THE ATLANTIC Journal of Medical Science and Research

Atlantic J Med Sci Res 2025;5(2):51-8
DOI: 10.5455/atjmed.2025.05.05

Review Article

Neuroscientific detection of covert consciousness in disorders of consciousness

Mostafa Eissa

Independent Researcher and Freelance Consultant, Department of Pharmaceutical Sciences, Nasr City, Egypt

Received: 05 May, 2025
Accepted: 03 June, 2025
Published: 17 June, 2025

Corresponding Author: Mostafa Eissa, Independent Researcher and Freelance Consultant, Department of Pharmaceutical Sciences, Nasr City, Egypt
Email: mostafaessameissa@yahoo.com

CITATION
Eissa M. Neuroscientific detection of covert consciousness in disorders of consciousness. Atlantic J Med Sci Res. 2025;5(2):51-8. DOI: 10.5455/atjmed.2025.05.05

Abstract

The subjective experience of consciousness, a cornerstone of human existence, is profoundly disrupted in disorders of consciousness (DOC) arising from severe brain injuries, spanning-states from coma to the minimally conscious state. A significant challenge in clinical practice is the phenomenon of covert consciousness, in which individuals may retain awareness despite the absence of overt behavioral responsiveness. Diagnosis based solely on observable behavior is inherently limited by factors such as co-occurring motor impairments, the fluctuating nature of consciousness, and subjective interpretation, potentially leading to misclassification. To overcome these limitations, neuroscientific methodologies have advanced significantly. To address these limitations, neuroscientific methods have advanced considerably. Functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) provide objective evidence of preserved brain activity and cognitive processing, enabling detection of willful modulation and offering prognostic insight. Electrophysiological techniques—including electroencephalography (EEG), event-related potentials (ERPs), transcranial magnetic stimulation combined with EEG (TMS-EEG), and advanced downstate analysis—further reveal dynamic neural patterns indicative of residual awareness. The detection of covert consciousness has profound ethical, clinical, and societal implications. It necessitates a re-examination of patient rights, end-of-life decision-making, the use of brain-computer interfaces, and societal conceptions of personhood. This evolving understanding mandates a shift towards integrating objective neuroscientific assessments with compassionate, person-centered care, aiming to preserve dignity and navigate the complex ethical landscape of severe brain injury.

Keywords: Covert consciousness, functional magnetic resonance imaging, positron emission tomography, electroencephalography, minimally conscious state, unresponsive wakefulness syndrome

INTRODUCTION

The subjective experience of consciousness, a defining characteristic of human awareness and self-perception, remains a profound enigma in scientific exploration (1). Its vulnerability is starkly evident in disorders of consciousness (DOC), a diverse group of conditions resulting from severe brain injuries that fundamentally impair this core aspect of human existence (2). Traditionally, DOCs are classified along a continuum that includes coma, unresponsive wakefulness syndrome (UWS), and the minimally conscious state (MCS). These states present substantial challenges for clinicians, researchers, and ethicists alike, particularly in the realms of diagnosis, prognosis, and ethical decision-making (2).

A particularly complex and ethically charged dimension of DOCs is the growing recognition of 'hidden' or 'covert' consciousness – a state where awareness may persist despite the absence of discernible behavioral responses (3). This phenomenon compels a re-evaluation of conventional diagnostic paradigms and raises critical questions about the true extent of conscious experience in individuals traditionally considered unresponsive (4).

This review explores the enigmatic phenomenon of covert consciousness by critically examining the limitations of relying solely on behavioral assessments for diagnosing consciousness. It also highlights significant advancements in neuroscientific techniques capable of detecting sub-behavioral awareness and addresses the profound ethical and societal implications emerging from evolving understandings of consciousness in these highly vulnerable populations (5-8). The exploration of hidden consciousness prompts a critical re-evaluation of the fundamental definitions of awareness, personhood, and the essence of human experience in the wake of severe neurological damage.

The development of this review article on hidden consciousness in DOCs employed a systematic and ethical approach. The process comprised three key stages: identifying and acquiring data sources, retrieving targeted information and critically selecting relevant material, and finally, synthesizing the integrated data to generate the textual content.

The initial phase focused on acquiring data from publicly accessible literature found in databases such as PubMed and Web of Science, alongside clinical practice guidelines and credible science news outlets, drawing upon an existing knowledge base. The second phase utilized keyword searches, prioritizing high-quality sources and the most convenient, relevant information, implicitly curating the data (9-12). The third phase involved synthesizing the information based on identified themes to construct the narrative.

The Constraints of Diagnosis Based Solely on Behavior in Disorders of Consciousness

Historically, the diagnostic approach for DOC has heavily relied on clinical evaluations at the bedside that focus on a patient's observable behaviors (13,14). In the case of UWS, formerly known as the vegetative state, the diagnosis is characterized by a clinical dissociation between wakefulness and awareness (15). Wakefulness is identified by the presence of sleep-wake cycles and basic reflexes, while awareness, defined by purposeful, voluntary interaction, is considered absent (16). Patients in UWS may exhibit preserved brainstem reflexes but lack consistent, intentional behavioral responses to various sensory inputs (15).

In contrast, the diagnostic criteria for the MCS require minimal but unambiguous behavioral evidence of awareness (17,18). These behaviors, although often variable, can include following simple commands, producing verbal or gestural responses, engaging in purposeful movements such as visual tracking or reaching, and displaying emotionally appropriate reactions to context (19). Despite these diagnostic distinctions, relying exclusively on observable behavior to determine consciousness in DOCs presents considerable challenges (20), particularly given the potential for hidden consciousness in individuals who appear behaviorally unresponsive.

A major limitation of behavior-based assessment in DOCs is the frequent co-occurrence of severe motor impairments resulting from the underlying brain injury (21,22). Conditions like traumatic brain injury or stroke can lead to paralysis or other motor deficits that severely hinder a patient's capacity to express consciousness through movement or communication (23). As a result, some individuals may retain full consciousness but remain unable to demonstrate it behaviorally—closely resembling a form of the locked-in state (24). This underscores the inadequacy of behavior-centric methods in capturing the full spectrum of conscious experience in DOC patients (22).

The inherent variability and unpredictable fluctuations in consciousness, particularly within the MCS spectrum and potentially in UWS, introduce further diagnostic ambiguity (19). Consciousness exists on a gradient, and levels of awareness can change over brief periods (22). Subtle, transient moments of responsiveness can be overlooked during routine clinical evaluations, potentially leading to an underestimation of the patient's actual conscious state (14). Although standardized tools such as the Coma Recovery Scale–Revised (CRS-R) have improved diagnostic reliability, repeated and longitudinal assessments are essential for detecting inconsistent signs of awareness (19,25). Nevertheless, even these structured behavioral protocols are inherently constrained by their reliance on overt behavioral manifestations (22).

Beyond motor impairments and fluctuations in arousal, subjectivity in interpreting subtle behaviors further contributes to diagnostic uncertainty and inter-observer variability in DOCs (26). The clinical interpretation of ambiguous movements or expressions can be subjective, influenced by the clinician's biases, resulting in inconsistent diagnoses (24). Although standardized scales are designed to improve reliability with defined criteria, the subjective element in observing and interpreting borderline behaviors cannot be entirely eliminated, especially given the subtle, inconsistent nature of responses in DOCs (27).

This inherent subjectivity underscores the urgent need for objective neurophysiological measures to complement traditional behavioral assessments. Tools such as functional neuroimaging and electrophysiological monitoring offer more accurate and reliable methods for detecting residual awareness in patients who may appear unresponsive on clinical examination (24,28).

Neuroimaging Techniques: Illuminating Covert Brain Activity

Recognizing the substantial limitations of relying solely on bedside behavioral assessments for diagnosing (DOC) (29), the field of consciousness research has undergone a significant paradigm shift (30). This shift is marked by the growing integration of objective neuroimaging and electrophysiological techniques (31), which enable direct investigation of brain function and the detection of residual awareness (32), effectively circumventing the need for overt behavioral responses (33). The integration of these objective neuroimaging techniques marks a pivotal advancement in understanding DOC (31,32).

DOI: 10.5455/atjmed.2025.05.05

However, as this field rapidly evolves, it is essential to critically appraise the evidence supporting each method's diagnostic and prognostic capabilities, acknowledging both their considerable strengths and current limitations in clinical application.

Functional magnetic resonance imaging (fMRI), a powerful non-invasive tool that measures brain activity by detecting changes in cerebral blood flow, has emerged as a particularly valuable method for identifying covert consciousness. It has demonstrated the capacity to reveal sub-behavioral neural responses in patients clinically diagnosed with UWS (33).

A landmark study in 2006 by Owen and colleagues (34) represented a pivotal moment in consciousness research, offering the first compelling neuroscientific evidence of willful brain activity and covert awareness in a patient clinically diagnosed as being in a persistent vegetative state. In this seminal work, the patient demonstrated distinct activation patterns in expected cortical regions when instructed to perform mental imagery tasks—such as imagining playing tennis or navigating through her home (35). Remarkably, these activation patterns were statistically indistinguishable from those observed in healthy control participants performing the same tasks (34).

This groundbreaking finding provided strong neurobiological evidence of command following and volitional thought modulation in the absence of any observable behavioral response (36), effectively challenging the long-held assumption that behavioral irresponsiveness equates to a complete lack of conscious awareness (37).

Building upon the foundational work by Owen and colleagues (34), subsequent fMRI studies have significantly advanced our understanding of covert consciousness in DOCs. In a landmark 2010 study, Monti and colleagues (38) conducted a larger multi-center replication and extension, demonstrating robust, willful brain activity in response to verbal commands in a substantial subset of patients behaviorally diagnosed with UWS (39).

Notably, this study also pioneered the use of fMRI to establish a rudimentary communication channel. By instructing patients to perform different mental imagery tasks corresponding to “yes” or “no” answers, researchers were able to decode responses based on distinct activation patterns—effectively enabling some clinically unresponsive patients to answer simple binary questions using only their brain activity (38,35). This innovative technique represented a remarkable step toward overcoming the behavioral limitations of traditional diagnostic frameworks (30).

Moving beyond basic binary communication (38), fMRI has also been employed to investigate higher-order cognitive processing in patients with DOC (40). Research has revealed compelling evidence of preserved language comprehension (40), semantic processing (41), and even subtle emotional responsiveness in a subset of individuals behaviorally diagnosed with UWS, despite their apparent clinical unresponsiveness (41).

Moreover, longitudinal fMRI studies have demonstrated that the capacity for willful brain activation—assessed via standardized mental imagery tasks—can serve as a robust predictor of subsequent behavioral recovery in DOC patients (42,43). These findings underscore the significant prognostic value of fMRI in forecasting long-term outcomes and informing individualized care strategies (44).

Positron emission tomography (PET) is another invaluable neuroimaging modality in the assessment of DOC, offering data that complement fMRI by directly measuring regional cerebral metabolic activity—an indicator of neuronal energy consumption and processing capacity (45). PET studies have consistently shown a clear and clinically meaningful gradient of metabolic activity across the DOC spectrum (45). Specifically, patients diagnosed with a MCS, and those who subsequently emerge from UWS, exhibit significantly higher levels of global and regional cerebral metabolism—particularly within frontoparietal cortical regions essential for consciousness—compared to patients who remain in UWS (46,47).

These pronounced metabolic differences are believed to reflect the degree of underlying neuronal integrity required for the emergence and maintenance of conscious awareness (47). Moreover, longitudinal PET studies have revealed that measurable increases in regional metabolism, especially in frontal and parietal association cortices, can often precede and reliably predict subsequent behavioral improvements and clinical recovery in DOC patients (46,48). These findings further support the prognostic value of PET in forecasting the potential for recovery of consciousness and guiding long-term patient care strategies (48).

Electrophysiological Techniques: Capturing Brain Dynamics

Electroencephalography (EEG) remains a widely accessible, clinically practical, and cost-effective neurophysiological tool for measuring the brain’s dynamic electrical activity through scalp-placed electrodes (49). It offers a complementary approach to investigating consciousness in DOC, particularly in clinical settings where advanced neuroimaging modalities such as fMRI and PET may not be readily available (50).

While fMRI and PET offer powerful insights into covert brain activity and cognitive processing, their broader application in routine clinical diagnostics for DOC is often constrained by factors that contrast with the accessibility of tools like EEG (49,50). These factors can include substantial equipment and operational costs, the requirement for specialized personnel and infrastructure, challenges related to patient stability and transport for these advanced imaging procedures, and complexities in data interpretation that continue to be areas of active research and standardization efforts. Consequently, their routine use, while invaluable for research and in specialized centers, may be limited in many clinical environments, reinforcing the need for accessible complementary methods.

EEG-based measures of brain complexity and functional connectivity have shown considerable promise as clinically translatable biomarkers for distinguishing levels of consciousness and detecting residual awareness in behaviorally unresponsive patients (51). Quantifying neural complexity and integration provides valuable insights into the large-scale neuronal interactions thought to be fundamental to conscious experience (49). EEG-based techniques offer distinct advantages in terms of accessibility and practicality for assessing brain dynamics in DOC patients (49). While these electrophysiological measures show considerable promise as clinically translatable biomarkers for distinguishing levels of consciousness and detecting residual awareness (51), a careful and ongoing consideration of the level of evidence for different EEG markers is warranted. This ensures their appropriate application in clinical decision-making and prognostic evaluation, alongside other diagnostic information.

Numerous EEG studies have demonstrated significantly reduced complexity and connectivity in patients with UWS compared to those in a MCS and healthy control subjects, reflecting impaired information integration essential for consciousness (50). These EEG-derived metrics often correlate with fMRI findings of covert consciousness and have shown predictive value for behavioral recovery, establishing EEG as a critical tool for both diagnostic refinement and prognostic evaluation in DOC patients (51).

Event-related potentials (ERPs)—voltage fluctuations in the brain's electrical activity that are time-locked to specific sensory or cognitive events—offer a non-invasive method for assessing the integrity of information processing in patients with DOC (52). Although ERPs are often reduced or absent in patients diagnosed with UWS, studies have identified subtle yet statistically significant responses to salient stimuli, such as a patient's own name, meaningful words, or structured patterns, even in individuals who appear clinically unresponsive (53).

The elicitation of these subtle ERPs suggests the preservation of cognitive processing at a sub-behavioral level (54). Specific ERP components—including the mismatch negativity (MMN), P300, and N2pc—have been associated with distinct stages of sensory discrimination, attentional orientation, and higher-order processing. These components provide valuable insights into residual levels of awareness in DOC patients (55).

Transcranial magnetic stimulation combined with electroencephalography (TMS-EEG) represents an active, interventional technique for assessing cortical excitability and effective connectivity associated with consciousness (56). In this approach, TMS is used to non-invasively perturb cortical activity, while the resulting EEG response captures the brain's dynamic reaction to the stimulation (57). By analyzing the complexity and spatiotemporal characteristics of these TMS-evoked responses, researchers can quantify levels of cortical integration and differentiation—both of which are considered fundamental to the emergence of conscious experience (58).

Studies have demonstrated significantly reduced complexity and temporal persistence of TMS-evoked responses in patients with UWS compared to those in MCS or healthy controls, reflecting impaired large-scale cortical integration and disrupted consciousness (59). TMS-EEG thus provides direct, mechanistic insight into the brain dynamics underlying consciousness, offering a valuable complement to passive neuroimaging and electrophysiological techniques while advancing the objective classification of conscious states (60,61).

Downstate EEG Research: A Novel Biomarker For Hidden Consciousness

The emerging focus on the detailed analysis of "downstates" in ongoing EEG activity in patients with DOC marks a promising and potentially transformative advancement in EEG-based approaches for detecting covert consciousness (62,63). Cortical neuronal activity is characterized by dynamic rhythmic oscillations, including alternating phases of heightened excitability (upstates) and relative neuronal quiescence (downstates) (62). These up–down state transitions are increasingly recognized as fundamental components of cortical information processing and may represent core neural mechanisms underlying conscious awareness (62,64).

Researchers are actively exploring the hypothesis that the intricate characteristics and temporal patterning of these downstates may be systematically altered across the spectrum of DOCs and serve as novel, sensitive biomarkers for accurately distinguishing consciousness levels and predicting patient recovery (65,66). Emerging evidence suggests that specific quantitative characteristics of downstate patterns can reliably differentiate patients in UWS who later recover from those who remain unresponsive (65,66).

Notably, in some patients who eventually regain consciousness, downstate patterns recorded at the time of initial UWS diagnosis resemble those observed in healthy individuals, despite the absence of overt behavioral signs of awareness (67). This line of research underscores the growing potential of advanced EEG analysis to enhance the objective detection, classification, and understanding of consciousness in severe brain injury. It marks a significant shift from traditional EEG metrics toward a more nuanced and mechanistically grounded characterization of the spatiotemporal dynamics of cortical activity (67).

Ethical and Societal Imperatives: Re-evaluating Care and Dignity

Recent advancements in the detection of covert consciousness in patients with DOC carry profound ethical and societal implications, directly challenging long-standing clinical assumptions about awareness, personhood, and dignity in the context of severe brain injury (68,69). The ability to objectively identify sub-behavioral awareness in individuals who appear behaviorally unresponsive calls into question the adequacy of traditional diagnostic frameworks based solely on observable

DOI: 10.5455/atjmed.2025.05.05

behavior, thereby necessitating a critical re-evaluation of our moral obligations toward these patients (70).

The recognition that individuals previously labeled as "vegetative" may retain internal cognitive activity, emotional experience, or awareness compels a fundamental shift in how we understand and treat these patients. Persisting in approaches that presume unconsciousness—despite growing neuroscientific evidence to the contrary—raises serious ethical concerns related to patient rights, autonomy, and the imperative for compassionate, person-centered care (68,71). As our understanding of consciousness deepens, so too must our commitment to upholding the dignity and humanity of individuals with DOC.

This enhanced capacity to detect covert consciousness has significant implications for end-of-life decision-making in patients with DOC (72). Ethical considerations surrounding the withdrawal of life-sustaining treatment are fundamentally altered when acknowledging that a patient—despite lacking outward behavioral communication—may still retain conscious awareness (73). Proceeding with the withdrawal of life support in such cases would be ethically indefensible and could violate the individual's right to life and human dignity (73).

Accordingly, accurate diagnosis using sensitive and validated neurodiagnostic tools is essential to ensure that decisions regarding continuation or withdrawal of life-sustaining interventions are ethically and legally justifiable in complex DOC cases (74). Clinicians bear a moral and professional responsibility to communicate findings, diagnostic uncertainties, and the potential implications of covert consciousness transparently to families. This transparency is crucial for empowering family members in shared decision-making processes and aligning care decisions with both ethical principles and the patient's best interests (75,76).

Beyond diagnosis, the identification of preserved consciousness in behaviorally unresponsive patients has opened the door to the use of brain-computer interfaces (BCIs) as a means of establishing direct communication (77,78). BCI technology offers the potential to enable otherwise isolated individuals to express their thoughts, restore a degree of autonomy, and potentially enhance their quality of life (77,78).

However, the deployment of BCIs in this population raises critical ethical considerations. These include ensuring the validity of informed consent, preventing misuse or coercion, managing expectations regarding the capabilities of the technology, and safeguarding patient privacy and data security (79-81). As BCI systems become more sophisticated and clinically viable, it is essential to embed their use within a robust ethical framework that prioritizes patient rights, autonomy, and well-being.

These scientific advancements extend to broader societal and legal domains, prompting a re-evaluation of definitions of death and personhood, which often rely on observable consciousness and communication (82,83). As diagnostic tools uncover covert awareness, complex legal and policy challenges emerge. These include issues of guardianship, the interpretation and applicability of advance directives in light of evolving diagnostic capabilities, and the equitable allocation of healthcare resources for the long-term care and support needs of individuals with DOC (84,85).

Addressing these challenges requires policy frameworks that are informed by current neuroscience, grounded in ethical reflection, and guided by a commitment to justice, dignity, and person-centered care (82). Furthermore, enhancing public awareness and education is essential to fostering empathy, reducing stigma, and promoting the social inclusion of individuals with DOC and their families. This shift is critical for challenging dehumanizing perceptions and building a more compassionate, informed approach to care and advocacy (86).

Importantly, following the transparent communication of diagnostic findings and their inherent uncertainties, a comprehensive care approach should also actively address the significant emotional and psychological needs of families (75,76). This includes facilitating access to ongoing support and providing educational resources aimed at demystifying the complexities of DOC, which can help in fostering empathy and mitigating societal stigma that can affect individuals with DOC and their families (86,87). Such an approach recognizes that compassionate, person-centered care necessarily extends to the patient's family, acknowledging their crucial role and the burdens they may carry in the context of these challenging conditions (71).

CONCLUSION

Toward a Person-Centered Paradigm of Consciousness

The investigation of covert consciousness in DOCs represents a critical interdisciplinary frontier at the intersection of neuroscience, medicine, ethics, and societal values. The well-documented limitations of traditional behavior-based diagnostic frameworks necessitate a paradigm shift—one propelled by advancements in neuroimaging techniques (e.g., fMRI, PET) and electrophysiological methods (e.g., EEG, TMS-EEG, and downstate analysis). These technologies offer objective, replicable means of detecting sub-behavioral awareness, moving the field beyond an exclusive reliance on observable responses.

This technological and conceptual evolution carries profound ethical, legal, and societal implications. It compels a re-examination of patient rights, informed end-of-life decision-making, the ethical deployment of BCIs, and the relevance of current legal and guardianship frameworks. Addressing these challenges requires sustained, ethically grounded, and collaborative discourse among neuroscientists, clinicians, bioethicists, policymakers, and, critically, patients and their families.

The central insight emerging from this body of work is that the pursuit of consciousness science—especially in the context of severe brain injury—must remain anchored in humanistic values.

DOI: 10.5455/atjmed.2025.05.05

Scientific innovation must be matched by a commitment to dignity, personhood, and equitable care. Ultimately, recognizing consciousness in its most subtle and elusive forms reinforces a shared sense of humanity and the collective responsibility to protect and uplift the most vulnerable among us.

Conflict of Interests
The authors declare that there is no conflict of interest in the study.

Financial Disclosure
The authors declare that they have received no financial support for the study.

REFERENCES

1. Glattfelder, J.B. Subjective Consciousness: What am I?. In: Information—Consciousness—Reality. The Frontiers Collection. Springer, Cham. 2019;395-449.
2. Golden K, Bodien YG, Giacino JT. Disorders of consciousness classification and taxonomy. Phys Med Rehabil Clin N Am. 2023;35:15-33.
3. Kuehlmeyer K, Racine E, Palmour N, et al. Diagnostic and ethical challenges in disorders of consciousness and locked-in syndrome: a survey of German neurologists. J Neurol. 2012;259:2076-89.
4. Young MJ, Edlow BL, Bodien YG. Covert consciousness. NeuroRehabilitation. 2024;54:23-42.
5. Armstrong MJ. Developing the disorders of consciousness guideline and challenges of integrating shared decision-making into clinical practice. J Head Trauma Rehabil. 2019;34:199-204.
6. Giacino JT, Katz DI, Schiff ND, et al. Practice guideline update recommendations 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. Neurology. 2018;91:450-60. Erratum in: Neurology. 2019;93:135.
7. Plum F. Coma and related global disturbances of the human conscious state. In: Peters A, Jones EG, eds., Normal and Altered States of Function. 1st edition. Plenum Press, New York, 1991;359-425.
8. Fins JJ. The complicated legacy of Terry Wallis and his brain injury. Issues Sci Technol. 2023;29:41-7.
9. UNC Library. Subject research guides. Systematic reviews: step 3: conduct literature searches. https://guides.lib.unc.edu/systematic-reviews/search access date 03.05.2025.
10. University of Westminster. LibGuides: Literature reviews: synthesis. https://libguides.westminster.ac.uk/literature-reviews/synthesis access date 03.05.2025.
11. ATLAS.ti. Guidelines for writing a literature review | rules & requirements. https://atlasti.com/guides/literature-review/literature-review-guidelines access date 03.05.2025.
12. Sukhera J. Narrative reviews: flexible, rigorous, and practical. J Grad Med Educ. 2022;14:414-7.
13. Gilutz Y, Lazary A, Karpin H, et al. Detailed behavioral assessment promotes accurate diagnosis in patients with disorders of consciousness. Front Hum Neurosci. 2015;9:87.
14. Giacino JT, Katz DI, Schiff ND, et al. 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. Neurology. 2018;91:461-70.
15. van Erp WS, Lavrijsen JCM, Vos PE, et al. Unresponsive wakefulness syndrome: outcomes from a vicious circle. Ann Neurol. 2020;87:12-8.
16. American Academy of Physical Medicine and Rehabilitation. Disorders of Consciousness. https://www.aapmr.org/about-physiatry/conditions-treatments/rehabilitation-of-central-nervous-system-disorders/disorders-of-consciousness access date 04.05.2025.
17. Giacino JT, Ashwal S, Childs N, et al. The minimally conscious state: definition and diagnostic criteria. Neurology. 2002;58:349-53.
18. Murtaugh B, Shapiro Rosenbaum A. Clinical application of recommendations for neurobehavioral assessment in disorders of consciousness: an interdisciplinary approach. Front Hum Neurosci. 2023;17:1129466.
19. Bareham CA, Allanson J, Roberts N, et al. Longitudinal assessments highlight long-term behavioural recovery in disorders of consciousness. Brain Commun. 2019;1:fcz017.
20. Bodien YG, Katz DI, Schiff ND, Giacino JT. Behavioral assessment of patients with disorders of consciousness. Seminars in Neurology. 2022;42:249-58. Erratum in: Semin Neurol. 2022;42:e1.
21. Toeback J, Depoortere S, Kerckhoffs MC, Slooter JC. Diagnostic approach of a patient presenting with altered consciousness in critical care. https://de-intensivist.nl/diagnostic-approach-of-a-patient-presenting-with-altered-consciousness-in-critical-care/ Accessed May 4, 2025.
22. Fitzpatrick-DeSalme E, Long A, Patel F, Whyte J. Behavioral assessment of patients with disorders of consciousness. J Clin Neurophysiol. 2022;39:4-11.
23. Guldenmund P, Stender J, Heine L, Laureys S. Mindsight: diagnostics in disorders of consciousness. Crit Care Res Pract. 2012;2012:624724.
24. Bai Y, Lin Y, Ziemann U. Managing disorders of consciousness: the role of electroencephalography. J Neurol. 2021;268:4033-65.
25. Porcaro C, Nemirovsky IE, Riganello F, et al. Diagnostic developments in differentiating unresponsive wakefulness syndrome and the minimally conscious state. Front Neurol. 2022;12:778951.

26. Beveridge A. Time to abandon the subjective–objective divide?. Psychiatric Bulletin. 2002;26:101-3.
27. Sanz LRD, Thibaut A, Edlow BL, et al. Update on neuroimaging in disorders of consciousness. Current Opinion in Neurology. 2021;34:488-96.
28. Zheng H, Tian L, Cai J. Meta-analysis of the diagnostic value of functional magnetic resonance imaging for distinguishing unresponsive wakefulness syndrome/ vegetative state and minimally conscious state. Front Neurosci. 2024;18:1395639.
29. Scolding N, Owen AM, Keown J. Prolonged disorders of consciousness: a critical evaluation of the new UK guidelines. Brain. 2021;144;1655-60.
30. Kazazian K, Monti MM, Owen AM. Functional neuroimaging in disorders of consciousness: towards clinical implementation. Brain. Published online February 9, 2025. doi: 10.1093/brain/awaf075
31. Kondziella D, Bender A, Diserens K, et al; EAN Panel on Coma, Disorders of Consciousness. European Academy of Neurology guideline on the diagnosis of coma and other disorders of consciousness. Eur J Neurol. 2020;27:741-56.
32. Edlow BL, Claassen J, Schiff ND, Greer DM. Recovery from disorders of consciousness: mechanisms, prognosis and emerging therapies. Nat Rev Neurol. 2021;17:135-56.
33. Gosseries O, Di H, Laureys S, Boly M. Measuring consciousness in severely damaged brains. Annu Rev Neurosci. 2014;37:457-78.
34. Owen AM, Coleman MR, Boly M, et al. Detecting awareness in the vegetative state. Science. 2006;313:1402.
35. Boly M, Coleman MR, Davis MH, et al. When thoughts become action: an fMRI paradigm to study volitional brain activity in non-communicative brain injured patients. Neuroimage. 2007;36:979-92.
36. Fernández-Espejo D, Owen AM. Detecting awareness after severe brain injury. Nat Rev Neurosci. 2013;14:801-9.
37. Laureys S. The neural correlate of (un)awareness: lessons from the vegetative state. Trends Cogn Sci. 2005;9:556-9.
38. Monti MM, Vanhaudenhuyse A, Coleman MR, et al. Willful modulation of brain activity in disorders of consciousness. N Engl J Med. 2010;362:579-89.
39. Schnakers C, Perrin F, Schabus M, et al. Voluntary brain processing in disorders of consciousness. Neurology. 2008;71:1614-20.
40. Coleman MR, Rodd JM, Davis MH, et al. Do vegetative patients retain aspects of language comprehension? Evidence from fMRI. Brain. 2007;130:2494-507.
41. Di Perri C, Stender J, Laureys S, Gosseries O. Functional neuroanatomy of disorders of consciousness. Epilepsy Behav. 2014;30:28-32. Erratum in: Epilepsy Behav. 2014;36:153.
42. Wang F, Di H, Hu X, et al. Cerebral response to subject's own name showed high prognostic value in traumatic vegetative state. BMC Med. 2015;13:83.
43. Chennu S, Annen J, Wannez S, et al. Brain networks predict metabolism, diagnosis and prognosis at the bedside in disorders of consciousness. Brain. 2017;140:2120-32.
44. Demertzi A, Antonopoulos G, Heine L, et al. Intrinsic functional connectivity differentiates minimally conscious from unresponsive patients. Brain. 2015;138:2619-31.
45. Thibaut A, Bruno MA, Chatelle C, et al. Metabolic activity in external and internal awareness networks in severely brain-damaged patients. J Rehabil Med. 2012;44:487-94.
46. Stender J, Gosseries O, Bruno MA, et al.; Coma Science Group Collaborators. Diagnostic precision of PET imaging and functional MRI in disorders of consciousness: a clinical validation study. Lancet. 2014;384:514-22.
47. Stender J, Mortensen KN, Thibaut A, et al. The minimal energetic requirement of sustained awareness after brain injury. Curr Biol. 2016;26:1494-9.
48. Marini CP, Stoller C, McNelis J, et al. Correlation of brain flow variables and metabolic crisis: a prospective study in patients with severe traumatic brain injury. Eur J Trauma Emerg Surg. 2020;48:537-44.
49. Wutzl B, Golaszewski SM, Kenji Leibnitz, et al. Narrative review: quantitative EEG in disorders of consciousness. Brain Sci. 2021;11:697.
50. Liu Y, Zeng W, Pan N, et al. EEG complexity correlates with residual consciousness level of disorders of consciousness. BMC Neurol. 2023;23:140.
51. Lord V, Opacka-Juffry J. Electroencephalography (EEG) measures of neural connectivity in the assessment of brain responses to salient auditory stimuli in patients with disorders of consciousness. Front Psychol. 2016;7:397.
52. Gusatovic J, Gramkow MH, Hasselbalch SG, Frederiksen KS. Effects of aerobic exercise on event-related potentials related to cognitive performance: a systematic review. PeerJ. 2022;10:e13604.
53. Kotchoubey B. Event-related potentials in disorders of consciousness. In: Rosesetti AO, Laureys S, eds. Clinical Neurophysiology in Disorders of Consciousness. 1st edition. Springer; 2014:107-23.
54. Farzan F, Vernet M, Shafi MM, et al. Characterizing and modulating brain circuitry through transcranial magnetic stimulation combined with electroencephalography. Front Neural Circuits. 2016;10:73.
55. Chowdhury NS, Chiang AKI, Millard SK, et al. Combined transcranial magnetic stimulation and electroencephalography reveals alterations in cortical excitability during pain. Elife. 2023;12:e88567.
56. Das S, Puthankattil SD. Functional connectivity and complexity in the phenomenological model of mild cognitive-impaired Alzheimer's disease. Front Comput Neurosci. 2022;16:877912.

57. Amantini A, Riccardo Carrai, Fossi S, et al. The role of early electroclinical assessment in improving the evaluation of patients with disorders of consciousness. Funct Neurol. 2011;26:7-14.

58. Zhang L, Zhang R, Guo Y, et al. Assessing residual motor function in patients with disorders of consciousness by brain network properties of task-state EEG. Cogn Neurodyn. 2021;16:609-20.

59. Jain R, Ramakrishnan AG. Electrophysiological and neuroimaging studies – during resting state and sensory stimulation in disorders of consciousness: a review. Front Neurosci. 2020;14:555093.

60. Cai Z, Shi L, Wu W, et al. A scoping review of effects of acute exercise on executive function: evidence from event-related potentials. Front Psychol. 2025;16:1599861.

61. Pruvost-Robieux E, Marchi A, Martinelli I, et al. Evoked and event-related potentials as biomarkers of consciousness state and recovery. J Clin Neurophysiol. 2022;39:22-31.

62. Camassa A, Galluzzi A, Mattia M, Sanchez-Vives MV. Deterministic and stochastic components of cortical down states: dynamics and modulation. Journal of Neuroscience. 2022;42:9387-400.

63. Frohlich F, Toker D, Monti MM. Consciousness among delta waves: a paradox?. Trends Cogn Sci. 2021;144:2257-77.

64. Rosanova M, Fecchio M, Casarotto S, et al. Sleep-like cortical OFF-periods disrupt causality and complexity in the brain of unresponsive wakefulness syndrome patients. Nature Commun. 2018;9:4427.

65. Liu B, Zhang X, Wang L, et al. Outcome prediction in unresponsive wakefulness syndrome and minimally conscious state by non-linear dynamic analysis of the EEG. Front Neurol. 2021;12:510424.

66. Di Gregorio F, La Porta F, Petrone V, et al. Accuracy of EEG biomarkers in the detection of clinical outcome in disorders of consciousness after severe acquired brain injury: preliminary results of a pilot study using a machine learning approach. Biomedicines. 2022;10:1897.

67. Casarotto S, Comanducci A, Rosanova M, et al. Stratification of unresponsive patients by an independently validated index of brain complexity. Ann Neurol. 2016;80:718-29.

68. Friedrich O, Jox RJ. Disorders of consciousness and the use of neurotechnologies: an ethical perspective. In: Clausen J, Levy N, eds. The Routledge Handbook of Neuroethics. 1st edition. Routledge; 2017:chap 8.

69. Niikawa T. Moral status and consciousness. ANNALS of the University of Bucharest Philosophy Series. 2018;67:235-57.

70. Fisher CE, Appelbaum PS. Diagnosing consciousness: neuroimaging, law, and the vegetative state. J Law Med Ethics. 2010;38:374-85.

71. Septien S, Rubin M. Disorders of consciousness: ethical issues of diagnosis, treatment, and prognostication. Semin Neurol. 2018;38:548-54.

72. Jox RJ. End-of-life decision making concerning patients with disorders of consciousness. Res Cogitans. 2011;8:43-61.

73. Skene L, Wilkinson D, Kahane G, Savulescu J. Neuroimaging and the withdrawal of life-sustaining treatment from patients in vegetative state. Med Law Rev. 2009;17:245-61.

74. Rissman L, Paquette ET. Ethical and legal considerations related to disorders of consciousness. Current Opinion in Pediatrics. 2020;32:765-71.

75. Clark T, Edgley A, Kerry R. Making healthcare decisions on behalf of people in a disorder of consciousness. a “risk-making” theory of decisional practices. AJOB Neuroscience. Published online February 21, 2025. doi: 10.1080/21507740.2025.2464112.

76. Istace T. Empowering the voiceless. Disorders of consciousness, neuroimaging and supported decision-making. Front Psychiatry. 2022;13:923488.

77. Farwell LA, Donchin E. Talking off the top of your head: toward a mental prosthesis utilizing event-related brain potentials. Electroencephalogr Clin Neurophysiol. 1988;70:510-23.

78. Birbaumer N, Ghanayim N, Hinterberger T, et al. A spelling device for the paralysed. Nature. 1999;398:297-8.

79. McMenemy D. Ethical Issues in brain–computer interfaces. In: Eslambolchilar P, Komninos A, Dunlop M, eds. Intelligent Computing for Interactive System Design: Statistics, Digital Signal Processing, and Machine Learning in Practice. 1st edition. Association for Computing Machinery, New York, United States. 2021;273-5.

80. Glannon W. Ethical issues with brain-computer interfaces. Frontiers in Systems Neuroscience. 2014;8:136.

81. Klein E, Peters B, Higger M. Ethical considerations in ending exploratory brain–computer interface research studies in locked-in syndrome. Camb Q Healthc Ethics. 2018;27:660-74.

82. Jones OD, Marois R, Farah MJ, Greely HT. Law and neuroscience. J Neurosci. 2013;33:17624-30.

83. Bernat JL. The definition and criterion of death. Handb Clin Neurol. 2013:419-35.

84. Heywood R. Moving on from bland: the evolution of the law and minimally conscious patients. Medical Law Review. 2014;22:548-71.

85. Fins JJ. A Palliative ethic of care: clinical wisdom at life's end. 1st edition. Jones & Bartlett Learning; 2006.

86. Corrigan PW, Watson AC. Understanding the impact of stigma on people with mental illness. World Psychiatry. 2002;1:16-20.

87. Illes J, Bird SJ. Neuroethics: a modern context for ethics in neuroscience. Trends Neurosci. 2006;29:511-7.