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Review Article

Coma, Vegetative State, and Minimally Conscious State Distinguishing Disorders of Consciousness

Craig H Lichtblau[1*], Scott Raffa[2], Kaveh Assadi[3], Christopher Warburton[4], Gabrielle Meli[4], Allyson Gorman[5]

[1]Medical Director of The Osseointegration Program at The Paley Orthopedic and Spine Institute at St.,West Palm Beach, FL, USA; [2]Neurosurgeon, Paley Orthopedic and Spine Institute at St. Mary's Medical Center, West Palm Beach, FL, USA; [3]Consultant to Children's Medical Services for The State of Florida, District 9, St. Mary's Medical Center, West Palm Beach, Florida 33407, United States; [4]Department of Physical medicine, University of Miami Miller School of Medicine, Miami, FL, USA; [5]Department of Physical Medicine, Medical College of Wisconsin, Wauwatosa, Wisconsin, USA

ABSTRACT

Disorders of consciousness can be difficult to diagnose, but distinguishing specific disorders of consciousness is critical for gaining insight into prognosis and optimizing care. Specifically, understanding the realities related to patients' pain perception and abilities to communicate is key to minimizing suffering and determining the care path. Here we discuss the specific levels of consciousness as they pertain to coma, vegetative state, and minimally conscious state and provide information on prognosis, life expectancy, and the care required for each of these disorders of consciousness.

Keywords: Diagnose; Prognosis; Brain stem; Neuro transmission

INTRODUCTION

Consciousness is defined based on wakefulness and awareness [1]. Wakefulness depends on the potential for arousal, which relies on activity in the brainstem, basal forebrain, and diencephalic areas [2]. Awareness-and the ability to respond to stimuli-originates from functioning thalamocortical networks. When cerebral excitatory synaptic activity is impaired, disorders of consciousness can occur [3]. Disorders of consciousness refer to prolonged altered consciousness, which represents coma, vegetative state, or minimally conscious state [4]. While a meaningful understanding of consciousness has eluded us, we readily recognize abnormal consciousness when there is a dissociation between level of arousal and level of awareness.

Specific disorders of consciousness can be challenging to diagnose, with vegetative state and minimally conscious state being particularly difficult to distinguish [4,5]. Nonetheless, precisely defining the disorder of consciousness is critical for a variety of reasons [6]. For instance, understanding consciousness level provides insight into prognosis and enables the assignment of appropriate caretaking, including whether and how to address pain, rehabilitation, and communication. Here we discuss coma, vegetative state (both persistent and permanent), and minimally conscious state and how these disorders of consciousness differ in terms of patients' level of consciousness, their prognosis and life expectancy, and the care they require. Distinctions in these groups of patients can be viewed in tables 1 and 2 [4,7,8].

Disorder of consciousness	Definition	Consciousness/ Communication	Sleep-Wake Cycle	Experience Pain
Coma	Unawake, unaware	None	Absent	No
Persistent Vegetative State	Awake, unaware	None	Present	No
Permanent Vegetative State	Awake, unaware	None	Present	No

Correspondence to: Craig H. Lichtblau, Physical Medicine and Rehabilitation Consultant to the Paley Orthopedic and Spine Institute, St. Mary's Medical Center, West Palm Beach, Florida, USA, E-mail: c.lichtblau@chlmd.com

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Minimally Conscious State	Awake, some signs of awareness	Some	Present	Yes

Table 1: Disorders of consciousness differ in levels of wakefulness and awareness

Disorder of Consciousness	Motor	Auditory	Visual
Coma	Reflexive Only	None	None
Persistent Vegetative State	Purposeless Withdraws to noxious stimuli	Startle	Startle
Permanent Vegetative State	Purposeless Withdraws to noxious stimuli	Startle	Startle
Minimally Conscious State	Inconsistent but purposeful behaviors	Can localize sound	Can fixate/ pursue visual stimuli

Table 2: Patients with different disorders of consciousness respond distinctly to stimuli

LITERATURE REVIEW

Coma involves unconsciousness, with a complete loss of arousal

The complete loss of arousal is the defining clinical feature of coma [4]. Those in a coma are unconscious, do not open their eyes, and demonstrate no reflex responses, including often failing to respond reflexively to noxious stimuli [2,4,9]. Patients who are in a coma demonstrate no sleep-wake cycles and feel no pain. Comas occur in those with brainstem lesions, white matter damage, or other diffuse cortical destruction [4]. The World Federation of Nonsurgical Societies classifies comas as Grades I-IV based on physical examination criteria [10]. Regardless of the grade, recovery from coma occurs *via* several mechanisms that drive the restoration of excitatory neurotransmission across corticocortical, thalamocortical, and thalamostriatal networks [3].

Prognosis for those in a coma depends largely on the cause of the coma and the duration of the coma. Compared to those who suffer a traumatic injury-induced coma, those whose coma occurs due to a nontraumatic injury have a poorer prognosis [11]. More than 85% of adults who suffer a coma immediately following a nontraumatic injury die within a month. Patients who survive a coma will normally transition to a vegetative state or minimally conscious state within 4 weeks [2,4]. However, the first 24 hours of a coma are critical for predicting outcomes [10,12]. Between 1% and 12% of those in a coma for more than 24 hours will transition to a persistent vegetative state [9]. For those who have remained in a coma for 3 days, chances of a good or moderate recovery is only 7% [12]. By the 14th day, this number drops to 2%.

Unlike those in a coma, those in a vegetative state are 'awake'

Those who awake from coma but remain without communicative abilities were defined in the 1970 as living in a vegetative state, which had previously been referred to as apallic syndrome or coma vigil [13]. Compared to those in a coma, those in a vegetative state open their eyes spontaneously [2,4]. Patients in a vegetative state are therefore described as 'awake but unaware', showing some reflexes but no meaningful reaction to their environments [9,14]. Some functions are preserved in those in a vegetative state, including some form of sleep-wake cycles, autonomous nervous system functioning, digestion, respiration, and thermoregulation [2,13]. Despite the presence of these functions, those in a vegetative state-like those in a coma-do not seem to experience pain. Evidence of the lack of pain comes from research demonstrating that high-intensity electrical stimulation that causes pain in control patients fails to activate parts of the brain that are critical for pain processing in those in a vegetative state [1]. Both vegetative state duration and brain activation that occurs beyond the primary sensory cortices are associated with recovery [8]. It has been reported that the mean survival for those in a vegetative state for a month is only 2 to 5 years [15]. However, for those who have already survived a year in a vegetative state, the annual mortality diminishes, and there have been instances of patients surviving for more than 20 years in a vegetative state. While functional recovery is similar in adults and children in both posttraumatic and nontraumatic vegetative states, children in a posttraumatic vegetative state recover their consciousness at a slightly higher rate compared to adults [1]. Research has shown that nearly 1 out of 4 children in a vegetative state following a severe head injury recovered consciousness within 3 months. The same study showed that at one year, 9% of the children had died, whereas 62% had regained consciousness. After a year, no more children recovered consciousness.

Persistent and permanent vegetative states differ in terms of duration of disordered consciousness

Persistent vegetative state' was coined in 1972 by Jennett and Plum, who described the syndrome in The Lancet [16]. Those deemed to be in a persistent vegetative state have remained in a vegetative state for 30 days [2]. Life span is significantly reduced in those in a persistent vegetative state, with average life expectancy reported as 2 to 5 years [17]. Survival beyond 10 years is rare. After 12 months in a posttraumatic persistent vegetative state, recovery of consciousness is unlikely in both adults and children [17]. Recovery is exceedingly rare after 3 months in a nontraumatic persistent vegetative state. For these reasons, experts now refer to those who have been in a vegetative state for 3 months following global ischemia or one year following traumatic brain injury as in a 'permanent vegetative state [2,13,17]. Given that cause of injury-i.e. traumatic *versus* anoxic-as well as the time since condition onset both play a role in prognosis, the American Congress of Rehabilitation Medicine recommends that these factors are always documented in those in a vegetative state [8].

Though life expectancy in those in a permanent vegetative state appears to be lower when ventilators and/or gastrostomy feeding tubes are required, these patients can survive for many years with the proper medical care [1,4,18]. For example, life expectancy for a 15 year-old who has been in a vegetative state for 1 year is 10.5 additional years. Because mortality rates

decline with each year of survival, the life expectancy for a 15-year-old who has been in a vegetative state for 4 years is even higher at 12.2 years [18].

'Minimally conscious state' indicates some level of awareness

Those in a minimally conscious state-also referred to as minimally responsive state-cannot communicate but do show some signs of awareness [19,20]. These patients were once characterized as being in a vegetative state, but the subtle behavioral differences observed in these patients-and the recognition that the presence of these behaviors are associated with better outcomes-catalyzed the classification of the minimally conscious state [4,21]. The American Academy of Neurology provided a definition for minimally conscious state in 2002 to separate it from non-communicative patients in a vegetative state [7,13]. The Aspen Neurobehavioral Workgroup has defined minimally conscious state as "a condition of severely altered consciousness in which minimal, but definite, behavioral evidence of self or environmental awareness is demonstrated [14,22]. According to this workgroup, minimally conscious state diagnosis requires that at least one of the following four behaviors are produced repeatedly upon physical examination:

- Follows simple commands
- Gives yes or no responses verbally or with gestures
- Verbalizes intelligibly
- Demonstrates other purposeful behaviors relevant to environmental stimuli

Though in many ways, those in a minimally conscious state resemble those in a vegetative state, level of consciousness distinguishes these groups of patients. While the latter are unconscious with no awareness and thus unable to experience pain, the former have some degree of consciousness and awareness and can therefore experience pain to some degree, though the level of suffering is often difficult to determine [14]. Corticothalamic connections are maintained in those in a minimally conscious state, which likely accounts for the preserved capacity for cognitive processing [4]. While outcomes for those in minimally conscious state appear better than for those in a vegetative state, these outcomes are heterogeneous [2,23,24]. Unlike with other disorders of consciousness, duration of minimally conscious state does not appear predictive of outcomes. Further, because the minimally conscious state is not as well understood as the vegetative state, we have not established a point at which minimally conscious state should be considered permanent [14].

DISCUSSION

As with outcomes, functional recovery in minimally conscious patients is also heterogeneous. This heterogeneity has led to the subcategorization of MCS to MCS- and MCS+, with the former meaning the patient displays nonreflex movements and the latter meaning that the patient can respond to commands [6]. Classification of MCS occurs through a combination of Positron Emission Tomography (PET) and behavioral testing. Life expectancy for those in a minimally conscious state depends on several factors including age, comorbid conditions, quality of care, and decisions around withdrawing life-sustaining therapy [25]. More than 4 out of 5 of young patients survive 8 years.

Consciousness level has implications for level of care required

Because a coma is a medical emergency, acute care providers are required when someone becomes comatose [26]. Once someone has transitioned to a vegetative state or minimally conscious state, however, treatment options become more complex. For instance, four levels of treatment have been defined for those in a vegetative state [11]. These treatments include:

- Technological "rescue" treatments such as mechanical ventilation, cardiopulmonary resuscitation
- Medications and supplemental oxygen
- Nutrition and hydration
- Home care or nursing care aimed at maintaining hygiene and personal dignity

Because people in a persistent vegetative state are thought to have such a poor prognosis, Jennett and colleagues believed 3 months should be the point at which withdrawing care becomes appropriate [27]. Nonetheless, patient survival across all disorders of consciousness depends in part on the intensity and quality of the care the patient receives, with preventive care being of primary importance [11,28-33].

CONCLUSION

In 2018, new practice guidelines for disorders of consciousness were put forth by the American Academy of Neurology, with the intent of providing recommendations for care of those with prolonged disorders of consciousness, as well as updating the 1995 definition of persistent vegetative state and the 2002 definition of minimally conscious state. These recommendations were endorsed by the American Academy of Physical Medicine and Rehabilitation, the American College of Surgeons Committee on Trauma, and the Child Neurology Society. Several factors, including clinical history, age, and behavioral assessment can help inform prognosis in those with disorders of consciousness. However, when more consciousness remains, it is likely that less severe brain damage has occurred, and it is thus critical to determine consciousness level in these populations of patients. This information can provide substantial insight into what the patient is experiencing, how they can best be nurtured through medical care, and what their ultimate prognosis and life expectancy may be. This knowledge helps not only the patient and the care team but also the loved ones and caregivers who must make crucial decisions about what support to provide.

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