Commentary

# *Commentary: Further Considerations in Using Functional Neuroimaging in Patients with Disorders of Consciousness*

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In this issue of *Neuroethics*, Mackenzie Graham and colleagues analyze the ethical hazards that must be navigated by physicians who consider ordering functional neuroimaging in patients with disorders of consciousness (DOC).[1] The authors offer ethically sound and clinically useful guidance. First, they clarify that functional neuroimaging paradigms, such as functional MRI (fMRI), remain research tools of unproven value in DOC patients. They emphasize physicians' singular duty to clearly and accurately communicate with surrogate decisionmakers. They explain the complexities of surrogate consent in DOC patients given the inherent ambiguities in diagnosis and prognosis. They show how harms to patients could result if these tools were used inappropriately, interpreted incorrectly, or communicated unclearly. In my commentary, I pursue several aspects of their analysis that I believe merit further elaboration.[2]

The current diagnostic nosology of DOC is based upon fulfilling criteria for a clinical syndrome. Syndromic diagnostic classification requires determining the presence or absence of certain qualifying signs.[3] For example, vegetative state (VS or unresponsive wakefulness syndrome) requires the absence of any evidence of awareness of self and environment plus the presence of cycles of eyes-closed-sleep and eyes-open-wakefulness. Because syndromes are diagnostic categories within which patients share certain features, they contain cases spanning a spectrum of severity and of diverse pathologies. As a consequence, each syndrome comprises a heterogeneous mixture of cases that, while sharing certain common essential features, are often vastly different.

A critical question for surrogate decisionmakers about treatment of the DOC patient is the prognosis for recovery of awareness. Given the assortment of differing pathologies and severities of cases encompassed within each syndrome, it is no surprise that prognosis correlates more closely with specific patient factors—such as underlying pathology, location and size of brain lesions, age, and chronicity—than it does with the mere membership in a diagnostic syndrome.[4] Thus, physicians determining prognosis must individualize each patient, and assess and weigh a unique combination of factors. Because of data limitations, physicians usually can provide only a statistical prognosis for recovery of awareness. Although a statistical pronouncement frames prognosis most accurately, it is often unsatisfying for surrogates and family members who desire greater specificity about what recovery to expect. Physicians must explain why their ability to prognosticate individual cases specifically is not possible, and share with surrogates the reasons for the limitation to their knowledge.[5]

Graham and colleagues pointed out that surrogates' interpretation of functional neuroimaging in DOC patients may be erroneous. This inaccuracy is compounded by the formidable technical challenges to physicians in obtaining consistent

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and reliable fMRI blood-oxygen-level-dependent (BOLD) signals in diffusely brain-injured patients. As Bardin and colleagues showed, fMRI testing paradigms produced much more consistent and reliable BOLD signals when normal volunteer research subjects were tested than when actual DOC patients were tested.[6] The presence of diffuse or multifocal brain damage impairs DOC patients' ability to generate the signals measured in the fMRI paradigms. Moreover, DOC patients' BOLD signals often vary from hour to hour and day to day because of the interposition of fluctuating metabolic and toxic factors that are common in critically ill patients but uncommon in healthy volunteers.[7]

Graham and colleagues thoughtfully describe the complexity of surrogate decisionmaking in DOC patients. One additional factor is the intrinsic limitation of accuracy of surrogate decisionmaking in any circumstance. Typically, the substituted judgment standard is used, in which the surrogate is asked to attempt to reproduce the exact decision the patient would have made if such were possible. Although this standard is sound ethically and legally, it produces inaccuracies. In the largest meta-analysis of the accuracy of substituted judgment, comprising 16 published studies totaling nearly 20,000 surrogate-patient pairs, the authors found an accuracy rate of only 68%.[8] Because approximately one-third of surrogate decisions purportedly made to follow the wishes of the patient were erroneous, prevailing standards of surrogate decisionmaking impart irreducible error. In my clinical experience with hundreds of DOC patients, I find that, given the uncertainties and statistical nature of prognosis, most surrogates understandably prefer the "treat, wait, and see" approach, rather than to make an early decision to discontinue life-sustaining therapy, especially in young patients.[9]

'Collaborative communication' is the term Graham and colleagues used to describe the ideal blending of physician opinion and surrogate preference in shared decisionmaking. They mentioned that physicians' personal values and biases about treatment in DOC patients can influence conversations with surrogates over decisions to continue or withdraw life-sustaining therapy. Physician bias exerts its negative effect through framing, that is, in *how* physicians present data on prognosis and disability. The power of framing in physicians' influence on surrogate decisions is well known. This effect can be harmful when negatively biased framing unjustifiably manipulates the surrogate into discontinuing treatment in the DOC patient.[10]

Graham and colleagues' analysis focused on surrogate decisionmaking for DOC patients. But additionally, there may be a limited direct role of the DOC patient. In a few reported instances, DOC patients with covert consciousness have been taught to communicate using separate ideational motor fMRI paradigms to indicate "yes" and "no" responses. In these cases, the DOC patient's communication predicament is analogous to that of the locked-in syndrome patient for whom communication is limited because of profound paralysis. But a vocabulary restricted only to a "yes" or "no" fMRI response has the same limitations for patient medical decisionmaking as it does for the patient in the locked-in syndrome. Most physicians would be loath to withdraw life-sustaining therapy based solely on a patient's "yes" or "no" response to a question without having the opportunity to engage the patient in a detailed conversation to assure that the "yes" or "no" response indicated a rational and informed decision.[11]

A final additional point is to emphasize the importance of neuropalliative care of the DOC patient. Whether or not the patient has demonstrated the presence of

covert consciousness, assiduous control of pain and potential suffering should be an essential neuropalliative element of every medical care plan.[12]

## Notes


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2. For further discussion and references on these issues, see Bernat JL. The medical practice impact of functional neuroimaging studies in patients with disorders of consciousness. In: Monti MM, Sannita WG, eds. *Brain Function and Responsiveness in Disorders of Consciousness*. Heidelberg: Springer; 2016, at 157–69.
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4. Bernat JL. Prognostic limitations of syndromic diagnosis in disorders of consciousness. *American Journal of Bioethics: Neuroscience* 2016;7(1):46–8.
5. Bernat JL. Ethical aspects of determining and communicating prognosis in critical care. *Neurocritical Care* 2004;1:107–18.
6. Bardin JC, Fins JJ, Katz DI, Hersh J, Heier LA, Tabelow K, et al. Dissociations between behavioural and functional magnetic resonance imaging-based evaluations of cognitive function after brain injury. *Brain* 2011;134:769–82.
7. Rohaut B, Eliseyev A, Claassen J. Uncovering consciousness in unresponsive ICU patients: Technical, medical and ethical considerations. *Critical Care* 2019;23:78. https:/doi.org/10.1186/s13054-019-2370-4.
8. Shalowitz DI, Garrett-Mayer E, Wendler D. The accuracy of surrogate decision makers: A systematic review. *Archives of Internal Medicine* 2006;166:493–7.
9. See note 5, Bernat 2016.
10. Fins JJ, Bernat JL. Ethical, palliative, and policy considerations in disorders of consciousness. *Neurology* 2018;91:471–5.
11. Bernat JL. Medical decision-making by patients in the locked-in syndrome. *Neuroethics* 2018. epub, published online. https://doi.org/10.1007/s12152-018-9358-7.
12. See note 10, Fins, Bernat 2018.