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Review

Mental imagery paradigms for the assessment of awareness in patients with disorders of consciousness: a systematic literature review

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SUMMARY

Introduction

Behavioural assessments are the current gold standard tool for determining the level of awareness in disorders of consciousness (DoC), but cannot be applied in all patients. Neuroimaging and/or neurophysiological responses to mental imagery tasks are emerging as a potentially more sensitive tool for assessing awareness, especially in patients with injuries to the motor systems that often accompany impairments in consciousness. This review summarises and critically appraises the current evidence to determine if functional magnetic resonance imaging (fMRI) and electroencephalography (EEG) based mental imagery paradigms are viable tools for assessing awareness in patients with DoC.

Methods

We conducted a systematic literature review according to the PRISMA guidelines. PubMed, Embase, and PsycInfo databases were searched for studies investigating fMRI or EEG based mental imagery paradigms for detecting awareness in patients with DoC.

Results

A total of 17 studies were identified for inclusion in this review (eleven investigating fMRI paradigms and six EEG protocols). Across all fMRI studies and five out of the six EEG studies, mental imagery paradigms were able to detect awareness in patients with DoC, with different degrees of accuracy. In one fMRI and one EEG study, mental imagery paradigms were a useful tool for communication with patients.

Discussion

There is promising evidence that both fMRI and EEG based mental imagery paradigms could become viable tools for assessing awareness in patients with DoC. Further research is needed to validate preliminary findings in larger samples of patients with different aetiologies and including longitudinal assessments.

Key words: awareness, disorders of consciousness, electroencephalography, functional magnetic resonance imaging, mental imagery

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Introduction

Patients with disorders of consciousness (DoC) have a condition characterised by severely impaired wakefulness and awareness, as a result of a broad range of pathologies such as acquired brain injury [1] and progressive brain degeneration [2]. The clinical assessment of consciousness in this patient population, as well as in neurological conditions resulting in transiently altered conscious states, relies on an important distinction between the dimensions of arousal and awareness [3-8]. Arousal ('level of consciousness') refers to the ability to demonstrate physical signs of wakefulness, whether that be opening the eyes or unprompted movements. On the other hand, awareness ('content of consciousness') is the ability to have subjective experiences. The bidimensional model of consciousness has proven particularly useful in the assessment of epilepsy-induced transient alterations of consciousness, often based on patients' retrospective accounts [5,8-12]. In the context of prolonged DoC, it is often difficult to confidently ascertain whether a patient is having a conscious experience because of the impairment in communication that defines this population [13-15]. Currently, the gold standard method for evaluating awareness in patients with DoC is a bedside behavioural assessment focusing on observable responses to external stimuli. The most commonly used behavioural assessment tools are the Glasgow Coma Scale (GCS) and the Coma Recovery Scale-Revised (CRS-R), with proven usefulness in this patient population [16]. The GCS was developed in 1974 and quantifies the functioning of three behavioural domains related to the level of consciousness: eye opening, verbal and motor response [17]. The CRS-R was developed in 1991 [18] and revised in 2004 to align its behavioural criteria with the new definition of MCS [19,20]. The CRS-R assesses auditory, visual and motor functioning, as well as verbal responsiveness, communication, and arousal [19]. Since damage to motor systems frequently accompanies DoC, a significant percentage of patients with impaired consciousness might still retain some degree of awareness, but have insufficient voluntary control over their movements to demonstrate this through observable behaviours [21]. Other confounders include sensory and cognitive impairment, as well as pain, potentially resulting in subtle or fluctuating behavioural signs that may be easily missed [13]. Combined with observer bias, these factors account for a relatively high frequency of misdiagnosis of DoC based on behavioural assessments - as high as 40% [22].

The clinical spectrum of DoC ranges from coma and vegetative state (VS) to minimally conscious state (MCS) [23-25]. Coma is the most severe DoC, as patients show no evidence of arousal; based on behavioural assessments, it is assumed that they have no awareness either [26]. When patients with coma gradually regain consciousness, their diagnosis is often initially changed to VS, also referred to as unresponsive wakefulness syndrome (UWS) [27-29]. Patients with UWS/VS retain sleep-wake cycles (arousal) and stimulus-induced movements (e.g. pupil dilation, apparently random movements of the limbs, chewing, teeth grinding). Despite the absence of clear and consistent behavioural evidence of awareness, inconsistent signs can be observed. Patients with MCS display inconsistent but reproducible behavioural responses, indicating awareness. In case of less obvious behavioural signs (e.g., a small hand or eye movement), assessments often need to be protracted over longer periods of time to achieve a confident diagnosis 30. It has been proposed to split the MCS diagnosis into MCS- and MCS+: patients with MCS- are thought to have the capacity for only a restricted range of rudimentary conscious contents (behaviourally expressed as visual pursuit, localization of noxious stimulation or appropriate smiling/crying to emotional stimuli), whereas patients with MCS+ are presumed to be able to enjoy a considerably wider range of conscious contents, involving a greater degree of cognitive sophistication, as shown by verbalised responses, command following, and intelligible verbalizations [16,31,32]. Patients with locked-in syndrome lie outside the clinical spectrum of DoC, as both arousal and awareness are preserved, as shown by voluntary control of eye movements and blinking, despite inability to speak and complete paralysis of the limbs [4].

Over the last few decades, other assessment strategies have been developed to provide additional or more reliable information about awareness in patients with DoC. The most promising tools to complement behavioural assessments are neuroimaging and neurophysiology, either in isolation or in combination [33-35]. Neuroimaging proved useful in reliably detecting differences in resting state brain activity and metabolism between patients with impaired consciousness and healthy controls, as well as in discriminating between patients with different levels of consciousness [36-39]. In neuroimaging-based mental imagery paradigms, patients with DoC are instructed to engage in an imagination task and responses are recorded using fMRI or EEG [31,40]. Patients can be asked to perform either complex motor imagery tasks, such as imagining playing tennis, or more simple motor tasks, such as imagining moving the right hand. They can also be asked to engage in spatial imagery - for example, imagining walking around each room in their house. A differential increase in activity in specific brain regions demonstrates that the patient successfully engaged with the task at hand. This also provides evidence for significant levels of consciousness (arousal) coupled with relevant contents of consciousness (awareness), as imagery tasks require understanding of and compliance to specific instructions. This promising research avenue is attracting an increasing amount of interest because of its clinical and theoretical implications. We therefore set out to conduct a systematic literature review to assess whether the available evidence indicates that fMRI and EEG based mental imagery paradigms are viable tools for assessing awareness in patients with DoC.

Methods

The present systematic literature review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [41]. On 25/05/2024, we performed a search on the PubMed, Embase, and PsycInfo databases for original studies in which fMRI or EEG imagery paradigms were used to assess awareness in patients with DoC. For our search, we combined the terms 'minimally conscious' OR 'vegetative' OR 'disorders of consciousness' AND 'awareness' OR 'consciousness' AND 'imag*' OR 'magnetic resonance' OR 'electroencephalograph*' (the search strategies for the three databases are detailed in the Supplementary Material). The reference lists of eligible articles were manually screened to identify any further relevant articles.

We included studies on patients diagnosed with any form of DoC following behavioural assessments according to the GCS, the CRS-R, or equivalent diagnostic measures. We restricted our search to studies that used fMRI or EEG approaches to mental imagery-based paradigms for assessing awareness in patients with DoC. Neuroimaging studies focusing on neural resting states instead of mental imagery were excluded, as they did not directly address our research question. Both case series and controlled studies were included in this review. Case studies of single patients were excluded. We excluded from our review studies published in languages other than English and studies published before 2004, the year in which the CRS-R was made available. By excluding the studies that used outdated instruments, we have focused our review on current gold standard methodology for the behavioural assessment of DoC.

Two independent reviewers (T.L.C., A.E.C.) collected data from each report without using automation tools. The reviewed studies contained all the relevant information and therefore there was no need to implement any processes for obtaining or confirming data from study investigators. The Crowe Critical Appraisal Tool (CCAT) was used to perform quality assessment on the reviewed studies [42]. The CCAT has eight sections: preliminaries, introduction, design, sampling, data collection, ethical matters, results, discussion. Each section is awarded a minimum of 0 points and a maximum of 5 points, with higher points indicating higher methodological quality. In the present review, scores were awarded as follows: 0-1 points indicated a section with a degree of flawed methodological quality that resulted in exclusion of the study from the review; 2 points indicated at least two methodological flaws leading to bias in the relevant section; 3 points indicated one methodological flaw likely leading to bias; 4 points indicated one methodological flaw unlikely to lead to bias; and 5 points indicated that any possible methodological flaws did not lead to bias. The sum of the scores of the eight sections yielded a combined CCAT score (0-40), with higher scores indicating higher methodological quality.

Results

In total, eleven fMRI studies and six EEG studies were selected for inclusion in this review, with research being conducted across nine different countries. The article selection process is summarised in the PRISMA flow diagram (Fig. 1).

Five out of the 17 studies took place in the United States [43-47], two each in Austria [48,49], Israel [50,51], and Italy [52,53], and one each in Australia, Belgium, China, and Germany [54-57]. Two further studies [58,59] were conducted across two countries, Belgium and the United Kingdom. All studies took place in specialist centres for the clinical management of patients with DoC resulting from acquired brain injury. The CRS-R was used as a behavioural measure in all studies except for the one by Liang et al. [54], who used the GCS and equivalent scales. The GCS was also used alongside the CRS-R in three studies [46,47,59]. Twelve out of the 17 studies recruited age-matched healthy controls to validate the mental imagery tasks by verifying the feasibility of detecting specific neural activity in response to a command as a standard

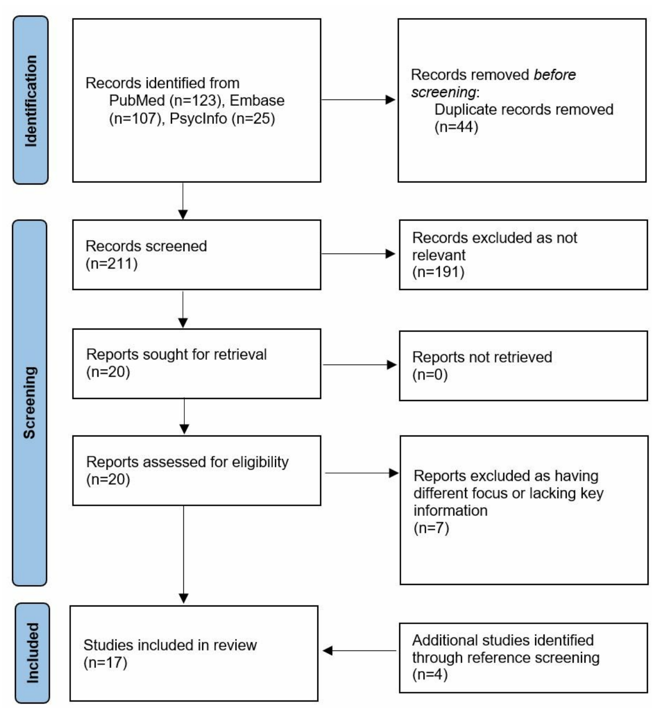

FIGURE 1. *PRISMA flow diagram outlining the identification, screening, assessment for eligibility, and inclusion of studies in the present review.*

indicator of awareness [43,45,46-48,51,52,54-56,58,59].
Mental imagery was assessed by asking participants to imagine carrying out specific tasks that required them to use either their motor or spatial imagery. Seven out of the 17 studies used both motor and spatial imagery tasks [43,49,50,54,55,57,59]. One very typical way to assess motor imagery was to ask patients to imagine playing a simple game that requires the same repetitive action, preferably with the same arm. Specifically, participants were instructed to "imagine playing tennis" in seven studies [43,45,49,54,55,57,59], and to "imagine swimming" in three studies [43,44,49]. Alternative commands to determine the presence of motor imagery included "imagine opening and closing your hand" and "imagine squeezing your hand", which were utilised in six studies [45-48,53,58]. In two further studies, patients were instructed to raise their hand [56] and to hold their hand firm [48], respectively. Spatial imagery was most commonly assessed by asking patients to imagine navigating through their house (five studies 4[9, 54, 55, 57, 59]). Personally familiar face imagery was used in two studies [51,54], whereas in one instance patients were asked to imagine objects from their kitchen [50]. Finally, two studies utilised instructions that were different from these simple commands. Along with a simple hand squeezing test, Naro and Calabrò [53] also asked subjects to imagine dancing, either while being shown simultaneous footage of people dancing in a video, or independent of external visual stimuli. Claassen et al. [47] took a slightly different approach: instead of asking patients with no behavioural response to motor commands to imagine moving their hand, they asked their participants to actually try carrying out that motor task.
A summary of the eleven studies using a fMRI mental imagery paradigm to investigate awareness in patients with DoC is provided in Table I. Data were collected for a total of 252 patients with DoC: 79 patients diagnosed with MCS, 74 patients with UWS/VS, 3 patients in a coma, and 96 patients with unspecified DoC. The aetiological processes leading to DoC were documented as follows: 95 patients had a traumatic brain injury, 39 an anoxic brain damage, 16 a cerebrovascular accident, and 4 other conditions, including infectious diseases. Two patients in the study by Monti et al. 59 had two pathologies each (traumatic brain injury and anoxia, traumatic brain

TABLE I. *Summary of studies using a fMRI mental imagery paradigm to investigate awareness in patients with disorders of consciousness.*

Study	Country	N. (aetiology)	DoC	Behavioural measure	Imagery paradigm	Main findings	CCAT score
Monti et al., 2010 [59]	Belgium, United Kingdom	54 ABI (31 TBI, 1 TBI + ABD, 1 TBI + infection, 15 ABD, 3 CVA, 3 infection) 16 HC	23 UWS/VS 31 MCS	CRS-R, GCS	Motor imagery: playing tennis; spatial imagery: mental navigation in own house	5/54 patients showed fMRI activation in imagery tasks (4/5 with UWS/VS); communication tested in 1 imagery responsive patient with UWS/VS (classified 5/6 answers with 100% accuracy)	37/40
Bardin et al., 2011 [43]	United States	5 ABI (3 TBI, 1 ABD, 1 CVA) 14 HC	5 MCS	CRS-R	Motor imagery: playing tennis or swimming; choice task: responding yes/no through imagery to matching/unmatching cards	2/5 patients showed fMRI activation in motor imagery task; 1 patient showed fMRI activation in choice task	36/40
Bick et al., 2013 [50]	Israel	11 ABI (7 TBI, 4 ABD)	6 UWS/VS 5 MCS	CRS-R	Preliminary auditory task; imagery: playing ball game, humming song, walking home, visualizing objects from kitchen	7/11 patients showed fMRI activation in preliminary auditory task; 5/7 showed fMRI activation in at least one imagery task (1/7 in all four tasks)	33/40
Sharon et al., 2013 [51]	Israel	4 ABI (2 ABD, 2 TBI) 13 HC	4 UWS/VS	CRS-R	Personally familiar face imagery: visualization of parent's face	All patients and HC showed fMRI activation in familiar face imagery task; strongest brain connectivity in the 2 patients who later recovered	35/40

TABLE I. .

Study	Country	N. (aetiology)	DoC	Behavioural measure	Imagery paradigm	Main findings	CCAT score
Vogel et al., 2013 [57]	Germany	22 ABI (10 ABD, 6 CVA, 6 TBI)	10 UWS/VS 12 MCS	CRS-R	Motor imagery: playing tennis; spatial imagery: mental navigation in own house	14/22 patients showed fMRI activation in imagery tasks (5/14 with UWS/VS, transitioned to MCS at follow-up); 8/22 patients did not show fMRI activation (5/8 with UWS/VS, did not transition to MCS at follow-up)	37/40
Forgacs et al., 2014 [44]	United States	26 ABI (NS)	NS	CRS-R	Motor imagery: swimming	4/26 patients showed fMRI activation in motor imagery task (3/4 with MCS, 1/4 with emerging MCS)	35/40
Liang et al., 2014 [54]	Australia	5 ABI (4 TBI, 1 other) 11 HC	3 UWS/VS 2 MCS	GCS, GOS, WHIM	Motor imagery: playing tennis; spatial imagery: mental navigation in own house; personally familiar face imagery; counting up from 10 by 7s	2/5 patients (1 UWS/VS, 1 MCS) showed fMRI responses to imagery tasks, producing activations in similar areas to HC	35/40
Stender et al., 2014 [55]	Belgium	70 ABI (NS) 16 HC	NS	CRS-R	Motor imagery: playing tennis; spatial imagery: mental navigation in own house	Agreement between CRS-R and mental imagery fMRI was recorded in 44/70 patients; mental imagery fMRI predicted 56% of all known outcomes	36/40
Bodien et al., 2017 [45]	United States	10 ABI (10 TBI) 10 HC	1 coma 4 UWS/VS 2 MCS- 3 MCS+	CRS-R	Motor imagery: playing tennis, squeezing hand	2/10 patients showed fMRI activation in tennis playing motor imagery task (0/2 with behavioural evidence); 3/10 patients showed fMRI activation in hand squeezing motor imagery task (2/3 with behavioural evidence)	35/40
Edlow et al., 2017 [46]	United States	16 ABI (16 TBI) 16 HC	2 coma 3 UWS/VS 3 MCS- 8 MCS+	CRS-R, GCS	Motor imagery: squeezing hand	11/16 HS and 7/16 patients showed fMRI activation in hand squeezing motor imagery task (3/7 with behavioural evidence)	35/40
Wang et al., 2019 [56]	China	29 ABI (16 TBI, 7 ABD, 6 CVA) 15 HC	21 UWS/VS 8 MCS	CRS-R	Motor imagery: raising hand	4/29 patients (2 MCS, 2 UWS/VS) showed fMRI activation in hand raising motor imagery task	35/40

Abbreviations. ABD, anoxic brain damage; ABI, acquired brain injury; CCAT, Crowe Critical Appraisal Tool; CRS-R, Coma Recovery Scale-Revised; CVA, cerebrovascular accident; DoC, disorders of consciousness; fMRI, functional magnetic resonance imaging; GCS, Glasgow Coma Scale; GOS, Glasgow Outcome Scale; MCS, minimally conscious state (+/-, with/without verbalised responses to environmental stimuli); NS, not specified; TBI, traumatic brain injury; UWS, unresponsive wakefulness syndrome; VS, vegetative state; WHIM, Wessex Head Injury Matrix.

TABLE II. *Summary of studies using an EEG mental imagery paradigm to investigate awareness in patients with disorders of consciousness.*

Study	Country	N. (aetiology)	DoC	Behavioural measure	Imagery paradigm	Main findings	CCAT score
Cruse et al., 2011 [58]	Belgium, United Kingdom	16 ABI (9 ABD, 5 TBI, 2 CVA) 12 HC	16 UWS/VS	CRS-R	Motor imagery: squeezing hand, wiggling toe	3/16 patients and 9/12 HC showed significant differences in EEG activity in motor imagery task; mean (range) imagery classification accuracy with EEG activity: ABI 70% (61-78%), HC 68% (60-91%)	37/40
Höller et al., 2013 [48]	Austria	14 ABI (6 CVA, 4 ABD, 4 TBI) 22 HC	9 UWS/VS 5 MCS	CRS-R	Motor imagery: opening/closing hand, holding hand firm	No significant differences in EEG activity after correcting for false positives	36/40
Horki et al., 2014 [49]	Austria	6 ABI (3 TBI, 1 TBI + CVA, 2 ABD)	6 MCS	CRS-R	Motor imagery: playing sport, moving foot; spatial imagery: mental navigation in own house	Significant differences in EEG activity for all imagery paradigms (higher accuracy for motor imagery than for spatial imagery)	35/40
Mangia et al., 2014 [52]	Italy	5 ABI (4 TBI, 1 TBI + ABD) 5 HC	1 UWS/VS 4 MCS	CRS-R	Motor imagery: moving hand/foot; communication task: responding yes/no through hand/foot movement imagery	Mean imagery classification accuracy with EEG activity: ABI 85%, HC 82%; mean communication classification accuracy with EEG activity: ABI 92%, HC 81%	36/40
Claassen et al., 2019 [47]	United States	104 ABI (39 CVA, 33 ABD, 15 TBI, 17 other) 10 HC	47 coma 27 UWS/VS 30 MCS	CRS-R, GCS	Motor imagery: opening and closing right/left hand	16/104 patients showed significant differences in EEG activity in motor imagery task (8/16 with coma, 3/16 with UWS/VS, 5/16 with MCS); 44% of patients who showed cognitive-motor dissociation (covert consciousness) reported improvement at 12-month follow-up behavioural assessment	38/40
Naro and Calabrò, 2020 [53]	Italy	20 ABI (8 TBI, 7 ABD, 5 CVA)	11 UWS/VS 9 MCS	CRS-R	Visuomotor-guided imagery: dancing while watching group dance video; simple motor imagery: squeezing hand; advanced motor imagery: dancing without visual guidance	7/20 patients showed significant differences in EEG activity in visuomotor-guided imagery task (1/11 with UWS, 6/9 with MCS); 4/20 patients showed significant differences in EEG activity in simple motor imagery task (0/11 with UWS/VS, 4/9 with MCS); 4/13 patients showed significant differences in EEG activity in simple motor imagery task (1/7 with UWS/VS, 3/6 with MCS)	38/40

Abbreviations. ABD, anoxic brain damage; ABI, acquired brain injury; CCAT, Crowe Critical Appraisal Tool; CRS-R, Coma Recovery Scale-Revised; CVA, cerebrovascular accident; DoC, disorders of consciousness; EEG, electroencephalography; GCS, Glasgow Coma Scale; MCS, minimally conscious state; NS, not specified; TBI, traumatic brain injury; UWS, unresponsive wakefulness syndrome; VS, vegetative state.

injury and infection). The aetiology of 96 patients who underwent fMRI in the studies by Forgacs et al. [44] and Stender et al. [55] was not specified. A total of 121 healthy controls were recruited across eight studies [43,45,46,51,54-56,59]. The mean age of patients ranged from 27 years [45] to 46 years [57]. The youngest patient across all studies was 8 years old [56] and the oldest was 75 years old [44].

Each fMRI study that was eligible for inclusion in this review demonstrated successful evidence of engagement in mental imagery tasks upon command by at least some of the patients. Between one third and one fourth of the combined sample (76/252 or 30%) demonstrated brain activation in response to mental imagery tasks. The proportion of patients able to engage in these tasks with evidence of mental imagery ranged from 5/54 (9%) [59] to 4/4 (100%) [51]. Monti et al. [59] also found that fMRI based mental imagery paradigms could be used successfully as a communication tool to answer simple yes/no questions, although this was only investigated in one patient.

A summary of the six studies using an EEG mental imagery paradigm to investigate awareness in patients with DoC is provided in Table II. A total of 165 patients were included for analysis, along with over 42 healthy controls. Höller et al [48] did not specify the number of controls used to validate the imagery tasks. Only Horki et al [49] did not include a control group. The most common diagnosis was UWS/VS (64 patients), followed by MCS (54 patients) and coma (47 patients). All patients who were in a coma were recruited by Claassen et al. [47]. With regard to aetiology, 55 patients had an anoxic brain damage, 52 a cerebrovascular accident, and 39 a traumatic brain injury. Two patients had two pathologies each: one patient with traumatic brain injury and cerebrovascular accident in the study by Horki et al. [49] and one patient with traumatic brain injury and anoxia in the study by Mangia et al. [52]. The remaining 17 patients in the study by Claassen et al. [47] had other, non-specified conditions. The mean age of patients ranged from 41 years [58] to 51 years [48], with the youngest patient being 14 years old [58] and the oldest being 78 years old [53].

The reviewed EEG studies reported how accurately EEG data could signal mental imagery engagement compared to rest conditions. Five out of the six EEG studies found that EEG based paradigms could detect awareness [47,49,52,53,58], with degrees of accuracy ranging from 19% [58] to 86% [52]. Naro and Calabrò [53] found distinctions between the neural response to commands in different subgroups of patients with DoC. Classification accuracy between resting and task-related electrical activity was validated in controls and although the difference in response was weaker in MCS patients than in controls, classification accuracy was still statistically significant for all mental imagery tasks in this patient subgroup. On the other hand, patients with UWS/VS did not consistently demonstrate responses to mental imagery. Naro and Calabrò [53] also found that motor imagery tasks outperformed spatial imagery tasks in terms of classification accuracy in patients with MCS. Visuomotor assisted imagery had the greatest classification accuracy in patients with MCS, but did not perform significantly better than simple motor imagery tasks. In the study by Cruse et al. [58], 19% of patients could repeatedly and reliably generate appropriate EEG responses to two distinct commands, despite being behaviourally entirely unresponsive (mean accuracy 70%). Mangia et al. [52] found that EEG based mental imagery paradigms were able to classify responses into 'yes' or 'no' during communication trials with 97% accuracy. Claassen et al. [47] found that 15% of patients in a coma had significant neural responses to the command to move their hand, even without the presence of physical movement: like mental imagery, this cognitive-motor dissociation establishes some level of awareness, with a degree of preserved cognitive ability. The study by Höller et al. [48] was the only outlier. These authors found that their EEG based paradigm could accurately distinguish between times when an unspecified number of controls were engaging in mental imagery, and times when they were not (79% accuracy). However, these findings were not replicated in their series of 14 patients with DoC after correction for false discovery.

Discussion

The ability to assess DoC using fMRI or EEG based mental imagery paradigms is a relatively novel approach that has significant advantages over behavioural testing alone. Our literature search identified 17 original studies presenting high-quality data on the use of fMRI and EEG based mental imagery paradigms for detecting awareness in patients with DoC. The combined results of the reviewed studies indicate that mental imagery paradigms developed within experimental settings have the potential to become reliable tools for the assessment of covert consciousness in this patient population.

The strongest levels of evidence were provided by neuroimaging findings, documenting successful mental imagery in at least some of the patients in each clinical sample. Four out of the five fMRI studies that included data about DoC subgroups found that patients diagnosed with less severe forms of DoC, such as MCS or emerging MCS, were more likely to demonstrate engagement in mental imagery tasks than patients with more severe impairments in consciousness, such as UWS/VS or coma [43,44,56,57]. In the study by Vogel et al. [57], all the patients with UWS/VS who demonstrated mental imagery responses had their diagnosis changed to

MCS or emerging MCS by their follow-up assessment, suggesting that fMRI may be able to predict recovery of awareness more accurately than behavioural assessments. In 2016, a systematic review and meta-analysis of studies using active, passive, and resting state fMRI or EEG paradigms [60] found that patients with MCS show signs of preserved consciousness more frequently than patients with UWS/VS across both active and passive paradigms. A more recent meta-analysis of neuroimaging studies published between 2005 and 2017 found that active and passive cognitive tasks rely on well-segregated patterns of fMRI activations [61].

The results of five out of the six reviewed EEG studies were broadly in agreement: EEG based paradigms were found to be reliable tools for assessing awareness in patients with DoC, as they could accurately differentiate cortical activity when engaging in mental imagery tasks from resting state activity [47,49,52,53,58]. Moreover, the study by Claassen et al. [47] showed that alongside mental imagery, cognitive-motor dissociation (evidence of covert consciousness) was predictive of better recovery of consciousness at 12-month follow-up, highlighting its sensitivity for detecting awareness in the early stages of recovery. The study by Naro and Calabrò [53] included data about DoC subgroups, showing that changes in EEG activity in response to mental imagery were detectable in less severe forms of DoC, such as MCS, but not in patients with a diagnosis of UWS/VS. The same authors also found that visuomotor-guided imagery paradigms had a 16% higher classification accuracy than standard motor imagery paradigms in patients with MCS. In turn, Horki et al. 49 found motor imagery to be significantly more sensitive at detecting awareness than spatial imagery paradigms, raising the possibility of clinically relevant differences across imagery paradigms in their sensitivity to detect signals of awareness.

The implementation of mental imagery paradigms as a communication tool in patients with DoC was explored in two of the reviewed studies, using different techniques. In the fMRI study by Monti et al. [59], a single patient with a diagnosis of UWS/VS who demonstrated evidence of awareness was able to answer five out of six questions with 100% accuracy using mental imagery to communicate ‘yes’ or ‘no’. The authors noted that it remained impossible to establish any form of communication with this patient at the bedside assessment. Similar findings were obtained in the EEG study by Mangia et al. [52], where classification accuracy between ‘yes’ and ‘no’ answers provided using motor imagery was 92% in patients with a diagnosis of MCS. In addition to allowing meaningful communication, these approaches open up new avenues for a more fine-grained assessment of the broader spectrum of cognitive functions affected by DoC [62]. Mental imagery-based studies attempting to obtain volitional responses from patients with DoC could detect their command-following capability and therefore may provide an effective means to communicate with selected patients [63].

Despite the general trend of agreement between studies, their estimations of the proportion of patients with DoC who retain awareness and the accuracy of mental imagery paradigms in detecting awareness were characterised by high variability. One of the possible reasons for the discrepancy in findings is the intrinsic difficulty in establishing validity. For example, across both fMRI and EEG studies, it is unclear whether studies with lower classification accuracy included a higher number of patients who failed to produce a detectable response to an imagery task or used mental imagery paradigms with lower sensitivity. Differences in sampling/analysis techniques and sample sizes could also account for a few discrepancies between the findings of the reviewed studies. For example, the fMRI study by Bick et al. [50] reported a high proportion (5/7 or 71%) of patients demonstrating evidence of mental imagery, however the authors recruited patients whose families believed they were showing signs of consciousness, raising the possibility that their clinical sample was biased towards patients with more intact consciousness. Most of the reviewed studies had relatively small sample sizes, often due to the large number of patients who did not meet the eligibility criteria [43,45,46,48-52,54,58]. In 2018, a systematic review and meta-analysis focusing on the relationship between brain data and clinical outcomes of patients with DoC [64] found that insufficient power and lack of an appropriate description of patient selection characterized about half of the reviewed neuroimaging and neurophysiology studies. Small sample sizes with participant selection bias could be at least partly responsible for variability of findings across studies and poor generalisability to the wider DoC population.

In the reviewed studies, measures of awareness provided by mental imagery paradigms were compared with structured behavioural assessments as the existing gold standard methodology. All studies used the CRS-R as the behavioural measure of choice, with the exception of the study by Liang et al. [54], who used the GCS and equivalent scales. It has been highlighted that the limitations of the GCS as a measure of consciousness include its suboptimal inter-rater reliability [65] and over-reliance on eye response to stimuli [66]. The CRS-R has been proposed as a more accurate and reliable tool for assessing awareness based on behavioural evidence [67]. However, its implementation can be problematic because of the need for multiple assessments over time and its reliance on the patients’ ability to convey physical manifestations of awareness which, depending on injuries to their motor systems, might not be consistently possible. As for the non-behavioural protocols, a significant advantage of the fMRI technique is its higher accuracy at localising responses to specific brain regions (e.g. supplementary motor areas for motor imagery tasks and parahippocampal gyrus for spatial imagery tasks). This increases confidence that the detected neural activity is a direct effect of intended execution of the required mental imagery task, rather than simply a response to auditory feedback or other environmental stimuli. An obvious disadvantage is its impractical use, which is prevented in the case of patients with surgical implants that make them unsuitable for this neuroimaging approach [33]. Despite lower spatial localisation power, the practicality of using EEG equipment makes neurophysiology investigations better suited for the patient's bedside assessment.

The implementation of mental imagery paradigms in a multimodal approach to assess awareness in patients with DoC could significantly increase diagnostic accuracy, leading to better informed decisions regarding care and rehabilitation programmes. Moreover, it has been argued that patients with DoC demonstrating neuroimaging evidence of covert consciousness may benefit from early adapted rehabilitation [68]. One of the developments of artificial intelligence is in the integration of mental imagery paradigms with brain computer interfaces [69]. As part of neurofeedback protocols, both fMRI and EEG signals can be converted into meaningful responses to facilitate communication [70]. Importantly, the available evidence suggests that imagery-based fMRI and EEG paradigms have the potential to outperform behavioural assessments in generating prognostic data to predict recovery trajectories in patients with DoC [71,72]. Coupled with the findings of resting state activity studies, functional neuroimaging studies implementing mental imagery paradigms allow for increasingly more reliable network mapping of connectivity alterations in DoC, which in turn paves the way for targeted neuromodulation [73].

Our systematic literature review has limitations. First, we deliberately focused on research published in English language during the last 20 years, possibly leaving out relevant studies. Second, although the reviewed studies were rated as having satisfactory methodological quality, they were mostly conducted in specialist centres across Europe [48,49,52,53,55,57-59] and North America [43-47], resulting in a geographical bias of the patient population. Third, the process of combining and comparing findings from heterogeneous studies was hindered by inter-individual variability in the behavioural assessment of consciousness and differences in the mental imagery paradigms. Finally, few studies presented data on the longitudinal trajectories of patients with DoC [47,51,55,57], thus limiting generalisations about the stability of findings over time.

Despite these limitations, the present review provides evidence that both fMRI and EEG mental imagery paradigms could become viable tools for assessing awareness in patients with DoC. A review published in 2022 covering studies that were conducted within the previous ten years showed that about 40% of patients with DoC can be misdiagnosed because specifically designed behavioural scales are not employed or improperly administered [74]. To improve diagnostic accuracy for these patients, the authors suggested that neuroimaging and electrophysiological techniques can play an important role in the differentiation between VS/UWS and MCS patients. Based on the available literature, mental imagery paradigms might prove more sensitive than behavioural assessments at detecting awareness, and could successfully be used as communication tools, especially in patients with compromised motor responses. These findings have important clinical and theoretical implications, paving the way to improved management of DoC and shedding light on the neural correlates of consciousness [75].

In order to overcome the limitations of relatively underpowered studies, further research should be conducted on larger sample sizes to establish the feasibility of mental imagery paradigms as a reliable method of assessing awareness in patients with DoC and to establish the consistency and specificity of findings across different patient subgroups. It would be especially important to incorporate healthy controls in the study design to confirm the generalisability of previously validated paradigms and to assess the validity of novel mental imagery paradigms, such as the visuomotor guided imagery task [49]. Overall, future research should focus on the further development of more sensitive imagery paradigms that can generate stronger neural responses in a reproducible manner and in a wide range of DoC, thus facilitating the implementation of these paradigms in a clinical setting. Longitudinal studies with follow-up assessments at 3, 6, and 12 months would provide useful indications about the predictive power of mental imagery paradigms about the long-term outcomes of patients with DoC. Finally, it would be essential to conduct further research combining both fMRI and EEG mental imagery paradigms within the same clinical samples, in order to allow direct comparisons between non-behavioural methods of assessing awareness in DoC. Advances in this field would play a crucial role in promoting the incorporation of mental imagery paradigms in improved diagnostic protocols for patients with DoC, alongside validated behavioural assessments.

Conflict of interest statement

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References

1. Fernández-Espejo D, Owen AM. Detecting awareness after severe brain injury. Nat Rev Neurosci. 2013;14:801-809. https://doi.org/10.1038/nrn3608
2. Huntley JD, Fleming SM, Mograbi DC, et al. Understanding Alzheimer's disease as a disorder of consciousness. Alzheimers Dement. 2021;7:e12203. https://doi.org/10.1002/trc2.12203
3. Zeman A. Consciousness. Brain. 2001;124:1263-1289. https://doi.org/10.1093/brain/124.7.1263
4. Laureys S, Owen AM, Schiff ND. Brain function in coma, vegetative state, and related disorders. Lancet Neurol. 2004;3:537-546. https://doi.org/10.1016/S1474-4422(04)00852-X
5. Monaco F, Mula M, Cavanna AE. Consciousness, epilepsy, and emotional qualia. Epilepsy Behav. 2005;7:150-160. https://doi.org/10.1016/j.yebeh.2005.05.018
6. Zeman A. What do we mean by "conscious" and "aware"? Neuropsychol Rehabil. 2006;16:356-376. https://doi.org/10.1080/09602010500484581
7. Cavanna AE, Shah S, Eddy CM, et al. Consciousness: a neurological perspective. Behav Neurol. 2011;24:107-116. https://doi.org/10.3233/BEN-2011-0322
8. Nani A, Cavanna AE. The quantitative measurement of consciousness during epileptic seizures. Epilepsy Behav. 2014;30:2-5. https://doi.org/10.1016/j.yebeh.2013.09.007
9. Cavanna AE, Monaco F. Brain mechanisms of altered conscious states during epileptic seizures. Nat Rev Neurol. 2009;5:267-276. https://doi.org/10.1038/nrneurol.2009.38
10. Bagshaw AP, Cavanna AE. Brain mechanisms of altered consciousness in focal seizures. Behav Neurol. 2011;24:35-41. https://doi.org/10.3233/BEN-2011-0312
11. Lambert I, Bartolomei F. Why do seizures impair consciousness and how can we reverse this? Curr Opin Neurol. 2020;33:173-178. https://doi.org/10.1097/WCO.0000000000000794
12. Blumenfeld H. Arousal and consciousness in focal seizures. Epilepsy Curr. 2021;21:353-359. https://doi.org/10.1177/15357597211029507
13. Demertzi A, Vanhaudenhuyse A, Bruno MA, et al. Is there anybody in there? Detecting awareness in disorders of consciousness. Expert Rev Neurother. 2008;8:1719-1730. https://doi.org/10.1586/14737175.8.11.1719
14. Zeman A. The problem of unreportable awareness. Prog Brain Res. 2009;177:1-9. https://doi.org/10.1016/S0079-6123(09)17701-4
15. Schnakers C. Assessing consciousness and cognition in disorders of consciousness. NeuroRehabilitation. 2024;54:11-21. https://doi.org/10.3233/NRE-230140
16. Bruno MA, Vanhaudenhuyse A, Thibaut A, et al. From unresponsive wakefulness to minimally conscious PLUS and functional locked-in syndromes: recent advances in our understanding of disorders of consciousness. J Neurol. 2011;258:1373-1384. https://doi.org/10.1007/s00415-011-6114-x
17. Gabbe BJ, Cameron PA, Finch CF. The status of the Glasgow Coma Scale. Emerg Med. 2003;15:353-360. https://doi.org/10.1046/j.1442-2026.2003.00474.x
18. Teasdale G, Jennett B. Assessment of coma and impaired consciousness. A practical scale. Lancet. 1974;2:81-84. https://doi.org/10.1016/s0140-6736(74)91639-0
19. Giacino JT, Kezmarsky MA, DeLuca J, Cicerone KD. Monitoring rate of recovery to predict outcome in minimally responsive patients. Arch Phys Med Rehabil. 1991;72:897-901. https://doi.org/10.1016/0003-9993(91)90008-7
20. Giacino JT, Kalmar K, Whyte J. The JFK Coma Recovery Scale-Revised: measurement characteristics and diagnostic utility. Arch Phys Med Rehabil. 2004;85:2020-2029. https://doi.org/10.1016/j.apmr.2004.02.033
21. Kalmar K, Giacino JT The JFK Coma Recovery Scale-Revised. Neuropsychol Rehabil. 2005;15:454-460. https://doi.org/10.1080/09602010443000425
22. Owen AM, Coleman MR. Detecting awareness in the vegetative state. Ann N Y Acad Sci. 2008;1129:130-138. https://doi.org/10.1196/annals.1417.018
23. Cavanna AE, Cavanna SL, Servo S, Monaco F. The neural correlates of impaired consciousness in coma and unresponsive states. Discov Med. 2010;9:431-438.
24. Zasler ND, Aloisi M, Contrada M, Formisano R. Disorders of consciousness terminology: history, evolution and future directions. Brain Inj. 2019;33:1684-1689. https://doi.org/10.1080/02699052.2019.1656821
25. Golden K, Bodien YG, Giacino JT. Disorders of consciousness: classification and taxonomy. Phys Med Rehabil Clin N Am. 2024;35:15-33. https://doi.org/10.1016/j.pmr.2023.06.011
26. Schnakers C. Update on diagnosis in disorders of consciousness. Expert Rev Neurother. 2020;20:997-1004. https://doi.org/10.1080/14737175.2020.1796641
27. Jennett B, Plum F. Persistent vegetative state after brain damage: a syndrome in search of a name. Lancet. 1972;1:734-737. https://doi.org/10.1016/s0140-6736(72)90242-5
28. von Wild K, Laureys ST, Gerstenbrand F, et al. The vegetative state: a syndrome in search of a name. J Med Life. 2021;5:3-15.
29. Laureys S, Celesia GG, Cohadon F, et al. Unresponsive wakefulness syndrome: a new name for the vegetative state or apallic syndrome. BMC Med. 2010;8:68. https://doi.org/10.1186/1741-7015-8-68
30. Giacino JT, Ashwal S, Childs N, et al. The minimally conscious state: definition and diagnostic criteria. Neurology. 2002;58:349-353. https://doi.org/10.1212/wnl.58.3.349
31. Bayne T, Hohwy J, Owen AM. Reforming the taxonomy in disorders of consciousness. Ann Neurol. 2017;82:866-872. https://doi.org/10.1002/ana.25088
32. Wannez S, Heine L, Thonnard M, et al. The repetition of behavioral assessments in diagnosis of disorders of consciousness. Ann Neurol. 2017;81:883-889. https://doi.org/10.1002/ana.24962
33. Harrison AH, Connolly JF. Finding a way in: a review and practical evaluation of fMRI and EEG for detection and assessment in disorders of consciousness. Neurosci Biobehav Rev. 2013;37:1403-1419. https://doi.org/10.1016/j.neubiorev.2013.05.004
34. Bagshaw AP, Rollings DT, Khalsa S, Cavanna AE. Multimodal neuroimaging investigations of alterations to consciousness: the relationship between absence epilepsy and sleep. Epilepsy Behav. 2014;30:33-37. https://doi.org/10.1016/j.yebeh.2013.09.027
35. Hauger SL, Schanke AK, Andersson S, et

al. The clinical diagnostic utility of electrophysiological techniques in assessment of patients with disorders of consciousness following acquired brain injury: a systematic review. J Head Trauma Rehabil. 2017;32:185-196. https://doi.org/10.1097/HTR.0000000000000267

36 Bagshaw AP, Cavanna AE. Resting state networks in paroxysmal disorders of consciousness. Epilepsy Behav. 2013;26:290-294. https://doi.org/10.1016/j.yebeh.2012.09.020

37 Marino S, Bonanno L, Giorgio A. Functional connectivity in disorders of consciousness: methodological aspects and clinical relevance. Brain Imaging Behav. 2016;10:604-608. https://doi.org/10.1007/s11682-015-9417-1

38 Bodien YG, Chatelle C, Edlow BL. Functional networks in disorders of consciousness. Semin Neurol. 2017;37:485-502. https://doi.org/10.1055/s-0037-1607310

39 Soddu A, Gómez F, Heine L, et al. Correlation between resting state fMRI total neuronal activity and PET metabolism in healthy controls and patients with disorders of consciousness. Brain Behav. 2015;6:e00424. https://doi.org/10.1002/brb3.424

40 Owen AM, Coleman MR, Boly M, et al. Detecting awareness in the vegetative state. Science. 2006;313(5792):1402. https://doi.org/10.1126/science.1130197

41 Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA. 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71. https://doi.org/10.1136/bmj.n71

42 Crowe M, Sheppard L, Campbell A. Reliability analysis for a proposed critical appraisal tool demonstrated value for diverse research designs. J Clin Epidemiol. 2012;65:375-383. https://doi.org/10.1016/j.jclinepi.2011.08.006

43 Bardin JC, Fins JJ, Katz DI, et al. Dissociations between behavioural and functional magnetic resonance imaging-based evaluations of cognitive function after brain injury. Brain. 2011;134:769-782. https://doi.org/10.1093/brain/awr005

44 Forgacs PB, Conte MM, Fridman EA, et al. Preservation of electroencephalographic organization in patients with impaired consciousness and imaging-based evidence of command-following. Ann Neurol. 2014;76:869-879. https://doi.org/10.1002/ana.24283

45 Bodien YG, Giacino JT, Edlow BL. Functional MRI motor imagery tasks to detect command following in traumatic disorders of consciousness. Front Neurol. 2017;8:688. https://doi.org/10.3389/fneur.2017.00688

46 Edlow BL, Chatelle C, Spencer CA, et al. Early detection of consciousness in patients with acute severe traumatic brain injury. Brain. 2017;140:2399-2414. https://doi.org/10.1093/brain/awx176

47 Claassen J, Doyle K, Matory A, et al. Detection of brain activation in unresponsive patients with acute brain injury. N Engl J Med. 2019;380:2497-2505. https://doi.org/10.1056/NEJMoa1812757

48 Höller Y, Bergmann J, Thomschewski A, et al. Comparison of EEG-features and classification methods for motor imagery in patients with disorders of consciousness. PLoS One. 2013;8:e80479. https://doi.org/10.1371/journal.pone.0080479

49 Horki P, Bauernfeind G, Klobassa DS, et al. Detection of mental imagery and attempted movements in patients with disorders of consciousness using EEG. Front Hum Neurosci. 2014;8:1009. https://doi.org/10.3389/fnhum.2014.01009

50 Bick AS, Leker RR, Ben-Hur T, Levin N. Implementing novel imaging methods for improved diagnosis of disorder of consciousness patients. J Neurol Sci. 2013;334:130-138. https://doi.org/10.1016/j.jns.2013.08.009

51 Sharon H, Pasternak Y, Ben Simon E, et al. Emotional processing of personally familiar faces in the vegetative state. PLoS ONE. 2013;8:e74711. https://doi.org/10.1371/journal.pone.0074711

52 Mangia AL, Pirini M, Simoncini L, Cappello A. A feasibility study of an improved procedure for using EEG to detect brain responses to imagery instruction in patients with disorders of consciousness. PLoS One. 2014;9:e99289. https://doi.org/10.1371/journal.pone.0099289

53 Naro A, Calabrò RS. Towards new diagnostic approaches in disorders of consciousness: a proof of concept study on the promising use of imagery visuomotor task. Brain Sci. 2020;10:746. https://doi.org/10.3390/brainsci10100746

54 Liang X, Kuhlmann L, Johnston LA, et al. Extending communication for patients with disorders of consciousness. J Neuroimaging. 2014;24:31-38. https://doi.org/10.1111/j.1552-6569.2012.00744.x

55 Stender J, Gosseries O, Bruno MA, et al. Diagnostic precision of PET imaging and functional MRI in disorders of consciousness: a clinical validation study. Lancet. 2014;384:514-522. https://doi.org/10.1016/S0140-6736(14)60042-8

56 Wang F, Hu N, Hu X, et al. Detecting brain activity following a verbal command in patients with disorders of consciousness. Front Neurosci. 2019;13:976. https://doi.org/10.3389/fnins.2019.00976

57 Vogel D, Markl A, Yu T, et al. Can mental imagery functional magnetic resonance imaging predict recovery in patients with disorders of consciousness? Arch Phys Med Rehabil. 2013;94:1891-1898. https://doi.org/10.1016/j.apmr.2012.11.053

58 Cruse D, Chennu S, Chatelle C, et al. Bedside detection of awareness in the vegetative state: a cohort study. Lancet. 2011;378:2088-2094. https://doi.org/10.1016/S0140-6736(11)61224-5

59 Monti MM, Vanhaudenhuyse A, Coleman MR, et al. Willful modulation of brain activity in disorders of consciousness. N Engl J Med. 2010;362:579-589. https://doi.org/10.1056/NEJMoa0905370

60 Kondziella D, Friberg CK, Frokjaer VG, et al. Preserved consciousness in vegetative and minimal conscious states: systematic review and meta-analysis. J Neurol Neurosurg Psychiatry. 2016;87:485-492. https://doi.org/10.1136/jnnp-2015-310958

61 Berlingeri M, Magnani FG, Salvato G, et al. Neuroimaging studies on disorders of consciousness: a meta-analytic evaluation. J Clin Med. 2019;8:516. https://doi.org/org/10.3390/jcm8040516

62 Lull N, Noé E, Lull JJ, et al. Voxel-based statistical analysis of thalamic glucose metabolism in traumatic brain injury: relationship with consciousness and cognition. Brain Inj. 2010;24:1098-1107. https://doi.org/10.3109/02699052.2010.494592

63 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. https://doi.org/10.3389/fnins.2020.555093

64 Kotchoubey B, Pavlov YG. A systematic review and meta-analysis of the relationship between brain data and the outcome in disorders of consciousness. Front Neurol. 2018;9:315. https://doi.org/10.3389/fneur.2018.00315

65 Gill MR, Reiley DG, Green SM. Interrater reliability of Glasgow Coma Scale scores in the emergency department. Ann Emerg Med. 2004;43:215-223. https://doi.org/10.1016/s0196-0644(03)00814-x

66 Majerus S, Gill-Thwaites H, Andrews K, Laureys S. Behavioral evaluation of consciousness in severe brain damage. Prog Brain Res. 2005;150:397-413. https://doi.org/10.1016/S0079-6123(05)50028-1

67 La Porta F, Caselli S, Ianes AB, et al. Can we scientifically and reliably measure the level of consciousness in vegetative and minimally conscious States? Rasch analysis of the Coma Recovery Scale-Revised. Arch Phys Med Rehabil. 2013;94:527-535.

https://doi.org/10.1016/j.apmr.2012.09.035

68 Sanz LRD, Thibaut A, Edlow BL, et al. Update on neuroimaging in disorders of consciousness. Curr Opin Neurol. 2021;34:488-496. https://doi.org/10.1097/WCO.0000000000000951

69 Carelli L, Solca F, Faini A, et al. Brain-computer interface for clinical purposes: cognitive assessment and rehabilitation. Biomed Res Int. 2017:1695290. https://doi.org/10.1155/2017/1695290

70 Vatrano M, Nemirovsky IE, Tonin P, Riganello F. Assessing consciousness through neurofeedback and neuromodulation: possibilities and challenges. Life. 2023;13:1675. https://doi.org/10.3390/life13081675

71 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;91:450-460. https://doi.org/10.1212/WNL.0000000000005926

72 Scolding N, Owen AM, Keown J. Prolonged disorders of consciousness: a critical evaluation of the new UK guidelines. Brain. 2021;144:1655-1660. https://doi.org/10.1093/brain/awab063

73 Mencarelli L, Biagi MC, Salvador R, et al. Network mapping of connectivity alterations in disorder of consciousness: towards targeted neuromodulation. J Clin Med. 2020;9:828. https://doi.org/10.3390/jcm9030828

74 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. https://doi.org/10.3389/fneur.2021.778951

75 Young MJ, Fecchio M, Bodien YG, Edlow BL. Covert cortical processing: a diagnosis in search of a definition. Neurosci Conscious. 2024;1:niad026. https://doi.org/10.1093/nc/niad026