

ETHICS CASE

Neuroethics and Disorders of Consciousness: Discerning Brain States in Clinical Practice and Research

Commentary by Joseph J. Fins, MD

Abstract

Decisions about end-of-life care and participation in clinical research for patients with disorders of consciousness begin with diagnostic discernment. Accurately distinguishing between brain states clarifies clinicians' ethical obligations and responsibilities. Central to this effort is the obligation to provide neuropalliative care for patients in the minimally conscious state who can perceive pain and to restore functional communication through neuroprosthetics, drugs, and rehabilitation to patients with intact but underactivated neural networks. Efforts to bring scientific advances to patients with disorders of consciousness are reviewed, including the investigational use of deep brain stimulation in patients in the minimally conscious state. These efforts help to affirm the civil rights of a population long on the margins.

Case

Sam had been driving his SUV when his car skidded on ice as he crossed the bridge around the corner from his apartment. The car tumbled over the guardrail and landed in the icy river below, causing Sam to lose consciousness. The first responders estimated that Sam had spent at least ten minutes underwater before two civilians were able to remove him from the car and pull him to the riverbank. The civilians immediately began CPR, but Sam never regained consciousness after the incident.

Sam's parents refused to give up hope and decided to send him to a rehabilitation center. One day while searching online for studies on persistent vegetative state (PVS) patients, Sam's mother came across a study that examined new ways to communicate with patients. The researchers had discovered that some PVS patients were actually in a minimally conscious state (MCS) and could communicate with the researchers with the right technology.

Molly was a bright neurology resident who had decided to take a research year while preparing her application for a fellowship. She had chosen to work on the MCS project after seeing families struggle with end-of-life decisions for PVS and brain-dead patients.

When she witnessed her mentor use the team's technology to interact with a patient who had been considered to be in PVS for the past five years, she was hooked.

Despite the breathtaking nature of their technology, however, the team members didn't pretend to be miracle workers. They realized their technology was still in its infancy and would require thorough testing before it could be implemented across the country. Until then, use of the technology adhered to strict rules. It could only be used to elicit yes or no answers from the patients to questions that were limited to a specific list: *Is the sky blue? Is the grass purple?* The researchers didn't want to ask anything serious that could potentially upset the study's participants.

Molly's mentor thought that Sam would be an ideal participant for the study. He had been a young healthy adult in his prime at the time of the accident, which had also occurred less than a year ago. The entire team was optimistic going into the testing session.

As Sam was wheeled into the testing room, his mother pulled Molly aside. "I know you're only supposed to ask him specific questions, but can you ask him if he wants all of this?" she asked. "Can you ask if he's in pain? Does he want us to keep providing care?"

Commentary

Before responding to whether a patient with a disorder of consciousness—a condition subsuming coma, the vegetative state, and the minimally conscious state (MCS) [1]—should be enrolled in a clinical trial or withdrawn from life support, we need to define relevant terms and be precise in our queries. The case concerns a patient who was thought to be in a persistent vegetative state but who might be in a minimally conscious state—two distinct conditions that are too often confused [2]. The case raises a number of ethical questions: Do we need to differentiate between patients who are in the vegetative versus the minimally conscious state when providing care to or withdrawing life support from patients? Is it ethical for someone who cannot give consent to participate in research? To answer these questions, we need to be clinically precise and differentiate these two brain states. As the old adage goes, good ethics begins with good facts.

Distinguishing Between the Vegetative State and the Minimally Conscious State

The persistent vegetative state was first described by the Scottish neurosurgeon Bryan Jennett and the American neurologist Fred Plum in a landmark 1972 article published in the *Lancet*. They described it as a "syndrome in search of a name" and characterized the condition as a paradoxical state of "wakefulness without awareness" in which the eyes are open but there is no awareness of self, others, or the surrounding environment [3]. Physiologically, patients in the vegetative state have an intact brain stem but no higher

integrative functions. They can maintain respiration and cardiac function, have sleep-wake cycles, and demonstrate a startle reflex [4].

Clinically, the vegetative state can be quite disconcerting and prone to misconstrual. Families naturally assume that the eye-opening, which marks the transition from coma to the vegetative state, indicates awareness and ability to interact with others. Because this is not the case in a patient who is vegetative, the realization can bring devastating disappointment, requiring sympathy and guidance from practitioners.

The vegetative state came to international prominence in the 1976 right-to-die case of Karen Ann Quinlan, a young woman in the vegetative state whose parents requested that she be taken off her ventilator when she did not regain consciousness [5]. Chief Justice Richard J. Hughes of the New Jersey Supreme Court asked Dr. Plum to serve as a court-appointed expert witness, where he confirmed the vegetative state diagnosis. Based upon his testimony, the court allowed for the removal of Ms. Quinlan's ventilator because there was "no realistic possibility of returning to any semblance of cognitive or sapient life" [6]. When the ventilator was removed, Ms. Quinlan survived, for a number of years, maintaining respiration with an intact brain stem. Dr. Plum, who was my teacher, told me he knew this would occur [7]. He had done an apnea test as part of his court-sanctioned neurological exam to assess brain stem function and differentiate the vegetative state from whole brain death [8]. To her parents and to members of the general public, however, Ms. Quinlan's survival was unexpected and suggested some important points of ethical and clinical relevance about what clinicians can do to help manage family members' expectations about loved ones in conditions like Ms. Quinlan's.

A Clinical Distinction that Makes an Ethical Difference

When the vegetative state was first described, it was only spoken of as the persistent vegetative state, but the nomenclature was updated in a 1994 Multi-Society Task Force report published in the *New England Journal of Medicine*: a vegetative state becomes persistent if it lasts for a month and permanent if it continues three months after anoxic injury and a year after traumatic injury [9, 10].

The prognosis for anoxic brain injury following the use of therapeutic hypothermia, when chilled intravenous saline is administered as a neuroprotective following a cardiac arrest, is evolving [11]. Therapeutic hypothermia was not administered to the patient in the present case, but his submersion in icy cold water following his car accident may have had a similar neuroprotective effect. This variable would need to be considered in his evaluation. Indeed, in assessing for brain death, patients who are hypothermic need to be warmed *before* they can undergo evaluation of brain stem function [12].

Returning to the categorization of the vegetative state, the distinction between persistence and permanence is critical because, until the vegetative becomes

permanent, patients can migrate into the MCS, a brain state introduced into the literature in 2002 [13]. Unlike the vegetative state, MCS is a state of consciousness. Patients in MCS can demonstrate intention, attention, and memory. They can track a loved one who enters the room, grasp for a cup, or even say their own name. Given the crucial difference between persistent and permanent vegetative states, we should strive for semantic clarity and abjure the confusing abbreviation *PVS*, which could indicate persistence or permanence. “PVS” may be the most dangerous abbreviation in all of medicine. As a philosopher might say, the distinction between the persistent and permanent vegetative state is a distinction that makes a difference.

Diagnostic Challenges

Beyond the relevance of the distinction between the persistent versus the vegetative state, the diagnosis of MCS is complicated by the fact that behaviors, which might indicate consciousness in the MCS patient, are manifested episodically and intermittently. As such, they can be missed.

When families report a behavior that might suggest consciousness, their claims can be discounted by clinicians as wishful thinking or evidence of deep denial [14]. For example, family members might sometimes see a loved one occasionally look up when they enter the room. Clinicians unschooled in these nuances do not expect patients labeled as “vegetative” to demonstrate evidence of consciousness. Families’ observations to the contrary might be doubted by clinicians because they seem to defy the diagnostic fixity of the vegetative state and what seemed to be an authoritative diagnosis made upon discharge from the hospital.

The problem with this formulation is that these conditions are not fixed diagnoses but rather brain states that can evolve in a way that defies recognition. While a patient discharged from the hospital with diabetes will not shed the diagnosis over time, patients who are discharged as being in the persistent vegetative state can evolve into the minimally conscious state. This evolution, coupled with the episodic demonstration of behaviors, which might indicate consciousness, can have implications for the accuracy of clinical assessment. Indeed, a startling paper found that 41 percent of traumatic brain injury patients in chronic care facilities who were thought to be vegetative were in fact in MCS when assessed with bedside neuropsychological testing [15, 16]. In other words, these patients appeared vegetative but were in fact minimally conscious.

The possibility that MCS patients might appear as if they were in a vegetative state is explained by the biology of the two conditions. In contrast to patients who are vegetative, those who are in MCS have intact neural networks [17, 18]. When these networks are inactive, the patients appear to be vegetative, but when the networks are activated, these patients can demonstrate evidence of consciousness either behaviorally or, as we shall see, on [neuroimaging](#) without an overt behavioral correlate [19].

Ethical Deliberation under Conditions of Clinical Uncertainty

In the case described above, the patient, Sam, has an ambiguous history. The case suggests both traumatic and anoxic brain injury from submersion of “at least ten minutes.” Generally, anoxia of this duration results in brain death, so perhaps the patient floated above the surface or benefited from the neuroprotective hypothermia of the ambient icy river water, as discussed above [11]. We just don’t know. As previously discussed, initial emergency care would need to warm the patient, since hypothermia is a contraindication to brain death testing [12].

The etiology of Sam’s brain injury is a critical part of his clinical history since traumatic brain injury (TBI) has a more favorable outcome than an anoxic injury [12]. This prognostic distinction is evident in the story of Don Herbert, a fireman who sustained anoxic injury in a house fire when his head was struck by a falling rafter [20]. He was initially communicative and then appeared vegetative. He spoke again nine years later, seemingly defying both what was thought to be a permanent vegetative state and the sequelae of anoxic brain injury. In retrospect, it became clear that Herbert had been in the minimally conscious state all those years and that his predominant injury was more traumatic than anoxic. Although he did sustain smoke inhalation, it was tempered by his oxygen mask which was askew, but near him when he was rescued. This mitigating factor likely yielded the more favorable outcome of traumatic injury [21].

Covert consciousness becomes the fundamental issue that should undergird our ethical obligations to patients in MCS [22]. First among these is a neuropalliative ethic of care [23], since MCS patients have the potential to experience pain, whereas vegetative patients do not. This creates an ethical mandate both to distinguish these brain states and to address the pain management needs of patients in MCS, who often are thought to be insensate and have invasive procedures done to them *without* proper analgesia. By knowing that a patient is in MCS, a clinician can help ensure that when these patients have potentially painful procedures they receive pain medication.

Research on Patients with Disorders of Consciousness

Returning to the question of how Molly should respond to Sam’s mother’s question about research participation prompts consideration of whether research should be done on patients with disorders of consciousness. Although important, this question is a moot. Research is happening, with a modicum of early success. Neuroimaging studies have further elucidated MCS and demonstrated the possibility of cognitive motor dissociation in which patients who appear behaviorally to be vegetative demonstrate activity on passive and active paradigms with functional studies [24]. In one notable case, neuroimaging was used as a means of functional communication [25]. Pharmacological studies have helped foster, restore, or accelerate recovery into overt demonstrations of consciousness [26, 27].

I was a co-investigator on a study on [deep brain stimulation](#) (DBS) in MCS, which was published in *Nature* in 2007 [28] (I designed the ethical framework for the study [29, 30]). That study introduced bilateral electrodes into the intralaminar nuclei of the thalamus. An MCS participant who could only sometimes communicate with eye movement, was dependent on percutaneous endoscopic gastrostomy feeding, and had poor muscle tone, was able—with stimulation—to say six- or seven-word sentences, recite the first 16 words of the Pledge of Allegiance, go shopping with his mother and voice a preference about clothing, and tell his mother he loved her. He could also eat by mouth for the first time in six years, maintain secretions and masticate, and also sit up with improved tone.

Research in patients with disorders of consciousness was not always accepted, however. Ethically, to get the MCS study done, I needed to justify it as a phase I clinical trial that had only a hypothetical benefit and more than minimal risk to a participant who could not provide consent [30]. As I describe in *Rights Come to Mind: Brain Injury, Ethics, and the Struggle for Consciousness* [29], providing such a justification was seemingly an impossible task, but I made the argument that the risks were proportionate to the benefits, since DBS was vetted as a safe and reimbursed treatment for drug-resistant Parkinson's disease and that analogies to the dark legacy of psychosurgery were ill-placed. Psychosurgery, typified by lobotomy, was crude and ablative and done in an unregulated era [31]. In contrast, DBS for MCS was [neuromodulation](#) and did not destroy tissue. Moreover, unlike the earlier psychosurgery era, the research would be (and was) done with multiple IRB approvals and under a Food and Drug Administration Investigational Device Exemption [28]. Moreover, we chose participants who could be theoretically helped but not incrementally injured by DBS. We identified MCS participants with intact but under-activated networks and those for whom the likelihood of naturally occurring recovery had passed [28-30].

To critics who contended that DBS for patients in the minimally conscious state was unethical, I argued that as a field we were confusing informed consent with the Belmont Report's central ethical principle of respect for persons [29, 32]. It is one thing to do something to people without their consent or over their objections. This would entail a breach of self-determination and a disrespect of persons. It is quite another issue to demand consent from participants who cannot provide it, especially when the object of the intervention is to provide them with a neuroprosthetic that might allow the patient who is in MCS to communicate and participate in decisions that are relevant to them, including the decision of whether to continue therapy [29, 32-34].

Conclusion

So should participants with disorders of consciousness be enrolled in a clinical study? In theory, yes, if there is an appropriate trial with a plausible hypothesis and surrogate authorization. And what about Sam? I am less optimistic about the utility of any

intervention in his case given the more dire prognosis of anoxic injury and the lack of any evidence of minimal consciousness in the case report. The likelihood of restored functional communication would appear low, and it would be important not to foster false expectations and a [therapeutic misconception](#) [35, 36].

My counsel therefore is to be clinically vigilant for signs of improvement, acknowledging that those who are conscious have a civil right to be properly identified, diagnosed, and welcomed back from the exile imposed by injury [29, 37, 38]. With evolving neuroprosthetics, restoration of functional communication is within our grasp for properly identified patients [39, 40]. This is a worthy aspiration for clinical practice and research [41].

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