ASK THE NEURO-ETHICIST

Should Patients in Disordered States of Consciousness Be Enrolled in Research? How to Decide

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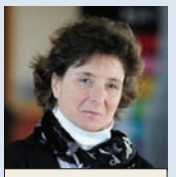
Thirty-four-year-old Sally Smith has been in a minimal state of consciousness (MCS) for approximately eight months after suffering a severe traumatic brain injury (TBI). She sustained multiple intracerebral, bilateral subarachnoid, and subdural hemorrhages in a head-on motor vehicle collision. Initially in a coma, in the early weeks after her injury Smith began to show some minimal responses during examination. She would at times track objects or faces with her eyes and on a few occasions was seen to move her right arm purposely towards an object held in her visual field. Family members also reported Smith occasionally smiled when spoken to by loved ones. She did not follow commands and the majority of the time when examined, did not show any responsiveness. Brainstem reflexes were intact and she had increased tone in all extremities. Both plantar responses were upgoing and reflexes brisk. Over the last eight months she has shown no further improvement and her neurological exam has remained stable. Repeat imaging has shown evolution of her hemorrhages with no new lesions.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The medical center near the rehabilitation facility where she receives full care has recently launched a research program that uses functional MRI to detect signals of consciousness and has been testing this line of research with less expensive, more portable EEG. As readers of *Neurology Today* will surely know, the question of whom to enroll in these studies and on what basis enrollment should be decided can be a vexing one [see "A More Portable EEG Used to Assess Consciousness in Patients in Vegetative State," in the Dec. 1, 2011, issue: http://bit.ly/yK30H2]. Should enrollment be based on advanced directives? On the principle of best interest? On substituted judgment? The researchers will have to work this out as their institutional review board can be fussy about the choice of ethical framework and will require a clear articulation and justification of the chosen approach.

In the best-case scenario, the decision to enroll Smith would be made based on a research advanced directive put in place when Smith was competent. But this is perhaps the easiest option to dismiss since it is unlikely that such a directive exists. While there is a growing literature on research advance directives, few are applied today. Most of the discussion has focused on dementia research. In one paper, published in 2002 in the journal *Ethics and Human Research,* the author argued that research advance directives promote autonomy and protect subjects and personal identity in the face of dynamic, progressive disease. Outside of the dementia context, however, a 2005 study in the *American Journal of Psychiatry* reported that little more than 10 percent of prospective participants complete a research advance directive. Furthermore, these results are based on participation in studies at NIH clinical centers, where one would expect a higher completion rate than that in the general population. Given these numbers, it is safe to assume that Smith does not have a research advance directive.

The next best-case scenario would be to use the principle of substituted judgment, described in a 2011 paper in the *Journal of Clinical Ethics*. The decision to enroll the patient would be made as if the decision-maker were the patient — what would Smith have decided to do when she was competent? A next-of-kin surrogate decision-maker, for example, would make the best guess as to what Smith would have wanted in her current situation, based on her knowledge of Smith's values prior to the injury.

There is good reason to argue that this is the principle to invoke. On the one hand, the risks and harms to Smith are minimal, especially since she will have had multiple neuroimaging exams already as part of her routine clinical work up. The research scan could be thought of as an extension of the physical exam and other clinical investigations. The patient has been in the hospital and health care system for some time now in this state, so the substituted judgment has likely already been involved in all decisions up to this point.

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But how likely is it that the surrogate decision-maker would know whether Smith would have consented to participating in the research study? In the absence of a research advance directive, it would be hard to make that decision. The person who has to decide may feel pressure to invent patient preferences and may not be able to separate emotionally from the effect that research may have on this individual and their family. Furthermore, since the implications of this research for communication, long-term prognosis, care, and end-of-life decision-making remain unresolved, surrogate decision-makers may not be in a position to make meaningful judgments.

The third approach is to use the principle of best interest discussed in the 1983 *Journal of Medical Philosophy* and elsewhere: the decision to enroll Smith in the neuroimaging study would be made on her behalf by a surrogate decision-maker who must decide whether the research will benefit the patient in some way. As we suggested in the case description, research using fMRI has been yielding positive results of what are interpreted as signals of consciousness in the roughly 17 percent of the clinically vegetative patients shown to be responsive with fMRI, and 3 percent of the clinically MCS patients, according to a 2010 paper in the *New England Journal of Medicine*. More recently, with EEG, 19 percent of clinically vegetative patients and 31 percent of clinically MCS patients have been shown to be responsive, according to a 2011 paper in *The Lancet*. Importantly, 15 of these were TBI, like Smith, and of those 15, 47 percent were responsive. The data thus suggest possible benefit to Smith. However, there remain plenty of questions about what to do with the positive

This hypothetical case was debated among neurology residents, faculty, and neuroethics trainees during a clinical neuroethics program devoted to the topic of neuroimaging and MCS in November 2011. We thank all participants, and are especially grateful to special guest Adrian Owen, PhD, Canada Excellence Research Chair in Cognitive Neuroscience and Imaging at the University of Western Ontario, and Marleen Eijkholt, PhD, and James Anderson, PhD, at the National Core for Neuroethics, University of British Columbia, for their leadership on the debate material and participation.

information, and researchers currently conducting these studies are cautious to assert that a negative research result is not necessarily prognostically negative. Therefore, it is not clear that the best interest principle is the most suitable path for the researchers to follow.

So, where do the researchers go from here? We argue for harnessing the complementary strengths of two principles — a decision for enrollment can be based on what the patient might be known to have wanted (substitute judgment) and what would benefit her (best interest). Researchers and proxies can support this strategy by sharing the decision-making and maintaining an open dialogue about the risks and benefits, hopes, and hype. Indeed, it is likely that both principles have already been invoked in Smith's case where next of kin, as well as other health care professionals, have been working together to make decisions on her behalf.

Meanwhile, as the knowledge around imaging and MCS advances, researchers will need to attend ever more acutely to the host of ethical issues that are arising alongside the science. We have yet to uncover and understand the full range translational demands and interests of society, health care systems, and policy-makers about the management of patients in this historically marginalized population.•

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