

# Can they suffer?

## The ethical priority of quality of life research in disorders of consciousness

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### Abstract

There is ongoing ethical and legal debate about withdrawing life support for patients with disorders of consciousness (DOCs). Frequently fueling the debate are implicit assumptions about the value of life in a state of impaired consciousness, and persistent uncertainty about the quality of life (QoL) of these persons. Yet there are no validated methods for assessing QoL in this population, and a significant obstacle to doing so is their inability to communicate. Recent neuroscientific discoveries might circumvent that problem and help shed light on QoL in DOCs. There is an ethical imperative to prioritize QoL research in this patient population, to provide evidence to inform treatment, research, and end of life decisions. A minimalist and pragmatic model of QoL is proposed, targeting positive and negative affects as domains for which there is potential to reach across the communication gap, and restore to these voiceless persons some measure of control.

**Key terms:** Vegetative state, disorders of consciousness, minimally conscious state, quality of life, functional neuroimaging

### “... the question is not, Can they reason? nor, Can they talk? but, Can they suffer?” [1]

The matter of withdrawing life support for persons with disorders of consciousness (DOCs) has given rise to much legal and ethical controversy, but it is also a source of anguished debate for families faced with making life or death decisions on behalf of loved ones. Frequently fueling debate are implicit assumptions about the value of life in a state of impaired consciousness, and a large source of discomfort about what to do for the DOC patient is persistent uncertainty about the quality of life (QoL) of these patients. A significant obstacle to assessing QoL in DOC patients is their inability to verbally communicate. Recent neuroscientific advances hold out the hope of reaching across that communication gap for some patients. As research on DOCs proceeds, there is an ethical imperative to prioritize research on QoL, which should consider both how and what to measure in persons with DOCs. The reasons are threefold:

1. Those who contemplate end of life decisions for individual patients have an urgent need for answers about QoL, but information is also important for therapeutic decisions, e.g. the need for pain relief or environmental enhancement.

2. DOC patients are a highly vulnerable patient group, unable to consent to research participation or treatment. Decisional proxies should have information about the potential burdens and benefits for patients of treatment options and research participation, and QoL is a critical piece of that information.

3. Without the ability to assess QoL, the ability to measure the success or failure (in terms of patient well-being) of therapeutic measures is also lacking. QoL is itself an important part of outcome measurement, and should be viewed as an end point in treatment decisions.

Additionally, it is possible that QoL research in DOC patients will benefit other groups of patients who are unable to communicate, but for whom QoL concerns are equally pressing: infants, the elderly demented, and persons with severe cognitive or intellectual disabilities. Before considering the case for prioritizing QoL research, I'll discuss why QoL assessment is particularly problematic in DOC patients, and propose a minimalist and pragmatic model of QoL appropriate to this population.

### Disorders of Consciousness

DOCs include coma, vegetative state/unresponsive wakefulness syndrome (VS/UWS)<sup>1</sup>, and the minimally conscious state (MCS). Locked-in Syndrome (LIS) is not a DOC, as persons in the LIS do not have impaired consciousness, but the condition can behaviorally mimic VS/UWS and coma in that the LIS patient is unresponsive as a result of paralysis.

LIS points to a problematic feature of DOCs. There are at least two conceptions of the VS/UWS at work in clinical diagnosis: a behavioral conception, confirmed by bedside examination (i.e. the patient is in a state of eyes-open behavioral unresponsiveness), and a defini-

1 Unresponsive Wakefulness Syndrome is a new designation for the vegetative state recently proposed by the European Task Force on Disorders of Consciousness. UWS avoids the negative connotation and stigma attached to the term “vegetative”, and is a more accurate description of the syndromic nature of VS, i.e. it acknowledges that these patients are human beings (and not mere “vegetables”), it includes wakefulness and unresponsiveness to stimuli, and does not make a claim about awareness. This distinguishes UWS, which acknowledges that some patients may be conscious but behaviorally unresponsive, from VS, which defines the unresponsive patient as unconscious [2].

tional one, based on inference, in which the unresponsive patient is by definition unconscious, i.e. unaware of self or environment.<sup>2</sup> Whether or not patients are considered conscious, then, is based not on our actual ability to directly access their minds, but on their ability to exhibit behaviors from which we can infer something about their mental life. This inference is suspect, as the example of LIS patients shows, and is driven by the problem of other minds: subjective consciousness is not directly observable. Clinically distinguishing between the VS/UWS, the MCS, and the LIS depends on a behavioral examination that relies on subjective interpretation of inconsistent behaviors that can be limited by motoric dysfunction [4]. Moreover, a subset of patients, who may have complicating, undetected language or movement deficits such as aphasia, agnosia or apraxia, is behaviorally unresponsive despite being conscious. Diagnosing DOCs is thus challenging, and there is an unacceptably high rate of misdiagnosis, with the incidence of conscious patients misdiagnosed as unconscious estimated to be as great as 43% [5,6,7]. Misdiagnosis can persist for years: the diagnosis of LIS takes on average 2.5 months, but in some cases takes up to 6 years [8] during which time the LIS patient is presumed to be comatose; in the striking case of Terry Wallis, his progression from VS to MCS remained undetected for nearly two decades [9].

DOCs essentially did not exist until the advent of intensive care measures that kept comatose patients alive, particularly the development of artificial respirators, which gained widespread use in the 1960s. In 1972, Jennett & Plum coined the term “persistent vegetative state” (PVS) to describe patients who awaken from coma into a state of chronic unresponsiveness [10]. In parts of Europe, the vegetative state was referred to as apallic syndrome or coma vigil. It was also in the 1970s that the PVS became (and has remained) the focal point of the “right to die” movement and intense ethical debate about the value of life in a state of permanent unconsciousness (e.g. the 1976 Karen Ann Quinlan case [11]). In 2002, the MCS was defined to describe those patients who emerged from the VS into a condition of partial awareness [12]. More recently, the MCS was bifurcated into MCS- and MCS+, to distinguish patients who, respectively, exhibit low-level behavioral responses (e.g. visual pursuit, localization of noxious stimuli, or appropriate responses to emotional stimuli) and those who exhibit high-level responses (e.g. command following, intelligible verbalizations or non-functional communication) [13]. Several notable developments in DOCs involve the discovery that some patients

who appear on standard behavioral assessment to be unconscious are “covertly aware”, able to respond to questions and commands through willful modulation of brain activity detectable only through paraclinical neuroimaging [14,15]. A proposed diagnosis for such patients is functional locked-in syndrome (fLIS), to designate persons with extreme motor dysfunction and identifiable higher cognitive functions only measurable by functional neuroimaging [13]. Monti et al argue that functional neuroimaging can reveal “brain behaviors” that are otherwise covert and inaccessible, and that such brain activity is an objective and reliable indicator of consciousness [16]. As with bedside examination, however, it remains the case that lack of detectable “brain behavior” is not dispositive of a lack of awareness, as it has been shown that some healthy controls are not able to reliably generate detectable results on functional neuroimaging. New neuroimaging paradigms have led to renewed interest in DOCs, and give hope that reliable, validated tools for more accurate diagnosis and prognosis will soon emerge.

### Quality of Life and Disorders of Consciousness

The QoL of patients in apparently permanent DOCs, whether the VS/UWS, MCS, or fLIS, is of significant ethical concern because a poor prognosis may prompt contemplation of discontinuing medical treatment and/or life sustaining measures. In the legal and bioethical context, when treatment withdrawal is considered, QoL is sometimes covertly considered under the guise of the “best interests” of DOC patients. QoL is a broad and complex concept about which there is no consensus concerning its definition or the factors that influence it. Nonetheless, it is one of those concepts that is intuitively understood, and which figures prominently in many bioethical discussions, whether about end of life care or about the benefits of medical treatment. There is consensus that QoL is inherently subjective, and refers to the subjective experience of an individual, and should be assessed from the perspective of the individual relative to his or her own values [17,18,19]. The challenge of QoL assessment is to quantify what is inherently qualitative and subjective, to measure, as it were, what it is like to be.

Three distinct conceptions of QoL are found in the literature: i) Subjective well-being, which includes positive and negative affect, life satisfaction, and physical and mental health status; ii) Achievements in the major domains of life (work, social relationships, housing, health); and iii) Utility, which quantifies preferences for various health states based on population samples [20]. The three dominant domains of QoL within these conceptions are physical, psychological, and social functioning. For reasons that will be outlined below, subjective well-being is the appropriate measure of QoL in

2 Shewmon argues that there is another distinct definitional domain of the VS as well, the anatomical definition: “the abolition of cortical structure or function in the context of an intact and functioning brainstem” [3]. There is, Shewmon argues, a suspect inference from behavioral VS/UWS to anatomical VS/UWS [3]. Such an inference is at odds with recent neurological findings of patients in the VS/UWS who exhibit intact but disconnected islands of cortical functioning.

brain-injured and DOC patients. There is no consensus as to the best method for assessing QoL [17], and instruments for measuring QoL, along with their acronyms, have proliferated in recent years [20]. Most measure QoL through a patient self-assessment questionnaire [17], and an issue cutting across all approaches is the ability of persons to self-report on the measured aspects of their own well-being. This presents particular challenges for assessing patients with brain injuries, who may have deficits in the ability to communicate, as well as in self-awareness and self-insight, all of which impair self-reporting [21, 22].

### Generalizing from other patients with brain injuries

There are a few instruments that measure QoL in persons with brain injuries, but all require further validation [18]. It remains empirically unresolved how reliable brain-injured patients are as self-reporters [20], but research shows that a sizable percentage of the general population also encounters difficulty completing some complex QoL questionnaires [20]. Thus, if subjective well-being is a reasonable indicator of QoL in healthy persons, it ought to be equally so in those with brain injuries, and the burden of proof is on those who would assume that this population is unreliable as self-reporters of their own subjective QoL.<sup>3</sup>

One of the shortcomings of instruments that measure QoL in patients with brain injury is the relative salience of different domains of well-being. For example, cognitive and communication deficits, and chronic pain have a significant impact on QoL in persons with brain injuries, but many instruments lack sufficient sensitivity to these dimensions. While an achievement such as meaningful employment is an important QoL domain in the general population, it may be less important to persons with cognitive deficits that preclude employment, while existential dimensions of well-being, such as successful readjustment of one's life perspective, feelings of estrangement from oneself and others, and social dimensions such as isolation, intimacy, and relationships with loved ones and friends may be relatively more important when other areas of fulfillment recede. Generic QoL instruments for the general population may be insensitive to the shifting needs and priorities of persons with brain injuries [18].

The phenomenon of "response shift" can result in a recalibration or reprioritization of value in persons living with brain injuries, such that they assess pain or

cognitive deficits differently, or modify the relative importance of different domains of life [20]. Response shift can result in persons coming to accept a QoL that they might, previous to their injury, have deemed unacceptable, and is a possible explanation for the so-called "disability paradox", in which people with serious disabilities report, contrary to expectations, that their QoL is good [23]. Response shift might also explain why significant others often rate the brain injured person's QoL much lower than the patient herself does [24], thus making proxy informant reports of QoL of questionable use. Studies of patients with LIS reveal that a large majority judge their QoL "good", and comparable to the QoL of healthy controls [24,25]. If nothing else, such results show that even profoundly disabled brain-injured persons often confound expectations when it comes to their QoL. The same may not be true of DOC patients, but generalizing from other brain-injured patients emphasizes the need to learn more about their actual QoL, rather than relying on population-based norms and preconceptions, or proxy reports with poor patient-proxy concordance [17] that might significantly mis-estimate QoL in DOCs or mis-value continued life.

There is an ethically serious flaw in assessing QoL in brain-injured persons by assuming that healthy individuals are the norm, or constitute a "gold standard" of sorts. Brain-injured persons experience many losses – social and functional losses, losses of ability, friendships, and of memories – but some nonetheless achieve subjectively good QoL. Looked at prospectively, however, a life of profound disability might seem incompatible with good QoL. We ought to find out, whenever possible, how an individual's life is actually going, not how it measures up to some pre-injury or healthy exemplar. The disability paradox, and the possibility that response shift as well as lack of self-insight might result in subjective QoL being higher in DOC patients than healthy persons would expect are ethically significant.

No existing QoL instrument is capable of assessing QoL in DOC patients, and some authors express skepticism about the very possibility of measuring QoL in unconscious or minimally conscious patients [18]. The inability to communicate or self-report is a significant barrier to assessing QoL, but in VS/UWS patients, there is a further hurdle: it is not known if these patients experience anything at all. It is conceivable that they are aware of nothing that might be recognized as a lived experience, and a life that is not experienced by an individual has no subjective quality. Thus, there is a sense in which unconsciousness might count against one possibly having a good life. A life with nothing of any value in it would count for many as a life not only barely lived, but a life not worth living. However, given the high rate of misdiagnosis in DOCs, it behooves us to consider QoL in those who may be covertly aware.

<sup>3</sup> There is an interesting epistemological question concerning whether it matters if brain injured patients are not "accurate" reporters of their own QoL (and even what it would mean to say that one might be wrong about one's subjective state of well-being). If an individual perceives the quality of his or her life to be good, is it not, by definition, subjectively good? Much more could be said about this issue, but it is somewhat beyond the scope of this paper, and so must be set aside.

## A minimalist and pragmatic model of quality of life

A concept of QoL, scaled to the norms and preferences of the general population, is inappropriate in patients whose QoL would inevitably be rated as abysmal. For example, on a standard health-related QoL index, DOC patients could not possibly have a good or high QoL due to their low level of physical and/or cognitive functioning. A conception of QoL as subjective well-being, sensitive to the functional status and interests of DOC patients, is needed. McMillan proposes a model of QoL that is useful and appropriate as a conceptual starting point, for it identifies two fundamental affective domains of QoL [17], which, propitiously, are the very domains that at present are potentially accessible in DOC patients who have minimal or no ability to communicate. The two domains are “negative affect” and “positive affect”.<sup>4</sup> The “negative affect” domain includes affective states of discomfort, both physical in origin (e.g. pain, illness) and emotional in origin (depression, boredom, etc.) [17]. The “positive affect” domain consists of pleasant affective states of physical or emotional origin, such as physical contact, social companionship, and mental stimulation [17].

Limiting the domains for assessment to positive and negative affect is not grounded in an epistemic claim that only those domains matter. In most persons, positive and negative affect barely scratch the surface of what is considered important to one’s well-being. Rather, these limited domains are emphasized because they are fundamental to QoL and undoubtedly do matter, if anything does, and because they actually have potential to be assessed in DOC patients. One could argue that positive and negative affect, and things that impact positive and negative affect, are all that matter for QoL in persons with profound disabilities, but nothing like that claim is being made here about DOC patients. What is offered here, rather, is a minimalist and pragmatic model of QoL based not on a claim about what matters, but rather on a claim about what matters that we can at the same time assess.

While QoL assessment has traditionally been the domain of the social sciences, recent developments suggest a role for neuroscience in accessing subjective information locked inside DOC patients. There is a serendipitous synergy between potential objective measures of QoL and innovative, objective tools for diagnosis and prognosis, so QoL research might plant two trees with one seed. Several potential contributions for neuroscience are here proposed, with the caveat that much more research is needed, particularly to develop, validate, and ascertain the reliability of neuroimaging modalities for assessing QoL in DOC patients.

<sup>4</sup> McMillan calls the domains “comfort-discomfort” and “pleasure” [17].

## Negative affect

The International Association for the Study of Pain has defined pain as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage” [26]. This distinguishes pain, as an experienced psychological state, from nociception which refers to “activity induced in the nociceptor and nociceptive pathways by a noxious stimulus” [26]. Although the proximate physical cause of experienced pain may be nociception, “the experience of pain is more than a simple sensory process. It is a complex perception involving higher levels of the central nervous system, emotional states, and higher order mental processes” [27]. Experiencing painfulness requires nociception and emotional reaction, which are “processed by the brain in areas anatomically and physiologically distinct from one another” [28].

The physiological effects of nociception, even if not perceived, may have longterm repercussions for QoL. Nociception in the absence of pain awareness induces a physiological stress response [28]; chronic neuropathic signaling can result in a “persistent and sometimes self-sustaining cascade of neural and endocrine responses that degrades physical and psychological well-being” [29], as well as neuronal damage and compromised immune functioning [29]. With evidence that neuroplasticity can play a role in recovery from VS/UWS [30], the capacity for nociception and untreated pain to negatively affect recovery should be explored. For purposes of assessing subjective QoL, whether or not a person experiences pain and suffering matters most.

There has been significant attention in recent years to the study of pain in DOCs. Several studies show that pain processing differs between the VS/UWS and the MCS [31]. Boly et al found widespread activation of the “pain matrix” along with preserved functional connectivity in MCS patients, comparable to controls [32]. Most studies with VS/UWS patients suggest likely nonconscious pain processing [31,33], Markl et al. found that 30% of VS/UWS patients showed responses in the affective pain network, leading the researchers to conclude that some can experience pain [34]. A recently developed behavioral test, the Nociception Coma Scale shows potential usefulness as a sensitive tool for assessing nociception in severely brain-injured patients, and for distinguishing, on the basis of reactivity to nociceptive stimuli, between the VS/UWS and the MCS [31, 35].

Objective evidence of the capacity for pain, and for the presence of pain, would be important pieces of the QoL puzzle for DOC patients. Additionally, pain is an aspect of QoL for which there is hope of remedy through the provision of analgesic or psychoactive medications. Thus, while pain research on a clinical population incapable of providing informed consent is fraught with ethical concerns, not least because it may involve the

intentional infliction of pain, such research also has the potential to directly benefit the research subjects by bringing to light the need for pain treatment.

Suffering, of course, has many potential causes besides physical pain, including depression, isolation, stress, and grief, all of which are common in persons with brain injuries. Psychological suffering in DOC patients is an important consideration. Evidence suggests that there may be more going on in the minds of MCS patients than is apparent from their behavior [16, 36, 37, 38], including evidence of potential cognition, such that some patients may have insight into their own condition [36, 39, 40]. There is also evidence of emotional response and processing [41, 42, 43], which suggests the possibility that some DOC patients could experience mental distress or pleasure. None of the evidence is yet unequivocal, but it rises to the level of possibility with sufficient force to obligate consideration of the psychological domains of QoL for persons in the MCS and fLIS.

### Positive affect

There is clear reason for ethical concern about negative affect and suffering, but positive affect is also an important component of subjective well-being. A person who suffers pain, grief, and isolation may also be a person for whom existence includes compensatory positive experiences and emotions as well. The truly tragic case would be one in which there are no compensatory positive experiences or affects, but only a life of unremitting misery. Such suffering would, presumably, result in an unacceptably low QoL, and a life that may not be worth living. A life without the possibility of positive experiences and emotions – a life without joy, love, humor, fun – even in the absence of suffering, would still be a poor life. Positive affect may make the difference between a life of flourishing (however relatively diminished that life might seem compared the flourishing of healthy individuals) and a life of mere languishing. Revealing the potential for positive affect in a patient may importantly have the positive effect of prompting others to engage in activities (talking, playing, touching, etc.) that could enhance QoL in DOC patients. As positive affect has been demonstrated to enhance cognitive functioning, resilience, and immune responses [44, 45], the therapeutic role of positive affect in cognitive disability and rehabilitation in DOC patients should not be overlooked.

The neuroscience of happiness is still in its infancy, but a few “hedonic hotspots” have been identified in the brain [46], and all pleasures appear to involve the same hedonic brain systems [46]. Neuroscience offers clues about the potential for brain injuries to abolish some pathways to positive affect by diminishing or even eliminating normal sensory pleasures. E.g. lesions to the ventral pallidum appear to abolish hedonic “liking” reactions to sweetness and replace them with disgust

[47]. Miller et al report a patient who, following bilateral damage to the ventral pallidum, reported feelings dominated by depression, hopelessness, and anhedonia [48]. It would be meaningful to know if such diminution of positive affect has occurred in a DOC patient. As with nociception and experienced pain, it would be overly reductive to assume that there is a simple correspondence between so-called “hedonic” brain activity and happiness or pleasure. The behavioral and neuro-anatomical evidence for positive and negative affect provide only a crude picture: we might infer that there is pleasure or pain, or positive or negative affect, without being able to measure its intensity or know how salient it is for the patient all things considered [49]. Does a pain bother him a lot? Is her pleasure very pleasing? The minimalist and pragmatic conception of QoL is rudimentary, and only begins to provide answers.

### Rethinking Quality of Life Assessment

Communication is a significant hurdle for QoL assessment in DOC patients, but if there were technology-mediated channels of communication – so-called brain-computer interfaces (BCIs) – DOC patients could simply be asked about their QoL given appropriately designed questionnaires suitable for individuals with severe brain injuries and communication deficits [4, 50]. Some neuroimaging paradigms that currently show potential for assessing QoL are likewise possible means of directly communicating with some DOC patients about their QoL. For example, using fMRI, Owen asked a VS/UWS patient if he was in pain, and he responded to indicate “no” [51, 52]. There remain significant limitations inherent in BCIs, not least of which is that a lack of a response by a patient can be interpreted in several ways (e.g. the patient is confused, or doesn’t understand the question, or was distracted). It is not necessarily the case that a lack of answer to a question like “Are you in pain?” equates to a negative answer, just as it is not the case that a lack of response to a test of covert consciousness proves lack of consciousness.

DOCs require a paradigm shift in how we think about QoL assessment, both in terms of the what (as noted above) and the how. A multidisciplinary effort that includes affective and clinical neuroscientists and social scientists is required for the how: to design and implement appropriate QoL assessments suited to the level of disability and diminished cognitive and communicative capacities of DOC patients, including those communicating via BCIs. In addition to developing the role of functional neuroimaging, modifications might include simplified questions (e.g. yes/no questions), and queries framed to target population- and individual-specific concerns and needs. QoL assessment has always attempted to objectively quantify subjective states of well-being: the aim of using neuroimaging and technol-

ogy is no different, even if the instruments employed are radically different.

### The ethics of Quality of Life research

DOC patients, like other persons with profound cognitive disabilities, are vulnerable persons who lack autonomy, and are unable to consent to research participation. However, research on QoL has the potential to directly benefit DOC patient-participants. The research may involve some discomfort for some patients, but it is comparable in risk/burden to current diagnostic tests that are already administered to these patients, as well as to experimental diagnostic/prognostic measures such as fMRI which have the potential to become standard tools. Moreover, the information gained can benefit research participants with empirical evidence of the need to treat pain or distress, or prompt the provision of positive and enjoyable stimuli, or inform decisions to end life-sustaining measures if doing so is compatible with the known values and desires of the patients and their proxies. Because of the minimal risk, the comparability or identity to already experienced risks/burdens and procedures, and the potential for direct benefits to the patients, such research can be ethically conducted in this vulnerable group with proxy consent. Additionally, information about the QoL of an individual allows for an evidence-based assessment of the potential benefits and burdens of research or treatment. In the absence of paradigms for assessing QoL in these patients, before and after therapeutic interventions, we risk worsening their plight in ways that are ethically unacceptable. After all, being unconscious, or lacking insight into one's level of disability, social impairment, and isolation may be psychologically protective for some DOC patients, and may enhance the ability to cope with disability [36, 54]. Altering the cognitive status of DOC patients with, e.g., treatments that aim to increase their level of awareness, may alter their QoL for good or bad. Having a baseline notion of what life is like for the patient, together with data on QoL in other DOC patients, may inform treatment and research decisions. The benefits might extend beyond individual participants, by helping inform treatment and nontreatment choices in those patients who still cannot be reached through the means available to us now or in the near future. Finally, the empirical evidence acquired may help guide the way in developing treatments and rehabilitative strategies that are responsive to the actual needs of DOC patients.

### Conclusion: the ethical imperative

DOC patients can be subjected to clinical neglect and nihilism: on the belief that nothing can be done for them, nothing is done for them. This benign neglect is

one reason for the unacceptably high rate of misdiagnosis. Once patients are deemed "permanent", they are not reevaluated for changes in neurological status that might reveal an emergence to consciousness, unless the patient exhibits dramatic changes in behavior. New research might begin to fill the empirical lacuna and reduce this neglect. The dearth of research on QoL in the DOC patient population likewise demands addressing. This neglect is based on the belief that QoL assessment is not possible in patients who have such limited capacities that they are not capable of self-assessment or self-reporting. Yet just as QoL is an important ethical consideration in the care of newborns, the elderly demented, and other patients incapable of communication and self-assessment, it is critically important in patients with DOCs. Presuppositions about their QoL prejudice our thinking about the value of life-sustaining treatment for such patients. Questions persist about what is in the best interests of these patients, and are especially contentious with patients in the MCS or fLIS, who are conscious, and may therefore suffer both physically and psychologically from being perpetually trapped in a state of profound disability [54, 55, 56, 57]. Is existence torture for them? Or does life allow for compensatory benefits, as it does for others with severe disabilities? These are questions for which answers are urgently needed, not because the answers by themselves are sufficient to justify end of life or treatment decisions, but because they are necessary for such decisions.

Given the place of prominence QoL has in our beliefs about whether life is worth living for DOC patients, the ethical importance of finding reliable and valid measures of QoL in this population can hardly be overstated. There is an ethical imperative to prioritize research towards developing QoL assessments suitable for DOC patients using available and emerging paradigms. Such research, which goes hand in hand with efforts to improve the accuracy of diagnosis and prognosis, should be prioritized over experimentation on treatments and therapies for DOCs. While this is a strong claim, the priority is justified because an understanding of QoL, of what it is like to be in a state of diminished or disordered consciousness, is a precondition for ethical research on treatment modalities that could potentially alter the QoL of these patients, for better or worse. For individual patients, assessing QoL could help inform therapeutic decisions, such as providing pain relief, or social/environmental enhancements, or, in some cases, decisions to withdraw life sustaining treatments. Making decisions based on false beliefs about the subjective value of life for DOC patients denies these persons what little proxy-mediated self-rule remains to them, and also denies their proxies the information they need to make the right decisions for them. In the absence of reliable and valid information about QoL, decisions are made in a void, based on inference, suppositions, and preconceptions that we

have good reason to question. Finding a way to assess QoL would give these voiceless patients some measure of control, and help us reach some small distance across the abyss that separates them from their families, their community, and their world.

**Conflicts of interest:** None.

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## Zusammenfassung

### Können sie leiden? Ethische Priorität der Lebensqualitätsforschung bei Bewusstseinsstörungen

Gegenwärtig wird eine ethische und rechtliche Debatte über den Abbruch lebenserhaltender Massnahmen bei Patienten mit Bewusstseinsstörungen geführt. Diese Debatten sind gewöhnlich von impliziten Annahmen über den Lebenswert und von Unsicherheit über die Lebensqualität der Menschen mit Bewusstseinsstörungen geprägt. Bislang gibt es keine validierten Methoden, um die Lebensqualität dieser Patienten zu messen, wobei ein wesentlicher Grund dafür in deren Kommunikationsunfähigkeit besteht. Neue neurowissenschaftliche Entdeckungen könnten dazu beitragen, dieses Problem zu umgehen und Licht auf Lebensqualitätsaspekte bei Bewusstseinsstörungen zu werfen. Es besteht ein ethischer Imperativ, die Lebensqualitätsforschung bei dieser Patientengruppe prioritär zu behandeln, um bessere Evidenzen für Behandlung, Forschung und Lebensende-Entscheidungen zu gewinnen. Es wird ein minimalistisches und pragmatisches Lebensqualitätsmodell vorgeschlagen, das auf positive und negative Gemütsbewegungen ausgerichtet ist, die das Potential in sich tragen, die Kommunikationslücke zu überwinden und bei Personen, die ihre Stimme verloren haben, Kontrollmassnahmen zu ermöglichen.

## Résumé

### Peuvent-ils souffrir ? La priorité éthique de la recherche sur la qualité de vie dans les pathologies de la conscience

On assiste actuellement à un débat éthique et juridique sur la question de l'interruption des mesures de maintien en vie pour les patients atteints de pathologies de la conscience (DOC). Le débat est régulièrement alimenté par des suppositions concernant la valeur de la vie des personnes dans un état de conscience diminué, ainsi que par une incertitude persistante concernant leur qualité de vie (QoL). C'est qu'il n'existe pas de mé-

thode validée pour évaluer la qualité de vie dans cette population de patients, et un obstacle important à cela vient de leur incapacité à communiquer. Des découvertes neuroscientifiques récentes pourraient cependant contourner cette difficulté et permettre de jeter quelque lumière sur la qualité de vie des patients DOC. Or, il existe un impératif moral de donner la priorité à la recherche sur la qualité de vie de cette population de patients, de rassembler des données pour guider le traitement, la recherche et les décisions de fin de vie. Cet article propose un modèle minimaliste et pragmatique de qualité de vie, ciblant les émotions positives et négatives comme étant des domaines où l'absence de communication pourrait être surmontée, afin de redonner à ces personnes sans voix un certain contrôle sur leur vie.

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## References

1. Bentham J. An introduction to the principles of morals and legislation. [Burns JH and Hart HLA, editors.] 1970. London; The Athlone Press. 1970.
2. Laureys S, Celesia GG, Cohadon F, Lavrijsen J, León-Carrión J, Sannita WG, Szabon L, Schmutzhard E, von Wild, KR, Zeman A, Dolce G, the European Task Force on Disorders of Consciousness. Unresponsive wakefulness syndrome: a new name for the vegetative state or apallic syndrome. *BMC Med.* 2010;8(68):online. <http://www.biomedcentral.com/1741-7015/8/68>.
3. Shewmon DA. A critical analysis of conceptual domains of the vegetative state: Sorting fact from fancy. *NeuroRehabilitation.* 2004; 19:343-347.
4. Naci L, Monti MA, Cruse D, Kübler A, Sorger B, Goebel R, Kochoube B, Owen AM. Brain-Computer Interfaces for communication with nonresponsive patients. *Ann Neurol.* 2012;72:312-323.
5. Childs NL, Mercer WN, Childs HW. Accuracy of diagnosis of persistent vegetative state. *Neurology.* 1993;43(8):1465-1467.
6. Andrews K, Murphy L, Munday R, Littlewood C. Misdiagnosis of the vegetative state: retrospective study in a rehabilitation unit. *BMJ.* 1996;313(7048):13-16.
7. Schnakers C, Vanhaudenhuyse A, Giacino J, Ventura M, Boly M, Majerus S, Moonen G, Laureys S. Diagnostic accuracy of the vegetative and minimally conscious state: Clinical consensus versus standardized neurobehavioral assessment. *BMC Neurol.* 2009; 9(35):no page numbers.
8. Laureys S, Pellas F, Van Eeckhout P, Ghorbel S, Schnakers C, Perrin F, Berré J, Faymonville M, Pantke K, Damas F, Lamy M, Moonen G, Goldman S. The locked-in syndrome: what it is like to be conscious but paralyzed and voiceless? In: S. Laureys, editor. *Progress in Brain Research*; vol 150. Elsevier 2005. Chapter 34;p.495-511.
9. Wijdicks EFM. Minimally Conscious State vs Persistent Vegetative State: The Case of Terry (Wallis) vs the Case of Terri (Schivo). *Mayo Clin Proc.* 2006;81(9):1155-1158.
10. Jennett B, Plum F. Persistent vegetative state after brain damage: A syndrome in search of a name. *Lancet.* 1972 April;299(7753): 734-737.
11. Meisel A. Quality of life and end-of-life decisionmaking. *Qual Life Res.* 2003;12(Suppl.1):91-94.

12. Giacino JT, Ashwal MD, Childs N, Cranford MD, Jennett B, Katz DI, Kelly JP, Rosenberg JH, Whyte J, Zafonte RD, Zasler ND. The minimally conscious state: Definition and diagnostic criteria. *Neurology*. 2002;58:349–353.
13. Bruno M, Vanhaudenhuyse A, Thibaut A, Moonen G, Laureys S. From unresponsive wakefulness to minimally conscious PLUS and functional locked-in syndromes: recent advances in our understanding of disorders of consciousness. *J Neurol*. 2011 June 16;(published online) DOI 10.1007/s00415-011-6114-x.
14. Owen AM, Coleman MR, Boly M, Davis MH, Laureys S, Pickard JD. Detecting awareness in the vegetative state. *Science*. 2006 Sept 8;313:1402.
15. Monti MM, Vanhaudenhuyse A, Coleman MR, Boly M, Pickard JD, Tshibanda L, Owen AM, Laureys S. Willful modulation of brain activity in disorders of consciousness. *N Engl J Med*. 2010 Feb 3;362:NEJMoa0905370.
16. Monti MM, Coleman MR, Owen AM. Behavior in the brain: Using functional neuroimaging to assess residual cognition and awareness after severe brain injury. *J Psychophysiol*. 2010;24(2):76–82.
17. McMillan FD. Quality of life in animals. *JAVMA* 2000 June 15; 276(12):1904–1910.
18. Bullinger M and the TBI Consensus Group. Quality of life in patients with traumatic brain injury—basic issues, assessment and recommendations: Results of a consensus meeting. *Restor Neurol Neurosci*. 2002;20:111–124.
19. Osoba D. Lessons learned from measuring health-related quality of life in oncology. *J Clin Oncol*. 1994;12:608–616.
20. Dijkers MP. Quality of life after traumatic brain injury: A review of the research approaches and findings. *Arch Phys Med Rehabil*. 2004 April;85(suppl 2):S21–35.
21. Prigatano GP. Impaired self-awareness after moderately severe to severe traumatic brain injury. *Acta Neurochir*. 2005;Suppl(93):39–42.
22. Sherer M, Hart T, Nick TG, Whyte J, Nakase R, Yablon SA. Early impaired self-awareness after traumatic brain injury. *Arch Phys Med Rehabil*. 2003 February;84:168–176.
23. Koskinen S. Quality of life 10 years after a very severe traumatic brain injury (TBI): the perspective of the injured and closest relative. *Brain Inj*. 1998;12(8):631–648.
24. Lulé D, Zickler C, Häcker S, Bruno MA, Demertzi A, Pellas F, Laureys S, Kübler A. Life can be worth living in locked-in syndrome. In: S. Laureys et al, editor. *Progress in Brain Research*; vol 177. Elsevier 2009. Chapter 23;p.339–351.
25. Bruno MA, Bernheim JL, Ledoux D, Pellas F, Demertzi A, Laureys S. A survey on self-assessed well-being in a cohort of chronic locked-in syndrome patients: happy majority, miserable minority. *BMJ Open*. 2011;doi:10.1136/bmjopen-2010-000039.
26. Merskey H, Albe-Fessard DG, Bonica JJ. Pain terms: a list with definitions and notes on usage: recommended by the IASP Subcommittee on Taxonomy. *Pain* 1979;6:249–252.
27. Osterwels R, Kleinman A, Mechanic D. Institute of Medicine Committee on Pain, Disability, and Chronic Illness Behavior: Pain and Disability, Clinical Behavioral and Public Policy Perspectives. 1987. National Academies Press.
28. Lowery CL, Hardman MP, Manning N, Hall RW, Anand KJS. Neurodevelopmental changes of fetal pain. *Semin Perinatol* 2007; 31:275–282.
29. Chapman CR, Gavrin J. Suffering: the contributions of persistent pain. *Lancet*. 1999 June 26;353:2233–2237.
30. Voss HU, Uluç AM, Dyke JP, Watts R, Kobylarz EJ, McCandliss BD, Heier LA, Beattie, BJ, Hamacher KA, Vallabhajosula S, Goldsmith SJ, Ballon D, Giacino JT, Schiff, ND. Possible axonal regrowth in late recovery from the minimally conscious state. *J Clin Invest*. 2006;116(7):2005–2011.
31. Schnakers C, Chatelle C, Demertzi A, Majerus S, Laureys S. What about pain in disorders of consciousness? *AAPS J*. 2012; 14(3):437–444.
32. Boly M, Faymonville ME, Schnakers C, Peigneux P, Lambermont B, Phillips C, Lancellotti P, Luxen A, Lamy M, Moonen G, Maquet P, Laureys S. Perception of pain in the minimally conscious state with PET activation: an observational study. *Lancet Neurol*. 2008; 7(11): 1013–1020.
33. Kassubek J, Juengling FD, Els T, Spreer J, Herpers M, Krause T, Moser E, Lücking CH. Activation of residual cortical network during painful stimulation in long-term postanoxic vegetative state: a <sup>15</sup>O-H<sub>2</sub>O PET study. *Neuro Sci*. 2003;212:85–91.
34. Markl a, Yu T, Vogel D, Müller F, Kotchoubey B, Lang S. Brain processing of pain in patients with unresponsive wakefulness syndrome. *Brain Behav*. 2013;3(2):95–103.
35. Schnakers C, Chatelle C, Vanhaudenhuyse A, Majerus S, Ledoux D, Boly M, Bruno A, Boveroux P, Demertzi A, Moonen G, Laureys S. The Nociception Coma scale: A new tool to assess nociception in disorders of consciousness. *Pain*. 2010;148:215–219.
36. Schiff ND, Giacino JT, Fins JJ. Deep Brain Stimulation, neuroethics, and the Minimally Conscious State: Moving beyond proof of principle. *Arch Neurol*. 2009 June;66(6):697–702.
37. Schnakers C, Majerus S, Laureys S. Bispectral analysis of electroencephalogram signals during recovery from coma: preliminary findings. *Neuropsychol Rehabil* 2005;15:381–388.
38. Menon DK, Owen AM, Williams EJ, et al. Cortical processing in persistent vegetative state. Wolfson Brain Imaging Centre Team. *Lancet* 1998;352:200.
39. Perrin F, Schnakers C, Schabus M, Degueldre C, Goldman S, Bredart S, Faymonville E, Lamy M, Moonen G, Luxen A, Maquet P, Laureys S. Brain response to one's own name in vegetative state, minimally conscious state, and locked-in syndrome. *Arch Neurol*. 2006;63:562–569.
40. Boly M, Faymonville M, Peigneux P, Lambermont B, Damad P, Del Fiore G, Degueldre C, Franck G, Luxen A, Lamy M, Moonen G, Maquet P, Laureys S. Auditory processing in severely brain injured patients: Difference between the minimally conscious state and the persistent vegetative state. *Arch Neurol*. 2004;61:233–238.
41. Bekinschtein T, Niklison J, Sigman L, Manes F, Leiguarda R, Armory J, Owen A, Carpintero S, Olmos L. Letter: Emotion processing in the minimally conscious state. *J Neurol Neurosurg Psychiatry*. 2004;75:788.
42. Owen AM, Menon DK, Johnsrude IS, et al. Detecting residual cognitive function in persistent vegetative state. *Neurocase*. 2002; 8:394–403.
43. Kotchoubey B, Kaiser J, Bostanov V, et al. Recognition of affective prosody in brain-damaged patients and healthy controls: a neurophysiological study using EEG and whole-head MEG. *Cogn Affect Behav Neurosci* 2009;9:153–167.
44. Zautra AJ, Johnson LM, Davis MC. Positive affect as a source of resilience for women in chronic pain. *J Consult Clin Psychol*. 2005 April;73(2):212–220.
45. Fredrickson BL, Losada MF. Positive affect and the complex dynamics of human flourishing. *Am Psychol*. 2005 October;60(7): 678–686.
46. Kringelbach ML, Berridge KC. Towards a functional neuroanatomy of pleasure and happiness. *Trends Cogn Sci*. 2009;13(11):479–487.
47. Berridge KC, Kringelbach ML. Building a neuroscience of pleasure and well-being. *Psychol Well Being*. 2011;1(3).
48. Miller JM, Vorel SR, Tranguch AJ, Kenny ET, Mazzoni P, van Gorp WG, Kleber HD. Anhedonia after a selective bilateral lesion of the globus pallidus. *Am J Psychiatry*. 2006;163(5):786–8.
49. Demertzi A, Racine E, Bruno M-A, Ledoux D, Gosseries O, Vanhaudenhuyse A, Thonnard M, Soddu A, Moonen G, Laureys S. Pain perception in disorders of consciousness: Neuroscience, clinical care, and ethics in dialogue. *Neuroethics*. 2013;6:37–50.
50. Chatelle C, Chennu S, Noirhomme Q, Cruse D, Owen AM, Laureys S. Brain-computer interfacing in disorders of consciousness. *Brain Inj*. 2012;1–13.
51. Doyle K. Can we “talk” to vegetative patients via fMRI? *Popular Mechanics*. 2012 November 14. url: <http://www.popularmechanics.com/science/health/neuroscience/can-we-talk-to-vegetative-patients-via-fmri-14733177> [accessed 24 May 2013].
52. Walsh F. Vegetative patient Scott Routley says ‘I’m not in pain.’ *BBC News*. 2012 November 12. <http://www.bbc.co.uk/news/health-20268044> [accessed 24 May 2013].
53. Lo B, Dornbrand L, Wolf LE, Groman M. The Wendland case— withdrawing life support from incompetent patients who are not terminally ill. *N Engl J Med*. 2002 May 9;346(19):1489–1493.
54. Johnson LSM. The right to die in the minimally conscious state. *J Med Ethics*. 2011;37:175–178.
55. Glannon W. Burdens of ANH outweigh benefits in the minimally conscious state. *J Med Ethics*. 2013;Online: doi:10.1136/medethics-2012-100882 [accessed 5/17/2013].
56. Kahane G, Savulescu J. Brain damage and the moral significance of consciousness. *J Med Philos*. 2009;34:6–26.
57. Wilkinson DJ, Kahane G, Horne M, Savulescu J. Functional neuroimaging and withdrawal of life-sustaining treatment from vegetative patients. *J Med Ethics*. 2009;35:508–511.