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Comprehensive Systematic Review Update Summary: Disorders of Consciousness

Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology; the American Congress of Rehabilitation Medicine; and the National Institute on Disability, Independent Living, and Rehabilitation Research

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Abstract

Objective: To update the 1995 American Academy of Neurology (AAN) practice parameter on persistent vegetative state and the 2002 case definition for the minimally conscious state (MCS) by reviewing the literature on the diagnosis, natural history, prognosis, and treatment of disorders of consciousness lasting at least 28 days.

Methods: Articles were classified per the AAN evidence-based classification system. Evidence synthesis occurred through a modified Grading of Recommendations Assessment, Development and Evaluation process. Recommendations were based on evidence, related evidence, care principles, and inferences according to the AAN 2011 process manual, as amended.

Results: No diagnostic assessment procedure had moderate or strong evidence for use. It is possible that a positive EMG response to command, EEG reactivity to sensory stimuli, laser-evoked potentials, and the Perturbational Complexity Index can distinguish MCS from vegetative state/unresponsive wakefulness syndrome (VS/UWS). The natural history of recovery from prolonged VS/UWS is better in traumatic than nontraumatic cases. MCS is generally associated with a better prognosis than VS (conclusions of low to moderate confidence in adult populations), and traumatic injury is generally associated with a better prognosis than nontraumatic injury (conclusions of low to moderate confidence in adult and pediatric populations). Findings concerning other prognostic features are stratified by etiology of injury (traumatic vs nontraumatic) and diagnosis (VS/UWS vs MCS) with low to moderate degrees of confidence. Therapeutic evidence is sparse. Amantadine probably hastens functional recovery in patients with MCS or VS/UWS secondary to severe traumatic brain injury over 4 weeks of treatment. Recommendations are presented separately.

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In simplest terms, consciousness is defined as the state of awareness of the self and environment.[1] Conscious behavior requires adequate arousal (i.e., wakefulness) and awareness of content (i.e., sensory, cognitive, and affective experience). Severe acquired brain injury (ABI) is a catastrophic event that disrupts the brain's arousal and awareness systems, which are mediated by the brainstem and cortex, respectively. The most severe injuries result in prolonged (i.e., lasting at least 28 days) disorders of consciousness (DoC), including the vegetative state (VS)[2] and the minimally conscious state (MCS).[3] VS is also referred to as postcoma unawareness[4] or unresponsive wakefulness syndrome (UWS).[5] In this guideline, the term UWS is used synonymously with VS. While this term has no special merit or mandate for use in clinical practice, it is included here because of its wide acceptance in Europe. Table e-1 (http://www.archives-pmr.org/A611) provides the definitions for VS and MCS and other key terms pertinent to DoC.

The cost of lifetime care for persons with prolonged DoC can exceed $1,000,000.[6] Despite the enormity of the problem, few practice guidelines are available. In 1995, the American Academy of Neurology (AAN) published diagnostic and prognostic guidelines for persistent VS (PVS)[7] following an evidence-based review completed by the Multi-Society Task Force (MSTF) on PVS.[2] In 2002, the Aspen Neurobehavioral Workgroup defined MCS and published consensus-based diagnostic criteria.[3] Both reports focused on diagnosis, as data addressing prognosis and treatment were sparse.

List of abbreviations:

AAN	**American Academy of Neurology**
CI	**confidence interval**
DoC	**disorders of consciousness**
eMCS	**emergence from minimally conscious state**
LEP	**laser-evoked potential**
LR	**likelihood ratio**
MCS	**minimally conscious state**
MSTF	**Multi-Society Task Force**
OR	**odds ratio**
PVS	**persistent vegetative state**
UWS	**unresponsive wakefulness syndrome**
VS	**vegetative state**

Based on available epidemiologic data,[8] the annual US incidence of VS is approximately 4,200 persons. The incidence of MCS is unknown largely because it has no diagnostic code in the International Classification of Diseases classification system. Prevalence figures for VS/UWS and MCS in the United States are hampered by economic factors that lead patients with DoC to be transferred from the acute care setting to long-term care facilities, where they are often lost to follow-up. Prevalence estimates range from 5,000 to 42,000 persons for VS/UWS[9–11] and 112,000 to 280,000 persons for MCS using a proxy definition.[12]

Published estimates of misdiagnosis among patients with DoC consistently approximate 40% in both US and European studies.[13–15] In the most recent study,[13] 41% of patients with a clinical diagnosis of VS/UWS based on team consensus (n = 44) were actually in MCS when reevaluated by the investigators using a standardized neurobehavioral scale. In addition, 89% of those with an uncertain diagnosis (n = 18) were found to have clear signs of consciousness on standardized examination. Findings from the other 2 studies[14,15] were in the same direction. Underlying visual or motor impairments interfering with detection of command-following and failure to detect visual pursuit are frequent causes of failure to recognize MCS. The rate of diagnostic error underscores the need for more refined evaluation methods. This concern extends to the criteria for emergence from MCS (eMCS), as some investigators suggest that the existing criteria lead to overdiagnosis of this condition.[16]

Now is an opportune time to reevaluate current diagnostic approaches. Apart from the extensive list of specialized neurobehavioral assessment instruments that have been released since the MSTF and Aspen Neurobehavioral Workgroup reports were published,[2,17] a growing body of research suggests that functional neuroimaging techniques, such as fMRI and PET, may be able to detect suggestions of conscious awareness in the absence of bedside evidence.[18–21]

Natural history studies of patients with prolonged DoC now include outcomes extending beyond 1 year. This provides an opportunity to reassess the 1994 MSTF introduction of the term permanent VS (supplemental data, available online only at http://www.archives-pmr.org/), which is questioned based on the methodology used to calculate the incidence of recovery of