

Nosologic Considerations in Disorders of Consciousness

Disorders of consciousness (DOC) comprise a group of clinical syndromes carved from the continuum of diffuse and multifocal brain damage.¹ Our current classification of DOC is simply a list of individual syndromes with their diagnostic criteria.² With our recent capacity to detect covert awareness using functional neuroimaging paradigms, this anecdotal classification has become inadequate. In this issue, Bayne and colleagues highlight the principal shortcomings of our current classification of DOC and insightfully analyze options for reforming it.³

Historically, the nosology of DOC encompasses several clinical syndromes. First, coma was defined as a pathologic state of eyes-closed unresponsiveness from which patients could not be aroused to wakefulness or awareness.⁴ In 1972, Jennett and Plum defined the vegetative state (VS) as a coma sequel in which unresponsive patients became wakeful with spontaneous eye opening, eye movements, and sleep–wake cycles, but to the fullest extent possible to test, their awareness of self and environment remained absent.⁵ In 2002, a committee defined the minimally conscious state (MCS) as a syndrome of profound unresponsiveness in which patients showed only limited or intermittent responses to stimuli.⁶ Subsequently, degrees of severity of MCS (MCS + and MCS –) were distinguished.⁷

Each DOC state was delineated as a syndrome into which patients were grouped who shared certain clinical features. Experts devised clinical diagnostic criteria for inclusion into or exclusion from each syndrome. Although syndromic classification is the usual initial step in nosology, once schemes based on pathophysiology become available, they supplant the syndromic approach. The most familiar example of this phenomenon is the many neurogenetic diseases that have been reclassified from a phenotypic to a genotypic nosology. This experience has shown the major limitation of syndromic nosology: that conditions differing pathologically and genetically can exhibit similar clinical signs and symptoms. The most scientifically sound basis for classification is by pathophysiology and genetics.⁸

Syndromic classification of DOC has several additional shortcomings. Patients who qualify for the diagnosis of VS or MCS may have reached the state by completely different mechanisms, such as by traumatic brain injury (TBI), stroke, or diffuse hypoxic–ischemic

neuronal damage. Furthermore, patients classified within each syndrome often vary in severity. For example, some VS patients have isoelectric electroencephalograms (EEGs), although most do not.⁹ The breadth of severity within each syndrome has led to the need to subclassify each syndrome, for example, by dividing MCS into MCS + and MCS –. Syndromic classification also has confounded prognosis, because accurate prognosis ultimately is a function of the pathophysiology producing the state, not membership in a syndrome. Thus, in early studies of VS, it became clear that VS resulting from TBI had a more favorable prognosis than similar-appearing VS resulting from diffuse neuronal hypoxia and ischemia.¹⁰

One limitation results from the choice of syndromic criteria. VS clinical criteria were delineated in the negative, that is, by stating those behaviors that VS patients could not perform. Irrespective of its accuracy, delineating clinical criteria in the negative has the unintended consequence of amplifying the frequency of false-positive diagnoses. Some VS patients may not be able to perform certain behavioral tasks (thereby qualifying for the diagnosis of VS) for reasons not directly resulting from their brain damage, such as from the sedating effect of anticonvulsant drugs. The problem of frequent false-positive diagnoses of VS remains frustratingly persistent.¹¹

The most serious shortcoming of syndromic classification of DOC is that behavioral responses count as the sole evidence of awareness. However, unresponsiveness in the setting of diffuse or multifocal brain damage does not necessarily imply unawareness. The bedside assessment of awareness is purely inferential, because it is impossible for any person to directly assess the conscious experience of another. The examiner interacts with the patient and infers the quality of the patient's conscious life by methodically assessing the patient's responses to a validated set of stimuli, such as those in the Coma Recovery Scale–Revised (CRS-R).¹²

Until the past decade, the skilled use of the CRS-R was believed to yield the most accurate assessment of the patient's level of awareness. However, novel functional neuroimaging paradigms using functional magnetic resonance imaging (fMRI) and fluorodeoxyglucose positron emission tomography (FDG-PET), in which patients are

instructed to ideate motor functions, have shown reproducible blood oxygen level–dependent signal patterns indicating the presence of awareness even when behavioral motor responses were completely absent.^{13,14} This ironic disconnect, called willful modulation of brain activity¹³ and covert cognition,¹⁵ has shown the categorical insensitivity of even the best clinical assessments of awareness.

The final shortcoming of current nosology is that DOC have been demarcated from the continuum of states of diffuse and multifocal brain damage within which it is arbitrary to erect boundaries defining clinical syndromes where none exist in biology. Resulting DOC diagnostic boundary issues are serious problems, not simply because of the ambiguities of borderline cases but because of epistemological and ontological consequences when the names of states imply what constitutes appropriate treatment of the patients.¹⁶

Bayne and colleagues correctly argue that our current syndromic nosology of DOC is inadequate because it relies solely on clinical assessment with the inevitable limitations of such a system. They point out that functional neuroimaging studies have opened a unique window for assessing awareness that in many documented cases can identify awareness when even the most sensitive physical examination cannot. This observation suggests that our current practice of clinical assessment systematically underestimates the conscious life of DOC patients. This important conclusion appears true for both VS and MCS.¹⁷

The most common cause of diagnostic error for VS or MCS is the dissociation of motor responsiveness from awareness, a phenomenon Schiff has called cognitive–motor dissociation.¹⁸ This situation is analogous to that of the patient with locked-in syndrome who remains aware but, because of profound paralysis, has limited response to the examiner’s stimuli and therefore may be wrongly judged to be comatose. Just as a normal EEG can reveal evidence of covert awareness in a locked-in patient, fMRI and FDG-PET responses to ideational commands can reveal evidence of covert awareness in some DOC patients.

Obviously, it is wrong to categorize a patient as VS once functional neuroimaging has demonstrated awareness, yet it is unclear how to diagnose such a patient within our current clinical nosology. A new nosology is necessary that incorporates ancillary testing including fMRI, FDG-PET, EEG, and evoked potentials, because they contribute unique information about awareness. At a minimum, a new system must provide for separate assessments of motor responsiveness and awareness to account for cognitive–motor dissociation. Of the options Bayne and colleagues discuss, the graded, multidimensional system seems best able to specifically describe individual cases given the great variability of DOC patients.

A related but distinct issue from nosology is DOC terminology. The names given to DOC states have been justly criticized for shortcomings. A European committee advocated renaming the VS to the “unaware wakeful state,” because it is a more accurate description and one free of the unintended but negative connotations of “vegetative.”¹⁹ Similarly, the name MCS was criticized for implying a low quantity of conscious life for patients who are minimally responsive on examination²⁰ but whose actual state of awareness often is found to be near normal when tested by fMRI responses.¹⁷ A new nosology using graded multidimensional ratings also could reform DOC terminology.

Potential Conflicts of Interest

Nothing to report.

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