

Memory During the Presumed Vegetative State: Implications for Patient Quality of Life

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Abstract: A growing number of studies show that a significant proportion of patients, who meet the clinical criteria for the diagnosis of the vegetative state (VS), demonstrate evidence of covert awareness through successful performance of neuroimaging tasks. Despite these important advances, the day-to-day life experiences of any such patient remain unknown. This presents a major challenge for optimizing the patient's standard of care and quality of life (QoL). We describe a patient who, following emergence from a state of complete behavioral unresponsiveness and a clinical diagnosis of VS, reported rich memories of his experience during this time. This case demonstrates the potential for a sophisticated mental life enabled by preserved memory in a proportion of patients who, similarly, are thought to be unconscious. Therefore, it presents an important opportunity to examine the implications for patient QoL and standard of care, both during the period of presumed unconsciousness and after recovery.

Keywords: disorders of consciousness; vegetative state; covert awareness; preserved cognition; memory; recovery; standard of care; quality of life

Introduction

Following severe brain injury, some patients progress to a state where they appear to be awake but completely unaware of themselves and their environment. When repeated behavioral assessments fail to elicit any voluntary motor responses, a patient is thought to lack consciousness and receives a clinical diagnosis of vegetative state (VS),¹ also known as “unresponsive wakefulness syndrome.”² This diagnosis is distinct from the locked-in syndrome (LIS), in which a person is almost completely paralyzed, but has preserved consciousness that can often be demonstrated by vertical eye movements.³ The clinical diagnosis of VS is based on behavioral assessment of the patient's responsivity at their bedside, which is especially challenging due to its subjective nature and because responses are often inconsistent and limited by motor constraints. This difficult situation is reflected in the high misdiagnosis rate of up to 43% in this group.^{4,5,6}

Many studies have now shown that functional neuroimaging can detect evidence of covert awareness and cognition in some patients, who show no signs of awareness according to clinical behavioral assessments.^{7,8,9,10,11,12,13,14,15,16,17} Some of these patients are able to demonstrate their covert awareness by wilfully modulating their brain activity to respond to instructions, such as “imagine playing tennis,”¹⁸ or convey the correct “yes” or “no” answers to questions posed by the researchers, by attending to either the word “yes” or “no.”¹⁹ These responses require a host of cognitive faculties, including intact auditory functioning, language processing, working memory, and response selection. In addition, some patients show brain activity that is synchronized to that of healthy controls during auditory or audio-visual movies, which tracks both the cognitive demands and the subjective emotion, for example, suspense, elicited by the plot, in the same way as healthy individuals.^{20,21,22,23} Synchronization of this sort provides evidence of covert

narrative capacity,²⁴ which relies on additional cognitive faculties, such as object/voice/face recognition, executive function, and emotion. It also suggests that other, more complex capacities, such as theory of mind and future-oriented thinking may be preserved in patients who can understand plot-driven narratives.^{25,26} To acknowledge these recent advances, the novel nosological distinction of “cognitive motor dissociation” (CMD) has been proposed to describe this subset of patients, who meet the behavioral criteria for the diagnosis of VS, but show neuroimaging evidence of conscious awareness.²⁷ However, the day-to-day life experience of any such patient remains unknown, which presents a major challenge for optimizing the patient’s standard of care and quality of life (QoL).

Memory and the Self

One area of cognition that is central to a person’s experience of everyday life is memory. The formation and retention of memories allows us to integrate past events with episodes from the present and thoughts about the future, to experience a sense of having a coherent self that persists over time. Philosophers have long argued that memory is key to allowing us to possess a sense of personal identity.^{28,29} Seeley and Sturm³⁰ distinguish between the “minimal” self and the “longitudinal” self. Although the “minimal” self refers to a person’s immediate online experience in the moment (e.g., their body state, conscious imagery, and internal dialogue), the presence of episodic autobiographical memory (i.e., memories of past events), and semantic self-knowledge (i.e., knowledge of one’s own traits) allows for the construction of the “longitudinal” self, that is extended across time. Damasio³¹ similarly proposed that consciousness could be divided into two levels: “core consciousness,” a basic integrated experience of the current moment, and “extended consciousness,” made possible by the accumulation of autobiographical memories that allow the creation of an internal world and projection beyond the present. Consistent with Seeley and Sturm,³² Damasio’s two levels of consciousness correspond to two different notions of “the self,” that is a transient, repeatedly reconstructed core self, and an autobiographical self, which provides a sense of lasting personal identity. Thus, memory plays a pivotal role in how we interpret our experiences of the world, and in turn, how these experiences impact our subjective QoL.

Furthermore, neuropsychological reports of patients with different types of brain damage have demonstrated that the presence of episodic memory is essential (although not necessarily sufficient) for maintaining a sense of identity over time.^{33,34,35} In addition to connecting the past experiences of a person, episodic memory is essential for mental time travel—a capacity that has been argued as the uniquely human capacity to disengage from the present and mentally project into the future.³⁶ The ability to internalize a sense of identity by reconstructing the past and imagining a future has been emphasized as an important factor in promoting positive psychological outcomes following suffering or negative life events.³⁷ The presence of episodic memory is, thus, extremely important to how a person experiences and makes sense of negative life events, such as brain injury, by enabling rumination as well as the ability to narrate one’s story in a particular way. Therefore, an understanding of whether some patients with CMD have preserved memory function, and thus may experience life with a sense of maintained personal identity over time, could provide us with important insights into the mental life of these patients.

To date, only one study has reported direct evidence of memory in a patient with CMD. Fernández-Espejo and Owen³⁸ described a patient who had a diagnosis of VS for 12 years. When asked to perform two mental imagery tasks (“imagine navigating around your house” and “imagine playing tennis”), the patient’s brain activity was indistinguishable from that of healthy participants completing the same command-following task, thus demonstrating that he was consciously aware. The researchers then used this mental imagery technique to ask the patient a series of yes/no questions—revealing that the patient remembered details from before his injury (such as the names of his family members), as well as information only learned since the injury (such as the name of his personal support worker from the hospital). However, the fact that relatively few yes/no questions can be asked during these effortful tasks substantially curtails what we can learn about any given patient’s inner experiences.

Where can we look for additional insights? Reports from patients, who recover from the VS and regain the ability to communicate, would be an invaluable addition to our knowledge in this area. Although rare, recovery from the VS occurs in some patients, as detailed in several case studies.^{39,40,41,42,43} However, these reports only discuss the patients’ experiences starting from the emergence from VS or minimally conscious state (MCS)⁴⁴ onwards.

To the best of our knowledge, there is only one report of a patient who was diagnosed as VS, recovered, and was able to report on his experience during that time.^{45,46} The patient described in these reports suffered an anoxic brain injury at 19 years old. He was admitted to the emergency room with a Glasgow Coma Score (GCS)⁴⁷ of 3 and following computed tomography, magnetic resonance imaging (MRI), and urine toxicology, was diagnosed with irreversible hypoxic ischemic encephalopathy. Five weeks postictus, he was transferred to the medical ward with a GCS of 8.

Three months after his injury, with a clinical diagnosis of VS, he visited the Robarts Research Institute at the University of Western Ontario for 4 days to take part in research protocols designed to look for signs of covert cognition and awareness. During this time, his behavioral abilities were repeatedly assessed with the Coma Recovery Scale-revised (CRS-R),⁴⁸ a standard clinical tool for the differential diagnosis of disorders of consciousness. The patient’s highest CRS-R score during his initial visit was 7, consistent with his clinical diagnosis of VS.

Within a few weeks after the research visit, the patient started to regain consciousness, and at 9 months postictus, he had recovered the ability to feed himself, write, and stand with assistance. Crucially, he also recovered the ability to speak, thus enabling researchers to directly ask him about his prior experience, during a second visit to Robarts Research Institute. In an open-ended interview, the patient recalled details about the procedures and materials he was presented, such as going on a stretcher into an MRI scanner and being asked to follow various objects with his eyes. His memory was also tested formally, with a personalized forced-choice recognition task that presented items that the patient had only encountered during his first visit, paired with “lure” objects, which he had not. He correctly performed these memory tests, and moreover, spontaneously reported richer details of his memories, such as correctly recalling the name of one of the researchers. The patient’s firsthand account of his covert awareness and preserved memory during the (presumed) VS, was further corroborated several months after the first imaging visit, with neuroimaging data from what had been a new experimental paradigm in

the earliest stages of development at the time.⁴⁹ These results demonstrated that, when presented with an engaging auditory narrative, the patient's brain activity was indistinguishable from that of healthy participants and followed the evolution of the plot over time.

Although a single case study, it demonstrated that it is possible for a patient, who is entirely behaviorally nonresponsive, to retain a much more sophisticated mental life than what can be inferred by their clinical diagnosis of VS. It is, therefore, important to consider the significance of preserved memory in any patient diagnosed as VS, what it would mean for their experience during and after the diagnosis of VS, and what the practical implications for clinicians and family members might be.

QoL during the Presumed VS

The World Health Organization has outlined six dimensions thought to be key to QoL in general: physical health, level of independence, psychological state, social relationships, environment, and spirituality/religion/personal beliefs.⁵⁰ However, the barriers to communication arising from disorders of consciousness, particularly during the VS, make it difficult to directly assess QoL in these patients. Indeed, the inability to communicate with patients with CMD, except for very limited yes/no communication that can take place in research settings,^{51,52,53} renders direct examination of QoL in this group uniquely challenging. Research from other and similar patient groups suggests that we should exercise caution in making assumptions about QoL. The term "disability paradox"⁵⁴ has been used to describe the finding that people with severe, persistent disabilities frequently report a good QoL, whereas, by contrast, external observers would imagine their life to be extremely undesirable due to their disability and situation. For example, Lulé et al.⁵⁵ reported that a significant number of patients with LIS maintain a good QoL despite their high levels of physical impairment, and that family members and primary caregivers of patients with chronic illness tend to underestimate their QoL. Another study found that the QoL of patients with LIS was no different than healthy controls' in all dimensions, except physical and social functioning.⁵⁶ Finally, Doble et al.⁵⁷ found that none of the patients with LIS who were followed after 11 years reported a desire to die. This contrasts with survey data from the general public indicating that 56% of healthy participants would not wish to be kept alive in a locked-in state.⁵⁸

Although patients with CMD differ from those in a LIS and other patients with significant disabilities in several ways—including the ability to communicate—the latter group exemplifies the shift in how patients evaluate their QoL after a devastating injury or illness, relative to prior. Indeed, the fact that healthy individuals and those with LIS differ so starkly in their evaluation of the latter's QoL suggests that the perceptions, assumptions, and values by which patients in similar states, such as those misdiagnosed as VS, evaluate their own wellbeing are different from those of healthy people.

To account for these differences, Tung et al.⁵⁹ developed the first QoL assessment tool for patients with disorders of consciousness (DoC), such as those in a VS or MCS. After identifying 42 dimensions used in other QoL assessments for other and similar patient groups, a multidisciplinary panel including healthcare professionals, bioethicists, and patient advocates rated which dimensions were important to include for patients with DoC using a Delphi consensus process. The top five most

highly rated dimensions were: bodily pain and discomfort, communication capacity, overall QoL, somatic complaints, and personal relationships.

This tool was developed in the absence of the evidence of preserved memory during the VS.^{60,61} Would this information change the dimensions that are considered central to QoL, and thus most important to assess, in patients with DoC? Below, we argue that several areas become more important to consider if memory is preserved in a patient thought to be in a VS. These include: social wellbeing (personal relationships and relationship with family), psychosocial wellbeing (sense of belonging), and mental wellbeing (experiencing anxiety, depression, positive and negative emotions, cognitive functioning, sense of identity, and experiencing loneliness). These dimensions provide a framework through which the potential impact of memory on patient QoL can be examined.

Impact of Memory on QoL during the Presumed VS

One important question concerns how the presence of intact memory changes our understanding of the QoL of behaviorally nonresponsive patients. If a person is forming and retaining memories during the period of a clinical diagnosis of VS, how does their lived experience differ from how it would be if memory was abolished? There is strong evidence that behaviorally nonresponsive patients can feel pleasure and pain; therefore, any decisions about treatment of these patients, including pain management, social and medical interactions, should take relevant fact this into account.⁶² Graham suggests that if higher-level cognitive capacities, such as memory, are present, these factors would impact on the patient's experience of pain and pleasure.⁶³ For example, anticipation or catastrophizing of an anticipated treatment or experience might increase how painful or uncomfortable the actual event is perceived to be, whereas overexposure to an initially pleasurable stimulus might render it aversive.

Given the importance of memory for shaping a patient's subjective experience, preserved memory, even in the absence of communication, has clear implications for patients' mental and emotional wellbeing. Some authors argue that the presence of memory can render life in a VS more distressing than it would be in the absence of memory. Kahane and Savelescu⁶⁴ argue that, when "*rationality and memory are essentially preserved*" but the "*ability to act in the external world...has been lost*" (p. 20), a person is likely to have desires and personal projects, but be unable to pursue them, and thus is cut off from the objective goods that make life meaningful. From this viewpoint, being aware of their situation and condition—including memories, desires and aims of their life prior to the injury—exacerbates a patient's suffering. Similarly, Hawkins⁶⁵ argues that extreme isolation makes it very unlikely that these patients will benefit from life.

These considerations notwithstanding, and in light of findings on the disability paradox, we argue that patients with CMD are capable of having positive experiences that can provide satisfaction. Social wellbeing constitutes a key dimension that could be positively impacted by the presence of memory, leading to an improvement in the patient's QoL. For example, a friend's visit to the patient's bedside could be a richer experience if the patient remembers their relationship. It would have meaning beyond the in-the-moment satisfaction, likely strengthening their sense of belonging. Even if memories prior to the injury are compromised, the ability to remember, for example, that a friend fulfils their commitment to visit, or to

hear about and follow a loved one's endeavors, provides the potential for meaningful interactions over time.

Finally, the presence of intact memory might expand the range of actions that can be taken by others to improve the patient's QoL. Novel communication methods may, in the future, enable patients with CMD to express wishes about their environment, opinions about their care schedule, and entertainment preferences⁶⁶ through the use of brain-computer interfaces.^{67,68,69} Recent work has demonstrated that neuroimaging paradigms have allowed patients to communicate yes/no answers to questions.^{70,71,72} Thus, it is plausible that, in the future, patients with CMD will be able to exert some control over their environment, and thereby satisfy interests that improve their QoL. Even in the absence of such communication systems, memory may allow the patients' interests to be satisfied in a way that would be impossible if memory was absent. For example, the provision of verbal stimulation to these patients demonstrates respect, dignity and concern for their interests and values.⁷³ The value of these interactions increases if a patient has an extended experience across time. Clinician guidelines on how to respond to requests for novel assessment/intervention methods, recommend that these are justified if they meet a goal of care.⁷⁴ The presence of memory expands the range of goals of care that are possible for these patients, beyond merely aiming to reduce/increase momentary pain or pleasure, to also include higher-order goals associated with the patient's mental state or social relationships.

Impact of Preserved Memory on QoL after Recovery

It is also important to consider how the experience of being aware and forming new memories, while being entirely behaviorally nonresponsive, might impact a person's QoL after they emerge from the VS. Cohort studies show that a small minority of patients do recover, although in most cases, they remain severely functionally impaired. In a prospective study of 50 patients with prolonged VS, six (12%) showed late recovery of consciousness.⁷⁵ A retrospective study reported no improvement in any of the 12 VS patients followed over 5 years, whereas 13 out of 39 patients diagnosed as MCS emerged after 1 year with severe disabilities.⁷⁶ Several other case reports detail late recovery following prolonged VS.^{77,78,79,80}

How does the experience of spending time in long-term care settings—aware and unable to communicate—impact on a patient's wellbeing upon recovery? One group that could provide insights are patients who experience accidental awareness under anesthesia (AAGA).⁸¹ A large-scale study found that 41% of patients who experienced accidental awareness reported moderate to severe long-term harm, such as flashbacks or nightmares, and posttraumatic stress disorder (PTSD).⁸² Furthermore, such long-term suffering was more likely in patients who experienced paralysis during AAGA, and, thus, were unable to communicate with their medical team.⁸³ The authors suggest that detection of AAGA and acknowledging it while it happens, by speaking to the patient, may protect from subsequent development of PTSD.⁸⁴ These findings underscore the importance of using neuroimaging techniques to assess the presence of covert awareness in severely brain-injured patients, wherever possible, and to acknowledge the patient's awareness if it is detected.

The presence of memory during the presumed VS has the potential to impact social relationships following recovery. As noted above, the capacity for forming new memories renders interactions with family members and clinicians meaningful

beyond the present moment; and can have a lasting impact on relationships, some of which carry over into life after functional recovery. Research shows that supportive relationships with family members facilitate positive health outcome following physical trauma⁸⁵ and childhood critical illness.⁸⁶ Similarly, it is likely that the ability to receive support from family members during the VS, will lead to better health outcomes upon emergence from this state. Therefore, creating environments and interactions that nurture the patients' personal and social wellbeing will help to facilitate their psychological adjustment, and in turn, will reduce the overall burden on the healthcare system, as they recover.

Conclusion

Research has established that at least 14%–19% of patients who are diagnosed as behaviorally nonresponsive show evidence of covert awareness with neuroimaging tasks.^{87,88} Although neuroimaging tasks can reveal preservation in a number of cognitive faculties in patients who are thought to lack awareness, the everyday life experience of these patients remains hard to ascertain. Despite a diagnosis of VS, the patient described earlier in this paper demonstrated covert awareness and a host of high-level cognitive faculties via neuroimaging testing protocols, and importantly, upon recovery, reported a rich memory of his experience during the time when he was deemed unconscious. This case demonstrates the potential for a sophisticated mental life in a proportion of patients, who, similarly, are thought to be unconscious. Therefore, it presents an important opportunity to examine how family members and medical care teams ought to interact with and treat these patients. Important societal discussions about our moral obligations to vulnerable patients and decisionmaking on their behalf, as well as regarding the preparation of advance directives, hinge on “what it is like” to be in the VS. The perspectives of different stakeholders, including clinicians, lay public, and family members, on what this experience can be like, and whether they would like to receive treatment are likely to be impacted by knowledge of the potential for intact memory during states of disordered consciousness.

Notes

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