REVIEW

Brain Circuitry of Consciousness: A Review of Current Models and a Novel Synergistic Model With Clinical Application

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How consciousness arises in the brain has important implications for clinical decision-making. We summarize recent findings in consciousness studies to provide a toolkit for clinicians to assess deficits in consciousness and predict outcomes after brain injury. Commonly encountered disorders of consciousness are highlighted, followed by the clinical scales currently used to diagnose them. We review recent evidence describing the roles of the thalamocortical system and brainstem arousal nuclei in supporting awareness and arousal and discuss the utility of various neuroimaging studies in evaluating disorders of consciousness. We explore recent theoretical progress in mechanistic models of consciousness, focusing on 2 major models, the global neuronal workspace and integrated information theory, and review areas of controversy. Finally, we consider the potential implications of recent research for the day-to-day decision-making of clinical neurosurgeons and propose a simple "three-strikes" model to infer the integrity of the thalamocortical system, which can guide prognosticating return to consciousness.

KEY WORDS: Consciousness, Traumatic brain injury, Global neuronal workspace, Integrated information theory, Thalamocortical loop

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Severe traumatic brain injury (TBI) typically results in disorders of consciousness (DoCs). It is generally believed that 2 essential components to consciousness exist, arousal and awareness, and individual conscious states are defined by varying content (awareness) and levels (arousal) of consciousness.[1] Plum and Posner[2] proposed that impairment of consciousness should be considered a form of organ failure, just as an elevation in creatinine represents kidney failure. Impairment of consciousness carries a significant risk of mortality, which is well-described in stroke,[3] TBI,[4] and seizure.[5] It is essential for clinicians to understand the brain circuitry that facilitates consciousness because clinical management may differ depending on which brain region is damaged.[5,6]

In this review, we provide an overview of DoCs and how to evaluate them and explore current theories of consciousness and the structures believed to facilitate it. We conclude with a representative TBI case to illustrate our approach to clinical decision-making for a comatose patient.

ABBREVIATIONS: anterior, anterior thalamic nuclei; **atr,** anterior thalamic radiations; **ARAS,** ascending reticular activating system; **CL,** central lateral nucleus; **CM,** centromedian nucleus; **CRS-R,** Coma Recovery Scale–Revised; **CSC,** cuneiform/subcuneiform complex; **DAI,** diffuse axonal injuries; **DMN,** default-mode network; **DoCs,** disorders of consciousness; **dtt_M,** delineated the medial; **dtt_L,** delineated the lateral; **DWI,** diffusion-weighted imaging; **FOUR,** ull Outline of Unresponsiveness Score; **GCS,** Glasgow Coma Scale; **GNW,** global neuronal workspace; **GPi,** globus pallidus internus; **HCP,** Human Connectome Project; **IIT,** information theory; **IML,** internal medullary lamina; **LD,** lateral dorsal nucleus; **LGN,** lateral geniculate nucleus; **LP,** lateral posterior nucleus; **MCS,** minimally conscious state; **mfb,** medial forebrain bundle; **MGN,** medial geniculate nucleus; **Midline,** midline thalamic nuclei; **MD,** mediodorsal; **pComm,** posterior commissural; **str,** superior thalamic radiations; **TBI,** traumatic brain injury; **VA,** ventral anterior nucleus; **VI,** ventral intermediate nucleus; **VL,** ventral lateral nucleus; **VPM,** ventral posterior medial nucleus; **VPL,** ventral posterior lateral nucleus; **VS/UWS,** vegetative state/unresponsive wakefulness syndrome.

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COMMON DoC

Neurosurgeons encounter DoC daily. They are classified as either acute or chronic. Acute DoCs, such as delirium and coma, are typically reversible. Chronic DoCs, however, are sometimes irreversible and include dementia, vegetative state/unresponsive wakefulness syndrome (VS/UWS), and minimally conscious state (MCS).[2,7] Identification of DoC is critical, as prognosis varies widely, and loved ones are often tasked with making medical decisions for these patients. Clinical criteria for diagnosis are extensively reviewed elsewhere.[8]

CLINICAL ASSESSMENT OF CONSCIOUSNESS

Objectively assessing consciousness is challenging. Currently, 3 behavioral tools are commonly used to assess consciousness. The Glasgow Coma Scale (GCS), designed in 1974, has been widely incorporated into clinical guidelines and scoring systems for rapid assessment of the level of consciousness in trauma patients.[9,10] The Full Outline of Unresponsiveness Score (FOUR) was designed to improve on the GCS by assessing brainstem reflexes and respiratory patterns in addition to eye-opening, verbal, and motor function.[11] Finally, the Coma Recovery Scale–Revised (CRS-R) grades patients on 6 subscales based on their responses to sensory stimuli administered in a standardized fashion.[12] These tools are described in Table 1.

CORE ANATOMY OF CONSCIOUSNESS

Clinicians have long sought to understand the physiological and neuroanatomic correlates of human consciousness. We outline the current literature supporting the role of brainstem arousal nuclei and the thalamocortical system as the neuroanatomic substrates for consciousness.

Critical Territory: Central Thalamus and Brainstem

Arousal is a prerequisite of consciousness.[1] The prevailing theory for the physiological basis of arousal hinges on excitatory input from the ascending reticular activating system (ARAS) to the corticothalamic circuit.[13,14] On electroencephalography (EEG), low-voltage fast activity predominates over high-voltage slow waves present during less wakeful states.[13] In animal studies, stimulation of the medial bulbar reticular formation in the pontine and midbrain tegmentum resulted in desynchronized EEG activity similar to waking from sleep.[13]

The ARAS pathways described by Moruzzi and Magoun were believed to begin in the reticular formation, a cluster of nuclei in the brainstem. This model held that the cuneiform and subcuneiform nuclei, and the pontis oralis, stimulate the cortex through thalamic excitation[14,15] (Figure 1). However, this model proved to be an oversimplification because it is now clear that the ARAS pathways originate from brainstem nuclei within and outside of the reticular formation proper. These arousal nuclei provide input to the hypothalamus, thalamus, basal forebrain, and cortex, with each pathway using a single neurotransmitter.[14]

The key thalamic nucleus for maintenance and regulation of arousal is the central lateral nucleus of the intralaminar nuclei (Figure 2).[16,17] The intralaminar nuclei facilitate large-scale corticocortical network activity in addition to providing direct input to the thalamocortical system.[16,18] Injury to the central thalamus severely impairs arousal.[16] Schiff's mesocircuit model[19] posits that deafferentation of the striatum by the cortex, after brain injury, leads to a central thalamic "downstate." This striatal deafferentation decreases its inhibition of the globus pallidus internus (GPi), increasing inhibitory tone from the GPi onto central thalamus. Positron emission tomography-MRI in patients with brain injury supports the mesocircuit hypothesis, revealing that increased GPi metabolic activity accompanied decreased activity in central thalamus and frontoparietal cortex.[20] In anesthetized macaques, increased activity in these structures correlated with the animal's level of consciousness.[21] Furthermore, central lateral stimulation augmented behavioral and electrophysiological markers of consciousness during anesthesia.[21,22] These results, in combination with the discovery that central thalamic deep brain stimulation (DBS) improved the level of consciousness in a MCS patient,[23] support the view that DBS may treat DoC. The patient regained the ability to communicate and use his limbs, years after injury, suggesting that thalamic stimulation may salvage residual functionality in patients with DoC. Therefore, the proposed anatomic basis of arousal lies within the brainstem ARAS pathways and the central thalamus. Understanding the circuitry supporting consciousness can help neurosurgeons evaluate DoC through imaging, where visualization of injuries to critical structures can guide subsequent treatment.

NEUROIMAGING

CT

CT is the diagnostic scan of choice in acute TBI because it allows for rapid characterization of life-threatening intracranial injuries that may require urgent neurosurgical intervention.[24] In particular, CT identifies patients at risk of brainstem injury from uncal herniation, which confers a high risk of developing a DoC because of its important role in arousal.[25]

Recently, the Rotterdam CT score has become a popular prognostic indicator in TBI.[26] Although the older Marshall scoring system evaluates mortality through findings of cistern obliteration and midline shift, the Rotterdam system also incorporates subarachnoid hemorrhage (SAH) and epidural hematoma.[27] Higher Rotterdam scores are significantly associated with unfavorable outcomes and increased mortality, making the scale useful in predicting early death after TBI.[26,28,29]

Structural MRI

Although CT is the best initial imaging modality to evaluate unconscious patients with TBI, structural MRI can better

TABLE 1. Behavioral Tools for Assessing Consciousness

Tool Features	GCS	FOUR	CRS-R
Range of score	3 to 15	0 to 16	0 to 23
Categories included	Eye response (4 max points)	Eye response (4 max points)	Auditory (4 max points)
	Verbal response (5 max points)	Motor response (4 max points)	Visual (5 max points)
	Motor response (6 max points)	Brainstem reflexes (4 max points)	Motor (6 max points)
		Respiration pattern (4 max points)	Oromotor/Verbal (3 max points)
			Communication (2 max points)
			Arousal (3 max points)
Score allocation	**Best eye response**	**Best eye response**	**Auditory function**
	1. No eye-opening	0. Eyelids remain closed with pain	0. None
	2. Eye-opening to pain	1. Eyelids are closed, but open in response to pain	1. Auditory startle
	3. Eye-opening to sound	2. Eyelids are close, but open to loud voice	2. Localization to sound
	4. Eyes spontaneously open	3. Eyelids are open, but are not tracking	3. Reproducible movement to command
	Best verbal response	4. Eyelids are open, or are opened, tracking or blinking to command	4. Consistent movement to command
	1. No verbal response	**Best motor response**	**Visual function**
	2. Incomprehensible sounds	0. No response to pain or generalized myoclonus status	0. None
	3. Inappropriate words	1. Extension response to pain	1. Visual startle
	4. Confused speech	2. Flexion response to pain	2. Fixation
	5. Intelligible and oriented speech	3. Localizes to pain	3. Visual pursuit
	Best motor response	4. Thumbs up, fist, or peace sign	4. Object localization: Reaching
	1. No motor response	**Brainstem reflexes**	5. Object recognition
	2. Abnormal extension to pain	0. Absence of pupil, cough or corneal reflex	**Motor function**
	3. Abnormal flexion to pain	1. Pupil and corneal reflexes are absent.	0. None/flaccid
	4. Withdrawal from pain	2. Pupil or corneal reflexes are absent.	1. Abnormal posturing
	5. Localizes to pain	3. One pupil wide and fixed	2. Flexion withdrawal
	6. Obeys motor commands	4. Pupil and corneal reflexes present	3. Localization to noxious stimulation
		Respiration pattern	4. Object manipulation
		0. Breathes at ventilator rate or apnea	5. Automatic motor response
		1. Breathes above ventilatory rate	6. Functional object use
		2. Not intubated, irregular breathing	**Oromotor/verbal function**
		3. Not intubated, Cheyne–Stokes breathing pattern	0. None
		4. Not intubated, regular breathing pattern	1. Oral reflexive movement
			2. Vocalization/oral movement

TABLE 1. Continued.

Tool Features	GCS	FOUR	CRS-R
			3. Intelligible verbalization
			Communication
			0. None
			1. Nonfunctional: intentional
			2. Functional: accurate
			Arousal
			0. Unarousable
			1. Eye-opening with stimulation
			2. Eye-opening without stimulation
			3. Attention

CRS-R, Coma Recovery Scale–Revised; FOUR, Full Outline of UnResponsiveness; GCS, Glasgow Coma Scale.

characterize the injury after patients are stabilized.[30] It is more sensitive for contusions, axonal injury, and extra-axial hemorrhage than CT and is recommended when neurological symptoms fail to improve or deteriorate.[30] Voxel-based morphometry on MRIs of patients with DoC after trauma revealed significantly more thalamic and midbrain atrophy, essential structures for maintenance of arousal.[31]

Diffusion tensor imaging (DTI) is particularly useful for assessing white matter abnormalities within the brain, such as traumatic axonal injury.[32] Tractography analysis of diffusion-imaged normal brains detailed the structural relationships within the ARAS arousal pathways of the human brainstem.[14] More recently, our work has demonstrated that DTI can be used to assess the structural integrity of thalamocortical projections and that preservation of these connections is associated with earlier command following after severe TBI.[33-35] Therefore, structural imaging methods can assess injuries to areas critical to consciousness and provide valuable prognostic information.

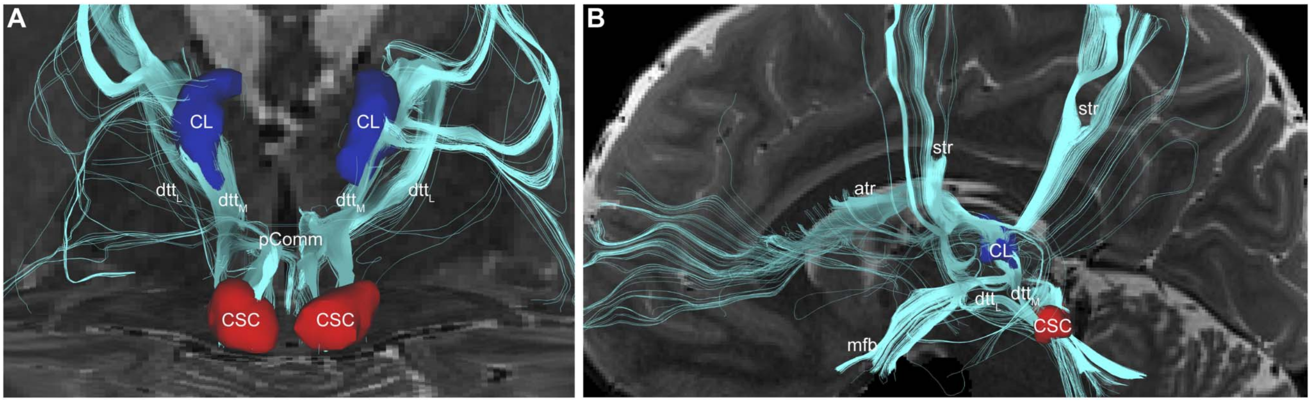

FIGURE 1. *Diffusion MRI tractography of the ascending reticular activating system in vivo, delineated by the human cuneiform–subcuneiform complex in the midbrain. Deterministic tractography from a 7T acquisition was performed in an individual subject from the HCP S1200 cohort ($b = 1000, 2000$ s/mm^2, TR/TE = 7000/71.2 ms, and slice thickness = 1.05 mm isotropic).* **A**, *Coronal and* **B**, *sagittal sections of the projections from the reticular formation to the intralaminar nuclei of the thalamus. The CSC was used as the seed, and the CL nucleus of the thalamus was the target. Tractography delineated the medial (dtt$_M$) and lateral (dtt$_L$) subdivisions of the dorsal tegmental tract. pComm fibers are visualized in* **A,** *at the level of the midbrain. In* **B**, *no termination masks were used to delineate the global white matter tracts that are projections from the dtt. Labeled neuroanatomic landmarks are mfb, atr, and str. atr, anterior thalamic radiations; CL, central lateral; CSC, cuneiform/subcuneiform complex; dtt$_M$, delineated the medial; dtt$_L$, delineated the lateral; HCP, Human Connectome Project; mfb, medial forebrain bundle; pComm, posterior commissural; str, superior thalamic radiations TE, echo time; TR, repetition time.*

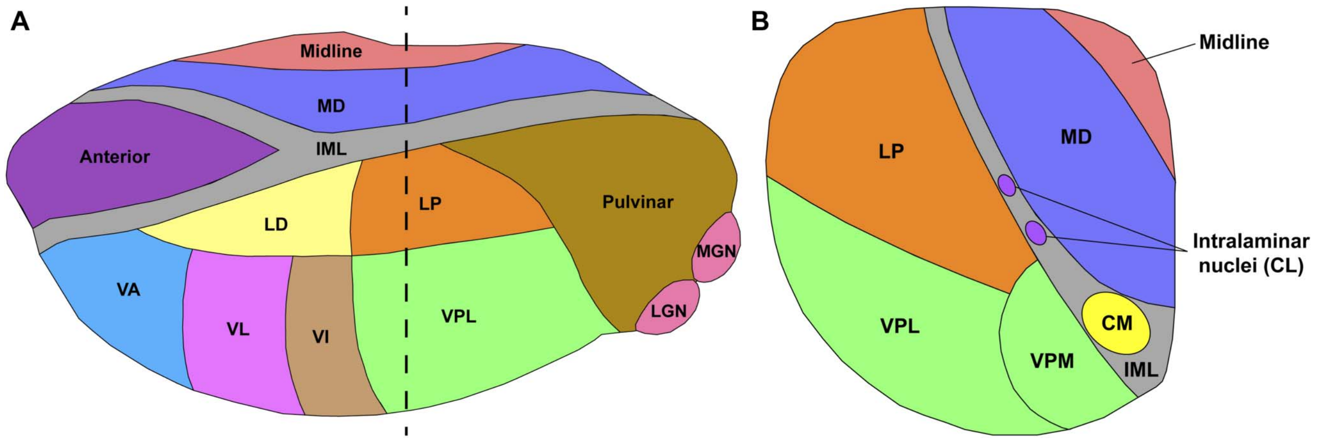

FIGURE 2. **A**, *Illustration of the various thalamic nuclei from a superior view. The dashed line represents the location of the cross-section shown in* **B**. *The CL is hypothesized to be integral to consciousness (arousal).*[17] *anterior, anterior thalamic nuclei; CL, central lateral nucleus; CM, centromedian nucleus; IML, internal medullary lamina; LD, lateral dorsal nucleus; LGN, lateral geniculate nucleus; LP, lateral posterior nucleus; MGN, medial geniculate nucleus; Midline, midline thalamic nuclei; MD, mediodorsal; VA, ventral anterior nucleus; VI, ventral intermediate nucleus; VL, ventral lateral nucleus; VPM, ventral posterior medial nucleus; VPL, ventral posterior lateral nucleus.*

TBIs and diffuse axonal injuries (DAI) are also commonly graded using a combination of histopathology and structural imaging to predict whether a patient may regain consciousness. Adams et al initially classified DAI based on histopathological findings; however, this grading scale was later translated to MRI findings by Gentry et al.[35,37] Although the prognostic validity of these grading scales is controversial, meta-analysis has supported the utility of MRI-based DAI grading scales in predicting functional outcomes.[38,39]

Functional MRI

Brain networks supporting consciousness are observable with both task-based and resting functional MRI (fMRI). Specifically, the return of consciousness after anesthesia was associated with increased brainstem, thalamic, hypothalamic, and anterior cingulate cortical activation and limited activation of frontal and parietal regions.[40] The latter cortical regions also exhibited increased functional connectivity in conscious individuals.[40] At rest, however, other structures are active, making up a so-called *default-mode network* (DMN).[41,42] The DMN, consisting of the posterior cingulate, precuneus, and medial prefrontal cortex, is correlated to the level of consciousness.[41] Studies on DMN functional connectivity during both conscious sedation[43] and anesthesia[44,45] have produced conflicting results. However, electrophysiological studies suggest that activity in the posteromedial DMN may be a substrate for conscious experience.[46,47]

Furthermore, task-based fMRI studies have also been used to assess the level of consciousness. These studies identified a subgroup of apparently unconscious patients who demonstrate brain activation during motor commands in the absence of a discernable behavioral response.[48-50] "Covert consciousness" can also be detected with EEG, underscoring the utility of these methods in assessing patients with DoC.[49,51]

THEORIES OF CONSCIOUSNESS

Understanding consciousness from a theoretical perspective has proved to be challenging. Two prevailing theories are the global

TABLE 2. **Overview of the 2 Main Theories of Consciousness**

Theory parameters	GNW	IIT
Neural correlate	Frontal, parietal cortex	Parietal cortex ("hot zone")[52]
Role of neural correlate	Global broadcasting of conscious information across interconnected prefrontal–parietal cortices	Posterior cortex generates the cause–effect power that allows for maximum integration of information
Central concept related to neural correlate	Ignition phase: top-down processing of a selected stimulus that has reached cortex level, higher-order GNW neurons	Phi (Φ): term used to quantify the integration of subsets of information based on the connectivity pattern, which together creates a conscious experience

GNW, global neuronal workspace; IIT, integrated information theory.

neuronal workspace (GNW) theory and the integrated information theory (IIT). We discuss these theories below and summarize them in Table 2.

GNW

Baars[53] postulated that a network of "unconscious specialized processors," capable of communicating with the rest of the system through the *global workspace*, facilitates conscious experience. Dehaene expanded on this model, stating that the specialized processors are bottom-up neural correlates carrying discrete pieces of information to create the content of consciousness when projected throughout the global workspace.[54,55]

According to GNW, conscious access occurs in 2 phases. In Phase I, a stimulus ascends the cortical hierarchy of specialized processors in a bottom-up fashion. If selected, based on salience and the individual's attention state, Phase II ensues. During Phase II, the *ignition phase*, the stimulus is amplified in a top-down manner and maintained by the sustained attention of GNW neurons throughout the global workspace, whereas other simultaneous stimuli are inhibited.[55] Ignition is posited to occur ∼250-500 ms after stimulus onset and is characterized by a broad cortical evoked potential, known as P3b.[55,56] P3b is a subcomponent of the event-related potential (ERP) known as P3 or P300, elicited on stimulus identification tasks.[56,57] P3b is believed to correlate with the subjective report of the target stimulus, thus implicating it in conscious processing.[55,56] However, whether this ERP is confounded by the motor response to target identification remains a question.[58-60]

Dehaene and colleagues[61] further elaborated on the GNW by distinguishing between subliminal and preconscious processing. They defined subliminal processing as bottom-up stimuli with minimal thalamocortical activation. Subliminal processing never reaches the global workspace and, therefore, is not conscious.[61] Alternatively, preconscious processing has sufficient thalamocortical activation but does not receive sufficient attention, rendering the information potentially accessible to conscious processing.[61] This distinction aligns with the no-report paradigm discussed later.

IIT

In 2004, Tononi introduced IIT,[62] which proposes a set of 5 phenomenological axioms, that is, consciousness exists and is structured, informative, integrated (irreducible), and exclusive (1 experience at a given time). These axioms have corresponding physical postulates, which specify the necessary properties of a system to generate a conscious experience. First, the system has causes and effects, including system elements (eg, neurons) having causes and effects within the system. Second, the elements of the system form higher-order mechanisms. Third, the interacting elements have different possible states representing concepts, called *conceptual structures*. Fourth, a conceptual structure is irreducible to independent elements. Information generated by the system, above and beyond the information generated by the individual elements of the system, is called *integrated information* also known by the term phi (Φ). Finally, only 1 set of elements, among all possible overlapping sets, gives rise to a conscious experience. According to IIT, the quality, or content, of each conscious experience corresponds to the conceptual structure. The quantity of the experience, or level of consciousness, corresponds to integrated information (Φ).[62,63]

Casali and colleagues[64] designed a measure to assess the integrated information content of EEG activity after transcranial magnetic stimulation (TMS). Their perturbational complexity index served as a proxy for Φ, estimating the cause–effect relationship of perturbation-induced activity and thus differentiating levels of consciousness.[64] In a recent study, investigators recorded local field potentials in macaques and discovered that activity in the parietal, thalamic, and striatal regions contributed most to Φ estimates during wakefulness, but not the frontal lobes.[65] Therefore, parietal circuits incorporating the striatum and thalamus best predicted consciousness.[65] This supports Tononi's original theory[62] that the thalamocortical system represents the neural correlates of consciousness (NCC), given the diversity of both intrathalamic and thalamocortical connections promoting information exchange across disparate brain regions. The structure–function relationship of this network facilitates the information integration critical to conscious experience.

AREAS OF CONTROVERSY

Theoretical Controversy

Although both GNW and IIT present theoretical models explaining consciousness, the 2 theories are incompatible. According to GNW, the frontal cortex is essential for consciousness, as represented by the importance of the ignition phase. To review, ignition is the top-down processing of a selected stimulus that has reached higher-order GNW neurons. Only stimuli aligning with the top-down goals of the cortical GNW neurons reach conscious awareness.[55] By contrast, proponents of IIT assert that the parietal and sensory cortices contain the true neural correlates of consciousness. As previously mentioned, recent evidence suggests that consciousness depends on integration of information (Φ) between the parietal cortex, thalamus, and striatum, not frontal cortex.[65] This gives rise to the so-called front vs back debate.[66] However, the controversy regarding the neural correlates of consciousness extends beyond GNW and IIT. We now address recent skepticism regarding the significance of both the thalamus and frontal lobes in consciousness.

Controversy Surrounding Thalamic Contributions to Consciousness

Despite evidence of the thalamic involvement in consciousness, its role is debated. In a retrospective cohort of patients with thalamic strokes, lesions limited to the thalamus did not severely affect the level of consciousness.[67] These results align with some previous rodent data[68] and support the belief that thalamic contributions to arousal may be due to its shared vascular supply with arousal-producing brainstem structures.[65] Similarly, a study on patients who survived hemorrhagic stroke found little evidence of impaired consciousness in individuals with thalamic lesions.[68] However, these lesions were not complete/bilateral.

Indeed, it is possible that the thalamus is critical for the content of consciousness, but not arousal. Our observations in patients with severe TBI and in silico have demonstrated that thalamic injury results in dysfunctional cortical networks with simplistic and repetitive characteristics, supporting the idea that thalamic input is crucial for the content of consciousness.[33]

Frontal Lobes: Can There be Reasonable Recovery with Frontal Lobe Damage?

Substantial evidence from both brain lesioning and stimulation studies undermines the importance of the frontal lobes in consciousness. Brickner[69] described the first patient to undergo bilateral frontal lobectomy sparing only Brodmann area 6 and Broca's area. Despite postoperative mood changes, the patient's examination was unremarkable. Interestingly, an epileptic patient who underwent complete bilateral prefrontal resection experienced an increase in his intelligence quotient.[70] A woman with significant bilateral prefrontal damage graduated high school and lived with intact consciousness.[71] Thus, lesion studies suggest that intact frontal lobes are not required for consciousness.

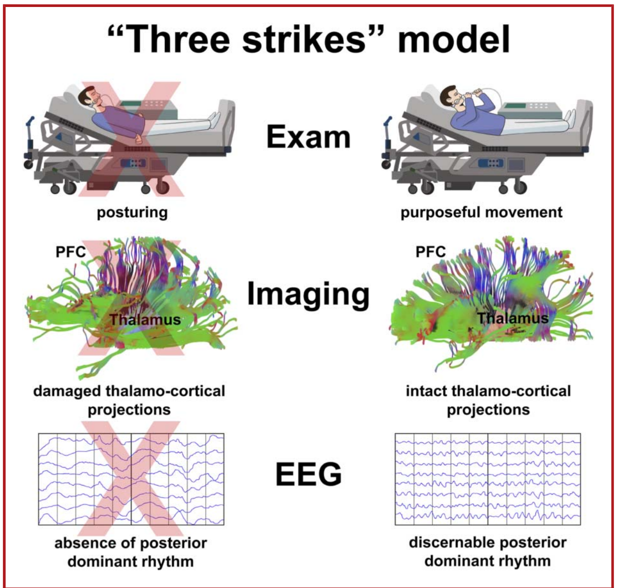

FIGURE 3. *Schematic of the proposed "three-strikes" model. Left: signs on neurological examination, diffusion-weighted imaging, and EEG that constitute a strike (red 'X'), suggesting a poorer prognosis. These signs include posturing, damaged thalamocortical projections, and the absence of a posterior dominant rhythm, respectively. Right: reassuring signs on neurological examination, diffusion-weighted imaging, and EEG including purposeful movement (localization to endotracheal tube), intact thalamocortical projections, and a discernable posterior dominant rhythm, respectively. These signs do not merit a strike. Tractography images from Mofakham et al, 2022.*[33] *© S Mofakham, used with permission.*

Boly and colleagues assert that areas of the parietal, temporal, and occipital lobes, known as the *posterior hot zone*, are more integral to consciousness than the frontal lobes.[6,72] Stimulation studies have corroborated this claim.[73-75] The case for a posterior hot zone aligns with findings from studies that used *no-report* paradigms, which separate the *experience* of consciousness from the *report* of consciousness. These paradigms typically do not cause frontal activation. The purpose of this paradigm is to isolate the NCC from the brain regions involved in the *report* of consciousness.[76,77] A key example is the binocular rivalry task implemented by Frassle and colleagues.[78] In this fMRI study, the authors presented competing visual stimuli to healthy participants who were instructed to indicate dominant stimuli by pressing a button (report). Importantly, eye movements that occurred independent of button-pressing allowed the authors to dissociate report from the perceptual experience. They found that that parietal and occipital cortices were activated even without report (button-pressing), whereas frontal cortex was not.[78] Therefore, the no-report paradigm further supports the idea that the frontal lobes are not critical for phenomenal consciousness (subjective experience).

"THREE-STRIKES" MODEL AND CASE APPLICATION

"Three-Strikes" Model for Prognosticating in TBI

Although previous TBI prognostic models have used clinical (GCS, FOUR, and CRS-R), radiological (Rotterdam, DAI, fMRI), or EEG findings in isolation, we felt that a more comprehensive prognostic model was necessary. Our proposed model—the "Three-Strikes" model—consists of integrating 3 key components: (1) the neurological examination, (2) imaging, and (3) the pattern of EEG activity (Figure 3). A poor result on any of these assessments constitutes a "strike," whereas a positive result does not. Prognosis is poorer with more strikes. Positive findings on examination include complex (nonposturing) responses to pain, spontaneous movements, reactive pupils, and an improvement in daily CRS-R assessment. On MRI, the presence of intact thalamocortical projections is another positive sign. These projections are best assessed through DTI, but more conventional diffusion-weighted sequences (diffusion-weighted imaging [DWI]) can also show these injuries.[79,80] Finally, low-amplitude, high-frequency activity (alpha and beta) on EEG is a positive prognostic indicator.[33,34,81,82] "Strike-earning" results on physical examination, imaging, and EEG include posturing, damaged thalamocortical projections, and absence of a posterior dominant rhythm, respectively.

Although the "Three-Strike" model's components may undoubtedly change during a patient's hospital course, the strength in this proposed model is its comprehensive nature. For example, if a patient were to suffer an adverse event during their hospital stay, such as recurrent apneic episodes, the "Three-Strike" model components can be easily reassessed for renewed prognostication.

Although an MRI may be cumbersome and expensive to reobtain, a thorough physical examination and EEG recordings can be easily reobtained cost-effectively. In addition, MRI structural findings are less likely to change acutely and dramatically compared with physical examinations and EEG.

We believe that incorporating this coarse framework into clinical practice can help neurosurgeons and families make informed decisions regarding TBI patient management. Notably, this conceptualization is not designed for quantitative predictions; we have proposed a three-point *Time to Follow Commands* score elsewhere for this purpose (high-impact trauma, a single fixed and dilated pupil, and poor Rotterdam CT score). Each gets a point, with three points indicating that command following is likely to return late or never.[29]

CONCLUSION

We have reviewed the current literature on consciousness and discussed its anatomic correlates, namely, the thalamus and cortex. We believe that thalamocortical connectivity is essential for the content of consciousness but nonetheless have addressed criticisms of prevailing theories of consciousness. Finally, we explored an illustrative case (see Supplemental Digital Content, http://links.lww.com/NEUOPEN/A57) and presented our three-strikes model to provide an approach for clinicians in diagnosing and prognosticating patients with DoC.

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Disclosures

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Case Illustration and Supplemental Figure.