

Minimally Conscious State vs Persistent Vegetative State: The Case of Terry (Wallis) vs the Case of Terri (Schiavo)

Miraculous awakening from prolonged coma is in the news again. This time it is the story of Terry Wallis. Newspapers and the blogosphere are covering it extensively, using eye-catching titles: “Miracle in Arkansas”¹; “Comatose man’s brain rewired itself, doctors say. While fibers were severed, nerve cells stayed intact allowing later recovery”²; “As man lay in coma-like state, his brain was busy rebuilding.”³

In this editorial, I place these claims into perspective and review recent knowledge about recovery from prolonged comatose states.

It is useful to briefly revisit the categories of outcome in a patient comatose from a structural injury. To produce prolonged coma, insult and injury to the brain or brainstem must be devastating and widespread. Generally speaking, coma due to a structural cause (eg, anoxia-ischemia, traumatic head injury, hemorrhagic stroke, or meningoencephalitis) is associated with a poor outcome, particularly if patients show no improvement in consciousness within the first weeks. Outcome is worse with any episodes of further neurological deterioration (after early clinical presentation) and possibly better with early therapeutic intervention (eg, antimicrobial drugs, placement of ventriculostomy, or control of increased intracranial pressure) in response to identifiable causes of that deterioration. Patients may never regain consciousness and may die if further brain swelling and herniation or systemic complications occur. Advanced directives or prior voiced wishes of the patient to the family to not provide critical care may lead to withdrawal of support.

Patients who survive acute brain injury may never regain consciousness but open their eyes, fail to focus or track objects, and typically develop sleep-and-wake cycles, all clinical telltale signs of an emerging persistent vegetative state (PVS). Patients who awake often have a disability, and many display little effective communication and a major physical and cognitive handicap. New in this nosology is the category of *minimally conscious state* (MCS), the most severe form of neurological disability in a conscious patient. These major categories of outcome are summarized in Figure 1.

Other factors that determine outcome from coma are age and multiorgan involvement. For example, traumatic injury

to the brain in young individuals may, after a protracted period, lead to a satisfactory outcome, whereas anoxic-ischemic injury after cardiopulmonary resuscitation in elderly persons is typically associated with few survivors. However, within this spectrum of outcomes, clinical experience shows us that, if there is a structural cause of coma, withdrawal of medical support is common, and full recovery or minimal deficit with return to gainful employment is unlikely. Transition from a poor outcome to a good outcome may occur, but frequently outcome is determined at the onset of brain injury.

Two terms that have recently received much attention in the medical literature and media are the *minimally conscious state* and the *persistent vegetative state*. As the late Ronald E. Cranford, MD, and I recently reviewed in *Mayo Clinic Proceedings*, PVS is a clinical diagnosis with clear criteria.⁴ It involves eyes-open unconsciousness with no evidence of any behavioral (ie, purposeful) response of the patient to stimuli. Families should have no expectations of significant improvement when the condition persists 6 to 12 months after the ictus.⁵⁻⁷ A recent clinical diagnosis, MCS indicates definitive evidence of awareness, albeit limited.⁸ The diagnostic criteria are far more difficult to define, and the boundaries are uncertain (how minimal and how maximal?). The clinical designation of MCS may include more specific clinical diagnoses such as akinetic mutism, in which the patient can improve after certain medical or surgical interventions. Clinically, MCS can easily be distinguished from PVS, but little data indicate that MCS has a specific clinical course, specific findings on neuroimaging, or specific autopsy findings. Minimally conscious state can follow PVS, but there are only a few verified cases in the literature. After such rare recovery from PVS, these severely disabled and fully dependent patients, victims of a tragic catastrophic injury, may be aware of their surroundings but barely remember parts of the day. If we accept legitimacy of MCS as a distinct clinical entity, and not everyone does, it is a far more common condition than PVS. It is remarkable that the acceptance of MCS has been rapid. Its quick assimilation into the medical lexicon may have been influenced by attorneys attempting to challenge the clinical diagnosis in the recent Robert Wendland and Terri Schiavo legal cases.^{9,10}

I now return to the case of Terry Wallis. Wallis is an unfortunate, severely brain-injured man, whose disability began after his truck careened off a 25-foot bluff. He remained comatose initially but then improved gradually. More exceptionally, Wallis started to speak after 19 years

Address correspondence to Eelco F. M. Wijdicks, MD, Department of Neurology, Mayo Clinic College of Medicine, 200 First St SW, Rochester, MN 55905 (e-mail: wijd@mayo.edu).

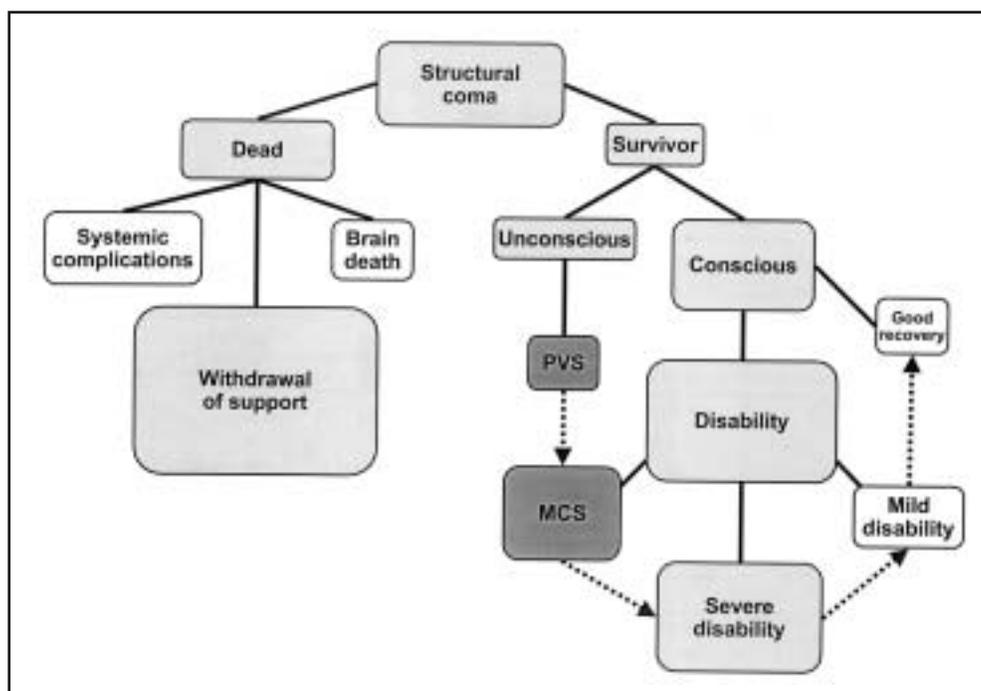


FIGURE 1. Major categories of outcome after structural cause of coma. (The size of the boxes estimates the frequency of occurrence of each category.) The dotted arrows represent possible transitions. MCS = minimally conscious state; PVS = persistent vegetative state.

of silence and grunts. This story, which at first look is amazing, had been in the news before. A television documentary that aired on the Discovery Health Channel in 2005 had covered the Wallis case in detail.¹¹ When physicians discussed prognosis with his mother, she was told that “Terry would probably never emerge.”¹¹ Physicians ignored his mother’s call that “Terry is in there, he just can’t communicate.” According to his mother, “they did not believe it, they just [said he is] in a coma and that is what he is going to be.” The documentary suggested that Wallis was in PVS and, if correct, that such a dramatic improvement implies that the concept of PVS is, at its core, deeply misleading. However I suspect that any neurologist who views the home video segments included in the Discovery Health Channel documentary will note that Wallis was not in PVS before his improvement. He looks about and responds quickly to his family. Although Wallis was not in PVS, it is unclear what state he really was in because he was not repeatedly examined by a neurologist.

Now a recent study from Weil Medical College of Cornell University has suggested that Wallis’ brain shows possible axonal regrowth.¹² The investigators evaluated the patient’s brain using magnetic resonance (MR) diffusion tensor imaging that specifically showed nerve fiber networks plus positron emission tomographic (PET) imaging that showed increased activity in the association cortex.

However, the clinical correlate of these MR and PET findings was not one of awakening from coma or transition from a PVS to conscious awareness. Rather, the neurological examination showed improvement of motor strength in limbs notwithstanding severe contractures (extension of the legs when held in a flexed position and elevation of the lower back when the legs were pushed down) and documented attention using tests such as auditory vigilance (eg, raising a hand when hearing sounds). Less incoherent talkativeness was also noted, but there was no change in word fluency. The investigators concluded that these MR and PET findings could explain Wallis’ improvement. The study indirectly implies that sophisticated neuroimaging may be better than clinical acumen. Additionally, it implies that there may be more than meets the neurologist’s eye. However, it is unclear whether the physicians were aware of the MR findings during clinical reexamination. Other factors (eg, training of the patient through repeated examination) may have played a role in Wallis’ performance test results. Furthermore, the investigators acknowledge that their interpretation was always an analysis post facto when baseline studies (ie, before major changes in communication occurred) were not available. That is, of course, exactly what was missing.

Wallis has been called “a miracle” by the family and attending physicians. How can we as physicians under-

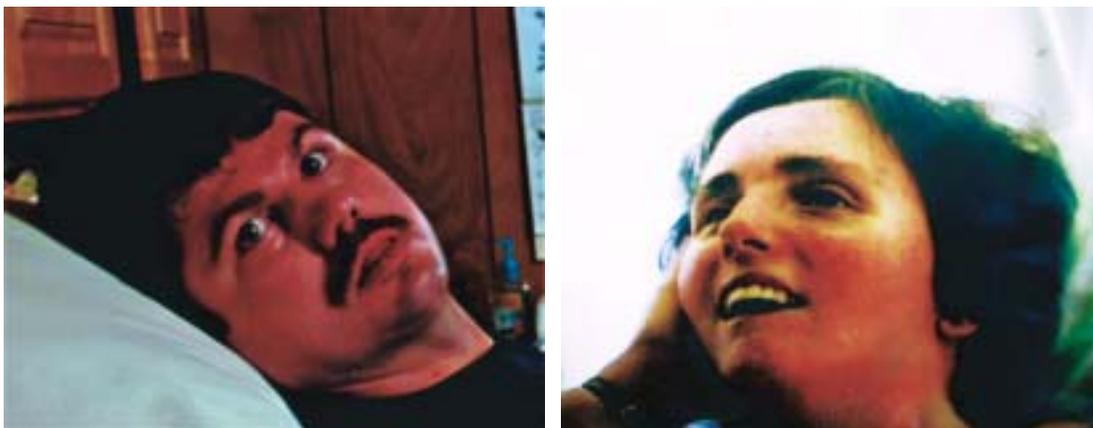


FIGURE 2. Terry Wallis (with permission from *The New York Times*) and Terri Schiavo (with permission from Getty Images) as portrayed in the media. Although the untrained eye may spot differences—Wallis seems to look into the camera—the facial expression is the least valuable feature that distinguishes minimally conscious state from persistent vegetative state. The 2 neurological states can certainly not be distinguished with quickly captured photographs.

stand these “miracle cases”? There is most likely a major distinction between *recovery* (meaning that the diagnosis is correct and there truly is exceptional improvement) and *discovery* (in which the diagnosis is incorrect and changes with more methodical examination). Some of these “miracle” patients may not have been in a coma but in a variant of a locked-in syndrome. Some of the news coverage of these cases highlights that communication was possible through eye blinking even before speech returned.¹³ Other patients suspected of being in MCS may have started to speak, often to the surprise of family members, when their tracheostomy was occluded and the cuff of the tracheotomy tube temporarily loosened. As such, attempts at discernable speech, which may have been impossible before, would now be mechanically possible. Washout of accumulated sedative drugs may play a role in speech resumption in such patients.

What is most interesting is that in many cases a fairly dramatic improvement in communication skills occurs over a period of hours or days, but then—if we believe the media coverage—the patients often typically relapse into the previous state. Not uncommonly, dopamine agonists or antidepressants have been introduced before clinical improvement, suggesting the possibility of neurotransmitter modulation in some patients in MCS. A systematic review of these cases would be useful, but the amassed information is likely to be fragmentary and difficult to interpret.

Certainly, research of coma is sparse, and new developments immediately attract attention. However, coverage of these so-called miracle recoveries is often hyperbole and serves little purpose. Physicians can raise concerns about the accuracy and validity of these individual reports, but these cases will inevitably be compared with the highly

publicized Terri Schiavo case. The questions that will be raised by those suspicious of physicians’ caution are the questions one may expect:

Question: Wallis was misdiagnosed as being in PVS (allegedly by nonneurologists who conversed with his mother). If this is the case, why was Schiavo not misdiagnosed as being in PVS as well?

Question: In the Schiavo case, many physicians were willing to submit affidavits claiming that she was not in PVS. Were they all wrong?

Question: If Wallis underwent rehabilitation and improved, should one not expect similar improvement had Schiavo been afforded similar rehabilitative therapy?

The answers to these questions lie in the fact that, unlike Wallis, Schiavo was unprecedentedly examined by no fewer than 7 board-certified neurologists, all of whom diagnosed her condition as PVS. As such, she could never have recovered to an independently functioning human being, able to care for herself. Strong opinions to the contrary emanated from others who did not actually examine Schiavo but instead watched videotapes of her examinations or edited videotapes provided by the parents. In the final analysis, it is fair to conclude that the neurological condition of Wallis and Schiavo bears no resemblance to each other (Figure 2).

To say that the case of Wallis is evidence of meaningful clinical improvement in a case of PVS is a simplistic generalization. To say instead that PVS is often overdiagnosed because the clinical state is uncommon and few physicians have the skill to examine patients appropriately seems a more reasonable conclusion. Such a criticism is well known in the neurology community and applies to many other neurological conditions. Fortunately there are second opinions.

Saying that the results of the recent MR and PET studies of Wallis may result in effective rehabilitation for patients in MCS or PVS is misleading, creates unsupported expectations, and eventually leads to frustration for all concerned. The facts show that PVS is the result of a brain that is badly, and chronically, injured, and meaningful clinical recovery from PVS is possible only in the hopes and dreams of patients' loved ones and supporters. The prognosis may not be much different with MCS. These latter ill-fated patients are bedbound, need full nursing care, are double incontinent, drift away during attempted conversation, and are unable to participate in rigorous rehabilitation programs as a result of their inability to perform complex tasks and retain information in their stored memory.

On the other hand, the recent MR and PET images of Wallis' brain should not be quickly dismissed. To say that the discoveries are simply "much ado about nothing" (ie, just more neuronal tracts formed over many years in an already awake and aware—and not comatose—patient) may be ignoring a valuable, interesting phenomenon. However, we should then accept that axonal sprouting from uninjured brain tissue is the correct interpretation of the MR images. This phenomenon has been demonstrated before and may be under the control of basic fibroblast growth factor or other neurotrophic factors. Nonetheless, leading experts in this area are unconvinced that such an intrinsic brain repair mechanism would lead to major clinical improvements, let alone awakening from coma.¹⁴ The more appropriate interpretation is that studies are needed in a much larger, clearly defined patient population, and the patients must be examined by skilled neurologists and the findings correlated with serial functional MR studies.

Can PET and functional MR imaging be helpful to clinical neurologists who care for patients like Wallis? I think they can. Admirable groundbreaking research from both the Cyclotron Research Center of the University of Liege¹⁵ and the Functional MRI Research Center of Columbia University¹⁶ has shown, for the first time, a glimpse into brain activity in PVS and MCS. Although it is not a major chore for a neurologist to distinguish the 2 conditions, these studies could help in identifying imaging correlates. Perhaps these studies could offer insights into the possible recovery from early stages of a vegetative state that is not persistent or permanent. A large amount of data

is emerging but from few patients, and it is still a major leap to interpret these studies as a way to understand "miracle recoveries."

It would not be surprising to learn that the media attention associated with the Wallis/MR/PET story was an unintended, regrettable consequence of the Cornell investigators' research. Scientific findings with doubtful generalizable conclusions, particularly when preliminary and based on a single case, should remain in academic circles for further debate and synthesis before being shared with the public. Most of the media cannot discern the subtleties of problems with interpretation, and most of the public may interpret wrongly. In these instances, it is the duty of neurologists to clarify, explain, and caution.

Eelco F. M. Wijdicks, MD
Division of Critical Care Neurology
Mayo Clinic College of Medicine
Rochester, Minn

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