FROM BIRTH TO DEATH AND BENCH TO CLINIC

THE HASTINGS CENTER BIOETHICS BRIEFING BOOK

for Journalists, Policymakers, and Campaigns

CHAPTER 4

Brain Injury: The Vegetative and Minimally Conscious States

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brain injury: the vegetative and minimally conscious states

by Joseph J. Fins

Framing the Issue

The debate over Terri Schiavo illustrated how questions about severe brain injury became central to the decade's most convulsive bioethics debate. As is well appreciated by anyone who witnessed the events of spring 2005, the Schiavo case divided a family—and much of the nation—over the question of whether it was ethically proper and legally permissible to remove a feeding tube from a young woman in a permanent vegetative state. Could a patient like Terri Schiavo ever recover? And beyond the question of prognosis, is a patient is such a brain state aware? Could she perceive starvation or feel pain?

Responses to questions like these, though decidedly settled in the negative for permanently vegetative patients like Ms. Schiavo, have increasingly become more nuanced in light of new evidence about severe brain injury and how the injured brain recovers. The advent of new diagnostic categories to describe both the severity of brain injury and its time course complicates questions about prognosis and perceptual awareness. Differences between these categories, or brain states, have ethical implications for patient care, scientific research, and public policy.

Terminology: Defining Different Brain States

Much to the confusion of lay readers, there are a host of newly defined brain states (and their acronyms, such as MCS and MCS-e) beyond the ubiquitous but still confusing PVS, or persistent vegetative state. These categories for different disorders of consciousness have both clinical and ethical implications.

The persistent vegetative state was first described in 1972 by the Scottish neurosurgeon Bryan Jennett and the American neurologist Fred Plum. In a landmark article in the British journal *The Lancet*, they described PVS as a state of "wakeful unresponsiveness" in which the eyes are open, but there is no awareness of self or others. Patients who are vegetative do not have cognitive or higher brain functions, such as the ability to think and reason. But they do have autonomic ones, such as the direction of cardiac and respiratory function and sleep-wake cycles, which originate in the brain stem—the lower part of the brain just above the spinal cord. Vegetative patients may also have a startle reflex, but this behavior is not intentional and involves only brain stem

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HIGHLIGHTS

- Not long ago, patients with severe brain injury and no apparent consciousness were presumed to be in a permanent vegetative state, without hope of recovery.
- New evidence shows that some of these patients are, in fact, misdiagnosed and actually minimally conscious, that they may comprehend speech, and that they may be able to, and occasionally do, speak and gesture.
- Unlike patients such as Terri Schiavo, who was in a permanent vegetative state, patients in the minimally conscious state can sometimes recover, even after a decade or more. Research suggests that they may also respond to experimental interventions.
- Differences between brain states have ethical implications for patient care, scientific research, and public policy.
- Distinguishing the vegetative state from the minimally conscious state requires careful clinical evaluation. As yet, no neuroimaging tools can make this distinction.

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activity.

As was evident in the Schiavo case, the vegetative state remains a disquieting one. It defies normal expectations about awareness and consciousness. Usually when the eyes are open there is awareness, but in the vegetative state a patient is stripped of ability to interact with others or the environment.

The vegetative state is often confused with a coma by nonclinicians. This is an important error to correct. Although comatose and vegetative patients are unresponsive and unarousable, there are important differences. Coma is an eyes-closed state, while the vegetative state is an eyes-open one. Moreover, coma is the initial presentation of severe brain injury and is self-limited, usually lasting a couple of weeks. A coma can progress in a number of ways, from brain death to complete recovery. The most ominous of comas progress to brain death, defined as the death of the whole brain, including brain stem and higher brain functions. Brain death is recognized as the equivalent of cardiopulmonary death in all states, although a couple of states allow for a religious or moral objection to this neurological definition of death.

Comatose states can also evolve into a vegetative state. A vegetative state is labeled as persistent once it lasts more than a month. It is considered permanent after three or 12 months, depending upon the nature of the initial injury. If the injury is from anoxia, or oxygen deprivation, as would be the case in a cardiac arrest or drowning accident, a vegetative state persisting for three months is considered permanent. In contrast, a vegetative state resulting from a traumatic brain injury, such as from a motor vehicle accident or a fall, would need to last for 12 months in order for it to be designated as permanent.

The different time courses to a permanent vegetative state relate to the nature of the injury. The potential for recovery for a traumatically injured brain exceeds that of the anoxically injured brain. This differential degree of recovery from anoxic injury helps explain why it takes longer for clinicians to conclude that a traumatic injury has resulted in a permanent vegetative state.

If a vegetative state has yet to become permanent, a patient may move into what has been described as minimally conscious state. MCS is a new clinical designation that has its origins in the Aspen Criteria published in the journal *Neurology* in 2002. Unlike the vegetative state—with which MCS may be confused—MCS is a state of consciousness. MCS patients demonstrate unequivocal but

Neuroimaging and Disorders of Consciousness

Diagnostic precision and intellectual honesty are important when we consider the biological underpinning of the minimally conscious state and emergence from MCS. Neuroimaging techniques may hold promise in improving diagnosis, although their use at this writing remains investigational. Consider the case of Terry Wallis, who was in an MCS state for 19 years. Studies using a functional magnetic resonance imaging (fMRI) technique called diffuse tensor imaging (DTI) by my colleagues at Weill Cornell Medical College revealed changes in his brain two decades after injury. Their study described "axonal sprouting"—or new connections between existing neurons—which may have had something to do with his late recovery from the minimally conscious state.

Other imaging studies from Weill Cornell Medical College and Columbia University have demonstrated the capability of minimally conscious brains to activate a widely distributed functional language network on imaging studies when exposed to spoken narratives. These studies suggested that the MCS patients retain the capability to process language and semantic content. This capability may even be retained in vegetative patients who have yet to reach the permanent vegetative state. A highly provocative 2006 study from the University of Cambridge in the United Kingdom, using another language paradigm, demonstrated the ability of a patient in the vegetative state to activate integrated networks. The patient had sustained traumatic brain injury five months earlier (so the vegetative state was not yet permanent).

In findings reported in *Science*, the patient was able to activate networks in the brain when asked to imagine walking in her home, playing tennis, or parsing linguistically ambiguous phrases. My colleague and I suggested in the *Hastings Center Report* that this patient was in a nonbehavioral MCS state as she responded to her environment with normal language and spatial brain networks, as evidenced by the flares identified on neuroimaging. At 11 months the patient was clearly engaging in behaviors that indicated she was in MCS, and two years after injury she was speaking, suggesting that what was seen on neuroimaging at five months was likely evidence of her transitioning from the vegetative to minimally conscious states.

While these data are intriguing, it is important to caution against viewing any of these neuroimaging modalities as anything but investigative tools. They have yet to be validated outside of the research context, and it is the consensus in the research community that it would be premature to disseminate them into routine clinical practice for the assessment of patients.

fluctuating evidence of awareness of self and the environment. They may say words or phrases and gesture. They also may show evidence of memory, attention, and intention. However, these behaviors may be fleeting. The inability to reproduce telltale signs of awareness is part of the biology of MCS and an expected and confounding part of the clinical picture.

A patient who reaches the minimally conscious state before becoming permanently vegetative is open to a degree of prognostic uncertainty about the possibility of further cognitive recovery. The prognosis can be fixed or open-ended, with rare occurrences of dramatic recoveries and emergence from MCS years and decades after injury.

Patients who have regained the ability to consistently engage with others and who reestablish functional communication are considered to have emerged from MCS. Emergence from MCS is taken to be the consistent and reproducible recovery of consciousness and an awareness of self, others, and the environment. In the last few years, there were two well-known cases of emergence from MCS in the United States.

Arkansan Terry Wallis emerged from MCS in 2003, bringing international media attention to this phenomenon against the backdrop of the evolving Schiavo saga. Wallis regained fluent speech after lingering for some 19 years in a nursing home after sustaining traumatic brain injury in a motor vehicle accident. During that time he had been labeled erroneously as being in a coma or vegetative state, although he was most certainly minimally conscious and recovered fluent speech from that prognostic milestone. In July 2003, he began to speak. His first words were "mom" and "Pepsi." In his mind it was still 1984, and Ronald Reagan was still president.

Another compelling case of emergence from MCS involved Don Herbert, a Buffalo firefighter. Herbert was injured in a 1995 fire, sustaining a mix of traumatic and hypoxic brain injury. For the first few months after his injury he met the criteria for MCS with occasional and episodic signs of awareness and verbalizations. For the next nine years he lingered, presumed to be vegetative, until he spontaneously regained fluent speech in 2005, emerging after a number of psychoactive drugs were given to him by a physiatrist.

On the Horizon: Towards Therapeutics for Severe Brain Injury

Taken together, neuroimaging data and other findings indicate that patients with severe brain injury may sustain late recoveries and that even severely injured brains may harbor residual functional capacity. Our group at Weill Cornell Medical College, along with colleagues at the Cleveland Clinic Foundation and JFK-Johnson Rehabilitation Center in New Jersey, are conducting a clinical trial using deep brain stimulation in the minimally conscious state.

Our results—the first to demonstrate that deep brain stimulation in MCS can promote late functional recovery after traumatic brain injury—were published in *Nature* in August 2007. We implanted electrodes, such as those used routinely to treat drug refractory Parkinson disease, into the brain of a 38-year-old man who had been in MCS for six years after traumatic brain injury. Prior to the study the subject was unable to eat without a feeding tube or to communicate reliably.

The procedure resulted in statistically validated improvements in cognitively-mediated behaviors, as well as the ability to eat by mouth and to control motor activity. The subject has regained the ability to communicate in six- to seven-word sentences when prompted and to interact more fully and consistently with his family.

Distinguishing the Vegetative and Minimally Conscious States

Invariably, people asked how Terry Wallis or Don Herbert could recover when experts were so definitive in asserting that Terri Schiavo was permanently unconscious. The answer to these questions is found in the diagnostic categories just reviewed and in the important biological differences between the permanent vegetative state of Schiavo and the minimally conscious states of Wallis and Herbert. Unlike patients in the permanent vegetative state, patients who are in MCS have preserved brain networks that retain the potential for activation. Both Wallis and Herbert emerged from their long period of quiescence from the minimally conscious state, not from the vegetative state. They each had reached MCS before the vegetative state became permanent, thus retaining the potential for additional recovery. While such dramatic recoveries are uncommon and should not be overstated, they should not be entirely discounted.

Because of the biological and prognostic differences between the minimally conscious and the permanent vegetative states, it is critical that these

RESOURCES

Web sites

- www.biausa.org – the Brain Injury Association of America. Includes relevant policy and legislation, research, links, and a bookstore.
- www.braintrauma.org – the Brain Trauma Foundation. Includes news, statistics, educational materials, and resources.

Recent news

- Timothy Gower, "Fatal Flaw," *Boston Globe*, March 9, 2008.

Rob Stein, "Technique May Revive Head Injury Victims," *Washington Post,* October 16, 2006/

- Benedict Carey, "Mental Activity Seen in a Brain Gravely Injured," *New York Times*, September 8, 2006.

Further reading

- Nicholas D. Schiff et al., "Behavioural Improvements with Thalamic Stimulation after Severe Traumatic Brain Injury," *Nature,* August 2, 2007.
- Joseph J. Fins et al., "Late Recovery from the Minimially Conscious State: Ethical and Policy Implications, " *Neurology,* January 2007.
- Joseph J. Fins and Nicholas D. Schiff, "Shades of Gray: New Insights from the Vegetative State," *Hastings Center Report*, November-December 2006.
- Adrian M. Owen et al., "Detecting Awareness in the Vegetative State," *Science*, September 8, 2006.
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- Joseph J. Fins, *A Palliative Ethic of Care: Clinical Wisdom at Life's End,* Jones and Bartlett, 2006.
- George J. Annas, "'Culture of Life' Politics at the Bedside—The Case of Terri Schiavo," *New England Journal of Medicine*, April 21, 2005.
- Joseph J. Fins, "Rethinking Disorders of Consciousness: New Research and Its Implications," *Hastings Center Report,* March-April 2005.
- Joseph T. Giacino et al., "The Minimally Conscious State: Definition and Diagnostic Criteria," *Neurology,* February 12, 2002.

patients be distinguished from each other. This is easier said than done because of the evolving nature of brain states after injury and because of discontinuity in care as patients are transferred from the hospital to chronic care facilities.

Patients may leave the hospital with a vegetative diagnosis that has yet to become permanent, and then over time migrate into MCS while in chronic care. If a clinician does not notice this change in status, the patient may be assumed to be in a permanent vegetative state. This potential for misdiagnosis is only compounded by the episodic nature of displays of consciousness in MCS. Typically, families will see behavioral evidence of awareness and seek to reproduce these signs for wary staff. But because these behaviors are only episodic in MCS, they are not reliably reproduced. Staff may conclude that family observations are the result of denial or wishful thinking. Perhaps a third of patients in nursing homes diagnosed as being in the vegetative state may in fact be in the minimally conscious state, according to estimates from small studies. Wallis and Herbert were among those who were misdiagnosed this way. Because of the diagnostic and prognostic importance of these brain states, greater precision in discussions about a patient's vegetative state is now recommended. Medical staff should avoid confusing terms like persistent or permanent and speak instead of the type of injury (anoxia or traumatic) and its duration. And an Institute of Medicine exploratory meeting on disorders of consciousness called for the establishment of registries to determine the number of patients in these brain states and to better delineate the natural history of these conditions.

Values, Ethical Considerations, and Legal Ramifications

Beyond scientific precision, it is important to avoid turning a diagnostic assessment into a values choice, as was the case with Schiavo. Attempting to assert that Ms. Schiavo was minimally conscious in order to forestall a decision to withdraw her feeding tube has implications for patients who are actually in MCS. Because Ms. Schiavo would never regain consciousness, labeling her as an MCS patient represents a disservice to patients who are actually in MCS because it implies that they, too, will never recover.

While each of us in a liberal democracy is entitled to place a moral valuation on life in a vegetative or minimally conscious state, we should be careful not to distort the diagnostic act. Neither ideological motivation nor scientific ignorance is an acceptable cause for diagnostic imprecision. Diagnostic errors of omission or commission have the potential to either perpetuate false hope in the

case of the permanently vegetative or to blind us to the recuperative potential of minimally conscious patients.

Disorders of consciousness highlight fundamental bioethical concerns. Modern American bioethics was founded on the centrality of patient self-determination and autonomy. These rights have coalesced in two discrete arenas: reproductive ethics (see chapter 2, "Assisted Reproduction") and end-of-life care (see chapter 11, "End-of-Life Care"). The evolution of the right to die is centrally linked to disorders of consciousness, most notably through the case of Karen Ann Quinlan, a New Jersey woman who was in a vegetative state following a drug overdose and anoxic brain injury. Her parents sought to remove her ventilator and allow her to die.

In a landmark 1976 ruling, the New Jersey Supreme Court permitted the removal of Ms. Quinlan's life support, citing the irreversible nature of her vegetative state. As the court opined, based on testimony given by Dr. Fred Plum, Ms. Quinlan had forever and irretrievably lost the possibility of returning to a "cognitive sapient state." The irreversible nature of her injury, and its futility, became the ethical and legal justification for the removal of her ventilator. This case, in turn, launched the era of patients' rights at life's end.

This right to die was further codified in other cases involving the vegetative state, including those of Nancy Beth Cruzan and Terri Schiavo, both young women in the permanent vegetative state. In *Cruzan v. Director* in 1990, the U.S. Supreme Court recognized the constitutional right of a competent person to refuse life-sustaining therapy, equated artificial nutrition and hydration with other life-sustaining therapies, and ruled that each state could set evidentiary standards for the withdrawal of these therapies. *Cruzan* also led to the increased use of advance directives. Justice Sandra Day O'Connor's decision was the inspiration for the Patient Self-Determination Act, which was signed into law on December 1, 1991. With the passage of the PSDA, which requires many hospitals and other health care providers to inform patients of their rights under state laws governing advance directives, advance directives gained a central role in efforts to improve end-of-life care in the 1990's.

The advent of new brain states like MCS and their potential treatment has upset many of the presumptions that gave rise to modern bioethics and the right to die. Where it was once presumed that severe brain injury was invariably as dire as the vegetative state, we now know that prognostic outcomes can be variable. Therefore, it is increasingly inappropriate to view brain injured patients as untreatable.

To pursue therapeutic possibilities without engendering false hope, it is critically important to diagnose brain states as precisely as possible in order to balance burdens and benefits. As I wrote in the journal *Palliative and Supportive Care*, clinicians and policymakers need to preserve the right to die, but also to affirm the right to care for those who might be helped. The purpose of this ethical imperative is to carefully distinguish the vegetative from minimally conscious states and to avoid the diagnostic shortfalls that stem from clinical ignorance or ideological intent.