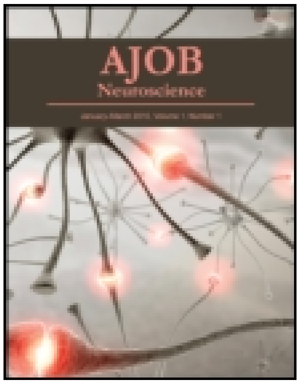

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Assessing Decision-Making Capacity in the Behaviorally Nonresponsive Patient With Residual Covert Awareness

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Target Article

Assessing Decision-Making Capacity in the Behaviorally Nonresponsive Patient With Residual Covert Awareness

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Recent neuroscientific findings suggest that functional magnetic resonance imaging (fMRI)-based brain–computer interfaces may be a viable strategy for detecting covert awareness in patients clinically diagnosed as being in a vegetative state. This research may open a promising new avenue for developing neuroimaging techniques that provide prognostic and diagnostic information that complements current behavioral tests for assessing disorders of consciousness, thereby increasing the effectiveness of diagnostic screening. These techniques may also permit patients who are behaviorally nonresponsive yet retain high levels of preserved cognition to meaningfully engage in clinical decision making. Before this application can occur, certain ethical issues associated with decision-making capacity must be addressed. Although it is not currently possible to assess decision-making capacity through neuroimaging methods, it may be in the future, provided that certain conceptual and empirical steps are taken to demonstrate that brain–computer interfaces satisfy requisite criteria of capacity assessment. In this article we lay out the conceptual foundations for a mechanistic explanation of capacity that would allow the necessary empirical steps for incorporating neuroimaging techniques into the standard capacity assessment battery utilized in clinical practice.

Keywords: Vegetative state, disorder of consciousness, fMRI, EEG, decision-making capacity, neuroimaging, MacCAT-T, MMSE, functionally locked in syndrome, minimally conscious state, neurology

NEW DIRECTIONS IN DETECTING COVERT AWARENESS IN BEHAVIORALLY NONRESPONSIVE PATIENTS

In 2006, researchers at the University of Cambridge successfully detected conscious awareness in a 23-year-old patient diagnosed as being in a vegetative state (Owen et al. 2006). By employing functional magnetic resonance imaging (fMRI), investigators discovered that this patient, despite her inability to demonstrate voluntary behavioral responses to repeated clinical examinations, could willfully modulate her brain activity in response to auditory commands. The patient was instructed to imagine one of two activities—playing tennis or navigating from room to room in her house—while lying inside an fMRI scanner. Imagining these activities induced blood-oxygen-level-dependent changes in specific regions of the brain, the supplementary motor area and the cortical network involved in spatial navigation, thereby allowing investigators to reliably detect willful brain modulation. Moreover, the patient's brain activity was shown to be indistinguishable from healthy participants' under similar experimental conditions (Boly et al. 2007). The patient's neural activation was statistically robust, reproducible, task appropriate, and sustained over 30-second intervals, thus precluding the possibility of an automatic, preconscious response to the verbal instructions (Owen 2013; Owen et al. 2007).

These findings led investigators to conclude that although patients may meet the standard diagnostic criteria indicative of the vegetative state, some may be consciously aware of their surroundings. Indeed, it is well established that misdiagnosis in this patient group occurs frequently. Due to varying diagnostic standards it is estimated that 40% of all patients diagnosed as vegetative may, in fact, be

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minimally conscious (Andrews et al. 1996; Childs, Mercer, and Childs 1993; Schnakers et al. 2009). Of the remaining 60%, patients in a subset (17–19%) retain awareness undetectable through bedside clinical examination (Cruse et al. 2011; Monti et al. 2010). Actively searching for patients who fall into this subset is of great interest to both physicians and investigators. As Owen and colleagues have shown (Cruse et al. 2011; Monti et al. 2010; Owen et al. 2006), some of these patients may retain the ability to volitionally modulate their brain activity through mental imagery, thereby demonstrating that they are consciously aware (Owen 2013).

In 2010, Owen and colleagues, along with collaborators at the University of Liege, Belgium, extended this mental imagery paradigm to allow binary communication with similar behaviorally nonresponsive patients by coding the two imagined activities with the answers "Yes" or "No" (Monti et al. 2010). Using this technique, investigators were able to pose several questions to one patient whose diagnosis was confirmed repeatedly over a 5-year period. These questions pertained to the patient's father, siblings, and the last country visited prior to the patient's accident. The patient's family subsequently confirmed that the answers provided were correct (Monti et al. 2010). These results suggest not only that this mental imagery paradigm could pave the way for effective brain–computer communication with similar patients (Naci et al. 2012), but that the inner mental lives of some patients clinically diagnosed as vegetative may be far richer than previously assumed (cf. Owen 2013).

These findings have significant implications for our nosological understanding of the vegetative state (cf. Fins et al. 2008). While there are many patients who are correctly diagnosed as vegetative through rigorous clinical testing at the bedside, some patients receive inaccurate diagnoses solely on the basis of their inability to behaviorally respond to commands. Clinical neurology has taught us that the only viable means of detecting conscious awareness is through reliable motor response to commands or nonreflexive response to noxious stimuli (Giacino, Kalmar, and Whyte 2004; Owen 2013; Sheil et al. 2000; Teasdale and Jennett 1974). Yet as Owen and colleagues have shown, fMRI can reveal mental responses in a minority of patients who are otherwise unable to meet the behavioral diagnostic criteria for conscious awareness.

In response to these findings, some have suggested reclassifying this patient group as *functionally locked in* (Bruno et al. 2011b). This new category would effectively capture behavioral nonresponsiveness while acknowledging residual cognitive function constitutive of awareness. Nevertheless, patients with such clinical presentations are still routinely diagnosed as vegetative under conventional diagnostic standards. This is due to the preferential weighting of overt behavioral evidence for diagnosis, rather than covert cognitive abilities detectable through neuroimaging techniques. In these cases, neuroimaging may indeed demonstrate that a patient is aware. However, due to formal diagnostic definitions, the patient will still satisfy the behavioral neurological criteria of the vegetative state (Owen 2013). To avoid this nosological confusion, we refer to this patient group as *behaviorally nonresponsive patients who retain residual covert awareness*.

Aside from diagnostic utility, what other applications might this neuroimaging method have for clinical practice? One possibility would be to use these techniques to allow behaviorally nonresponsive patients who retain high-level cognitive faculties to participate in decision making relevant to their own medical care. If patients can provide reliable answers to binary questions (Monti et al. 2010), they might well be able to provide answers to clinically relevant questions during fMRI scanning sessions. This may allow individuals from this patient group greater say in their own treatment and restore some modicum of autonomy.

Although clinical application of this research is promising, the technical limitations of this neuroimaging method make it difficult to evaluate a central ethical prerequisite for patient participation in medical decision making, namely, decision-making capacity (Peterson et al. 2013). Due to extensive brain injury, behaviorally nonresponsive patients with covert awareness are presumed to be decisionally impaired. Thus, such patients can only participate in clinically relevant decisions if their decision-making capacity can be established with the help of brain–computer interfaces (BCI). Although this subject has been raised in the ethics literature (Bendsten 2013; Fisher and Appelbaum 2010), no actual means of integrating active, passive, or anatomical imaging-based paradigms into the medical decision-making process has yet been developed.

In light of this, we present a conceptual strategy for assessing decision-making capacity in behaviorally nonresponsive patients with residual covert awareness using the fMRI mental imagery paradigm outlined earlier—the current "gold-standard" method for communicating with this patient group (Boly et al. 2007; Monti et al. 2010; Owen et al. 2006). We acknowledge that several theoretical and empirical steps must be completed before BCI neuroimaging paradigms can be successfully incorporated into the standard capacity assessment battery. However, we do believe that detailed analysis of decision-making capacity, and its modification for BCI communication, will ultimately determine whether such a procedure is feasible. A procedure like this, if developed, will benefit this patient group, their families, and the physicians that care for them.

DECISION-MAKING CAPACITY IN THE CLINICAL SETTING

To provide free and informed consent for medical treatment, a patient must possess decision-making capacity. Preservation of patient autonomy is a hallmark of ethical medical care (Berg, Lidz, and Parker 2001), yet in some cases patients may be unable to choose a course of therapy that is consistent with enhancing quality of life. Neurological conditions or the inability to understand sophisticated medical information, inter alia, may lead to diminished comprehension, and thus inhibit the patient's ability to make well-reasoned treatment decisions (Appelbaum 2007). In such instances, the responsibility for making clinically relevant choices is deferred to the patient's family or legally appointed guardian.

It is important to note the differences between the ethical definition of capacity and the legal concept of competence. While a patient may possess the requisite cognitive abilities to make medical decisions, she or he may nevertheless be legally incompetent to make such choices. Thus, the cognitive faculties constituting decision-making capacity can, in certain circumstances, be dissociated from those constituting legal competence (Faden and Beauchamp 1986). Decision-making capacity, therefore, is a necessary but not sufficient condition of competency. Indeed, this may raise important concerns in the future about the legal constraints placed on this patient group regardless of the presence of residual cognitive abilities necessary for medical decision making. In what follows, though, we focus solely on the ethical notion of capacity, and set aside the legal dimensions of competence for future study.

The operational definition of decision-making capacity has evolved over the past 25 years (Appelbaum 2007; Appelbaum and Grisso 1995; Buchanan and Brock 1986; Grisso and Appelbaum 1995; Grisso et al. 1995). It commonly consists of four criteria, which are understood to be independently necessary but jointly sufficient (see Table 1). First, a patient must be able to communicate a medical preference (Appelbaum 2007; Appelbaum and Grisso 1995; Grisso and Appelbaum 1995; Grisso et al. 1995). In the strictest sense, the patient must be able to engage in conversation with an interlocutor. However, in cases of restricted communication, this criterion may be minimally interpreted as a patient's ability to express a medical choice by any available means. Second, a patient must understand the treatment options presented (Appelbaum 2007; Appelbaum and Grisso 1995; Grisso and Appelbaum 1995; Grisso et al. 1995). Standard interpretation indicates that a patient has understood treatment options if medical information is adequately encoded and comprehended. Third, a patient must appreciate the consequences of the medical decision (Appelbaum 2007; Appelbaum and Grisso 1995; Grisso and Appelbaum 1995; Grisso et al. 1995). This criterion is satisfied if the patient can accurately relate diagnosis, prognosis, and treatment options to her- or himself, thereby realizing the consequences of choosing one therapy instead of another. Finally, the patient must show evidence of a reasoned decision by providing a logically consistent and coherent rationale for the clinically relevant choice (Appelbaum 2007; Appelbaum and Grisso 1995; Grisso and Appelbaum 1995; Grisso et al. 1995).

A standardized method for evaluating these criteria in the clinical setting is laid out in the MacCAT-T (Grisso et al. 1995). Here, decision-making capacity is evaluated through a structured disclosure of the patient's condition, treatment options, risks and benefits, and alternative courses of medical therapy. The patient responds by choosing a treatment option and providing reasons for making one decision as opposed to another. Embedded in this conversation are a series of questions that assess the patient's capacity to make responsible decisions while navigating an unfamiliar medical landscape.

To evaluate understanding, the physician will ask the patient to recapitulate the clinical information in her or his own words (Grisso et al. 1995, 1416). To evaluate reasoning, the physician will ask the patient to provide justification for the chosen treatment option, paying careful attention to the patient's ability to understand the consequences of the treatment—what Grisso and colleagues refer to as "consequential reasoning" (Grisso et al. 1995, 1416). Finally, to evaluate appreciation, the physician will assess whether the patient can sufficiently correlate the disclosed medical information with her or his actual condition (Grisso et al. 1995, 1416). Throughout this process, nonverbal cues, such as pauses or inflections, are taken into account.

Interview data acquired from the patient are then scored against a standardized 3-point scale (0 through 2), on which 0 denotes *inadequate response* and 2 denotes *adequate response*. Scores for the question sets probing the four components of decision-making capacity are tallied with the following ranges: understanding 0–6; appreciation 0–4; reasoning 0–8; communication 0–2. The maximum possible score is 20, with a minimal satisfaction threshold in each component category. Studies evaluating the validity of this measure suggest that individuals with no history of neurological or psychiatric disorders will tend to score between 15 and 20 (Grisso et al. 1995, 1417). A MacCAT-T score lower than 15 suggests diminished overall decision-making capacity, or a significant inhibition of understanding or reasoning.

Given the inherent complexity of this measure, the chance of gleaning similar information from behaviorally nonresponsive patients with residual covert awareness is small. The MacCAT-T evaluation requires the articulation of sophisticated medical information, which current BCI technology does not allow. This, in turn, precipitates the cautionary appraisal of using of BCI neuroimaging paradigms in the clinical setting (Fins and Illes 2008; Fins and Schiff 2010; Fins et al. 2008; Mackenzie 2013; Rich 2013). Since the mental imagery paradigm restricts communication to "Yes" or "No" questions, how could one possibly begin to satisfy the conditions of decision-making capacity as currently understood by the medical community?

ASSESSING DECISION-MAKING CAPACITY IN THE BEHAVIORALLY NONRESPONSIVE PATIENT WITH RESIDUAL COVERT AWARENESS

Is it possible to evaluate decision-making capacity in behaviorally nonresponsive patients with residual covert awareness by utilizing BCI neuroimaging paradigms? A first step in answering this question is to analyze the requisite cognitive faculties necessary for responsible decision making, and determine whether or not they can be operationalized in ways that are measurable with neuroimaging techniques. If this can be done, it may then be possible to examine the underlying intact cognitive functions of this patient group in order to assess the cognitive foundations of capacity. This approach follows the procedure developed in the MacCAT-T (i.e., evaluating understanding, appreciation, reasoning, and communication) (Grisso et al. 1995), yet extends the

Table 1. Standard decision-making capacity criteria

Decision-making capacity criterion	Description of criterion
Communication	The patient must have the means of displaying a medically relevant choice has been made, and what the particular choice is (Appelbaum 2007; Appelbaum and Grisso 1995; Grisso and Appelbaum 1995; Grisso et al. 1995; Buchanan and Brock 1986).
Understanding	The patient must understand the relevant information regarding the medical condition. This includes, but is not limited to, the proposed treatment, the possible risks of the proposed treatment, any alternative treatments that may be available, and their respective risks (Appelbaum 2007; Appelbaum and Grisso 1995; Grisso and Appelbaum 1995; Grisso et al. 1995; Buchanan and Brock 1986).
Appreciation	The patient must appreciate the gravity of the medical situation by acknowledging the possible negative consequences of refusing treatment, or choosing an alternative treatment relative to a physician's recommendation (Appelbaum 2007; Appelbaum and Grisso 1995; Grisso and Appelbaum 1995; Grisso et al. 1995; Buchanan and Brock 1986).
Reasoning	The patient must show evidence of a reasoned decision, rather than a decision based on compulsion or diminished decision-making capacity. In some cases, this may be understood as the patient exercising a unique set of values in the decision-making process (Appelbaum 2007; Appelbaum and Grisso 1995; Grisso and Appelbaum 1995; Grisso et al. 1995; Buchanan and Brock 1986).

Note. The assessment battery of decision-making capacity is decomposed into four criteria. These criteria are commonly interpreted as independently necessary, but jointly sufficient.

decomposition of these four criteria into smaller measurable components. If it is possible to develop operational definitions of these latent cognitive skills that allow patients to manipulate medical information in ways we refer to as, "communication," "understanding," "appreciation," and "reasoning," then BCI neuroimaging techniques may lead to an empirically adequate model of decision-making capacity that complements the MacCAT-T protocol.

Decomposing cognitive function in this way is a common method employed in mechanistic explanations of neuroscience (cf. Craver 2009). Investigators first use analytic methods to identify behavioral phenomena, and conceptually decompose them such that they can be operationalized for controlled measurement procedures. These a priori hypotheses are then tested empirically to correlate behavior with activity in specific brain areas.

A concern often raised regarding this type of neuroscientific explanation is the risk of conceptually decomposing phenomena incorrectly (cf. Sullivan 2010). It can be argued, for example, that, due to the variability of experimental interpretation, researchers may not be able to discriminate the phenomenon in question from confounds in experimental design. Thus, thoroughly explicating and decomposing the target phenomenon, along with controlling confounding variables, ensures the validity of experimental design. In the case of decision-making capacity, this initial a priori step amounts to conceptually explicating and decomposing the latent cognitive skills behind the four standard criteria in preparation for future empirical work.

Standard interpretations of communication, understanding, appreciation, and reasoning stipulated by the MacCAT-T suggest that a set of simple cognitive faculties, which permit language processing and information retention, underlies these higher order capacities. A preliminary set of these faculties may include the ability to ascertain auditory information in the form of speech; the ability to store that information in short-term memory; the ability to engage elements of working memory that distinguish descriptive, interrogative, and imperative sentences; and the ability to volitionally stipulate a clinically relevant choice. These respective cognitive faculties might be further decomposed into highly specific cognitive functions, which may be traceable through both the mental imagery paradigm and a number of alternative passive or anatomical techniques. Indeed, a significant amount of neuroimaging-based research has been devoted to the subject of speech processing (see Table 2). By examining this information, one may be able to identify the residual cognitive faculties that form one foundational pillar of decision-making capacity.

Language processing alone will not satisfy the more abstract cognitive requirements of decision-making capacity. Coherent and consistent application of a stable value set, for example, requires a far more sophisticated cognitive profile than language processing permits. However, there appears to be no principled reason why complex faculties like these cannot be analyzed in a similar fashion. By assessing these complex cognitive requirements, it can be demonstrated that they too are decomposable into discrete, operational cognitive functions, much like speech processing and information retention.

Take the more sophisticated ability that Grisso and colleagues refer to as "consequential reasoning" (Grisso et al.

Table 2. Decomposition of decision-making capacity criteria

Capacity criterion	Selected decomposed cognitive faculties associated with criterion	Selected fMRI and EEG investigations that may reveal these faculties
Communication	• Ability to process spoken language.	Cruse et al. 2012†; Bardin et al. 2012†; Sorger et al. 2012‡; Goldfine et al. 2011†; Cruse et al. 2011†; Monti et al. 2010†; Coleman et al. 2009†; Fernández-Espejo et al. 2008†; Coleman et al. 2007†; Schnakers et al. 2008†; Boly et al. 2007‡; Owen et al. 2006†; Bekinschtein et al. 2005†; Owen et al. 2005†; Schiff et al. 2005†
	• Ability to distinguish between declarative, interrogative, and imperative sentences.	Cruse et al. 2012†; Bardin et al. 2012†; Sorger et al. 2012‡; Goldfine et al., 2011†; Cruse et al. 2011†; Monti et al. 2010†; Boly et al. 2007‡; Owen et al. 2006†
	• Ability to recognize and respond task appropriately to an interlocutor (behaviorally or otherwise).	Naci and Owen 2013†; Naci et al. 2013‡; Cruse et al. 2012†; Bardin et al. 2012†; Sorger et al. 2012‡; Goldfine et al., 2011†; Cruse et al. 2011†; Monti et al. 2010†; Boly et al. 2007‡; Owen et al. 2006†
Understanding	• Ability to store information (e.g., instructions, and declarative information) in short-term memory.	Cruse et al. 2012†; Bardin et al. 2012†, Sorger et al. 2012‡; Goldfine et al. 2011†; Cruse et al. 2011†; Monti et al. 2010†; Boly et al. 2007‡; Owen et al. 2006†
	• Ability to sustain attention on a target phenomenon (e.g., the spoken language of an interlocutor) for periods of time.	Naci and Owen 2013†; Naci et al. 2013‡; Lehembre et al. 2012†; Lule et al. 2012†; Schnakers et al. 2008†
	• Ability to form new memories post ictus.	Fernández-Espejo and Owen † (in press)
Appreciation	• Ability to localize one's self in space and time.	Naci and Owen 2013†; Fernández-Espejo and Owen† (in press); Naci et al. 2013‡
	• Ability to relate medically relevant information to one's self (e.g., the patient is able to recognize he or she is the subject of the medical condition).	Fernández-Espejo and Owen † (in press); Naci and Owen 2013†
	• Ability to recognize temporal ordering in the environment.	Hampshire et al. 2013†; Naci and Owen 2013†; Fernández-Espejo and Owen† (in press)
Reasoning	• Ability to recognize and process basic logical inferences.	Hampshire et al. 2013†
	• Ability to engage dimensions of long-term memory (e.g., the patient is able to reference long-held beliefs while reasoning).	Fernández-Espejo and Owen † (in press); Naci et al. 2013‡ Naci and Owen 2013†; Monti et al. 2010†; Schnakers et al. 2008†
	• Ability to engage short-term memory (e.g., the patient is able to remember new information, which is then reasoned upon).	Naci and Owen 2013†; Naci et al. 2013‡; Hampshire et al. 2013†; Cruse et al. 2012†; Bardin et al. 2012†, Sorger et al. 2012‡; Goldfine et al. 2011†; Cruse et al. 2011†; Monti et al. 2010†; Boly et al. 2007‡; Owen et al. 2006†

Note. The received criteria of decision-making capacity can be decomposed into foundational cognitive faculties. These faculties can then be assigned operational definitions, which permit measurement with active, passive, or anatomical paradigms. This table reflects the decomposition process and provides a selection of constitutive cognitive faculties necessary for each capacity criterion. Neuroimaging investigations that reveal these underlying faculties are included in the third column. Some investigations reveal several cognitive faculties and thus have been included in multiple corresponding areas. The selected cognitive faculties outlined here *are not* indicative of the entire range of cognitive operations utilized in decision-making capacity. Likewise, the selected investigations *are not* indicative of the entire scope of empirical literature on these topics. ‡ = control study; † = patient study.

1995, 1416). On close analysis, this criterion can be decomposed into several simpler components, including the ability to retain new information; the ability to distinguish oneself from other objects and people; the ability to localize oneself in space and time; and the ability to appreciate temporal sequencing, such as knowing that event *X* happened before event *Y*. While these more basic cognitive faculties may not completely capture the essence of consequential reasoning, it is reasonable to assume that they constitute a regularly exercised set of cognitive faculties, which patients use when reasoning through the consequences of medical decisions. For example, a patient must be able to retain new medical information relating to diagnosis, prognosis, and treatment options. The patient must also recognize that this information pertains to her- or himself. The patient must then be able to understand where she or he is in space and time, thereby realizing that a medical choice made in the present will occur before its specific effects in the future.

We admit that this list of decomposed cognitive faculties does not exhaust the rich concept of decision-making capacity utilized in clinical practice. Additionally, we acknowledge that this conceptual approach to decomposing the four criteria of capacity may not be borne out sufficiently in empirical studies (e.g., Eyler et al. 2007). Nevertheless, given that these are a representative cross section of cognitive faculties constitutive of capacity, it seems plausible, in principle, that the cognitive foundations of decision-making capacity can be evaluated through neuroimaging techniques when the MacCAT-T cannot be applied. Rather than taking communication, understanding, appreciation, and reasoning as the targets of investigation, we can instead investigate the patient's underlying cognitive profile, through passive (Coleman et al. 2007; Coleman et al. 2009; Owen et al. 2005), active (Hampshire et al. 2013; Monti et al. 2010; Naci et al. 2013; Owen et al. 2006), and anatomical imaging paradigms (Fernández-Espejo et al. 2012). Indeed, current research into the residual cognitive functions of behaviorally nonresponsive patients has revealed a significant number of underlying cognitive abilities (see Table 2). Emerging neuroimaging techniques may reveal whether or not it is even possible for a given patient within this group to exercise any one of the four decision-making capacity criteria. If this strategy proves successful, clinicians can then build a model of the patient's residual cognitive faculties from the ground up (cf. Owen and Coleman 2008). Provided that a standard set of underlying cognitive functions is accepted as the necessary foundation of complex psychological phenomena, such as decision-making capacity, clinicians may then be able to infer the reasonable possibility of capacity by assessing its constitutive cognitive components through neuroimaging techniques.

PROBING THE COGNITIVE FACULTIES CONSTITUTIVE OF DECISION-MAKING CAPACITY

If this a priori decomposition of the four standard criteria into underlying cognitive functions proves to be a viable strategy for assessing decision-making capacity in behaviorally nonresponsive patients with residual covert awareness, the next step is to consider how these functions can be empirically probed in the clinical setting. Consider, as an example, a standard clinical measure used to evaluate rudimentary cognitive abilities: the Mini-Mental State Examination (MMSE; Folstein, Folstein, and McHugh 1975). This measure evaluates a patient's ability to understand the complex relationship between self, space, and time, as well as certain language and logical reasoning abilities. Since the MMSE is used as a standard screening instrument for capacity, we can reasonably conclude that satisfaction of the measure warrants further investigation into the preserved dimensions of decision-making capacity at the time the measure was completed. Moreover, employing measures like the MMSE may be especially useful in evaluating this patient group, since it can easily be translated for application in the mental imagery paradigm. Questions can simply be rephrased for binary (Yes/No) communication (see Table 3).

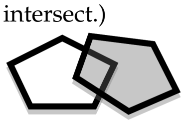
Of course, not all MMSE questions can be translated with absolute precision. In some cases the measurement parameters for the target phenomenon may not be sufficiently preserved. The pentagon drawing task, for example, evaluates memory, spatial reasoning, and motor skills, but it cannot be performed through BCI neuroimaging. In such cases, the task must be rendered in a form that is compatible with binary communication. This, for example, may be a task that probes the patient's ability to identify congruent or incongruent sets of auditory tones (see Table 3). Despite these differences, many other MMSE questions appear to maintain their semantic integrity regardless of phrasing.

While the MMSE may offer a promising first step in probing residual capacity through BCI neuroimaging, we acknowledge that it is not a satisfactory tool for capacity assessment on its own. It has been demonstrated, for example, that the MMSE's clinical utility cannot be precisely verified, since "no single cut off score yields high sensitivity and high specificity" (Appelbaum 2007). However, several investigations with Alzheimer's disease patients provide strong evidence that high and low score thresholds are reliably correlated with changes to a patient's decision-making capacity. MMSE scores below a threshold of 19 are strongly correlated with diminished capacity, while scores above 26 are strongly correlated with robust capacity (Karlawish et al. 2005; Kim and Caine 2002). Thus, by employing an empirically validated adaptation of the MMSE, along with several other adapted measures from the standard capacity screening battery, a promising strategy for integrate BCI neuroimaging paradigms into medical decision making might be developed.

DECISION-MAKING CAPACITY AS A THRESHOLD CONCEPT

Assessing capacity in behaviorally nonresponsive patients with residual covert awareness by evaluating their underlying cognitive profile may, in principle, provide sufficient evidence to warrant the participation of high-functioning patients in medical decision making. However, it would be hasty to presume that such findings would warrant participation in all medical decisions. Indeed, clinically relevant choices come in many shapes and sizes, and the appropriate level of capacity required should correspond to the significance of the decision at hand. Given that the strategy just outlined may reveal an adjusted form of decision-making capacity relative to the MacCAT-T, it is necessary to determine which medically relevant decisions are ethically permissible for any individual in this patient group to make. Treating decision-making capacity as a threshold concept, where the required level of capacity is calibrated to the stakes of the decision, may be the best way to address this problem.

Table 3. Revised MMSE for binary communication

MMSE scoring	Mini-Mental State Examination (MMSE)	Potential revisions to MMSE for use in binary communication
5	"What is the year? Season? Date? Day of the week? Month?"	Is the year XXXX? The season, XXXX? The date, XXXX? The day of the week XXXX? The month, XXXX?
5	"Where are we now: State? County? Town/city? Hospital? Floor?"	Are we in XXXX state/province? In XXXX country? In XXXX Town/city? In XXXX Hospital? On XXXX Floor?
3	The examiner names three unrelated objects clearly and slowly, then asks the patient to name all three of them. The patient's response is used for scoring. The examiner repeats them until patient learns all of them, if possible. Number of trials: ————	The examiner names three unrelated objects clearly and slowly. The examiner then repeats the list of unrelated objects, interspersed with several other objects unrelated to the original three. The examiner asks whether or not each object in the list was included in the original set of three. Number of trials: ————
5	"I would like you to count backward from 100 by sevens." (93, 86, 79, 72, 65, . . .) Stop after five answers. Alternative: "Spell WORLD backwards." (D-L-R-O-W)	"I will now count backward from 100 by sevens. (93, 86, 79, 72, 65, . . .) Answer whether or not each number is correct after the number is stated." Stop after five answers. Alternative: "Is WORLD spelled backwards the following way?" (D-L-R-O-W)
3	"Earlier I told you the names of three things. Can you tell me what those were?"	"Earlier I told you the names of three objects. Were these things X, Y, Z?" or "A, B, C?"
2	Show the patient two simple objects, such as a wristwatch and a pencil, and ask the patient to name them.	Expose the patient to two simple tones, such as a rooster call and a doorbell. Then ask the patient whether the first or second tone was a rooster or a doorbell. Do the same for the second tone.
1	"Repeat the phrase: 'No ifs, ands, or buts."'	Brain–computer interface is insufficient for this task
3	"Take the paper in your right hand, fold it in half, and put it on the floor." (The examiner gives the patient a piece of blank paper.)	Brain–computer interface is insufficient for this task
1	"Please read this and do what it says." (Written instruction is "Close your eyes.")	"Listen to these instructions and do what they say." (Auditory instructions are "Imagine playing tennis.")
1	"Make up and write a sentence about anything." (This sentence must contain a noun and a verb.)	Is the following set of words a sentence? Set #1 "Jane up blond." Set #2 "Jane is blond."
1	"Please copy this picture." (The examiner gives the patient a blank piece of paper and asks him/her to draw the symbol below. All 10 angles must be present and two must intersect.) 	"Are these two sets of auditory tones the same?" The examiner plays a recording containing a high pitch and low pitch in an alternating pattern. A second recording is then played with identical or deviant tone patterns.

Note. The MMSE is part of the standard screening process for capacity. The questions contained in the MMSE are easily translatable for binary communication, and may provide a promising strategy for probing underlying cognitive faculties in behaviorally nonresponsive patients. Adapted from Rovner and Folstein (1987) and Folstein, Folstein, and McHugh (1975).

We should note from the outset that an important aspect of this debate relates to controversial end-of-life decisions. Fins and Schiff (2010), for example, open their recent critique of neuroimaging research by envisaging a scenario in which an acutely brain-injured patient is asked to verify her do-not-resuscitate (DNR) status using a hypothetical fMRI paradigm. Their assessment rightly draws attention to the difficulty these high-stakes decisions pose when BCI neuroimaging is restricted to binary communication. "There is a risk of reading too much into these one sided interviews," they argue, which inevitably distorts an interrogator's interpretation of the patient's response (Fins and Schiff 2010, 22). Notwithstanding such concerns, this type of criticism, which draws on high-stakes decisions as examples, caricatures how BCI neuroimaging paradigms might realistically be employed in the clinical setting. For example, the patients assessed thus far have been from a chronic population ($n >$ 1 year post ictus) (Cruse et al. 2011; Monti et al. 2010; Owen et al. 2006), and are not reliant on the invasive life-sustaining technologies described by Fins and Schiff (2010). Thus, the decisions issued by these patients with the aid of BCI neuroimaging are unlikely to probe issues like DNR status. Rather than focusing on end-of-life decisions, we believe it would be far more useful to focus on strategies for improving quality of life for these patients and their families.

In their influential work on decision-making capacity, Buchanan and Brock (1986) discuss the connection between the type of clinical decision being made and the level of capacity required to make it. They argue that the standards of decision-making capacity are contingent on the stakes of the decision. The evaluative skill of the physician, the personality of the patient, and the timing of the given decision all bear on the level of capacity required to make the clinical choice (Buchanan and Brock 1986, 23). Aside from the clinical assessment of capacity, this view is certainly consistent with conventional wisdom. A cardiac surgeon, for example, presumably retains the capacity to make decisions related to ischemic heart disease. However, it is doubtful that this surgeon maintains the same capacity to make decisions relevant to the repair of an automobile engine. Likewise, we are likely to trust the decision-making capacity of a young and otherwise healthy individual who refuses an influenza vaccination. Yet we are less likely to trust the capacity of the same individual if the person refuses safe and effective treatment for an otherwise fatal disease. In this sense, decision-making capacity is not an analytically fixed, "all-or-nothing" concept (Buchanan and Brock 1986). Rather, capacity sits on a scale where the threshold for each clinical decision is contingent upon the relative importance of its outcome (see Table 4) (Buchanan and Brock 1986).

The application of this strategy in assessing decision-making capacity in behaviorally nonresponsive patients with residual covert awareness may effectively parse out which therapeutic questions are ethically permissible to ask using the mental imagery paradigm. According to Buchanan and Brock's (1986) strategy, the evaluation of a decision's significance is a function of its potential harms and benefits. When stakes are high, "where risk is a function of the severity of the expected harm and the probability of its occurrence," the threshold of capacity required to make the decision is also high (Buchanan and Brock 1986, 37). When the stakes are low, the threshold is as well (see Table 4).

For the time being, clinically relevant decisions with high-stakes outcomes (e.g., invasive procedures and end-life-decisions) should not be addressed through BCI neuroimaging paradigms since the conceptual and empirical foundations of this process are not yet satisfactorily established. However, once a robustly validated cognitive model of decision-making capacity is developed, it should, in principle, be ethically permissible to allow behaviorally nonresponsive patients with residual covert awareness to initially make decisions with low to medium stakes, provided that they demonstrate intact underlying cognitive faculties constitutive of an adjusted form of capacity. In practical terms, this includes decisions regarding administration of analgesics, a change in hospice conditions, or the appointment of a proxy decision maker. Because choices like these seek to reestablish autonomy, and thus improve quality of life, the relative probability of therapeutic benefit is high, which in turn suggests that the threshold of capacity for making such decisions is low. Thus, initially posing questions of this sort to individuals within this patients group who demonstrate the presence of certain intact, latent cognitive faculties appears to satisfy standard ethical constraints that govern decision making, and may lead to further application in high-stakes decisions of medical practice.

LIMITATIONS

There are two types of limitations that may hinder efforts to assess decision-making capacity through BCI neuroimaging paradigms. The first is an amalgam of technical obstacles inherent in neuroimaging technology and the mental imagery paradigm. These include imaging artifacts caused by patient movement in the fMRI scanner, an inability to identify true negative results, the restricted number of questions investigators can ask due to patient fatigue during imaging, and the high operating costs of scanning sessions (Peterson et al. 2013). The type and quantity of questions that can feasibly be asked using the mental imagery paradigm, meanwhile, may be difficult to reconcile with any reliable methods used to probe underlying cognitive faculties. For example, in the successful instance of BCI communication previously described (Monti et al. 2010), the patient who was able to communicate required 1 hour of imaging time to answer five questions (Peterson et al. 2013).

Nevertheless, these technical limitations are not insurmountable. Neuroimaging research in this patient group has advanced rapidly in the past 10 years. With reduced costs of imaging equipment, a larger patient population, and several recent innovations in BCI neuroimaging (Bardin et al. 2011; Bardin, Schiff, and Voss 2012; Cruse et al. 2011; 2012; Goldfine et al. 2011; Hampshire et al. 2013; Naci et al. 2012; Naci and Owen 2013; Sorger et al. 2012), it is likely these technical limitations will be resolved in the future.

The second type of limitation is the in-principle objection. Unlike the forgoing technical limitations, these objections derive from the position that assessment of decision-making capacity in this patient group with the aid of BCI neuroimaging is precluded on theoretical grounds. These objections take at least three forms: the argument from psychological health; the argument from phenomenal consciousness; and the argument from changing sets of values.

The first in-principle objection, the argument from psychological health, posits that clinical choices made through the mental imagery paradigm may be driven by underlying psychiatric conditions secondary to brain injury. This is not an unreasonable concern since several recent neuropsychiatric studies have drawn strong correlations between traumatic brain injury and various psychiatric ailments, including depression (Byers and Yaffe 2011; Shively et al. 2012; Yaffe et al. 2010). If, for example, it is suspected that severe brain injury negatively influences

Table 4. Decision-making capacity thresholds

Threshold of decision making capacity	Potential net balance of expected benefits and harms	Potential consequences of decision	Example of binary question	Stakes of decision
High threshold	Potential harms substantially outweigh the benefits relative to alternative treatments	Radical and irreversible	Do you consent to invasive research?	High
Medium threshold	Potential harms are equal to the benefits relative to alternative treatments	Radical yet reversible	Do you consent to appointing person *X* as your medical proxy?	Medium
Low threshold	Potential benefits substantially outweigh the harms relative to alternative treatments	Mundane and reversible	Do you wish to have more pain medications?	Low

Note. Medical choices can be organized in terms of the stakes of the decision's outcome. The stakes of each outcome can then be calibrated with the empirically verified presence of underlying cognitive faculties constitutive of decision-making capacity. High-stakes decisions will require a high threshold of capacity. Low stakes decisions will require a low threshold. Adapted from Buchanan and Brock (1986).

psychiatric health, regardless of the presence of residual covert awareness, then it may also be reasonable to assume that decision-making capacity is diminished as a result of these conditions.

One response to this argument is to devise a procedure that tests for the presence of psychiatric ailments that diminish decision-making capacity. For example, in neurologically healthy patients, the self-scored Beck Depression Inventory (BDI-I and BDI-II; Beck and Steer 1993a; 1993b; 1996) is used to assess clinical depression. If the BDI could be translated for binary interrogation, it might be possible to assess whether clinical preferences are driven by depression rather than a coherent and consistent rationale.

Another response to this argument appeals to the empirical literature. In a recent cohort study assessing the quality of life of a similarly nonresponsive patient group, chronically locked-in patients, participants were asked to self-assess their "global subjective well-being" on a 10-point scale (Bruno et al. 2011a). Of the 65 patients who provided responses, 47 reported overall happiness, while 18 reported overall unhappiness (Bruno et al. 2011a). Surprisingly, it was also found that a protracted duration spent in this neurological state was positively correlated with greater happiness (Bruno et al. 2011a). Even though the rates of occurrence remain to be established empirically, this would suggest that there is no necessary connection between severe brain injury and diminished psychiatric well-being. Surely, there will be cases of psychiatric illness secondary to severe brain injury, which will undermine decision-making capacity. However, the forgoing study suggests that in the case of patient groups with severe neurological insult, the prevalence of depression may be small.

A second in-principle objection, the argument from phenomenal consciousness, holds that BCI neuroimaging paradigms do not satisfactorily reveal the quality of consciousness in this patient group. This argument proceeds from the presumed explanatory gap between evidence acquired from the mental imagery paradigm and the subjective, phenomenal states of conscious experience. Even though we may be able to extract autobiographical information from this patient group, it is argued that this does not permit inference of subjective emotionality (Mackenzie 2013) or self-consciousness (Rich 2013). It has also been suggested that these particular phenomenal states are central components of robust decision-making capacity. Self-consciousness, for example, distinguishes humans from animals (Rich 2013), while emotionality allows one to exercise an overarching set of values (Mackenzie 2013). Since we cannot unequivocally confirm these phenomenal states with the mental imagery paradigm, it is reasoned that medical decision making should be precluded in this patient group.

In the context of BCI neuroimaging paradigms, we believe this objection is unfounded. For one, the concepts of subjective emotionality and self-consciousness are poorly defined. Even though these concepts are meaningful in the colloquial sense, it is unclear how they could be incorporated in an empirically adequate model of residual cognition. Because fMRI and clinical assessment of behaviorally nonresponsive patients proceed under controlled experimental conditions, the cognitive phenomena constitutive of consciousness—awareness and wakefulness—must be presented as well-circumscribed operational definitions. If they are not, it is unclear how they could be utilized in clinical practice or revealed by empirical tests. Indeed, whether one can even provide objective operational definitions for subjective phenomenal states may simply be a contradiction in terms.

To be sure, we acknowledge the importance of subjective phenomenal states in analyzing conscious experience.

But such an objection calls into question the very possibility of knowing whether any human, behaviorally nonresponsive or not, is, in fact, conscious at all. Because common sense tells us that awareness and wakefulness are satisfactory indicators of consciousness *simpliciter*, appealing to subjective phenomenal states as a genuine limitation to assessing decision-making capacity through BCIs is an incomplete objection at best, a mere pseudo-problem at worst.

A final in-principle objection is the argument from changing sets of values. A central criterion of decision-making capacity is the consistent application of a stable value set throughout the clinical reasoning process (Appelbaum 2007; Appelbaum and Grisso 1995; Buchanan and Brock 1986; Grisso and Appelbaum 1995; Grisso et al. 1995). If, hypothetically, a patient stipulates particular medical preferences in an advance directive, yet makes decisions inconsistent with these preferences after suffering a traumatic brain injury, it may be concluded that the patient has diminished capacity (cf. Cantor 1993). Indeed, this issue is further confounded by the communication restrictions inherent to the mental imagery paradigm.

In the face of uncertainty, however, it appears reasonable to allow such patients to participate in clinical decision making provided that the capacity threshold for the given medical choice is sufficiently low. Since it is unlikely that patients will provide evidence of preferences, such as an advance directive, for all medical decisions, worries related to comparing the stability of value sets before and after injury may simply be irrelevant to the quality-of-life decisions we have outlined thus far.

FUTURE DIRECTIONS

The use of fMRI to communicate with behaviorally nonresponsive patients with residual covert awareness may likely be integrated into the clinical setting in the future. Despite skepticism regarding the precise clinical and diagnostic application of fMRI, popular demand and legal precedence may undercut any preventative arguments advanced by the medical ethics community. Ethically responsible integration of this technology into the clinical setting should therefore be a principal focus of future research.

While it is not yet possible to assess decision-making capacity through BCI neuroimaging paradigms, these techniques may likely be integrated into the standard assessment battery. We have provided here a principled demonstration of how this integration could proceed. The central claim of this mechanistic explanation posits that the standard criteria of decision-making capacity can be sufficiently decomposed into underlying cognitive faculties. Accordingly, these can be measured through active, passive, and anatomical neuroimaging paradigms. Clinicians are then in the position to rebuild a model of a patient's residual cognitive profile and calibrate it to the requisite capacity threshold for any given medical decision. For these reasons, we believe there are no principled arguments that restrict the use of BCI neuroimaging paradigms to assess capacity. This approach, therefore, may open a promising way forward that allows this patient group to participate in making meaningful clinical decisions.

Before BCI neuroimaging can be incorporated into the standard capacity assessment battery, a number of theoretical and empirical concerns must be addressed. This future work, we believe, includes five principal components:

1. Broad consensus by the medical ethics community on the correct analysis of decision-making capacity, and its decomposition into operationalized cognitive faculties.
2. Further empirical studies that test the veracity of this mechanistic explanation of capacity.
3. Development of novel BCI neuroimaging paradigms that efficiently probe the constitutive cognitive faculties of decision-making capacity.
4. Development of a comprehensive question set, for binary communication, that efficiently probes the underlying cognitive faculties.
5. Development of a probability calculus that assigns specific probabilistic values to the respective probes, thereby facilitating a model of the patient's residual cognitive profile that is accurate and ethically responsible.

Given the theoretical and empirical interest generated by neuroimaging research in the past 10 years, we anticipate solutions to these problems may emerge in the future. In the interim, extensive discussion and reflection on these issues will be of substantial benefit to this patient group, their families, and the physicians who care for them.

REFERENCES

Andrews, K., L. Murphy, R. Munday and C. Littlewood. 1996. Misdiagnosis of the vegetative state: Retrospective study in a rehabilitation unit. *British Medical Journal* 313(7048): 13–16.

Appelbaum, P. S. 2007. Assessment of patients' competence to consent to treatment. *New England Journal of Medicine* 357(18): 1834–1840.

Appelbaum, P. S., and T. Grisso. 1995. The Macarthur treatment competence study. 1. Mental-illness and competence to consent to treatment. *Law and Human Behavior* 19(2): 105–126.

Bardin, J. C., J. J. Fins, D. I. Katz, et al. 2011. Dissociations between behavioural and functional magnetic resonance imaging-based evaluations of cognitive function after brain injury. *Brain* 134: 769–782.

Bardin, J. C., N. D. Schiff, and H. U. Voss. 2012. Pattern classification of volitional functional magnetic resonance imaging responses in patients with severe brain injury. *Archives of Neurology* 69(2): 176–181.

Beck, A., and R. Steer. 1993a. *Manual for the Beck Anxiety Inventory*. San Antonio, TX: Psychological Corporation.

Beck, A., and R. Steer. 1993b. *Manual for the Beck Depression Inventory*. San Antonio, TX: Psychological Corporation.

Beck, A., and R. Steer. 1996. *Manual for the Beck Depression Inventory–IT*. San Antonio, TX: Psychological Corporation.

Bekinschtein, T., C. Tiberti, J. Niklison, et al. 2005. Assessing level of consciousness and cognitive changes from vegetative state to full recovery. *Neuropsychological Rehabilitation* 15(3–4): 307–322.

Bendtsen, K. 2013. Communicating with the minimally conscious: Ethical implications in end-of-life care. *AJOB Neuroscience* 4(1): 46–51.

Berg, J. A. P., C. Lidz, and L. Parker. 2001. *Informed consent: Legal theory and clincal practice.* New York, NY: Oxford University Press.

Boly M., M. Coleman, M. Davis, et al. 2007. When thoughts become action: An fMRI paradigm to study volitional brain activity in non-communicative brain injured patients. *NeuroImage* 36(3): 979–992.

Bruno, M. A., J. L. Bernheim, D. Ledoux, F. Pellas, A. Demertzi, and S. Laureys. 2011a. A survey on self-assessed well-being in a cohort of chronic locked-in syndrome patients: Happy majority, miserable minority. *BMJ Open* 1(1).

Bruno, M. A., A. Vanhaudenhuyse, A. Thibaut, G. Moonen, and S. Laureys. 2011b. From unresponsive wakefulness to minimally conscious plus and functional locked-in syndromes: Recent advances in our understanding of disorders of consciousness. *Journal of Neurology* 258(7): 1373–1384.

Buchanan, A., and D. W. Brock. 1986. Deciding for others. *Milbank Quarterly* 64(Suppl. 2): 17–94.

Byers, A. L. and K. Yaffe. 2011. Depression and risk of developing dementia. *Nature Reviews Neurology* 7(6): 323–331.

Cantor, N. L. 1993. *Advance directives and the pursuit of death with dignity*. Indianapolis, IN: Indiana University Press.

Childs, N. L., W. N. Mercer, and H. W. Childs. 1993. Accuracy of diagnosis of persistent vegetative state. *Neurology* 43(8): 1465–1467.

Coleman, M. R., M. H. Davis, J. M. Rodd, et al. 2009. Towards the routine use of brain imaging to aid the clinical diagnosis of disorders of consciousness. *Brain* 132: 2541–2552.

Coleman, M. R., J. M. Rodd, M. H. Davis, et al. 2007. Do vegetative patients retain aspects of language comprehension? Evidence from fMRI. *Brain* 130: 2494–2507.

Craver, C. F. 2009. *Explaining the brain: Mechanisms and the mosaic unity of neuroscience*. New York, NY: Oxford University Press.

Cruse, D., S. Chennu, C. Chatelle, et al. 2011. Bedside detection of awareness in the vegetative state: A cohort study. *Lancet* 378(9809): 2088–2094.

Cruse, D., S. Chennu, D. Fernández-Espejo, W. L. Payne, G. B. Young, and A. M. Owen. 2012. Detecting awareness in the vegetative state: Electroencephalographic evidence for attempted movements to command. *PLoS One* 7(11).

Eyler, L. T., R. K. Olsen, G. V. Nayak, H. Mirzakhanian, G. G. Brown, and D. V. Jeste. 2007. Brain response correlates of decisional capacity in schizophrenia: A preliminary fMRI study. *Journal of Neuropsychiatry and Clinical Neurosciences* 19(2): 137–144.

Faden, R., and T. Beauchamp. 1986. *A history and theory of informed consent.* New York, NY: Oxford University Press.

Fernández-Espejo, D., C. Junque, P. Vendrell, et al. 2008. Cerebral response to speech in vegetative and minimally conscious states after traumatic brain injury. *Brain Injury* 22(11): 882–890.

Fernández-Espejo, D., A. Soddu, D. Cruse, et al. 2012. A role for the default mode network in the bases of disorders of consciousness. *Annals of Neurology* 72(3): 335–343.

Fernández-Espejo, D., and A. M. Owen. In press. Detecting awareness after severe brain injury. *Nature Reviews Neuroscience*.

Fins, J. J. and J. Illes. 2008. Lights, camera, inaction? Neuroimaging and disorders of consciousness. *American Journal of Bioethics* 8(9): W1–W3.

Fins, J. J., and N. D. Schiff. 2010. In the blink of the mind's eye. *Hastings Center Report* 40(3): 21–23.

Fins, J. J., J. Illes, J. L. Bernat, J. Hirsch, S. Laureys, and E. Murphy. 2008. Neuroimaging and disorders of consciousness: Envisioning an ethical research agenda. *American Journal of Bioethics* 8(9): 3–12.

Fischer C. E., and P. S. Appelbaum. 2010. Diagnosing consciousness: Neuroimaging, law, and the vegetative state. *The Journal of Law, Medicine & Ethics* 38(2): 374–385.

Folstein, M. F., S. E. Folstein, and P. R. McHugh. 1975. Mini-Mental State—Practical method for grading cognitive state of patients for clinician. *Journal of Psychiatric Research* 12(3): 189–198.

Giacino, J. T., K. Kalmar, and J. Whyte. 2004. The JFK Coma Recovery Scale–Revised: Measurement characteristics and diagnostic utility. *Archives of Physical Medicine and Rehabilitation* 85(12): 2020–2029.

Goldfine, A. M., J. D. Victor, M. M. Conte, J. C. Bardin, and N. D. Schiff. 2011. Determination of awareness in patients with severe brain injury using EEG power spectral analysis. *Clinical Neurophysiology* 122(11): 2157–2168.

Grisso, T., and P. S. Appelbaum. 1995. The Macarthur treatment competence study. 3. Measures of patients to consent to psychiatric and medical treatments. *Law and Human Behavior* 19(2): 149–174.

Grisso, T., P. S. Appelbaum, E. P. Mulvey, and K. Fletcher. 1995. The Macarthur treatment competence study. 2. Measures of abilities related to competence to consent to treatment. *Law and Human Behavior* 19(2): 127–148.

Hampshire, A., B. L. Parkin, R. Cusack, et al. 2013. Assessing residual reasoning ability in overtly non-communicative patients using fMRI. *NeuroImage: Clinical* 2: 174–183.

Karlawish, J. H. T., D. J. Casarett, B. D. James, et al. 2005. The ability of persons with Alzheimer disease (AD) to make a decision about taking an AD treatment. *Neurology* 64(9): 1514–1519.

Kim, S. Y. H., and E. D. Caine. 2002. Utility and limits of the Mini Mental State Examination in evaluating consent capacity in Alzheimer's disease. *Psychiatric Services* 53(10): 1322–1324.

Lehembre, R., O. Gosseries, Z. Lugo, et al. 2012. Electrophysiological investigations of brain function in coma, vegetative and minimally conscious patients. *Arch. Ital. Biol.* 150(2–3): 122–139.

Lule, D., Q. Noirhomme, S. C. Kleih, et al. 2013. Probing command following in patients with disorders of consciousness using a brain–computer interface. *Clinical Neurophysiology* 124(1): 101–106.

Mackenzie, R. 2013. Fragments of selves and the importance of emotionality: Ethicolegal challenges in assessing capacities, consent, and communicating with MCS patients and the need for guidelines. *AJOB Neuroscience* 4(1): 59–60.

Monti, M. M., A. Vanhaudenhuyse, M. R. Coleman, et al. 2010. Willful modulation of brain activity in disorders of consciousness. *New England Journal of Medicine* 362(7): 579–589.

Naci, L., R. Cusack, V. Z. Jia, and A. M. Owen. 2013. The brain's silent messenger: Using selective attention to decode human thought for brain-based communication. *Journal of Neuroscience* 33(22): 9385–9393.

Naci, L., M. M. Monti, D. Cruse, et al. 2012. Brain–computer interfaces for communication with nonresponsive patients. *Annals of Neurology* 72(3): 312–323.

Naci, L., and A. M. Owen. 2013. Making every word count for vegetative patients. *JAMA Neurology*. Epub ahead of print. Available at: archneur.jamanetwork.com/article.aspx?articleid=1724990 (accessed August 14, 2013).

Owen, A. M. 2013. Detecting consciousness: A unique role for neuroimaging. *Annual Review of Psychology* 64: 109–133.

Owen, A. M., M. R. Coleman, M. Boly, M. H. Davis, S. Laureys, and J. D. Pickard. 2006. Detecting awareness in the vegetative state. *Science* 313(5792): 1402.

Owen, A. M., and M. R. Coleman. 2008. Detecting awareness in the vegetative state. *Annals of the New York Academy of Sciences* 1129: 130–138.

Owen, A. M., M. R. Coleman, M. Boly, et al. 2007. Response to comments on "Detecting awareness in the vegetative state." *Science* 315(5816): 1221.

Owen, A. M., M. R. Coleman, D. K. Menon, et al. 2005. Using a hierarchical approach to investigate residual auditory cognition in persistent vegetative state. In *Boundaries of consciousness: Neurobiology and neuropathology*, ed. S. Laureys, 457–471. Amsterdam, The Netherlands: Elsevier Science.

Peterson, A., L. Naci, C. Weijer, and A. M. Owen. 2013. A principled argument, but not a practical one. *AJOB Neuroscience* 4(1): 52–53.

Rich, B. A. 2013. Distinguishing minimal consciousness from decisional capacity: Clinical, ethical, and legal implications. *AJOB Neuroscience* 4(1): 56–57.

Rovner, B. W., and M. F. Folstein. 1987. Mini-Mental-State-Exam in clinical practice. *Hospital Practice* 22(1A): 99, 103, 106, 110.

Schiff, N. D., D. Rodriguez-Moreno, A. Kamal, et al. 2005. fMRI reveals large-scale network activation in minimally conscious patients. *Neurology* 64(3): 514–523.

Schnakers, C., F. Perrin, M. Schabus, et al. 2008. Voluntary brain processing in disorders of consciousness. *Neurology* 71(20): 1614–1620.

Schnakers, C., A. Vanhaudenhuyse, J. Giacino, et al. 2009. Diagnostic accuracy of the vegetative and minimally conscious state: Clinical consensus versus standardized neurobehavioral assessment. *BMC Neurology* 9.

Shiel, A., S. A. Horn, B. A. Wilson, M. J. Watson, M. J. Campbell, and D. L. McLellan. 2000. The Wessex Head Injury Matrix (WHIM) main scale: A preliminary report on a scale to assess and monitor patient recovery after severe head injury. *Clinical Rehabilitation* 14(4): 408–416.

Shively, S., A. I. Scher, D. P. Perl, and R. Diaz-Arrastia. 2012. Dementia resulting from traumatic brain injury: What is the pathology? *Archives of Neurology* 69(10): 1245–1251.

Sorger, B., J. Reithler, B. Dahmen, and R. Goebel. 2012. A real-time fMRI-based spelling device immediately enabling robust motor-independent communication. *Current Biology* 22(14): 1333–1338.

Sullivan, J. A. 2010. Reconsidering 'spatial memory' and the Morris water maze. *Synthese* 177(2): 261–283.

Teasdale, G., and B. Jennett. 1974. Assessment of coma and impaired consciousness—Practical scale. *Lancet* 2(7872): 81–84.

Yaffe, K., E. Vittinghoff, K. Lindquist, et al. 2010. Posttraumatic stress disorder and risk of dementia among US veterans. *Archives of General Psychiatry* 67(6): 608–613.