



## Emerging Neuro-Technologies for Detecting Consciousness in Locked-In Syndrome: A Review of fMRI, EEG, and Machine Learning Applications

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### Abstract

**Introduction:** The clinical differentiation between disorders of consciousness (DOC), such as unresponsive wakefulness syndrome (UWS), and locked-in syndrome (LIS/CLIS) remains a formidable challenge, with misdiagnosis rates reaching up to 40%. Because traditional bedside assessments are motor-dependent, they fail to detect "covert consciousness" or "cognitive motor dissociation" (CMD) in patients who are cognitively aware but physically paralyzed. This review analyzes evidence on emerging neurotechnologies, specifically functional magnetic resonance imaging (fMRI), electroencephalogram (EEG), and machine learning (ML)—aimed to establish objective, motor-independent markers of awareness.

**Methods:** PubMed, Google Scholar and Scopus were searched for articles that focus on locked-in syndrome and the neurotechnologies that can detect consciousness, using keywords such as "Locked-in syndrome", "electroencephalography", "fMRI". Analysis was done from 22 studies, focusing on different technologies and different subgroups of unconsciousness.

**Results:** Out of 22 studies, transcranial magnetic stimulation-electro-EEG-derived perturbational complexity index reliably discriminates conscious from unconscious states with high sensitivity, providing a "gold standard" for bedside complexity mapping. Task-based fMRI and EEG detected command-following in 15% of behaviorally unresponsive acute patients, which serves as a powerful

predictor of 12-month functional recovery. In chronic cases, resting-state fMRI demonstrated that LIS patients maintain higher default mode network (DMN) connectivity than those in UWS. Machine learning models successfully automated the detection of awareness by training on pharmacological datasets and applying them to pathological states. For the transition to completely locked-in state (CLIS), metabolic signals from functional near-infrared spectroscopy (fNIRS) and invasive Brain-Computer Interfaces (BCI) using ECoG or LFP signals provided stable, long-term communication channels where traditional EEG paradigms often failed. Furthermore, hybrid systems integrating EEG with eye-tracking significantly improved communication accuracy in fluctuating states.

**Conclusion:** Emerging neurotechnologies have transformed the diagnostic landscape for locked-in syndrome, shifting reliance from overt behavior to internal neural dynamics. A multimodal diagnostic framework, combining the spatial resolution of fMRI, the temporal flexibility of EEG, and the predictive power of machine learning, is essential for accurate stratification. These advancements not only reduce misdiagnosis but also provide the technical foundation for permanent, high-speed communication interfaces for the most severely disabled patients.

**Keywords:** Locked-in syndrome, electroencephalography, machine learning, functional magnetic resonance imaging, consciousness

## Abbreviations

Amyotrophic lateral sclerosis (ALS)  
Brain-computer interface (BCI)  
Completely locked-in state (CLIS)  
Locked-in syndrome (LIS)  
Disorders of consciousness (DOC)  
Functional magnetic resonance imaging (fMRI)  
Resting-state functional magnetic resonance imaging (rs-fMRI)  
Electroencephalography (EEG)  
Near-infrared spectroscopy (NIRS)  
Functional near-infrared spectroscopy (fNIRS)  
Transcranial magnetic stimulation (TMS)  
Perturbational complexity index (PCI)  
Unresponsive wakefulness syndrome (UWS)  
Minimally conscious state (MCS)  
Default mode network (DMN)  
Electrocorticography (ECoG)  
Local field potential (LFP)  
Motor imagery (MI)  
Cognitive motor dissociation (CMD)  
Traumatic brain injury (TBI)

Intensive care unit (ICU)  
Glasgow Outcome Scale-Extended (GOS-E)  
Lempel-Ziv complexity (LZC)  
Power-law exponent (PLE)  
Machine learning (ML)  
Convolutional neural network (CNN)  
Support vector machine (SVM)  
Multimodal target recognition network (MTRN)  
Somatosensory evoked potential (SSEP)  
Auditory evoked potential (AEP)  
Non-rapid eye movement (NREM)  
Coma Recovery Scale-Revised (CRS-R)  
Oxygenated hemoglobin (HbO)  
Deoxygenated hemoglobin (HbR)  
Power spectral density (PSD)  
Global Outflow Scale (GOS)  
Hypoxic-ischemic encephalopathy (HIE)  
Subarachnoid hemorrhage (SAH)  
Intracerebral hemorrhage (ICH)

## Introduction

Locked-in syndrome (LIS) is a rare, one of the most complex conditions in neurointensive care, which can be described by complete paralysis and anarthria with retained consciousness. Individuals with LIS are only able to communicate using limited eye movements, such as blinking and vertical motion. It typically arises from injury to the anterior pontine region; however, there have been reports of lesions in the midbrain or bilateral internal capsules that result in similar presentations (18).

Stroke, traumatic brain injury, and neurodegenerative diseases like amyotrophic lateral sclerosis (ALS) are several causes of these lesions, which block the motor pathways leading to quadriplegia and loss of speech, while leaving arousal systems and thalamocortical projections unaltered, allowing patients to remain fully conscious (1, 2, 18). Due to total immobility and restricted means of communication, individuals with LIS remain vulnerable during the early phase. Nevertheless, if the disease is accurately diagnosed early and proper supportive care is provided, long-term survival is likely to be achieved (4). Regardless of the apparent clinical observation, it remains difficult to precisely detect consciousness in LIS and other disorders of consciousness (DoC), leading to a significant rate of incorrect diagnoses. Clinical assessments, such as the coma recovery scale – revised (CRS-R), rely on overt motor responses and therefore they demonstrate limitations in identifying completely motor-silent individuals, as in LIS. As a result, LIS with the coexistence of absent motor output and retained consciousness is more prone to being mistakenly categorized as barely conscious or even vegetative. Misdiagnosis can lead to

adverse outcomes, for instance, incorrect expectations of recovery, early discontinuation of life-sustaining therapies, exclusion from rehabilitation, and inability to make decisions related to care. From an ethical perspective, neglecting a patient's awareness compromises their right to make informed decisions (16).

Accordingly, techniques that can evaluate conscious states without relying on motor responses are essential for overcoming these challenges. Among recent advances in neurotechnology, functional magnetic resonance imaging (fMRI), electroencephalography (EEG), and machine learning-assisted applications play a key role in detecting covert consciousness. EEG delivers important bedside insights into the cognitive state by recording evoked responses that reflect retained sensory processing and the brain's ability to respond to commands (11). Perturbational techniques, mainly transcranial magnetic stimulation- electroencephalography (TMS-EEG) measurement of the perturbational complexity index (PCI), provide a measurable neural indicator that greatly helps in differentiating LIS from others (3). Additionally, by revealing connections within the default mode network (DMN) and frontoparietal networks (FPN) that remain unaltered, fMRI aids in differentiating LIS from other DoCs. Mental imagery tasks used in task-based fMRI have consistently shown reliable command-following, even in individuals previously labeled as unconscious (4, 8). Machine learning can be applied to techniques, for example, EEG, which allows relatively insignificant brain signals to be detected in a practical environment, which helps to improve the sensitivity and precision in classification (13,17).

Alongside these advances, (fNIRS), magnetoencephalography (MEG), electrocorticography (ECoG), autonomic and pupillometry measurements, transcranial focused ultrasound (tFUS), and brain-computer interfaces (BCI) are currently being recognized as helpful techniques to lower the risk of false-negative assessments, thus boosting the diagnostic precision (5,12).

Despite major advances, existing research on detecting consciousness in LIS continues to be limited by small, diverse cohorts and inconsistent methodologies, making it difficult to replicate and apply the findings in clinical practice. Moreover, a key challenge is validating the results of consciousness, as even advanced neurotechnologies are judged against imperfect references such as the CRS-S. In addition, other techniques, such as TMS-EEG, BCI, fNIRS, and MEG show great potential; however, they are rarely combined into a single diagnostic framework or monitored over time, which hinders the understanding of their reliability and utility (3,8,10).

By highlighting methodological deficiencies and obstacles to application in clinical settings, the objective of the review is to provide direction for future research and encourage the development of more reliable assessment strategies which will help to improve diagnostic precision, ethical decision-making and, patient care in LIS. This review assesses the status of neurotechnology development, with an emphasis on EEG, FMRI, and machine learning applications used to assess consciousness in individuals with LIS. Building on recent key research, this study aims to combine current evidence, strengths, and limitations of the aforementioned techniques and discuss the integration of other modalities to improve patient care in the future.

## Objectives

This review aimed to provide a comprehensive overview of current approaches used to assess consciousness in patients with locked-in syndrome.

## Methodology

Relevant studies were identified through a systematic search of major electronic databases, including PubMed, Google Scholar, and Scopus. In addition, previously published clinical review articles were examined, and their reference lists were screened to identify additional studies relevant to the topic. The search strategy was based on a combination of keywords related to locked-in syndrome and neurotechnological assessment methods. These included “locked-in syndrome,” “functional MRI,” “EEG,” “disorders of consciousness,” and “neuroimaging.” Boolean operators (AND/OR) were used to refine searches and adapt them to each database.

Studies were included if they were peer-reviewed, published in english, and directly relevant to locked-in syndrome or methods used to assess consciousness.

Studies were excluded if they were not peer-reviewed, lacked full-text availability, or were not directly relevant to the objectives of the review. Case reports with limited methodological detail and opinion-based articles were also excluded.

All articles identified were collected, and duplicates were removed. The remaining studies underwent a two-stage screening process. First, titles and abstracts were reviewed to assess relevance. Studies that appeared suitable were then examined in full to confirm eligibility. Only articles meeting all inclusion criteria after full-text review were included in the final selection.

After title and abstract screening and full-text screening, 22 studies were selected. The studies were then analyzed, based on locations of the aneurysms, and the key clinical outcomes such as mortality, rebleeding, vasospasm, and quality of life. Disagreements regarding selection were resolved by discussion and with the help of a third reviewer. At the end, 22 studies were selected for analysis.

## Results

A unifying trend among reviewed studies showed that EEG-based measurements consistently measured preserved neuromarkers of consciousness in locked-in syndrome. Task based EEG framework can detect command-following, providing objective evidence of preserved consciousness in patients who are behaviorally nonresponsive. TMG-EEG studies were able to demonstrate that locked-in patients had complex, widespread cortical responses comparable to conscious control (2, 3). Quantitative PCI values in locked-in syndrome fell within the conscious range, which confirmed preservation of consciousness in locked-in syndrome patients independent of motor output. Analysis of spontaneous EEG in locked-in syndrome patients and complete locked-in syndrome patients demonstrated that there is no single pattern that defines consciousness. Two patients with similar

clinical diagnosis can have drastically different EEG readings, for example low EEG amplitude, absent or weak alpha rhythm. The complexity and connectivity metrics reliably indicated consciousness states despite inter-individual variables (8). EEG analysis is a great tool for detecting consciousness when it is present, however a negative EEG reading does not rule out its absence and its role in detecting consciousness is highly limited. A common consensus among reviewed studies is that a negative EEG reading should be interpreted with caution, and this stresses for a need of a multimodal approach in measuring consciousness in patients exhibiting locked-in syndrome or complete locked-in syndrome to avoid misdiagnosis (12,16,17).

## FMRI

Early functional MRI (fMRI) studies in patients diagnosed with vegetative state (VS) or minimally conscious state (MCS) demonstrated that some behaviorally unresponsive individuals show cortical activation in response to auditory, emotional, or motor imagery tasks. These findings suggest preserved cognitive processing despite the absence of overt behavioral responses (Owen et al., 2006, Monti et al., 2007). Such observations challenge the traditional reliance on bedside behavioral assessments, which may underestimate awareness in patients with limited or inconsistent motor output (Giacino et al., 2009). To address this limitation, task-based fMRI paradigms—particularly motor imagery and command-following tasks—have been employed to detect covert cognition by comparing blood-oxygen-level-dependent (BOLD) responses during active versus rest conditions (Owen et al., 2006, Boly et al., 2007).

However, task-based fMRI depends on intact language comprehension, attention, and neurovascular coupling. As a result, false-negative findings may occur in patients who are sedated, fatigued, hemodynamically unstable, or otherwise unable to sustain task engagement. Importantly, a negative fMRI result does not exclude awareness, as absent activation may reflect technical limitations or altered physiological states rather than a true lack of cognition (Monti et al., 2010; Schiff, 2009). Resting-state fMRI (rs-fMRI) has therefore emerged as a complementary approach, allowing the assessment of functional connectivity without requiring task performance. By analyzing spontaneous BOLD signal fluctuations, rs-fMRI enables investigation of brain network organization in patients who are unable to follow commands (Fox & Raichle, 2007; Vanhaudenhuyse et al., 2010; Demertzi et al., 2015).

Multiple studies have demonstrated that the level of consciousness correlates with the integrity of functional connectivity within and between canonical brain networks, including the default-mode, frontoparietal, sensorimotor, visual, and language networks (Vanhaudenhuyse et al., 2010; Laureys & Maquet, 2014). A 2024 systematic review further reported that preserved resting-state connectivity is associated with higher levels of awareness and may carry prognostic value for recovery in disorders of consciousness (Di Perri et al., 2024). Large-scale and recent investigations have strengthened these findings. The largest multicenter study to date, examining cognitive motor dissociation, assessed 353 adults with disorders of consciousness across six international sites using task-based fMRI and EEG (Edlow et al., 2024). Complementary evidence comes from a 2025 study comparing 109 chronic DoC patients with healthy controls, which showed that the number and strength of preserved functional

networks, particularly visual, temporal, left frontoparietal, and default-mode networks, distinguished VS/UWS from MCS, achieving intermediate diagnostic discrimination (AUC 0.64–0.69) (Thibaut et al., 2025).

Beyond functional measures alone, multimodal imaging approaches combining fMRI with diffusion tensor imaging and structural MRI provide insight into whether preserved structural substrates support functional activation and connectivity (Laureys et al., 2009; Fernández-Espejo et al., 2011). Evidence suggests that the integrity of white-matter tracts underpins preserved functional networks, indicating that combined structural–functional biomarkers may improve the specificity of detecting residual consciousness (Fernández-Espejo et al., 2012). Despite substantial progress, significant limitations remain. Resting-state functional connectivity reflects statistical dependencies rather than direct measures of conscious awareness, and intact connectivity does not necessarily imply subjective experience (Boly et al., 2013; Demertzi et al., 2015). Practical barriers—including high costs, limited availability, the need for specialized expertise, and variability in acquisition and analysis methods across centers—continue to hinder routine clinical implementation (Laureys & Maquet, 2014).

Additionally, many studies rely on small and heterogeneous samples with varying etiologies and time since injury, and relatively few longitudinal datasets are available to validate prognostic accuracy. Key future priorities therefore include the development of normative databases, standardized task paradigms and rs-fMRI pipelines, and large-scale multicenter longitudinal studies linking neuroimaging findings to long-term outcomes (Giacino et al., 2018; Di Perri et al., 2024). Integrating fMRI with EEG, diffusion imaging, and perfusion measures may further enhance clinical utility and reduce false-positive and false-negative interpretations (Edlow et al., 2017).

In summary, task-based and resting-state fMRI have substantially advanced the understanding of covert consciousness by demonstrating that a meaningful proportion of behaviorally unresponsive patients retain brain activation or network connectivity consistent with cognition (Edlow et al., 2024; Thibaut et al., 2025). Nevertheless, methodological, interpretive, and logistical challenges currently limit widespread clinical application, underscoring the need for standardization, multimodal integration, and rigorous prognostic validation.

### Electroencephalography (EEG) and Perturbational Complexity

EEG-based technologies offer the most versatile bedside applications, particularly through the measurement of brain complexity and spectral dynamics. A landmark finding in this field is the validation of the Perturbational Complexity Index (PCI), derived from TMS-EEG. Study results indicate that a PCI value above a specific threshold (0.31) accurately identifies consciousness in "disconnected" patients (LIS) while showing low values in unconscious states such as NREM sleep or anesthesia (2, 3). This metric has been successfully used to detect the potential for consciousness in chronic UWS patients who were otherwise misdiagnosed based on behavioral scales (11). In the Completely Locked-In State (CLIS), EEG results reveal that while classic communication paradigms often fail, resting-state dynamics remain rich. Studies using Lempel-Ziv complexity (LZC) and the

power-law exponent (PLE) found that CLIS patients exhibit arousal fluctuations similar to healthy individuals, although their overall brain dynamics are often more "sluggish" or shifted toward lower frequencies (18, 22). In the first days following severe brain injury, EEG-based machine learning has detected brain activation in response to commands in 15% of unresponsive patients, and these patients were significantly more likely to achieve functional independence (GOS-E  $\geq 4$ ) at 12 months compared to those without such activation (10). Furthermore, multiscale entropy and Poincaré plot analysis of EEG signals have identified specific "windows" of high complexity in CLIS patients, suggesting that consciousness in these patients may not be constant but rather occurs in discrete periods of awareness (13, 15).

### Brain-computer interfaces (BCI) and invasive monitoring

The development of BCIs has moved from experimental labs to long-term clinical utility for LIS and CLIS. Results from studies on fully implanted ECoG systems show that patients can achieve high-speed, independent communication (using "brain clicks") with a high degree of accuracy and minimal long-term signal degradation (5). Similarly, intracortical microelectrode arrays (like BrainGate2) have demonstrated that Local Field Potentials (LFPs) remain stable over years, allowing patients with ALS and LIS to control communication software even as their physical condition progresses (9). For patients who have lost even eye movement (CLIS), vibro-tactile P300 and motor imagery BCIs have been tested; while success rates are lower than in LIS, some patients successfully achieve command-following and yes/no communication (6). Recent innovations include hybrid systems that integrate EEG P300 potentials with eye-tracking and pupillometry. Results show that by using a multimodal target recognition network (MTRN), the system can adaptively weight neural and ocular signals, significantly increasing communication accuracy for patients with fluctuating levels of consciousness (20).

### Functional near-infrared spectroscopy and machine learning

fnIRS has emerged as a portable alternative to fMRI, measuring the hemodynamic response at the bedside. Study outcomes show that fnIRS can detect residual awareness in prolonged DOC patients by monitoring oxygenated hemoglobin levels during motor imagery tasks (16). In a notable case of CLIS, a bedside NIRS-based BCI was the only modality that allowed the patient to communicate "yes" or "no" over several sessions, suggesting that metabolic signals might be more robust than electrical signals in the final stages of neurodegeneration (1). Machine learning has become the "engine" behind these technologies, providing the ability to classify states of consciousness with high precision. By training algorithms on "pharmacologically informed" datasets (e.g., healthy brains under anesthesia), models can now identify pathological states of unconsciousness in fMRI data with high sensitivity (12). Deep learning applications, specifically VGG16-based neural networks, have improved the classification of UWS versus MCS by extracting complex features from EEG frequency domains that surpass traditional

linear analysis (19). However, the literature also highlights the challenge of model selection, noting that while ML significantly improves diagnostic accuracy, there is a constant risk of overestimating accuracy if the same sample is used for both training and estimation (14).

## Conclusion

The evidence reviewed in this article demonstrates that consciousness in LIS and related conditions cannot be reliably inferred from behavioral output alone. Profound motor paralysis can obscure preserved awareness, necessitating objective, brain-based methods that bypass sensory-motor limitations. Advances in neurotechnology have therefore transformed the assessment of consciousness from indirect behavioral inference to direct neural evaluation.

Electrophysiological approaches, particularly EEG combined with perturbational techniques, have emerged as some of the most robust tools for detecting consciousness. Measures of brain complexity derived from transcranial magnetic stimulation-EEG paradigms consistently differentiate conscious from unconscious states. The PCI has been validated across diverse populations and reliably identifies preserved consciousness in behaviorally unresponsive patients, including those with LIS. Complementary EEG metrics—such as spectral activity, connectivity, and signal complexity—further reveal substantial neurophysiological heterogeneity within LIS and CLIS, underscoring the limitations of relying on any single index.

Functional neuroimaging studies provide converging, network-level evidence of awareness. The preservation of the default mode network and higher order frontoparietal networks in LIS, contrasted with their disruption in vegetative or unresponsive states, supports the diagnostic and prognostic utility of fMRI. Beyond detection, fMRI has also informed clinical decision-making by guiding electrode placement for invasive brain-computer interfaces, facilitating more precise neuroprosthetic interventions.

Portable and bedside-compatible techniques such as functional near-infrared spectroscopy (fNIRS) extend these capabilities to patients unable to tolerate MRI or visual paradigms. When combined with active motor imagery tasks and machine-learning classifiers, fNIRS and EEG have enabled command following and basic communication in subsets of LIS and minimally conscious patients, even without prior training.

Machine learning has further enhanced sensitivity to subtle neural signatures of awareness across modalities, reducing subjectivity and improving prognostic accuracy. Nevertheless, challenges remain, including inter-individual variability, limited sample sizes, methodological heterogeneity, and ethical concerns related to false-positive interpretations.

Overall, the reviewed literature strongly supports a multimodal, hierarchical approach that integrates EEG, fMRI, perturbational measures, and machine-learning-assisted analysis. Such frameworks offer the most reliable path toward accurate consciousness detection, ethical clinical decision-making, and meaningful communication for individuals with Locked-In Syndrome.

During the preparation of this work, the author(s) used Grammarly AI and Google Gemini. The application of these tools was strictly limited to improving grammar, spelling, style, and formatting. All intellectual content is the original work of the authors.

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