estimates of the prevalence of incidental findings in neuroimaging research vary widely due to differences in study population, image resolution, expertise of those reviewing scans, and definition of incidental finding. By any measure, however, incidental findings are common, and the ethical conduct of neuroimaging research demands that plans be in place for their management.[2]

Few dispute that a reliable finding of medical import should be disclosed to research participants. When imaging reveals a serious medical condition, researchers must disclose this to the participant so she can seek further investigation and treatment. Whether researchers should actively look for incidental findings, and whether disclosure of incidental findings of uncertain or low medical relevance is morally required is subject to debate.

To date, no consensus has emerged on how to comprehensively manage incidental findings in neuroimaging research. The diversity of study designs, imaging methods, and detectable incidental findings means that researchers are afforded considerable discretion in the application of available guidelines to particular studies. Surveys of neuroimaging researchers suggest that the ethical grey areas around incidental findings are of concern to the scientific community.[3] The development of large-scale population-based neuroimaging studies, such as the UK Biobank and the German National Cohort, highlights the urgency of developing comprehensive ethical guidance for the management of incidental findings.[4]

As Mackenzie Graham, Nina Hallowell, and Julian Savulescu demonstrate in this issue of the *Journal of Law, Medicine & Ethics*, any proposed solution to the problem of incidental findings involves navigating an array of intersecting issues, each characterized by pervasive uncertainty.[5] For brain anomalies of uncertain or low medical relevance, the prevalence, natural history, and harms and benefits of disclosure are unknown.[6] The authors argue that existing autonomy- and beneficence-based proposals for managing incidental findings answer the easy questions, but do not — and, indeed, cannot — answer the hard questions. For incidental findings of unknown or low import "whether disclosure is likely to benefit the participant, and moreover, whether this benefit is outweighed by the potential harms of disclosure, is often uncertain."[7] And while disclosure of an incidental finding of a serious medical condition will promote the autonomy of research participants by providing them with information they can

Nicholas Murphy, Ph.D., *Postdoctoral Fellow, Departments of Philosophy and Medicine, Western University.* **Charles Weijer, M.D., Ph.D.**, *Departments of Medicine, Epidemiology & Biostatistics, and Philosophy, Western University.*

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act on, it is not clear — from first principles at least — whether disclosing an incidental finding of uncertain medical relevance will enhance a particular participant's capacity for self-determination. "The problem," they conclude, "is that in many cases, the requirements of beneficence and autonomy are indeterminate."[8]

Graham and colleagues shed light on these grey areas of neuroimaging research by exploring what participants are owed as a matter of distributive justice. Building on the work of Douglas Mackay,[9] the authors maintain that the state cannot ethically authorize its agents to act in ways which prevent them from fulfilling the obligations of distributive justice, e.g., to provide access to basic healthcare to all citizens. For this reason, researchers whose work is sponsored directly or indirectly by the state "must carry out their research in a way that is consistent with this obligation, and not deprive research participants of the care to which they would normally be entitled outside the context of research."[10] In other words, the medical care to which research participants have a right is determined by the care owed to any citizen. Since neuroimaging of asymptomatic people is not a part of basic healthcare, Graham and colleagues conclude that researchers have no obligation to look for incidental findings, nor to disclose any but those of medical import.

The authors' view describes a principled method through which researchers can determine their obligations to research participants, and which offers a welcome level of clarity for the hard cases presented by neuroimaging research. Nonetheless, we have two reservations about their proposal.

First, in exploring the implications of their argument, Graham and colleagues speculate on how to deal with changes to the requirements of basic care in the context of evolving health care practices. If neuroimaging were to become a part of routine screening of healthy citizens, what would this mean for long-term studies whose initial consent documents stipulate that no incidental findings will be disclosed to participants? The authors "tentatively suggest that because the obligations of researchers depend on the standard of care in the wider health system, a significant change in the standard of care would require a shift in disclosure policy."[11] However, they then go on to describe countervailing considerations (e.g., the burdens on researchers from re-consenting participants) that, they suggest, would undermine these requirements. We wonder why this conclusion is only tentative, and indeed how these considerations could trump participants' access to what they are entitled to as a matter of basic care. The authors' argument entails that what someone has a right to is dynamic, and not a function of a consent document written years previously.

Second, and more problematic, is that while the authors demonstrate that researchers have a positive duty to participants, this is not a baseline from which they are free to depart. Rather, the proposal's logic suggests that it would be *impermissible* for researchers to disclose incidental findings of uncertain or low medical relevance. Graham and colleagues argue that researchers have justice-based obligations to society that are additional to those they have to participants. Since researchers are obligated to act in a way consistent with the state's duty to provide basic care to all citizens, disclosing an incidental finding of unknown consequence could trigger follow-up testing that would distort the just distribution of scarce health care resources. That is, "an increase in participants being referred to primary care for further assessment of incidental findings places a significant burden on the wider health system, and potentially deprives other patients who are entitled to care."[12]

We question whether researchers would welcome these limitations on their discretion. Researchers are required to protect the agent-relative interests of participants.[13] The authors rightly note that the distributive justice-based obligations of researchers "are

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in addition to their natural and professional obligations."[14] By imposing stringent antecedent conditions on the discretionary powers of researchers, the justice-based approach may come into conflict with the fiduciary obligations some have argued are inherent in the researcher-participant relationship.[15] While there is no obligation to actively look for or disclose incidental findings of uncertain or low medical import, there may yet be circumstances in which researchers feel compelled to do so for particular reasons, and this ought to be permitted.[16]

Graham, Hallowell, and Savulescu's proposal is a welcome — and largely compelling — contribution to the debate on incidental findings in neuroimaging research, one which offers a compass to help researchers navigate this ethical terrain. Yet, while the authors may be right that "[d]eferring to researcher judgement may be appropriate in individual cases, but it is not an appropriate standard for determining a general policy of disclosure…,"[17] we worry that their proposal solves one problem — uncertainty over researcher obligations in neuroimaging research — while introducing another: an unwarranted limitation on researchers' discretion. We hope that room can be found for researcher judgement regarding incidental findings of uncertain or low medical relevance.

Note

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6. See Wolf et al., *supra* note 1; Medical Research Council, *supra* note 2.
7. Graham, *supra* note 5.
8. Graham, *supra* note 5.
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13. See P.B. Miller and C. Weijer, "The Trust-Based Obligations of the State and Physician–Researchers to Patient-Subjects," *Journal of Medical Ethics* 32, no. 9 (2006): 542–547.
14. Graham, *supra* note 5.
15. See P.B. Miller and C. Weijer, "Fiduciary Obligation in Clinical Research," *Journal of Law, Medicine & Ethics* 34, no. 2 (2006): 424-440.
16. For example, some researchers may be moved by empirical evidence demonstrating that most research participants want to be informed of incidental findings, regardless of medical relevance. See, e.g., J.P. Phillips, C. Cole, J.P. Gluck, J.M. Shoemaker, L.E. Petree, D.L. Helitzer, R.M. Schrader, and M.T. Holdsworth, "Stakeholder Opinions and Ethical Perspectives Support Complete Disclosure of Incidental Findings in MRI Research," *Ethics & Behavior* 25, no. 4 (2015): 332-350.
17. Graham, *supra* note 5.

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