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Assessment of Covert Consciousness in the Intensive Care Unit: Clinical and Ethical Considerations

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Abstract

Objective: To propose a practical ethical framework for how task-based functional MRI (fMRI) and electroencephalography (EEG) may be used in the intensive care unit (ICU) to identify covert consciousness in patients with acute severe traumatic brain injury (TBI).

Methods: We present two clinical scenarios in which investigational task-based fMRI and EEG were performed in critically ill patients with acute severe TBI who appeared unconscious on the bedside behavioral assessment. From these cases, we consider the clinical and ethical challenges that emerge and suggest how to reconcile them. We also provide recommendations regarding communication with families about ICU patients with covert consciousness.

Results: Covert consciousness was detected acutely in a patient who died in the ICU due to withdrawal of life-sustaining therapy, whereas covert consciousness was not detected in a patient who subsequently recovered consciousness, communication, and functional independence. These cases raise ethical challenges about how assessment of covert consciousness in the ICU might inform treatment decisions, prognostication, and perceptions about the benefits and burdens of ongoing care.

Conclusions: Given that covert consciousness can be detected acutely in the ICU, we recommend that clinicians reconsider evaluative norms for ICU patients. As our clinical appreciation of covert consciousness evolves and its ethical import unfolds, we urge prognostic humility and transparency when clinicians communicate with families in the ICU about goals of care.

Keywords

coma; vegetative state; minimally conscious state; consciousness; traumatic brain injury; functional MRI; EEG; neuroethics; prognostication

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Early prognostication for patients with acute severe traumatic brain injury (TBI) is an uncertain art and science.¹ In the absence of reliable prognostic models, a clinician's judgment, beliefs, and communication style may influence a family's decision about life-sustaining therapy and lead to premature care decisions before a patient's prognosis becomes clearer. In this context, withdrawal of life-sustaining therapy accounts for up to 70% of TBI deaths in the intensive care unit (ICU), with decisions often made within 3 days of admission.^{2, 3} Too often a nihilistic bias points to decisions to withdraw life-sustaining therapy without a clear evidence base.⁴ Uninformed nihilism leads to countless acute severe TBI deaths when families are told that there is no hope for recovery. Over the past decade, investigational functional magnetic resonance imaging (fMRI) and electroencephalography (EEG) techniques have begun to complement the bedside behavioral examination by detecting covert consciousness in the chronic stage of recovery from severe TBI.^{5, 6} With a recent study showing that task-based fMRI can detect covert consciousness in some critically ill TBI patients who appear unconscious,⁷ clinicians must reconsider evaluative norms for these ICU patients as society considers the rights of all apparently unconscious patients.⁴

Beyond these normative considerations, the identification of covert consciousness may portend a physiologic receptivity to pharmacologic and neuroprosthetic interventions that might restore functional communication.⁵ Critically ill patients with covert consciousness, and intact distributed networks,⁸ may have the ability to perceive pain and hear bedside conversations by clinicians who erroneously believe the patient to be either insensate or unaware based on behavioral assessment. These distinctions have implications for emerging therapies, pain management,⁹ neuro-palliative care¹⁰ and clinical ethics.⁴

In order to better identify covert consciousness, here, we propose an ethical framework to inform how task-based fMRI and EEG might be employed in the acute management of patients with severe TBI as these technologies evolve and become integrated into clinical practice. While the use of these modalities remains in the proof-of-principle phase in the ICU, it is not too early to consider the ethical and practical challenges presented by their use. Our framework is intended to be practical yet contingent, built upon an inductive "bottom-up" approach rather than a deductive "top-down" approach.¹¹

We begin by presenting two clinical scenarios in which investigational task-based fMRI and EEG were performed in critically ill patients with acute severe TBI. From these cases, we consider the clinical and ethical challenges that emerge and suggest how to reconcile them. We conclude with recommendations regarding communication with families about ICU patients with covert consciousness.

Covert consciousness

Since the first report of covert consciousness by Owen and colleagues in 2006,¹² several terms have been proposed to describe patients who demonstrate volitional brain activity that is only detectable by a task-based fMRI or EEG technique. These terms include "non-behavioral minimally conscious state (MCS),"¹³ "covert cognition,"¹⁴ "functional locked-in syndrome,"¹⁵ "minimally conscious star (*),"¹⁶ and "cognitive motor dissociation".⁶ While

the terminology has evolved, the conceptual foundation is well established: covert consciousness has been defined by the presence of command-following on task-based fMRI or EEG in a patient whose bedside behavioral diagnosis suggests coma, vegetative state (VS), or a low-level minimally conscious state (i.e. MCS without language function [MCS-], which arguably may not fall within the category because of minimal behavioral responsiveness). Notably, the presence of passive brain responses to auditory or visual stimuli, even within higher-order association regions of the cerebral cortex, is not considered to be evidence of covert consciousness. Passive responses to stimuli may shed light on the brain's ability to perceive language or other complex stimuli,^{17–19} but perception does not necessarily imply conscious comprehension of the stimulus. Only a volitional response to a task (i.e. command-following) is considered dispositive evidence of consciousness, because a volitional response requires an *active* cognitive process that is not stimulus-dependent. The rationale for command-following as being essential for covert consciousness is supported by fMRI data from healthy subjects showing that passive responses to language persist in the human brain even when subjects are behaviorally unresponsive due to anesthetic sedation.²⁰

Covert consciousness is especially problematic in the ICU because the bedside behavioral examination is not always reliable for detecting consciousness in patients with acute severe brain injuries. Just as 40% of patients with chronic DoC who are diagnosed as being in VS based on consensus evaluation are found to be in MCS when a comprehensive Coma Recovery Scale-Revised (CRS-R)²¹ behavioral assessment is performed,^{22–24} Schnakers and colleagues found a similar (~30%) rate of misdiagnosis for patients with acute DoC who are believed to be in VS.²⁴ This alarming rate of misdiagnosis may be related to deficits in visual, auditory, motor, or language function that limit a patient's ability to demonstrate purposeful behavior. Notably, it is the use of a mirror for visual pursuit testing – a procedure rarely performed in the ICU – that provides the greatest increase in sensitivity for detecting consciousness with the CRS-R, as compared to standard ICU assessments like the Glasgow Coma Scale (GCS; as depicted in Figure 1).^{24, 25}

Yet even a comprehensive behavioral assessment with the CRS-R may fail to detect consciousness in approximately 20% of patients with VS and MCS-.^{7, 26, 27} Fluctuations in level of arousal, which are common in patients with DoC,²⁸ likely contribute to the limited sensitivity of the CRS-R. In some patients with DoC, serial CRS-R assessments may be necessary to detect consciousness,²⁹ but it may not be feasible to perform the CRS-R serially in the ICU due to intracranial hypertension or non-neurological risks that preclude frequent cessation of sedation. Given the imperfect sensitivity of the CRS-R and the difficulty of performing serial CRS-R assessments in the ICU, it may therefore be appropriate to perform fMRI and EEG to optimize detection of consciousness in critically ill patients with severe TBI, even if the sensitivity and specificity of fMRI and EEG in this patient population remain limited. It should be emphasized here that *the CRS-R remains a more sensitive test for detecting consciousness than fMRI or EEG*, and the CRS-R has far more evidence to support its routine use in clinical practice.^{27, 30} fMRI and EEG are therefore not to be considered replacement assessments, but rather ancillary or complementary assessments.

Task-based fMRI in the ICU

Task-based fMRI identifies volitional brain activity using measurements of the blood-oxygen level dependent (BOLD) signal.³¹ The BOLD signal is a surrogate for cerebral blood flow, and hence neuronal activity, as long as the neuronal activation-flow coupling mechanism is intact. The assumption of an intact activation-flow coupling mechanism is not always valid for patients with acute DoC in the ICU,³² a limitation we discuss in detail below, and there can be temporal and spatial dislocations on neuroimaging as well.^{33, 34} Task-based fMRI analyses for patients with DoC typically utilize a block design, in which a patient is asked to perform an imagery task (e.g. imagine squeezing your hand) for brief blocks of time (e.g. 15 to 30 sec) that are interspersed with rest blocks. Brain activation maps are derived from statistically significant differences in the BOLD signal between the task and rest blocks.³⁵

Task-based fMRI activation maps can be processed and analyzed in a variety of different ways, including global exploratory analysis, region-of-interest analysis, and multivariate pattern analysis. As the field of fMRI has matured, advances in hardware and data acquisition³⁶ have reduced the rate of false negatives, and stricter statistical models for data processing have reduced the rate of false positive activations.³⁷ Nevertheless, false negative and false positive results remain a possibility in any fMRI study, and some technical advances may not be generalizable to clinical MRI scanners used to image critically ill patients. For these reasons, only positive tests are potentially dispositive of covert consciousness.

Furthermore, acquiring fMRI data in patients with acute severe TBI involves practical challenges and safety considerations beyond those encountered in the subacute or chronic setting. Some patients require continuous intravenous sedation for safety or comfort, even in the comatose state (e.g. to treat bronchospasm or paroxysmal sympathetic hyperactivity).^{7, 38, 39} This can lead to pharmacologically induced negative results in patients who might otherwise demonstrate covert consciousness. Finally, the risk of intracranial hypertension associated with lying supine may necessitate a delay in fMRI data acquisition beyond the time period when a patient's surrogates are faced with the decision about continuation of life-sustaining therapy via tracheostomy and percutaneous gastric tube placement (typically 7–14 days post-injury).

Task-based EEG in the ICU

Task-based EEG identifies volitional brain activity based upon changes in the frequency and/or amplitude of cortical rhythms, as measured by scalp electrodes. As with fMRI, stimuli are presented in discrete blocks of time, and cortical rhythms during task blocks are compared to those during rest blocks. Whereas high-density or augmented electrode arrays are often used in the chronic setting,^{40–45} the need for intracranial pressure (ICP) monitoring in the ICU typically necessitates the use of low-density clinical “10–20” electrode arrays.⁴⁶ With fewer electrodes to record from, the statistical rigor with which task-based EEG paradigms can assess for command-following may be limited.^{7, 47} Nevertheless, emerging evidence suggests that reliable command-following can be detected from a small number of

scalp electrodes in certain patients.^{48, 49} Furthermore, given that task-based EEG does not require traveling out of the ICU or lying supine, EEG has several feasibility and safety advantages compared to fMRI for critically ill patients with acute brain injuries.

METHODS

Participants

We selected two patients with acute severe TBI from a cohort of 16 patients who were prospectively enrolled in an fMRI and EEG study aimed at detecting covert consciousness in the ICU.⁷ These two patients were selected for presentation here because of the ethical challenges raised by their investigational fMRI and EEG results. In addition, each case highlights the complex relationship between behavioral and advanced fMRI/EEG assessments of consciousness, as shown in Figure 1. The investigational fMRI and EEG protocol was approved by the Institutional Review Board, with written informed consent provided by the patients' surrogates/legally authorized representatives. fMRI and EEG were performed during a spoken language stimulus, music stimulus, and right hand squeeze motor imagery task, as previously described.^{7, 38}

RESULTS

Patient 1

A 51-year-old man was hit by a car as he stepped off the sidewalk. Bystander witnesses called 911 and his initial Glasgow Coma Scale (GCS) score assessed by Emergency Medical Services personnel was 3 (Eyes = 1, Motor = 1, Verbal = 1), consistent with coma. His pupils were 3 mm and sluggishly reactive bilaterally. He underwent endotracheal intubation and was transported to the nearest Level 1 Trauma Center Emergency Department, where he was tachycardic and hypertensive with normal oxygenation on mechanical ventilation. Comprehensive trauma evaluation revealed no thoracic, abdominal, or orthopedic injury. Head computed tomography (CT) demonstrated subarachnoid hemorrhage in the sulci and basal cisterns, intraventricular hemorrhage, right frontoparietal subdural hemorrhage, right frontal contusion, and multifocal subcortical hemorrhages in the bihemispheric white matter and splenium of the corpus callosum. An ICP monitor was placed with initially normal ICP, which became elevated intermittently in the ensuing days and required hyperosmolar therapy and intravenous sedation. His ICU course was also notable for expansion of the right frontal contusion, ventilator-associated pneumonia treated with antibiotics, and intermittent limb shaking that raised the possibility of seizures though there was no correlation on continuous EEG monitoring.

On post-injury day 8, the ICP monitor was removed after three "supine trials" did not cause a rise in ICP. He underwent clinical MRI and investigational fMRI later that day. Clinical sequences were performed during the first 30 minutes of the scan, with investigational sequences performed during the next 30 minutes. Immediately prior to the MRI, the patient's CRS-R demonstrated arousal (i.e. eye opening), but no evidence of awareness, indicating a behavioral diagnosis of VS. However, fMRI revealed superior temporal gyrus activation during language and music, and pre-motor cortex activation during the motor

imagery task (Figure 2), indicating covert consciousness (Figure 3). These fMRI responses were observed despite intravenous boluses of 50 mcg of fentanyl and 20 mg of propofol prior to imaging. The clinical MRI sequences confirmed the head CT findings and revealed additional foci of hemorrhagic traumatic axonal injury in the bilateral cerebral hemispheres, corpus callosum, and brainstem (i.e. grade 3 diffuse axonal injury). Over the next two days, the ICU clinicians conducted a series of meetings with the patient's family to discuss his prognosis. The family ultimately decided to withdraw life-sustaining therapy and transition to comfort-focused care, before preliminary fMRI data analysis was completed. He died the next day, post-injury day 11, with his family at the bedside.

Patient 2

A 19-year-old woman was an unrestrained passenger in a high-speed, head-on car collision. She was intubated by Emergency Medical Services personnel, and the first documented GCS score was 5T (Eyes = 1, Motor = 3, Verbal = 1T), consistent with coma. The left pupil was 3 mm and the right pupil was 2 mm, both sluggishly reactive. She was medflighted to a Level 1 Trauma Center, where her blood pressure, heart rate, and oxygenation were normal on arrival. A comprehensive trauma evaluation revealed a scalp laceration, but no thoracic, abdominal, or orthopedic injury. Head CT revealed sulcal subarachnoid hemorrhage and multifocal subcortical hemorrhages in the bihemispheric white matter and splenium of the corpus callosum. An ICP monitor was placed, and her initial ICP was elevated at 22 mmHg, requiring immediate hyperosmolar therapy. Over the next two days she received hyperosmolar therapy and intravenous sedation for intermittent ICP elevations. She also was treated with antibiotics for a ventilator-associated pneumonia.

On post-injury day 3, after a "supine trial," the ICP monitor was removed, and she underwent clinical and investigational MRI. As with patient 1, the clinical and investigational sequences were performed consecutively during a single 60-minute scanning session. Immediately prior to the MRI, her CRS-R was consistent with coma. fMRI did not reveal activation within the superior temporal gyrus during language or music stimuli, nor was there activation within the premotor cortex or supplementary motor area during the motor imagery task. The patient was treated with a continuous propofol infusion at 300 mg/hr before and during the fMRI, at the discretion of the ICU clinicians, to prevent bronchospasm. The clinical MRI sequences revealed hemorrhagic traumatic axonal injury in the bilateral cerebral hemispheres, corpus callosum, and brainstem (i.e. grade 3 diffuse axonal injury). The day after the MRI, an investigational EEG was performed with the same language, music, and motor imagery stimuli. CRS-R assessment indicated that the patient remained comatose at the time of EEG, which was performed without sedation. Again there were no detectable responses to language, music, or motor imagery. Later that day (post-injury day 4), the ICU clinicians met with the patient's family to discuss her prognosis, and the family decided to continue life-sustaining therapy. She opened her eyes on day 5, indicating a transition from coma to VS. Tracheostomy and percutaneous gastric tube placement were performed on day 6. She was weaned off the ventilator and transferred out of the ICU on day 10.

By the time of discharge from the Level 1 Trauma Center to an inpatient rehabilitation hospital, 26 days post-injury, her tracheostomy tube was removed and she was following verbal commands, indicating a behavioral diagnosis of high-level MCS (i.e. MCS+). She spent one month at the inpatient rehabilitation hospital, where she received physical, occupational, and speech therapy. Her percutaneous gastric tube was removed once she regained the ability to swallow without aspiration. She was treated with methylphenidate for deficits in multiple cognitive domains, particularly attention. By the time of discharge from the inpatient rehabilitation hospital, she had fully recovered consciousness, communication, and functional independence for activities of daily living. Six months after her injury, her Glasgow Outcome Score-Extended was 7, and her only persistent symptom was fatigue after performing cognitively-demanding tasks. She returned to college, graduated, and subsequently joined the work force.

DISCUSSION

The two patients presented here highlight the promise and peril associated with fMRI and EEG assessments of covert consciousness in the ICU. In the first case, covert consciousness was detected by fMRI and a decision to withdraw life-sustaining therapy was made before investigational data were available. In the second, although covert consciousness was not detected by fMRI or EEG, the patient recovered fully, regained independence and graduated from college. These cases raise ethical challenges about how assessment of covert consciousness in the ICU might inform treatment decisions, prognostication, and perceptions about the benefits and burdens of ongoing care.

What does a positive fMRI or EEG assessment mean?

Early emergence of *overt* consciousness on a behavioral assessment is associated with better long-term functional outcomes.^{50, 51} However, it is unknown whether this holds true for early emergence of *covert* consciousness. In the first study to systematically study covert consciousness with fMRI and EEG in the ICU, the small patient sample (n=16) provided insufficient statistical power to demonstrate the prognostic relevance of covert consciousness.⁷ Determination of the prognostic relevance of covert consciousness in the ICU is now the focus of ongoing studies (e.g. [ClinicalTrials.org](https://clinicaltrials.org/ct2/show/study/NCT03504709) number NCT03504709 and NCT02644265).

If fMRI and EEG are performed to complement the CRS-R behavioral evaluation, interpretation of a positive result and communication of the result with a patient's family is fraught with ethical challenges. If future research demonstrates that early emergence of covert consciousness is not associated with better long-term outcomes, a positive fMRI or EEG result could provide false hope. The presence of covert consciousness may influence a family's substituted judgment regarding a patient's perceived wishes to pursue an erroneously predicted good functional outcome. The resultant decision to continue life-sustaining therapy could condemn a patient to a poor quality of life that he or she finds unacceptable. Indeed, it is estimated that hundreds of thousands of patients worldwide currently live in chronic VS or MCS, receiving around-the-clock supportive care in long-term care facilities or in their homes.^{52–54} It is unknown what percentage of these patients

previously expressed that this quality of life would be unacceptable, but survey data suggest that a majority of adults in the United States would prefer a dignified death rather than living with an incurable disease that rendered them totally dependent.⁵⁵ Not surprisingly, attitudes toward these types of end-of-life issues are influenced by religion and culture.⁵⁶ For patients who believe living in a chronic dependent state is unacceptable, a positive fMRI or EEG result may deny them the right to a dignified death in the ICU via a transition to comfort-focused care.

Even if future studies show that fMRI or EEG detection of covert consciousness is associated with better long-term functional outcomes, the possibility of a false-positive result must be considered by clinicians and clearly communicated to families. Recent advances in hardware (e.g. high-field MRI scanners and multi-channel head coils),³⁶ software (e.g. simultaneous multi-slice BOLD imaging),⁵⁷ and post-processing (e.g. using a conservative cluster-thresholded Z-score of 3.1 as opposed to 2.3),³⁷ have reduced but not eliminated false positives. A fundamental unanswered question about the false positive rate is how the multifocal, heterogeneous pathophysiology of severe TBI affects the BOLD signal acutely. Traumatic blood-brain barrier disruption, hemorrhage, edema, or elevated ICP may disrupt the activation-flow coupling mechanism that links the BOLD signal to neuronal activity in the human brain.³² Without understanding the spatial and temporal properties of this disruption and its effects on the BOLD signal, there is potential for a false positive (and false negative) rate of uncertain magnitude. Thus, positive fMRI results must be analyzed with caution and interpreted in light of these potential confounders and limitations.

What does a negative fMRI or EEG assessment mean?

Negative fMRI and EEG results *do not* indicate that a patient's brain is incapable of volitional cognition. Up to 25% of healthy human subjects have negative fMRI or EEG results during command-following tasks,^{7, 58} for reasons that remain incompletely understood. In the largest study of patients with chronic DoC, fMRI failed to detect command-following in 55% of patients who were minimally conscious on the CRS-R.²⁷ Similarly, in the recent study of ICU patients with acute DoC, fMRI and EEG failed to detect command-following in 43% and 33%, respectively, of patients who followed commands on the CRS-R.⁷ The sensitivity of fMRI and EEG are thus insufficient for these tests to be used as a sole means of detecting consciousness, again highlighting the point that fMRI and EEG are ancillary tests that may be used to supplement the CRS-R, not replace it.

While the physiological mechanisms underlying the limited sensitivity of fMRI and EEG for detecting consciousness have not been fully elucidated in healthy subjects, several potential mechanisms have been identified in patients. The administration of sedative, anxiolytic, and analgesic medications is common in ICU patients, many of whom require these medications for comfort or safety. Even comatose patients may require sedative medications for control of ICP or bronchospasm caused by the endotracheal tube. For the second patient described here, administration of propofol may have contributed to the absence of fMRI responses. However, the absence of brain responses during the EEG, which was performed the next day without sedation, raises the possibility that the absence of responses during fMRI was

attributable to the brain injury itself and not the sedation. The relative effects of sedation and brain injury on fMRI and EEG measures of brain function are just beginning to be studied in patients with DoC,⁵⁹ but studies in healthy subjects clearly demonstrate decreased brain responses at higher doses of sedation.²⁰

The list of other possible explanations for a negative fMRI or EEG result in an *overtly* conscious patient is long. For example, a restless or confused patient may move during the fMRI or EEG, leading to degradation of the data by motion artifact. A patient may also fall asleep. The possibility that a negative fMRI or EEG result is not reflective of a patient's potential for consciousness is high; and for a patient who is truly conscious, but for whom command-following is not detected by fMRI or EEG, the negative test result can become a diagnostic stigma. Even if the CRS-R shows evidence of awareness (i.e. MCS), a negative fMRI or EEG result could be used to erroneously derive a worse prognosis or inappropriately limit access to inpatient rehabilitation. As we begin to consider the ethical implications of sharing investigational fMRI and EEG results with families (a topic covered below), we run the risk of creating a self-fulfilling prophesy, whereby negative fMRI or EEG results are erroneously perceived as being trustworthy and a family withdraws life-sustaining therapy, thereby statistically linking the negative result to the patient's death when no biological mechanism for such a link exists. It is therefore essential that any disclosure of information to families does not undermine the scientific validity of ongoing research studies,⁶⁰ a goal that will require clinicians to be diligent and dedicated to the accurate counseling of families.

Temporal considerations

Whatever the result, it is prudent to not make precipitous decisions based on early studies in the ICU. There is a contingency to both positive and negative data, and given this, the timing of decisions to withhold or withdraw therapy warrants further consideration as an ethical issue in its own right. Given that the temporal interactions between brain plasticity and recovery are incompletely understood,⁶¹ and that consciousness may emerge after an unpredictable delay of months or even years,⁶² it can be argued that patients and families should always be "given time" to allow for recovery of consciousness. The implication of this argument is that an initial decision to continue life-sustaining therapy is reversible, and a subsequent transition to hospice care is always an option. However, the operational, clinical, and ethical challenges associated with delayed withdrawal of life-sustaining therapy in the post-ICU setting may be far more complex and distressing for families than in the ICU, where patients often pass away comfortably within minutes to hours, or sometimes days. As evidenced by the experiences of multiple families and patients discussed in the public domain,^{4, 61, 63} the transition to hospice for a patient in the subacute or chronic stage of DoC may on the contrary play out over the course of many distressing weeks or months. While family experiences differ, some families report feeling that the patient's condition is one "worse than death."⁶⁴ Moreover, families may experience additional stress or guilt when life-sustaining therapy is withdrawn in the chronic stage of injury,⁶⁵ a phenomenon described as the "burden of witness."⁶⁶ This burden is associated with witnessing a loved one's physical appearance change during the 1–2 weeks that typically elapse between feeding tube removal and death.⁶⁶ The idea of "giving time," while appealing from an ethical and practical

perspective at first glance, is thus inherently problematic and warrants compassionate counseling by clinicians to families and other surrogate decision-makers in the ICU.

Should we try to identify covert consciousness in the ICU?

Given the many limitations, confounders, and ethical challenges associated with fMRI and EEG assessments of consciousness in patients with acute severe TBI, it is reasonable to ask whether there is a role for these assessment tools in the ICU. An uninformed faith in the utility of these tests by families or clinicians unquestionably poses a potential for harm to patients. For the second patient presented here, we must consider the possibility that if her family had been aware of the negative fMRI and EEG results, and if the limited sensitivity of fMRI and EEG had not been accurately communicated by the ICU clinicians, life-sustaining therapy may have been withdrawn on a patient who ultimately had an excellent functional and cognitive outcome. This hypothetical concern is particularly poignant when we consider that the patient had grade 3 diffuse axonal injury, an imaging finding that has historically been believed to portend a poor prognosis, even though recent evidence suggests it is compatible with a good outcome.^{67–69} One could thus invoke the precautionary principle, arguing that the potential for harm, even death, from an inaccurate prognosis and consequent withdrawal of life-sustaining therapy, is unacceptably high for task-based fMRI or EEG to continue in the ICU.

However, an ethical counterargument in support of task-based fMRI and EEG is that the presence of covert consciousness may be actionable. These patients may have a therapeutic physiologic receptivity to deep brain,⁷⁰ non-invasive,^{71, 72} or pharmacologic stimulation.⁷³ Moreover, the presence of covert consciousness might make a patient more amenable to standard rehabilitation. As critically, the presence of covert consciousness raises the possibility that patients might be able to express preferences, or simply say they are in pain, with the provision of therapy, rehabilitation, or assistive communication devices.⁷⁴ This, in and of itself, is an ethical mandate to seek to identify covert consciousness early in the course of care and to integrate their reemergent agency into conversations about care, as they are able to do so.⁷⁵

Communication with Families

Finally, we must consider a family's access to *research data* in the context of covert consciousness. Do surrogates have a right to these investigational data? In one Canadian survey, the chairs of Research Ethics Boards overwhelmingly supported dissemination of group-level, aggregate research data to study participants,⁷⁶ but attitudes of Research Ethics Boards toward dissemination of single-subject data have not been studied. Members of the DoC research community have argued that it is ethically appropriate to share single-subject data if families are fully informed of the performance characteristics of the assessments, such as their sensitivity and specificity.^{4, 60} We share this view, as long as clinicians are appropriately trained to disseminate the investigational data in an accurate and unbiased manner. Our arguments hinge on Richardson's conception of ancillary care obligations that clinical investigators have to subjects who otherwise do not have access to the care or expertise of investigators.^{4, 77, 78} We also note that task-based fMRI and EEG data are included as potentially relevant prognostic tests in the 2018 DoC management guideline

jointly published by the American Academy of Neurology, American Congress of Rehabilitation Medicine, and the National Institute on Disability, Independent Living, and Rehabilitation Research.^{79–82}

We acknowledge, however, that communication with families about investigational results is fraught with additional ethical challenges.^{83, 84} Even if clinicians are trained to disseminate investigational data about covert consciousness in an accurate manner, complete eradication of clinician bias is likely an unachievable goal. Indeed, survey studies suggest that even when clinicians value patient autonomy, and hence the surrogate judgment of a family, their approaches to end-of-life care vary greatly and are often influenced by culture, religion, and prior clinical experience.^{56, 85, 86} These influences may affect a clinician's tone or body language during a family discussion, potentially shaping family decision-making in a manner that has life-or-death consequences. Consultation of an ethicist to participate in these family discussions may be appropriate, but some clinicians may be reluctant to do so, and access to ethics consultation is limited in many hospitals. But when ethics consultation is available, such expert input may be useful in addressing normative issues. When this is not possible, we suggest adopting a process of inductive moral reasoning to address ethical challenges encountered in clinical practice, drawing on the American pragmatic tradition.^{87, 88}

Ultimately, the most effective way to minimize the influence of clinician bias and ensure that families receive accurate information is to discuss task-based fMRI and EEG data in the context of a multimodal approach to diagnosis and prognosis. No behavioral, serologic, radiologic, or electrophysiologic test – clinical or investigational – has sufficient prognostic utility to stand alone. By ensuring that task-based fMRI and EEG data about covert consciousness are never interpreted in isolation, the potential for over-interpretation of investigational data is lessened, as is the risk of life-or-death decisions being shaped by clinician biases.

Conclusions and future directions

As our clinical appreciation of covert consciousness evolves and its ethical import unfolds, we strongly urge prognostic humility and transparency when clinicians communicate with families in the ICU about goals of care. If we truly endorse informed consent and refusal, clinicians will need to provide informed counsel to families about covert consciousness, prognosis, and longitudinal recovery. The emerging evidence that covert consciousness can be detected by task-based fMRI and EEG in patients with acute severe TBI indicates that there may be new opportunities for the early initiation of rehabilitation. Parallel advances in assistive communication devices raise the possibility that covert consciousness could be translated into overt self-expression, a paramount goal for rehabilitative care in the ICU.

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Figure 1. Assessment of consciousness in the intensive care unit.

The standard behavioral assessment used to evaluate a patient's level of consciousness in the intensive care unit (ICU) is the Glasgow Coma Scale (GCS),⁸⁹ as depicted in the left panel. For a patient whose eyes are open and whose limb movements appear reflexive on the GCS, suggesting a vegetative state (VS), there is an approximately 40% chance that consciousness will be detected by a comprehensive behavioral assessment with the Coma Recovery Scale-Revised (CRS-R).²⁴ The use of a mirror for gaze tracking, as depicted in the middle panel, is the CRS-R procedure that is most likely to detect evidence of consciousness missed by the GCS.²⁵ For a patient whose CRS-R assessment suggests VS or a low-level minimally conscious state (MCS-), there is an approximately 20% chance that consciousness will be detected by task-based functional MRI (fMRI) or EEG.^{7, 26, 27} Task-based fMRI involves providing verbal instructions to a patient via earphones to perform a motor imagery task, which results in an increase in the blood-oxygen level dependent signal within the supplementary motor and premotor cortices, as shown in the right panel.

Figure 2. Functional MRI detection of covert consciousness in the intensive care unit.

A functional MRI (fMRI) scan was performed for Patient 1 with language stimuli, music stimuli, and a motor imagery task (i.e. imagine squeezing your right hand) on post-injury day 8, at which time the Coma Recovery Scale-Revised assessment suggested a behavioral diagnosis of vegetative state. fMRI revealed association cortex responses to language and music stimuli, as well as volitional command-following during the motor imagery task (arrow), indicating covert consciousness. Unaware of these investigational data, the patient's surrogates decided to pursue comfort care and he died on post-injury day 11 in the ICU. All fMRI data are shown as Z-statistic images thresholded at cluster-corrected Z scores of 3.1 (inset color bar) and superimposed upon T1-weighted axial images. In the bottom panel, a three-dimensional rendering of fMRI activation during the motor imagery task is shown

(arrow). Abbreviations: Ins = insula; LV = lateral ventricle; PMC = premotor cortex. Images adapted with permission from Edlow et al.⁷

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Figure 3. The three dimensions of assessing consciousness.

The patients reported here were evaluated for motor function and overt cognitive function via behavioral assessment with the Coma Recovery Scale-Revised (CRS-R). Covert cognition was assessed with functional MRI (fMRI) and EEG. Levels of consciousness indicated by overt cognition are defined as coma, vegetative state (VS), minimally conscious state without language function (MCS-), minimally conscious state with language function (MCS+), post-traumatic confusional state (PTCS), complete locked-in syndrome (CLIS), locked-in syndrome with preservation of minimal motor function (LIS), and full recovery.

Covert consciousness (i.e. cognitive motor dissociation [CMD]) is defined by fMRI or EEG evidence of command-following despite absence of behavioral evidence of language function. Higher-order cortex motor dissociation (HMD) is defined by fMRI *and* EEG responses within association cortex (e.g. Wernicke's area) during passive language or music stimuli despite absence of behavioral evidence of language. Using the behavioral diagnosis as the reference standard, patients without behavioral evidence of language (coma, VS, and MCS-) are classified as true negatives (TN) if there are no fMRI or EEG responses. Patients with behavioral evidence of language (MCS+, PTCS, CLIS, LIS, and full recovery) are classified as false negatives (FN) if there are no fMRI or EEG responses, and true positives (TP) if there are fMRI and EEG responses. Abbreviation: CAP = Confusion Assessment Protocol. Figure reproduced with permission from Edlow et al.⁷