Disorders of Consciousness:
State of the Science 2024
Guidelines for Diagnosis and Prognostication

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Brigham & Women's Hospital

Disclosure

Dr. Giacino has no significant financial relationship with any commercial or proprietary entity that produces healthcare-related products and/or services relevant to the content of this presentation.

Dr. Giacino occasionally receives honoraria for conducting Coma Recovery Scale-Revised training seminars.

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Outline

1. Definitions and distinguishing features of disorders of consciousness (DoC).
2. Natural history of recovery from DoC.
3. Evidence-based practice guidelines for maximizing diagnostic accuracy in DoC.
4. Evidence-based practice guidelines to inform prognostication in DoC.

Disorders of Consciousness: Definitions

1. ***Coma:*** State of *sustained pathologic unconsciousness* in which the *eyes remain continuously closed (Multi-Society Task Force, NEJM, 1994).*
2. ***Vegetative State:*** Condition in which there is *complete absence of behavioral evidence* for awareness of self and environment, with eye-opening and preserved sleep/wake cycles (*Aspen Workgroup, JHTR, 1997).*
3. ***Minimally Conscious State:*** Condition of severely altered consciousness in which there is minimal but definite (and often intermittent) behavioral evidence of self or environmental awareness *(Giacino et al., Neurology, 2002)*
   a. ***MCS +:*** Evidence of preserved language function *(Thibaut et al, J Neurol, 2020)*
   b. ***MCS-****:* Volitional behavior without evidence of language function *(Thibaut et al, J Neurol, 2020)*
4. ***Post-Traumatic (or Acute) Confusional State:*** A disorder of consciousness characterized by *reduced ability to focus or sustain attention*, *disorientation* to time and place, *impaired ability to encode and recall new information* and *symptom fluctuation*. *(Stuss et al, J Neurosurg,1999; Sherer et al, Arch Phys Med Rehabil, 2020).*

Disorders of Consciousness: Diagnostic features

Dimension		Behavior	Coma*	VS/UWS†	MCS-*	MCS+*	PTCS‡
Awareness		Reduced ability to focus or sustain attention.					
		Disorientation to place, time and situation.					
		Impaired encoding and recall of new information.					
		Symptom fluctuation over course of the day.					
		Reliable yes-no responses or functional object use.					
Awareness	+ Language	Consistent command-following					
		Reproducible command-following					
		Intelligible speech					
		Object recognition					
		Discernible but unreliable yes-no responses					
	- Language	Automatic motor behavior					
		Object manipulation					
		Object localization					
		Visual pursuit					
		Visual fixation					
		Localization to pain					
Arousal		No reproducible evidence of any behavior above					
		Eyes open spontaneously or to stimulation					
		Continuous eye closure					

∞ The designated behavior must be present

†Both designated behaviors must be present

*Any designated behavior must be present

‡All designated behaviors must be present

(Adapted from Giacino et al, Brain Injury Medicine, 2020)

NIDILRR National Institute on Disability, Independent Living, and Rehabilitation Research

AMERICAN ACADEMY OF NEUROLOGY

ACRM AMERICAN CONGRESS OF REHABILITATION MEDICINE

Published Ahead of Print on August 8, 2018 as 10.1212/WNL.0000000000005928

SPECIAL ARTICLE

Comprehensive systematic review update summary: Disorders of consciousness

Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology; the American Congress of Rehabilitation Medicine; and the National Institute on Disability, Independent Living, and Rehabilitation Research

Joseph T. Giacino, PhD, Douglas I. Katz, MD, Nicholas D. Schiff, MD, John Whyte, MD, PhD, Eric J. Ashman, MD, Stephen Ashwal, MD, Richard Barbano, MD, PhD, Flora M. Hammond, MD, Steven Laureys, MD, PhD, Geoffrey S.F. Ling, MD, Risa Nakase-Richardson, PhD, Ronald T. Seel, PhD, Stuart Yablon, MD, Thomas S.D. Getchius, Gary S. Gronseth, MD, and Melissa J. Armstrong, MD, MSc

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Neurology® 2018;00:1-10. doi:10.1212/WNL.0000000000005928

Abstract

Objective

To update the 1995 American Academy of Neurology (AAN) practice parameter on persistent vegetative state and the 2002 case definition for the minimally conscious state (MCS) by reviewing the literature on the diagnosis, natural history, prognosis, and treatment of disorders of consciousness lasting at least 28 days.

Methods

Articles were classified per the AAN evidence-based classification system. Evidence synthesis occurred through a modified Grading of Recommendations Assessment, Development and Evaluation process. Recommendations were based on evidence, related evidence, care principles, and inferences according to the AAN 2011 process manual, as amended.

Results

No diagnostic assessment procedure had moderate or strong evidence for use. It is possible that a positive EMG response to command, EEG reactivity to sensory stimuli, laser-evoked potentials, and the Perturbational Complexity Index can distinguish MCS from vegetative state/unresponsive wakefulness syndrome (VS/UWS). The natural history of recovery from prolonged VS/UWS is better in traumatic than nontraumatic cases. MCS is generally associated with a better prognosis than VS (conclusions of low to moderate confidence in adult populations), and traumatic injury is generally associated with a better prognosis than nontraumatic injury (conclusions of low to moderate confidence in adult and pediatric populations). Findings co… prognostic features are stratified by etiology of injury (traumatic vs nontraumatic) and diagnos… MCS) with low to moderate degrees of confidence. Therapeutic evidence is sparse. Amant… hastens functional recovery in patients with MCS or VS/UWS secondary to severe traumatic b… 4 weeks of treatment. Recommendations are presented separately.

RELATED ARTICLE

Articles

Practice guideline update recommendations summary: Disorders of consciousness: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology; the American Congress of Rehabilitation Medicine; and the National Institute on Disability, Independent Living, and Rehabilitation Research

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Ethical, palliative, and policy considerations in disorders of

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Neurology® 2018;00:1-11. doi:10.1212/WNL.0000000000005926

Abstract

Objective

To update the 1995 American Academy of Neurology (AAN) practice parameter on persistent vegetative state and the 2002 case definition on minimally conscious state (MCS) and provide care recommendations for patients with prolonged disorders of consciousness (DoC).

Methods

Recommendations were based on systematic review evidence, related evidence, care principles, and inferences using a modified Delphi consensus process according to the AAN 2011 process manual, as amended.

Recommendations

Clinicians should identify and treat confounding conditions, optimize arousal, and perform serial standardized assessments to improve diagnostic accuracy in adults and children with prolonged DoC (Level B). Clinicians should counsel families that for adults, MCS (vs vegetative state [VS]/unresponsive wakefulness syndrome [UWS]) and traumatic (vs nontraumatic) etiology are associated with more favorable outcomes (Level B). When prognosis is poor, long-term care must be discussed (Level A), acknowledging that prognosis is not universally poor (Level B). Structural MRI, SPECT, and the Coma Recovery Scale–Revised can assist prognostication in adults (Level B); no tests are shown to improve prognostic accuracy in children. Pain always should be assessed and treated (Level B)… discussed (Level B). Clinicians should prescribe …tic VS/UWS or MCS (4–16 weeks post injury) to …y in recovery (Level B). Family counseling con…ory of recovery, prognosis, and treatment are not …hat the term chronic VS/UWS should replace …dditional recommendations are included.

RELATED ARTICLES

Articles

Comprehensive systematic review update summary: Disorders of consciousness: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology; the American Congress of Rehabilitation Medicine; and the National Institute on Disability, Independent Living, and Rehabilitation Research

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Ethical, palliative, and policy considerations in disorders of consciousness

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AMERICAN ACADEMY OF NEUROLOGY

Level of Obligation

- Level A: Must
- Level B: Should
- Level C: May
- Level U: No recommendation supported

Diagnostic Assessment

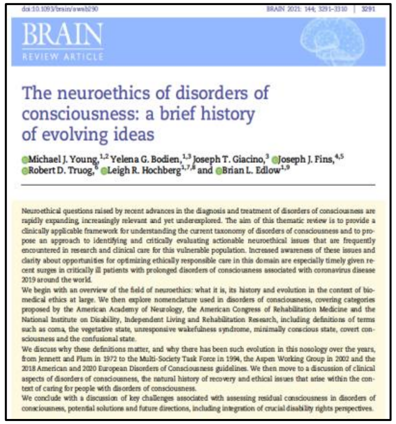
Guidelines for Diagnostic Assessment

Recommendation Statement 1

- Clinicians should refer patients with DoC who have achieved medical stability to settings staffed by multidisciplinary rehabilitation teams with specialized training to optimize diagnostic evaluation, prognostication, and subsequent management, including effective medical monitoring and rehabilitative care (**Level B**).

(Giacino et al., DoC Practice Guideline Update, Neurol 2018)

Algorithm for Diagnostic Assessment of DoC


doi:10.1093/brain/awab290 BRAIN 2021: 144; 3291–3310 | 3291

BRAIN
REVIEW ARTICLE

The neuroethics of disorders of consciousness: a brief history of evolving ideas

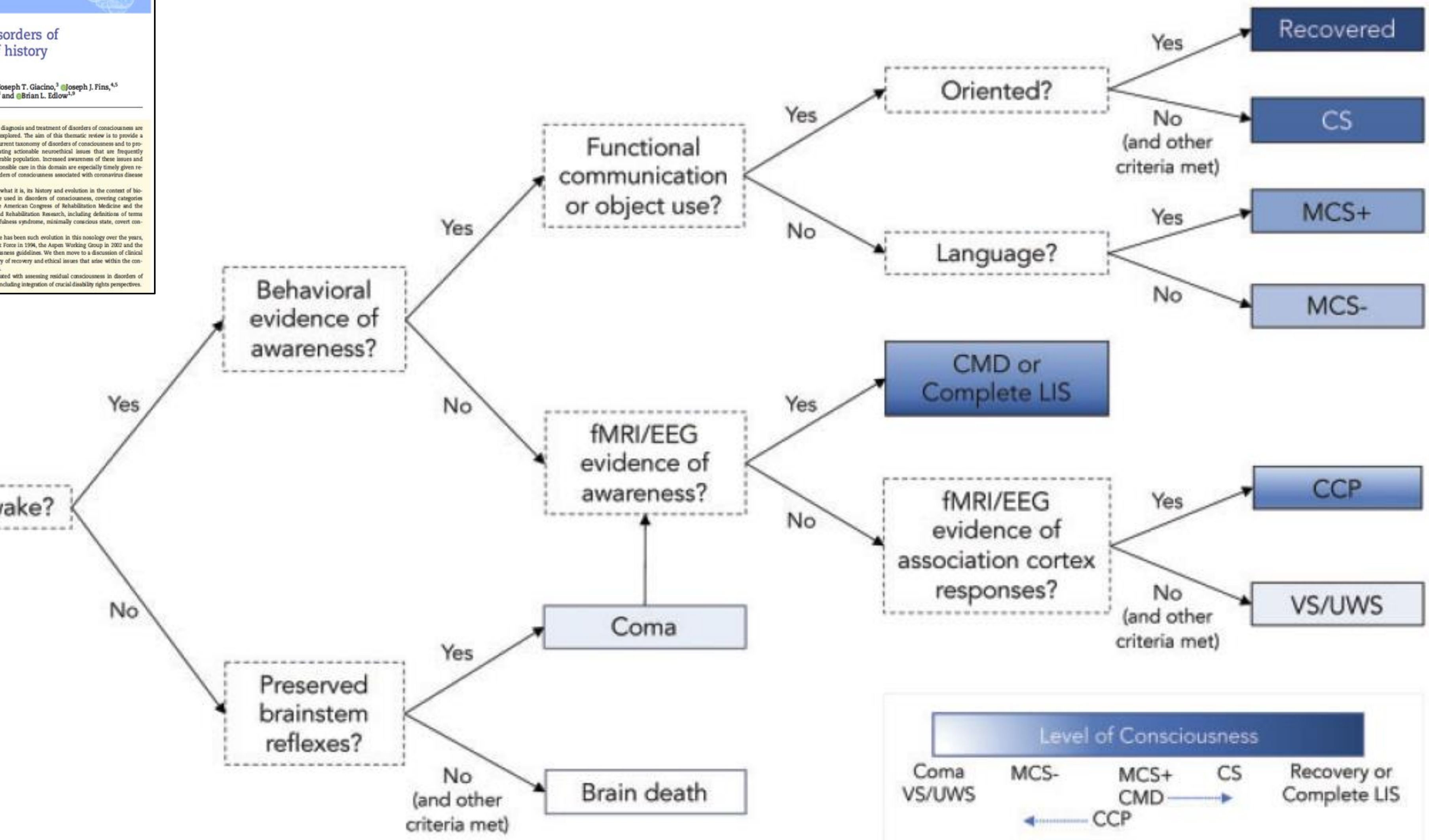
Michael J. Young,[1,2] Yelena G. Bodien,[1,3] Joseph T. Giacino,[3] Joseph J. Fins,[4,5] Robert D. Truog,[6] Leigh R. Hochberg[1,7,8] and Brian L. Edlow[1,9]

Neuroethical questions raised by recent advances in the diagnosis and treatment of disorders of consciousness are rapidly expanding, increasingly relevant and yet underexplored. The aim of this thematic review is to provide a clinically applicable framework for understanding the current taxonomy of disorders of consciousness and to propose an approach to identifying and critically evaluating actionable neuroethical issues that are frequently encountered in research and clinical care for this vulnerable population. Increased awareness of these issues and clarity about opportunities for optimizing ethically responsible care in this domain are especially timely given recent surges in critically ill patients with prolonged disorders of consciousness associated with coronavirus disease 2019 around the world.

We begin with an overview of the field of neuroethics: what it is, its history and evolution in the context of biomedical ethics at large. We then explore nomenclature used in disorders of consciousness, covering categories proposed by the American Academy of Neurology, the American Congress of Rehabilitation Medicine and the National Institute on Disability, Independent Living and Rehabilitation Research, including definitions of terms such as coma, the vegetative state, unresponsive wakefulness syndrome, minimally conscious state, covert consciousness and the confusional state.

We discuss why these definitions matter, and why there has been such evolution in this nosology over the years, from Jennett and Plum in 1972 to the Multi-Society Task Force in 1994, the Aspen Working Group in 2002 and the 2018 American and 2020 European Disorders of Consciousness guidelines. We then move to a discussion of clinical aspects of disorders of consciousness, the natural history of recovery and ethical issues that arise within the context of caring for people with disorders of consciousness.

We conclude with a discussion of key challenges associated with assessing residual consciousness in disorders of consciousness, potential solutions and future directions, including integration of crucial disability rights perspectives.



(Young, Bodien, Giacino et al, Brain 2021)

Incidence of diagnostic error

- 37% *(Childs et al, Neurol, 1993)*
- 43% *(Andrews et al, BMJ, 1996)*
- 41% *(Schnakers et al, BMC Neurology, 2009)*

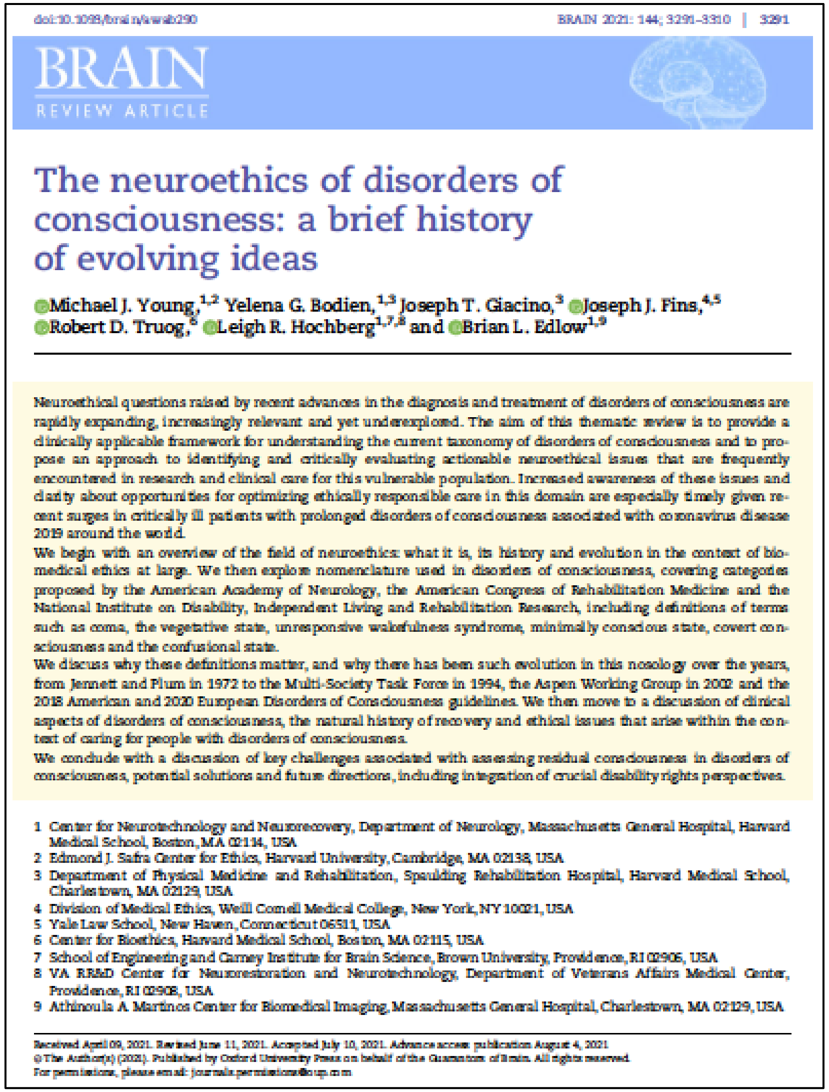
Diagnostic Error in DoC

Causes

- Reliance on qualitative assessment methods
- Inattention to baseline arousal level
- Failure to account for fluctuation in "state"
- Insufficient behavioral sampling
- Unrecognized medical complications/sedating agents

Consequences

- Inaccurate prognostic counseling
- Inappropriate decision-making about goals of care and treatment
- Family/Caregiver misinformation and distress



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Guidelines for Diagnostic Assessment

Recommendation 2a

- Clinicians should ***use standardized neurobehavioral assessment measures*** that have been shown to be valid and reliable (such as those recommended by the ACRM) to improve diagnostic accuracy for the purpose intended (**Level B** based on importance of outcomes and feasibility).

(Giacino et al., DoC Practice Guideline Update, Neurol 2018)

Guidelines for Diagnostic Assessment

BMC Neurology

BioMed Central

Research article

Open Access

Diagnostic accuracy of the vegetative and minimally conscious state: Clinical consensus versus standardized neurobehavioral assessment

Caroline Schnakers[1], Audrey Vanhaudenhuyse[1], Joseph Giacino[2], Manfredi Ventura[3], Melanie Boly[1,4], Steve Majerus[5], Gustave Moonen[4] and Steven Laureys*[1,4]

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This article is available from: http://www.biomedcentral.com/1471-2377/9/35

Table 2: Behavioral signs of consciousness found in patients misdiagnosed with VS and MCS or with uncertain clinical consensus diagnosis.

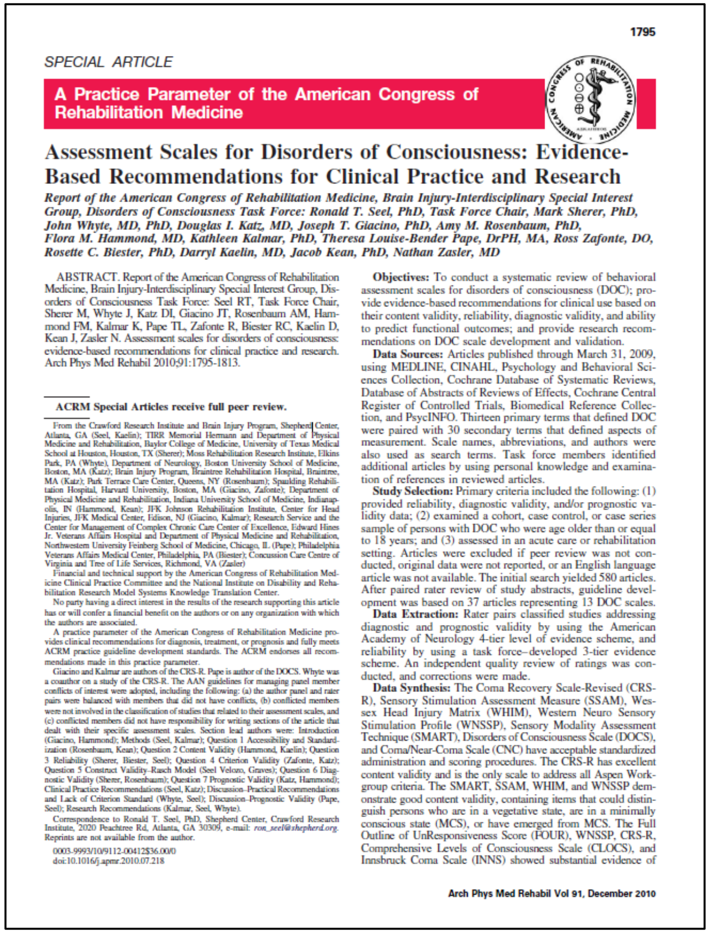
Behavior	VS	MCS	Unsure of diagnosis
1 – response to verbal order	4	*	4
2 – purposeful eye movements	8	*	6
3 – automatic motor response	1	*	1
4 – pain localization	1	*	1
5 – several criteria for MCS	4	*	4
6 – communication	*	1	*
7 – functional object use	*	1	*
8 – several criteria for EMCS	*	2	*
Total	18	4	16

Recommended DoC Assessment Scales

- Standardized assessment scales recommended for use in clinical practice with **minor** or moderate reservations)

  - **The Coma Recovery Scale-Revised (CRS-R)**
  - The Sensory Modality Assessment Rehabilitation Technique (SMART)
  - Sensory Stimulation Assessment Measure
  - The Western Neuro Sensory Stimulation Profile
  - Wessex Head Injury Matrix
  - Disorders of Consciousness Scale (DOCS)

(Seel et al., Assessment scales for DOC, Arch Phys Med Rehabil, 2010)



1795

SPECIAL ARTICLE

A Practice Parameter of the American Congress of Rehabilitation Medicine

Assessment Scales for Disorders of Consciousness: Evidence-Based Recommendations for Clinical Practice and Research

Report of the American Congress of Rehabilitation Medicine, Brain Injury-Interdisciplinary Special Interest Group, Disorders of Consciousness Task Force: Ronald T. Seel, PhD, Task Force Chair, Mark Sherer, PhD, John Whyte, MD, PhD, Douglas I. Katz, MD, Joseph T. Giacino, PhD, Amy M. Rosenbaum, PhD, Flora M. Hammond, MD, Kathleen Kalmar, PhD, Theresa Louise-Bender Pape, DrPH, MA, Ross Zafonte, DO, Rosette C. Biester, PhD, Darryl Kaelin, MD, Jacob Kean, PhD, Nathan Zasler, MD

ABSTRACT. Report of the American Congress of Rehabilitation Medicine, Brain Injury-Interdisciplinary Special Interest Group, Disorders of Consciousness Task Force: Seel RT, Task Force Chair, Sherer M, Whyte J, Katz DI, Giacino JT, Rosenbaum AM, Hammond FM, Kalmar K, Pape TL, Zafonte R, Biester RC, Kaelin D, Kean J, Zasler N. Assessment scales for disorders of consciousness: evidence-based recommendations for clinical practice and research. Arch Phys Med Rehabil 2010;91:1795-1813.

ACRM Special Articles receive full peer review.

From the Crawford Research Institute and Brain Injury Program, Shepherd Center, Atlanta, GA (Seel, Kaelin); TIRR Memorial Hermann and Department of Physical Medicine and Rehabilitation, Baylor College of Medicine, University of Texas Medical School at Houston, Houston, TX (Sherer); Moss Rehabilitation Research Institute, Elkins Park, PA (Whyte), Department of Neurology, Boston University School of Medicine, Boston, MA (Katz); Brain Injury Program, Braintree Rehabilitation Hospital, Braintree, MA (Katz); Park Terrace Care Center, Queens, NY (Rosenbaum); Spaulding Rehabilitation Hospital, Harvard University, Boston, MA (Giacino, Zafonte); Department of Physical Medicine and Rehabilitation, Indiana University School of Medicine, Indianapolis, IN (Hammond, Kean); JFK Johnson Rehabilitation Institute, Center for Head Injuries, JFK Medical Center, Edison, NJ (Giacino, Kalmar); Research Service and the Center for Management of Complex Chronic Care Center of Excellence, Edward Hines Jr. Veterans Affairs Hospital and Department of Physical Medicine and Rehabilitation, Northwestern University Feinberg School of Medicine, Chicago, IL (Pape); Philadelphia Veterans Affairs Medical Center, Philadelphia, PA (Biester); Concussion Care Centre of Virginia and Tree of Life Services, Richmond, VA (Zasler)

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No party having a direct interest in the results of the research supporting this article has or will confer a financial benefit on the authors or on any organization with which the authors are associated.

A practice parameter of the American Congress of Rehabilitation Medicine provides clinical recommendations for diagnosis, treatment, or prognosis and fully meets ACRM practice guideline development standards. The ACRM endorses all recommendations made in this practice parameter.

Giacino and Kalmar are authors of the CRS-R. Pape is author of the DOCS. Whyte was a coauthor on a study of the CRS-R. The AAN guidelines for managing panel member conflicts of interest were adopted, including the following: (a) the author panel and rater pairs were balanced with members that did not have conflicts, (b) conflicted members were not involved in the classification of studies that related to their assessment scales, and (c) conflicted members did not have responsibility for writing sections of the article that dealt with their specific assessment scales. Section lead authors were: Introduction (Giacino, Hammond); Methods (Seel, Kalmar); Question 1 Accessibility and Standardization (Rosenbaum, Kean); Question 2 Content Validity (Hammond, Kaelin); Question 3 Reliability (Sherer, Biester, Seel); Question 4 Criterion Validity (Zafonte, Katz); Question 5 Construct Validity–Rasch Model (Seel Velozo, Graves); Question 6 Diagnostic Validity (Sherer, Rosenbaum); Question 7 Prognostic Validity (Katz, Hammond); Clinical Practice Recommendations (Seel, Katz); Discussion–Practical Recommendations and Lack of Criterion Standard (Whyte, Seel); Discussion–Prognostic Validity (Pape, Seel); Research Recommendations (Kalmar, Seel, Whyte).

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0003-9993/10/9112-00412$36.00/0
doi:10.1016/j.apmr.2010.07.218

Objectives: To conduct a systematic review of behavioral assessment scales for disorders of consciousness (DOC); provide evidence-based recommendations for clinical use based on their content validity, reliability, diagnostic validity, and ability to predict functional outcomes; and provide research recommendations on DOC scale development and validation.

Data Sources: Articles published through March 31, 2009, using MEDLINE, CINAHL, Psychology and Behavioral Sciences Collection, Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects, Cochrane Central Register of Controlled Trials, Biomedical Reference Collection, and PsycINFO. Thirteen primary terms that defined DOC were paired with 30 secondary terms that defined aspects of measurement. Scale names, abbreviations, and authors were also used as search terms. Task force members identified additional articles by using personal knowledge and examination of references in reviewed articles.

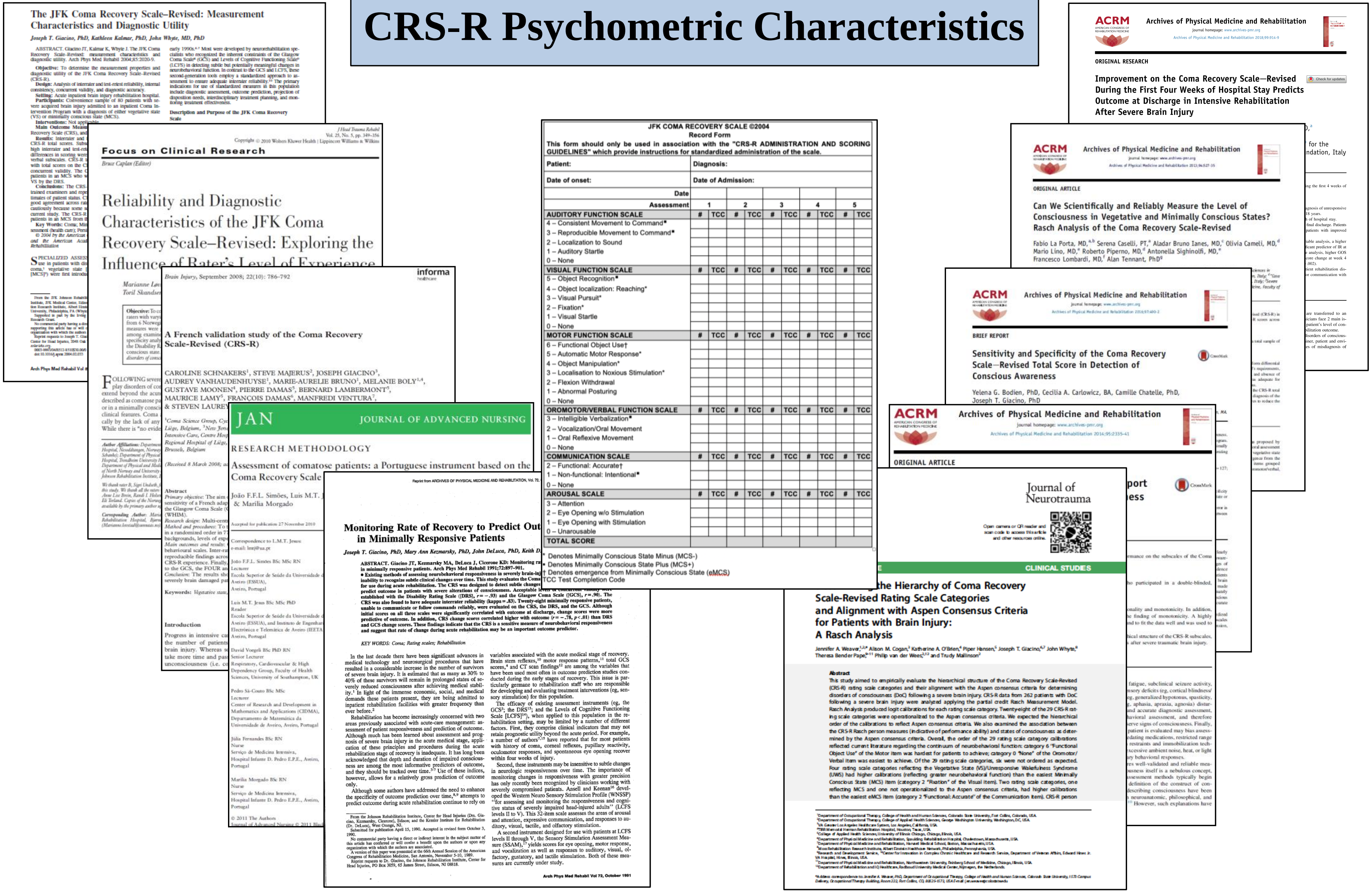
Study Selection: Primary criteria included the following: (1) provided reliability, diagnostic validity, and/or prognostic validity data; (2) examined a cohort, case control, or case series sample of persons with DOC who were age older than or equal to 18 years; and (3) assessed in an acute care or rehabilitation setting. Articles were excluded if peer review was not conducted, original data were not reported, or an English language article was not available. The initial search yielded 580 articles. After paired rater review of study abstracts, guideline development was based on 37 articles representing 13 DOC scales.

Data Extraction: Rater pairs classified studies addressing diagnostic and prognostic validity by using the American Academy of Neurology 4-tier level of evidence scheme, and reliability by using a task force–developed 3-tier evidence scheme. An independent quality review of ratings was conducted, and corrections were made.

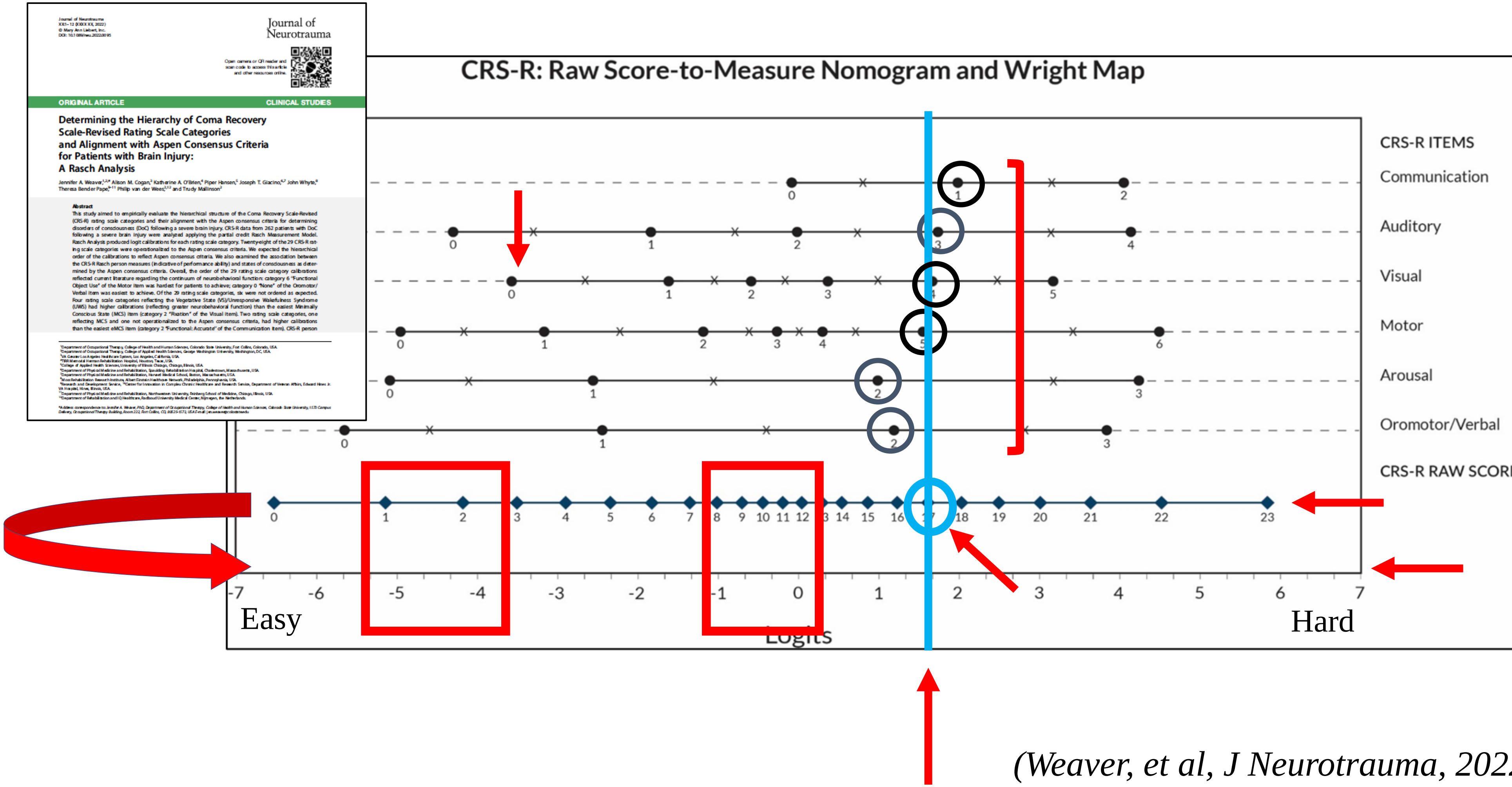
Data Synthesis: The Coma Recovery Scale-Revised (CRS-R), Sensory Stimulation Assessment Measure (SSAM), Wessex Head Injury Matrix (WHIM), Western Neuro Sensory Stimulation Profile (WNSSP), Sensory Modality Assessment Technique (SMART), Disorders of Consciousness Scale (DOCS), and Coma/Near-Coma Scale (CNC) have acceptable standardized administration and scoring procedures. The CRS-R has excellent content validity and is the only scale to address all Aspen Workgroup criteria. The SMART, SSAM, WHIM, and WNSSP demonstrate good content validity, containing items that could distinguish persons who are in a vegetative state, are in a minimally conscious state (MCS), or have emerged from MCS. The Full Outline of UnResponsiveness Score (FOUR), WNSSP, CRS-R, Comprehensive Levels of Consciousness Scale (CLOCS), and Innsbruck Coma Scale (INNS) showed substantial evidence of

Arch Phys Med Rehabil Vol 91, December 2010

CRS-R Psychometric Characteristics



CRS-R Recovery Ruler



(Weaver, et al, J Neurotrauma, 2022)

Challenges assessing consciousness in the ICU

- Sedation
  - When lifted, typically have only a few minutes for exam
- Peripheral injuries
- Medical complications (i.e., infection, seizure)
- Interruptions for clinical management
- Time constraints

Assessment of LoC in the ICU

GLASGOW COMA SCALE : Do it this way

GCS — EYES, VERBAL, MOTOR

Institute of Neurological Sciences NHS Greater Glasgow and Clyde

CHECK — For factors Interfering with communication, ability to respond and other injuries

OBSERVE — Eye opening , content of speech and movements of right and left sides

STIMULATE — Sound: spoken or shouted request. Physical: Pressure on finger tip, trapezius or supraorbital notch

RATE — Assign according to highest response observed

Eye opening

Criterion	Observed	Rating	Score
Open before stimulus	✓	Spontaneous	4
After spoken or shouted request	✓	To sound	3
After finger tip stimulus	✓	To pressure	2
No opening at any time, no interfering factor	✓	None	1
Closed by local factor	✓	Non testable	NT

Verbal response

Criterion	Observed	Rating	Score
Correctly gives name, place and date	✓	Orientated	5
Not orientated but communication coherently	✓	Confused	4
Intelligible single words	✓	Words	3
Only moans / groans	✓	Sounds	2
No audible response, no interfering factor	✓	None	1
Factor interferring with communication	✓	Non testable	NT

Best motor response

Criterion	Observed	Rating	Score
Obey 2-part request	✓	Obeys commands	6
Brings hand above clavicle to stimulus on head neck	✓	Localising	5
Bends arm at elbow rapidly but features not predominantly abnormal	✓	Normal flexion	4
Bends arm at elbow, features clearly predominantly abnormal	✓	Abnormal flexion	3
Extends arm at elbow	✓	Extension	2
No movement in arms / legs, no interfering factor	✓	None	1
Paralysed or other limiting factor	✓	Non testable	NT

Sites For Physical Stimulation

Finger tip pressure — Trapezius Pinch — Supraorbital notch

Features of Flexion Responses

Modified with permission from Van Der Naalt 2004 Ned Tijdschr Geneeskd

Abnormal Flexion: Slow Sterotyped, Arm across chest, Forearm rotates, Thumb clenched, Leg extends

Normal flexion: Rapid, Variable, Arm away from body

For further information and video demonstration visit www.glasgowcomascale.org

Teasdale and Jennett, Lancet, 1974

Multiple DoC diagnoses associated with same GCS score

Journal of Neurotrauma
38:3295–3305 (December 1, 2021)

DOI: 10.1089/neu.2021.0199

Journal of Neurotrauma

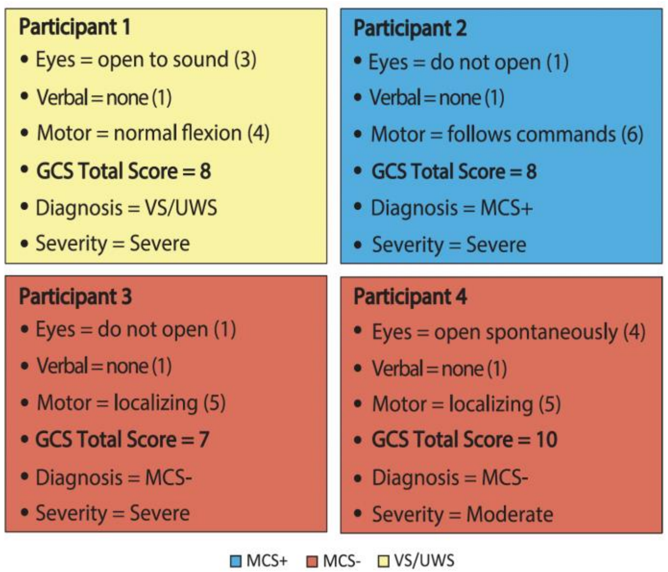
ORIGINAL ARTICLE CLINICAL STUDIES

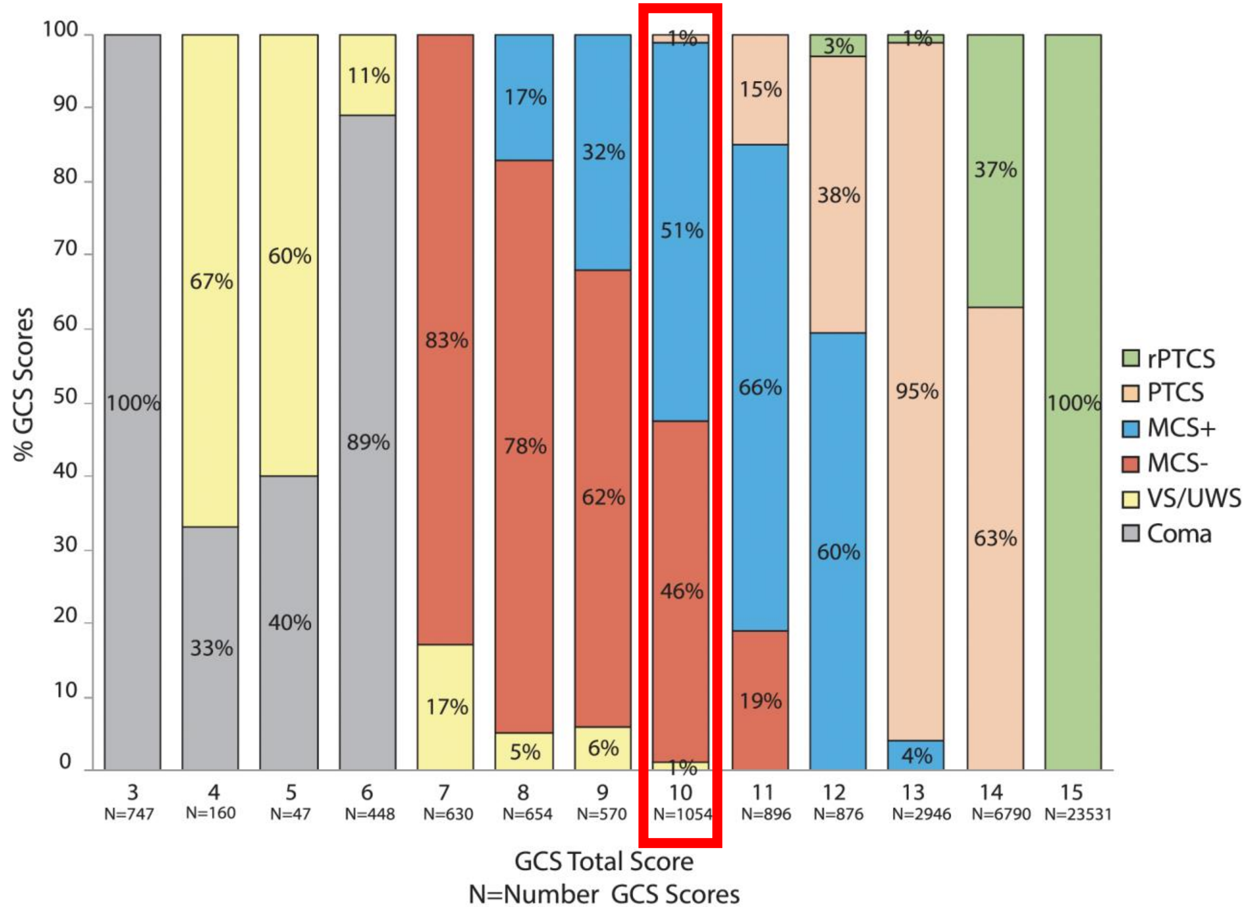
Diagnosing Level of Consciousness: The Limits of the Glasgow Coma Scale Total Score

Yelena G. Bodien,[1,2,*,**] Alice Barra,[1,3,4,**] Nancy R. Temkin,[5,6] Jason Barber,[5] Brandon Foreman,[7] Mary Vassar,[8] Claudia Robertson,[9] Sabrina R. Taylor,[8] Amy J. Markowitz,[8] Geoffrey T. Manley,[8] Joseph T. Giacino,[1,***] Brian L. Edlow[2,10,***]; and the TRACK-TBI Investigators[****]

Same score/ Different diagnosis

Same diagnosis/ Different score





CRSR for Accelerated Standardized Testing (CRSR-FAST)

BRIEF COMMUNICATION

Feasibility and Validity of the Coma Recovery Scale-Revised for Accelerated Standardized Testing: A Practical Assessment Tool for Detecting Consciousness in the Intensive Care Unit

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We developed and validated an abbreviated version of the Coma Recovery Scale-Revised (CRS-R), the CRS-R For Accelerated Standardized Testing (CRSR-FAST), to detect conscious awareness in patients with severe traumatic brain injury in the intensive care unit. In 45 consecutively enrolled patients, CRSR-FAST administration time was approximately one-third of the full-length CRS-R (mean [SD] 6.5 [3.3] vs 20.1 [7.2] minutes, $p < 0.0001$). Concurrent validity (simple kappa 0.68), test–retest (Mak's $\rho = 0.76$), and inter-rater (Mak's $\rho = 0.91$) reliability were substantial. Sensitivity, specificity, and accuracy for detecting consciousness were 81%, 89%, and 84%, respectively. The CRSR-FAST facilitates serial assessment of consciousness, which is essential for diagnostic and prognostic accuracy.

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Introduction

Bedside examination plays a key role in clinical management of patients with disorders of consciousness (DoC) in the intensive care unit (ICU) and, in addition to serving as the gold standard for diagnostic assessment, is the primary means of determining intensity of care, detecting complications, monitoring rate of recovery, establishing prognosis, and planning discharge disposition.[1] However, studies of diagnostic accuracy in patients with DoC conducted in both acute and post-acute settings consistently indicate that 30–40% of those judged to be unconscious on bedside examination actually retain some degree of conscious awareness.[2] Failure to detect signs of conscious awareness may inappropriately influence clinical decision-making, lead to premature withdrawal of life-sustaining therapy, and limit access to medical and rehabilitation services.

The Glasgow Coma Scale[3] and the Full Outline of UnResponsiveness[4] score are brief and widely used assessment scales developed to detect changes in level of consciousness in acutely injured patients. However, neither scale was designed to quantify level of consciousness or differentiate the minimally conscious state (MCS) from

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- Standardized assessment and scoring procedures improve consistency
- Item content accurately captures subtle behavioral signs of consciousness
- Adequate validity, interrater reliability, test-retest reliability, diagnostic accuracy (conscious/unconscious; MCS+/MCS-)
- Identifies factors confounding consciousness
- Rapid administration time facilitates serial assessment (<7 mins)
  - Discontinue on detection of first sign of consciousness

CRSR for Accelerated Standardized Testing (CRSR-FAST)

CRSR-FAST Record Form

Patient:____________ Date: ___________ Start Time:________(hh:mm) End Time:_____(hh:mm) Examiner:____

Administer each item per guidelines until a scoreable response is obtained		
Present (1=yes, 0=no)	**Item**	**Responses**
	Reproducible command following	___ ___ ___ ___ / ___ ___ ___ ___
	Fixation/Visual pursuit	___ ___ ___ ___ / ___ ___ ___ ___
	Automatic motor response	______________ / ______________
	Localization to noxious stimulation	___ ___ ___ ___
	Intelligible expression	______________ / ______________
Supplementary Items		
	Functional object use	_ _ _ _ / _ _ _ _
	Functional/accurate communication	_ _ _ _ _ _
	Non-Functional/intentional communication	_ _ _ _ _ _ _ _ _ _ _ _

Trial scoring key: 0 =no response; - = incorrect response; + = correct

Resting Posture	
RUE:	RLE:
LUE:	LLE:

Spontaneous Behaviors
Eye Opening:
Visual Tracking:
Active or Automatic Movements:

Psychoactive Medications/Paralytics (use Notes section for additional medications)			
Name	1.	2.	3.
Dose			
Time admin.	hh:mm	hh:mm	hh:mm
Time lifted			

Check all potential confounders to exam findings	
	Psychoactive agents not lifted for exam
	General anesthesia within 24 hrs
	Ictal event within 24 hrs
	Intubation
	Fever >99 within 2 hrs of exam
	Underarousal (i.e. sustained eye closure for >3 seconds)
	No confounding factors

Notes: Record observations or concerns that may influence or ambiguate scoring of any items

___:# times Arousal Facilitation Protocol administered

Test Completion Codes- circle one			
1	test completed in full, in person- results valid		
Test attempted, not completed due to:		**Test not attempted due to:**	
2.1	impaired sensory function (cortical or peripheral)	3.1	impaired sensory function (cortical or peripheral)
2.2	aphasia	3.2	aphasia
2.3	physical injury (e.g., fracture, brachial plexus, hemiparesis)	3.3	physical injury (e.g., fracture, brachial plexus, hemiparesis)
2.4	primary language barrier	3.4	primary language barrier
2.5	illness/medical instability	3.5	illness/medical instability
2.6	examiner error	3.6	examiner error
2.7	logistical reasons	3.7	logistical reasons
2.8	other (specify):	3.8	other (specify):

Present	CRSR-FAST Item
MCS+	Reproducible command following
MCS-	Visual fixation/pursuit
MCS-	Automatic motor response
MCS-	Localization to noxious stimulation
MCS+	Intelligible expression

Recommendations for Diagnostic Assessment

Recommendation Statement 2b

- To reduce diagnostic error in individuals with prolonged DoC after brain injury, ***serial standardized neurobehavioral assessments should be performed*** with the interval of reassessment determined by individual clinical circumstances (**Level B** based on cogency, feasibility, and cost relative to benefit).

(Giacino et al., DoC Practice Guideline Update, Neurol 2018)

Conduct serial examinations

TABLE 1. Misdiagnosis Rates of Patients After *n* CRS-R Assessments as Compared to the Reference Diagnosis

No. of CRS-R Assessments Used for Comparison With Reference Diagnosis	Misdiagnosis (reference diagnosis based on six CRS-R assessments, n = 123)	Effect Size (r = Z/sqrt(2n))	Misdiagnosis (reference diagnosis based on seven CRS-R assessments, n = 58)	Effect Size (r = Z/sqrt(2n))
One assessment	44 (36%) Z = 5.78***	0.37	28 (48%) Z = 4.62***	0.43
Two assessments	30 (24%) Z = 4.78***	0.30	20 (34%) Z = 3.92***	0.36
Three assessments	21 (17%) Z = 4.01***	0.26	15 (26%) Z = 3.41**	0.32
Four assessments	11 (9%) Z = 2.93*	0.19	10 (17%) Z = 2.80*	0.26
Five assessments	6 (5%) Z = 2.2; n.s.	0.14	6 (10%) Z = 2.2; n.s.	0.10
Six assessments	N/A	N/A	2 (3%) Z = 1.34; n.s.	0.03

***Corrected $p < 0.0005$; **corrected $p < 0.005$; *corrected $p < 0.05$; n.s. = not significant.
CRS-R = Coma Recovery Scale-Revised; N/A = not applicable.

(Wannez et al, Annals Neurol, 2017)

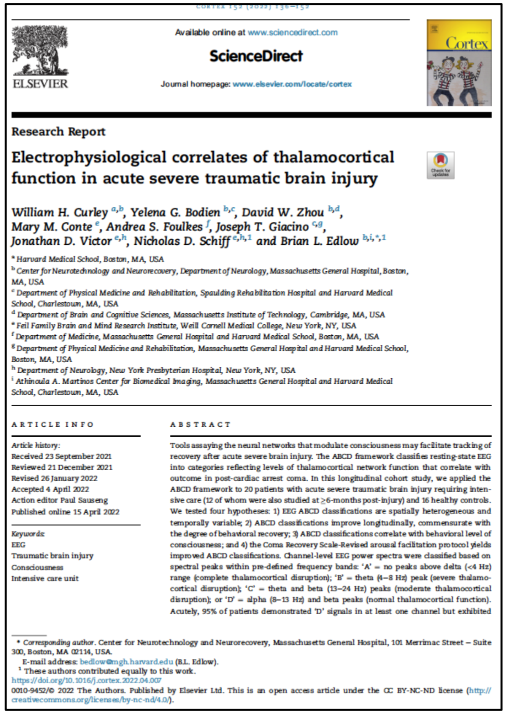
Recommendations for Diagnostic Assessment

Recommendation Statement 2c

- Clinicians should ***attempt to increase arousal*** before performing evaluations to assess level of consciousness anytime diminished arousal is observed or suspected (Level B based on importance of outcomes).

(Giacino et al., Neurol, 2018; Curley, et al, Cortex, 2022)

Factors Influencing Diagnostic Accuracy: Fluctuation in arousal level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ScienceDirect
Journal homepage: www.elsevier.com/locate/cortex

Research Report

Electrophysiological correlates of thalamocortical function in acute severe traumatic brain injury

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ABSTRACT

Tools assaying the neural networks that modulate consciousness may facilitate tracking of recovery after acute severe brain injury. The ABCD framework classifies resting-state EEG into categories reflecting levels of thalamocortical network function that correlate with outcome in post-cardiac arrest coma. In this longitudinal cohort study, we applied the ABCD framework to 20 patients with acute severe traumatic brain injury requiring intensive care (12 of whom were also studied at ≥6-months post-injury) and 16 healthy controls. We tested four hypotheses: 1) EEG ABCD classifications are spatially heterogeneous and temporally variable; 2) ABCD classifications improve longitudinally, commensurate with the degree of behavioral recovery; 3) ABCD classifications correlate with behavioral level of consciousness; and 4) the Coma Recovery Scale-Revised arousal facilitation protocol yields improved ABCD classifications. Channel-level EEG power spectra were classified based on spectral peaks within pre-defined frequency bands: 'A' = no peaks above delta (<4 Hz) range (complete thalamocortical disruption); 'B' = theta (4–8 Hz) peak (severe thalamocortical disruption); 'C' = theta and beta (13–24 Hz) peaks (moderate thalamocortical disruption); or 'D' = alpha (8–13 Hz) and beta peaks (normal thalamocortical function). Acutely, 95% of patients demonstrated 'D' signals in at least one channel but exhibited

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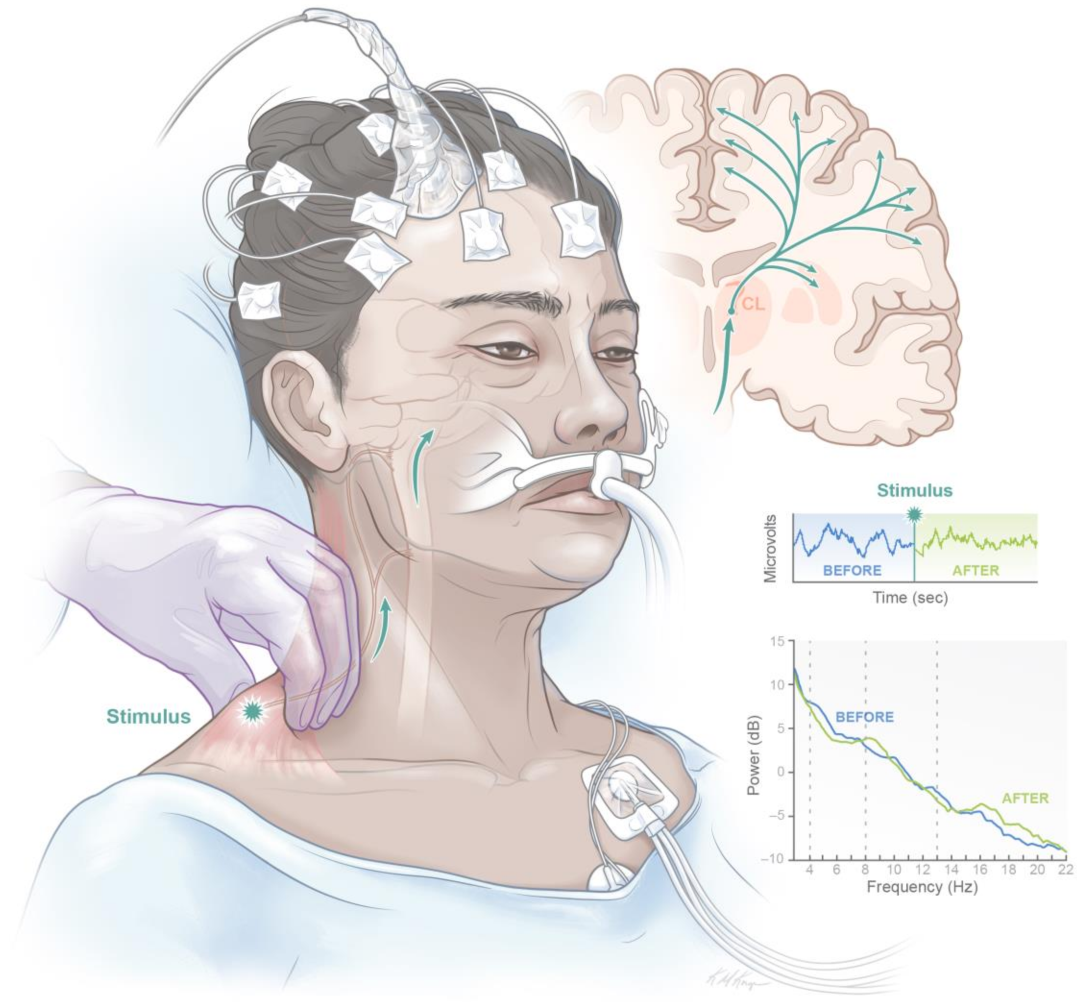
Arousal Facilitation



Curley et al. *Cortex* 2022

W. Curley

Recommendations for Diagnostic Assessment

Recommendation Statement 2d

- Clinicians should ***identify and treat conditions*** that may confound accurate diagnosis of a DoC prior to establishing a final diagnosis. **Level** B based on feasibility and cost.

Identify and treat confounding medical problems

ACRM
AMERICAN CONGRESS OF REHABILITATION MEDICINE

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JOURNAL-BASED CME ARTICLE

Medical Complications During Inpatient Rehabilitation Among Patients With Traumatic Disorders of Consciousness

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Statement of Need

Patients with DOCs have a high rate of medical complications early after injury. Many of these complications require brain injury expertise for optimal management. Active medical management appears to contribute to the reduction in new complications. An optimal system of care for DOC

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Table 2 Common events

Medical Complication	No. of Events	% of All Events	% Severe
Hypertonia/spasticity*	39	8.3	12.8
Agitation/aggression*	30	6.4	6.7
Urinary tract infection	30	6.4	3.3
Insomina/sleep disturbance*	29	6.2	3.4
Motor restlessness/hyperkinesia*	22	4.7	9.0
Vomiting	20	4.3	10.0
Other abnormal laboratory finding (including 8 cases of hyponatremia)	17	3.6	5.9
Pneumonia	14	3	64.3
Other GI problem (eg, GI bleeding, bowel obstruction, peritonitis)	13	2.8	38.5
Autonomic storm/PSH*	12	2.6	25.0
Skin rash	12	2.6	0.0
Diarrhea	12	2.6	8.3
Hydrocephalus*	10	2.1	70.0
Tachycardia	10	2.1	0.0
Upper respiratory tract infection	10	2.1	10.0
Total	280	59.8	

Abbreviation: GI, gastrointestinal.
*Problems that are characteristic of severe TBI and may require expertise with this patient population for optimal management.

Limitations of Behavioral Assessment

- Behavior is a poor proxy for conscious awareness
  - Eg, Cannot definitively differentiate volitional from involuntary or reflexive movement (eg, smiling)
- Confounds arising from co-existing sensory (eg, blindness), motor (eg, contractures) and cognitive impairments (eg, aphasia)
- Subjective bias of examiner

(Giacino & Smart, Curr Opin Neurol, 2007)

Practice Recommendations

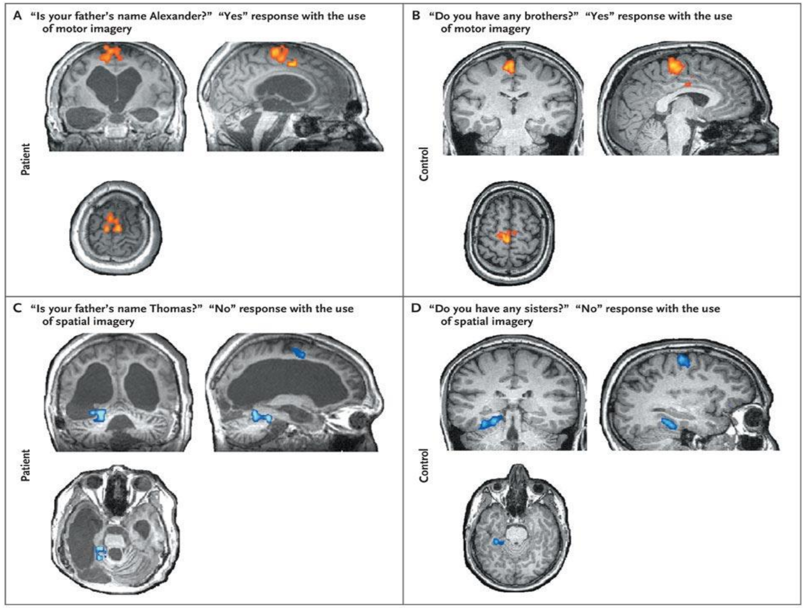
Recommendation Statements 2e

- In situations where there is continued ambiguity regarding evidence of conscious awareness despite serial neurobehavioral assessments, or where confounders to a valid clinical diagnostic assessment are identified, clinicians may use multimodal evaluations incorporating specialized functional imaging or electrophysiologic studies to assess for evidence of awareness not identified on neurobehavioral assessment that might prompt consideration of an alternate diagnosis (**Level C** based on assessment of benefit relative to harm, feasibility, and cost relative to benefit).

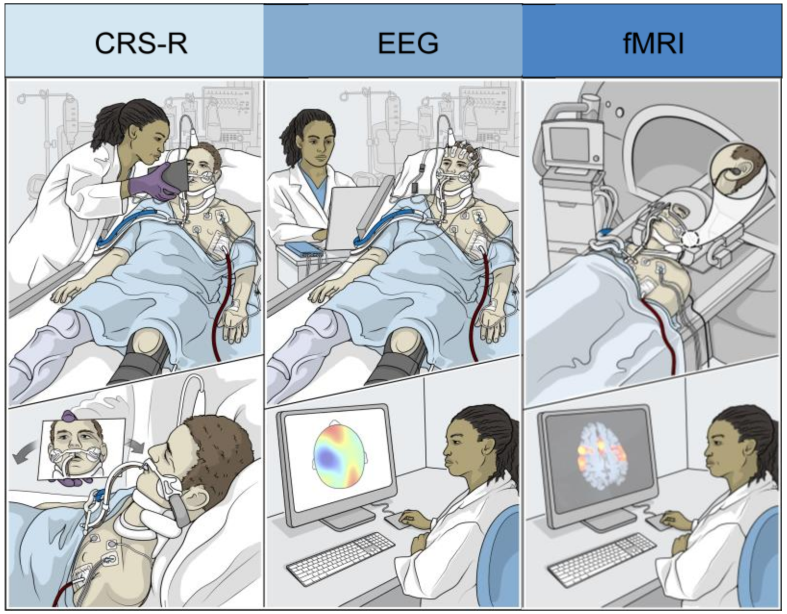
The Problem of Covert Consciousness

- Cognitive Motor Dissociation (CMD)

  Activation of language association cortex on fMRI and EEG studies in response to ***active*** *language stimuli (ie, verbal instructions to perform a task) when there is no evidence of volitional behavior on bedside examination (Schiff, JAMA Neurol 2015)*



(Owen, et al, Science, 2006, Monti, et al, NEJM, 2012)



(Edlow, et al., Brain, 2017)

Multimodal Assessment and the Level of Certainty Conundrum

	CRS-R		fMRI/PET		EEG		Family		Confidence Level
	+	-	+	-	+	-	+	-	
P1	x		x		x		x		High
P2		x		x		x		x	High
P3		x	x		x		x		Mod
P4		x	x		x			x	Mod
P5		x		x		x	x		Low
P6		x		x	x			x	Low

Natural History of Recovery

- *During inpatient rehabilitation*
- *Over the course of the first year post-injury*
- *Between 1 and 10 years post-injury*

Which behavioral signs of consciousness emerge first?

Annals of Physical and Rehabilitation Medicine 63 (2020) 263–269

Original article

Which behaviours are first to emerge during recovery of consciousness after severe brain injury?

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A R T I C L E I N F O

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Minimally conscious state
Outcome

A B S T R A C T

Background: Early detection of consciousness after severe brain injury is critical for establishing an accurate prognosis and planning appropriate treatment.
Objectives: To determine which behavioural signs of consciousness emerge first and to estimate the time course to recovery of consciousness in patients with severe acquired brain injury.
Methods: Retrospective observational study using the Coma Recovery Scale-Revised and days to recovery of consciousness in 79 patients (51 males; 34 with traumatic brain injury; median [IQR] age 48 [26–61] years; median time since injury 26 [20–36] days) who transitioned from coma or unresponsive wakefulness syndrome (UWS)/vegetative state (VS) to the minimally conscious state (MCS) or emerged from MCS during inpatient rehabilitation.
Results: Visual pursuit was the most common initial sign of MCS (41% of patients; 95% CI [30–52]), followed by reproducible command-following (25% [16–35]) and automatic movements (24% [15–33]). Ten other behaviours emerged first in less than 16% of cases. Median [IQR] time to recovery of consciousness was 44 [33–59] days. Etiology did not significantly affect time to recovered consciousness.
Conclusion: Recovery of consciousness after severe brain injury is most often signalled by reemergence of visual pursuit, reproducible command-following and automatic movements. Clinicians should use assessment measures that are sensitive to these behaviours because early detection of consciousness is critical for accurate prognostication and treatment planning.

1. Introduction

Severe brain injury frequently results in a period of altered consciousness characterized by impaired arousal and awareness [1,2]. Disorders of consciousness (DoC) include coma, a state of continuous eye closure and no behavioural signs of self or environmental awareness [3]; the vegetative state (VS), also referred to as unresponsive wakefulness syndrome (UWS), in which there is eye-opening but still no behavioural signs of awareness [4]; and the minimally conscious state (MCS), a condition characterized by reproducible but fluctuating behavioural signs of awareness. Emergence from MCS (eMCS) is marked by recovery of reliable communication and/or appropriate use of objects [5]. Detecting the transition from an unconscious to conscious state is critically important in clinical management, discharge disposition planning and family counselling. Unfortunately, diagnostic error remains high in this population, consistently reported to be around 40% [6–8].

The Coma Recovery Scale-Revised (CRS-R) [9], a standardized behavioural assessment scale consisting of 23 items hierarchically organized within 6 subscales that assess auditory, visual, motor, verbal, communication and arousal functions, is recommended for clinical use in patients with DoC by the American Congress of Rehabilitation Medicine in view of its strong psychometric properties [10]. Diagnostic assessment with the CRS-R has been

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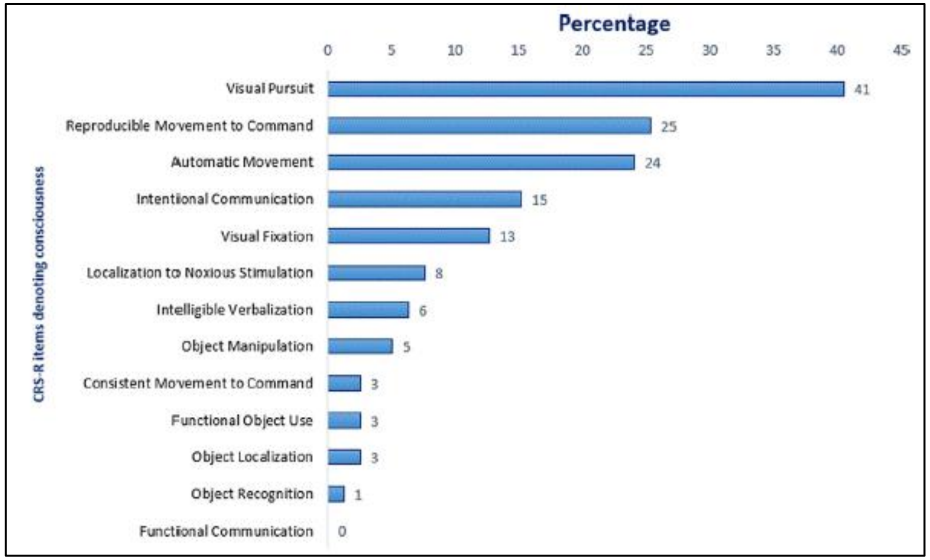

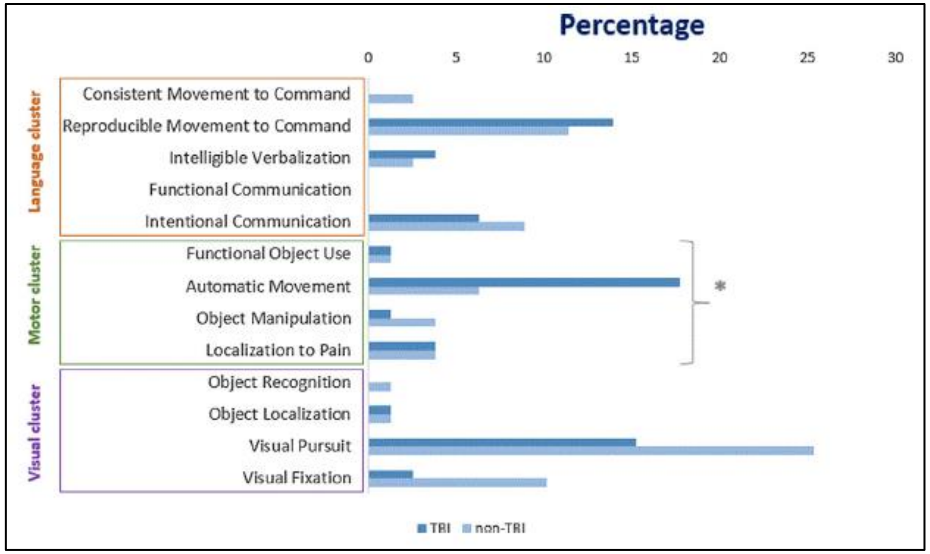

Recovery During Inpatient Rehabilitation

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Mary Ann Liebert, Inc.
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Behavioral Recovery and Early Decision Making in Patients with Prolonged Disturbance in Consciousness after Traumatic Brain Injury

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Flora M. Hammond,[7,8] David Long,[9] and Emilia Bagiella[10]

Abstract

The extent of behavioral recovery that occurs in patients with traumatic disorders of consciousness (DoC) following discharge from the acute care setting has been under-studied and increases the risk of overly pessimistic outcome prediction. The aim of this observational cohort study was to systematically track behavioral and functional recovery in patients with prolonged traumatic DoC following discharge from the acute care setting. Standardized behavioral data were acquired from 95 patients in a minimally conscious (MCS) or vegetative state (VS) recruited from 11 clinic sites and randomly assigned to the placebo arm of a previously completed prospective clinical trial. Patients were followed for 6 weeks by blinded observers to determine frequency of recovery of six target behaviors associated with functional status. The Coma Recovery Scale-Revised and Disability Rating Scale were used to track reemergence of target behaviors and assess degree of functional disability, respectively. Twenty percent (95% confidence interval [CI]: 13–30%) of participants (mean age 37.2; median 47 days post-injury; 69 men) recovered all six target behaviors within the 6 week observation period. The odds of recovering a specific target behavior were 3.2 (95% CI: 1.2–8.1) to 7.8 (95% CI: 2.7–23.0) times higher for patients in MCS than for those in VS. Patients with preserved language function ("MCS+") recovered the most behaviors ($p \leq 0.002$) and had the least disability ($p \leq 0.002$) at follow-up. These findings suggest that recovery of high-level behaviors underpinning functional independence is common in patients with prolonged traumatic DoC. Clinicians involved in early prognostic counseling should recognize that failure to emerge from traumatic DoC before 28 days does not necessarily portend unfavorable outcome.

Keywords: consciousness; MCS; outcome research; TBI; VS

Introduction

MONITORING BEHAVIORAL RECOVERY in patients who develop disorders of consciousness (DoC) after severe traumatic brain injury (TBI) is an essential component of diagnostic and prognostic assessment. Following emergence from coma, patients transition into the vegetative state (VS) or the minimally conscious state (MCS). In VS, sleep–wake cycles are restored but there is no behavioral evidence of awareness.[1] In MCS, there is at least one definitive behavioral sign of conscious awareness.[2] The diagnosis of "MCS+" (v. "MCS-") is made when the features of MCS include behavioral evidence of language comprehension or expression.[3] This dichotomy is supported by functional neuroimaging evidence of language network activation following exposure to verbal instructions in patients who meet diagnostic criteria for MCS.[4,5] Emergence from MCS is established when there are reliable yes–no responses to questions or reproducible instances of appropriate object use.[2] There is also evidence that re-emergence of specific behaviors foreshadows subsequent cognitive and functional recovery.[6–11]

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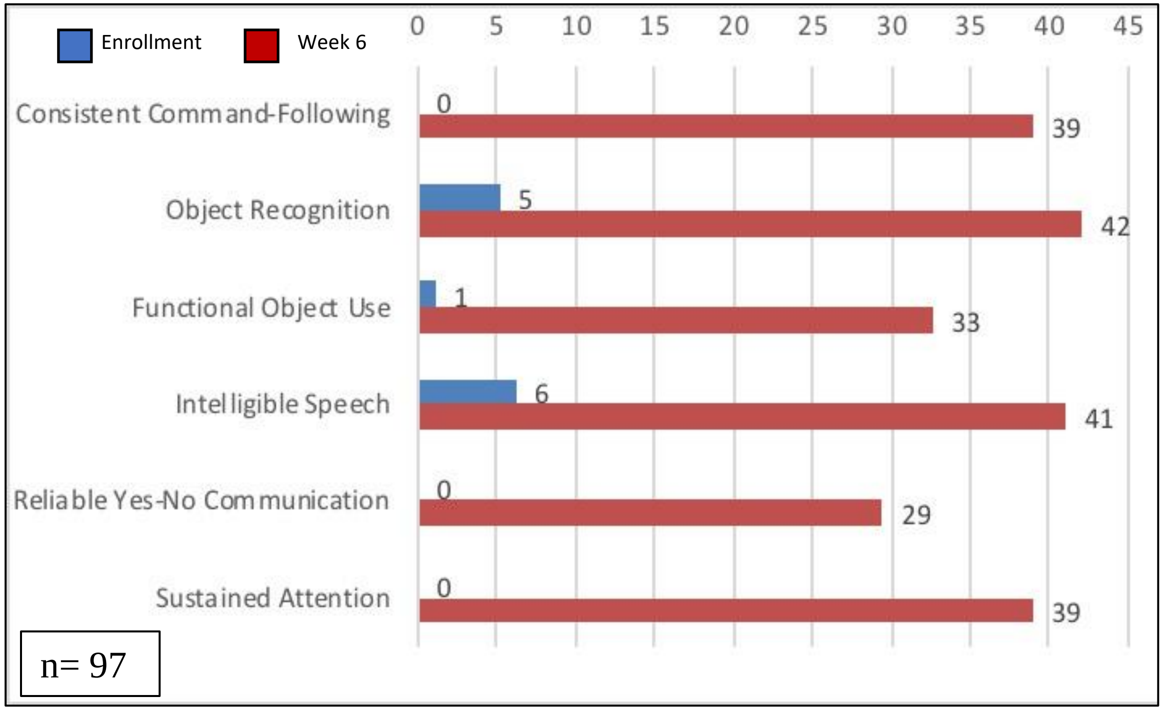
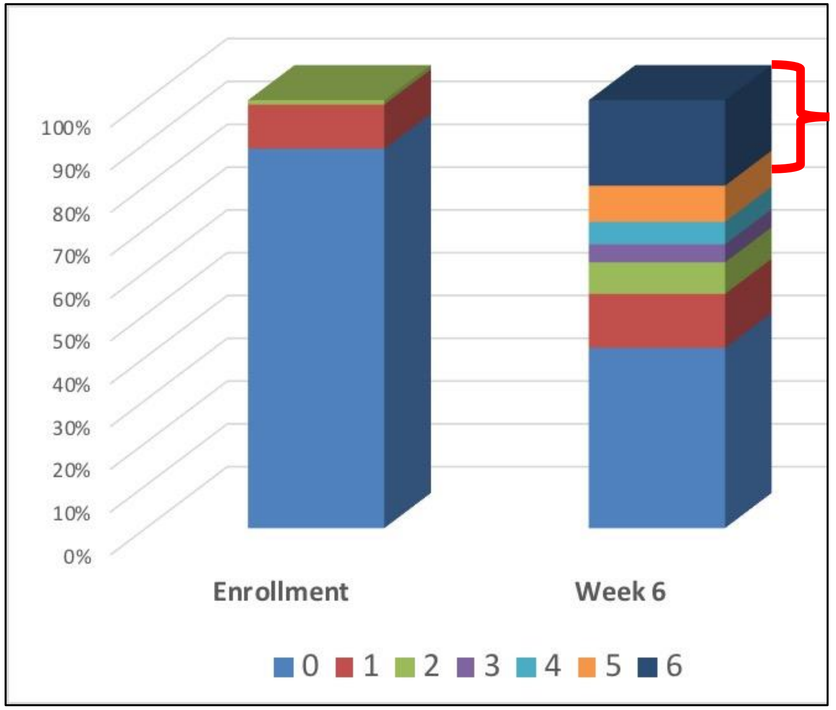
...Injury Program, Bryn Mawr Rehab Hospital, Malvern, Pennsylvania.
...for Biostatistics, Icahn School of Medicine at Mount Sinai, New York, New York.

- **Aim:** To determine the relationship between behavioral recovery over a 6-week observation period and degree of disability at rehab discharge.
- **Sample:** 97 adults diagnosed with traumatic VS or MCS who were enrolled in the placebo arm of the TBIMS amantadine trial at eight rehabilitation hospitals in the United States and three in Europe.
- **Outcomes:**
  - Proportion of sample demonstrating each target behavior (ie, highest-level item on each CRS-R subscale) within 6 weeks of enrollment
  - Total number of high-level behaviors present at week 6
  - Frequency of emergence from MCS by week 6
  - Median DRS score relative to the number of behaviors present at week 6.

TBIMS
Traumatic Brain Injury Model System
Since 1987

Key Findings





- *For each behavior recovered, DRS score improved by ≈ 2 points, resulting in a 12-point spread between patients who recovered all six behaviors and those who recovered none.*

Why These Findings Matter

- Critical prognostic decisions are generally made within 72 hours of injury, prior to recovery of command-following, speech and other conscious behaviors.

  ➡ Despite remaining in VS or MCS for a median of 47 days, 20% of the entire cohort recovered all six target behaviors within a 6-week observation period.

- Persistent VS (ie lasting at least 1 month) viewed as a dire condition with unfavorable prognosis for subsequent recovery.

  ➡ 20% of patients in VS at enrollment were consistently following commands by the end of the 6-week interval.

- Family members rank recovery of reliable communication among the most highly-valued outcomes.

  ➡ One in five patients who remained in traumatic VS or MCS for at least 4 weeks subsequently recovered the ability to communicate, verbalize intelligibly and/or follow commands.

Recovery of Consciousness and Function During Inpatient Rehabilitation

JAMA Neurology | Original Investigation

Recovery of Consciousness and Functional Outcome in Moderate and Severe Traumatic Brain Injury

Robert G. Kowalski, MBBCh, MS; Flora M. Hammond, MD; Alan H. Weintraub, MD; Risa Nakase-Richardson, PhD; Ross D. Zafonte, DO; John Whyte, MD, PhD; Joseph T. Giacino, PhD

Editorial
Supplemental content

IMPORTANCE Traumatic brain injury (TBI) leads to 2.9 million visits to US emergency departments annually and frequently involves a disorder of consciousness (DOC). Early treatment, including withdrawal of life-sustaining therapies and rehabilitation, is often predicated on the assumed worse outcome of disrupted consciousness.

OBJECTIVE To quantify the loss of consciousness, factors associated with recovery, and return to functional independence in a 31-year sample of patients with moderate or severe brain trauma.

DESIGN, SETTING, AND PARTICIPANTS This cohort study analyzed patients with TBI who were enrolled in the Traumatic Brain Injury Model Systems National Database, a prospective, multiyear, longitudinal database. Patients were survivors of moderate or severe TBI who were discharged from acute hospitalization and admitted to inpatient rehabilitation from January 4, 1989, to June 19, 2019, at 1 of 23 inpatient rehabilitation centers that participated in the Traumatic Brain Injury Model Systems program. Follow-up for the study was through completion of inpatient rehabilitation.

EXPOSURES Traumatic brain injury.

MAIN OUTCOMES AND MEASURES Outcome measures were Glasgow Coma Scale in the emergency department, Disability Rating Scale, posttraumatic amnesia, and Functional Independence Measure. Patient-related data included demographic characteristics, injury cause, and brain computed tomography findings.

RESULTS The 17 470 patients with TBI analyzed in this study had a median (interquartile range [IQR]) age at injury of 39 (25-56) years and included 12 854 male individuals (74%). Of these patients, 7547 (57%) experienced initial loss of consciousness, which persisted to rehabilitation in 2058 patients (12%). Those with persisting DOC were younger; had more high-velocity injuries; had intracranial mass effect, intraventricular hemorrhage, and subcortical contusion; and had longer acute care than patients without DOC. Eighty-two percent (n = 1674) of comatose patients recovered consciousness during inpatient rehabilitation. In a multivariable analysis, the factors associated with consciousness recovery were absence of intraventricular hemorrhage (adjusted odds ratio [OR], 0.678; 95% CI, 0.532-0.863; P = .002) and intracranial mass effect (adjusted OR, 0.759; 95% CI, 0.595-0.968; P = .03). Functional improvement (change in total functional independence score from admission to discharge) was +43 for patients with DOC and +37 for those without DOC (P = .002), and 803 of 2013 patients with DOC (40%) became partially or fully independent. Younger age, male sex, and absence of intraventricular hemorrhage, intracranial mass effect, and subcortical contusion were associated with better functional outcome. Findings were consistent across the 3 decades of the database.

CONCLUSIONS AND RELEVANCE This study found that DOC occurred initially in most patients with TBI and persisted in some patients after rehabilitation, but most patients with persisting DOC recovered consciousness during rehabilitation. This recovery trajectory may inform acute and rehabilitation treatment decisions and suggests caution is warranted in consideration of withdrawing or withholding care in patients with TBI and DOC.

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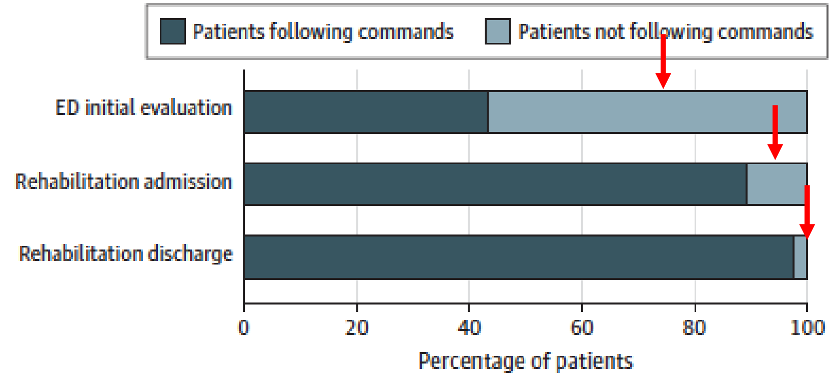
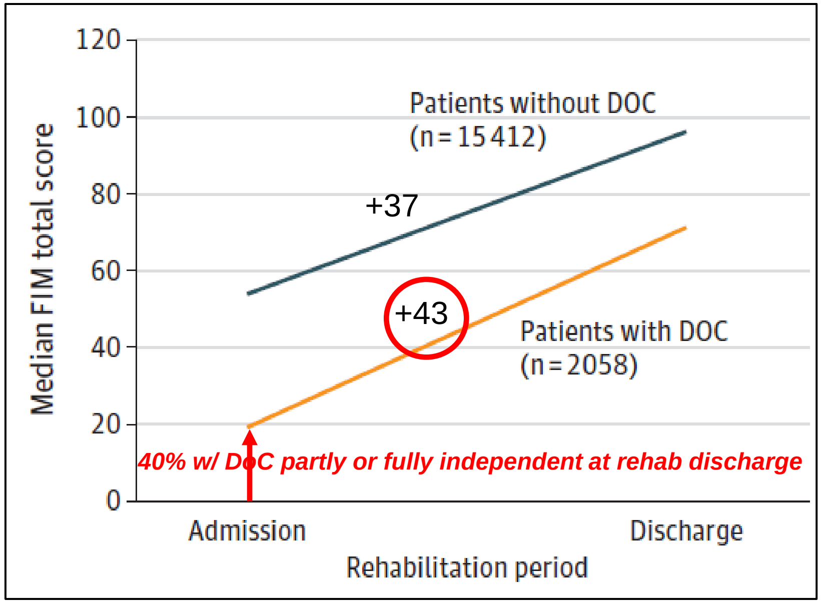
Figure 1. Progression in Percentage of Patients With Disorder of Consciousness During Treatment





Why These Findings Matter

- Protracted disturbance in consciousness is considered an ominous prognostic sign (high probability of severe disability).

  ➞ >80% of patients with DoC on admission to rehab recovered consciousness by rehab discharge.

- Lack of early improvement predicts lack of subsequent improvement.

  ➞ Patients with (v. w/o) DoC experienced *greater* absolute improvement during rehab
  ➞ Retain capacity for recovery of function but time course is delayed.

- Most frequent cause of death after TBI is WOLST, and the decision to stop treatment is typically made within 72 hours of the injury

  ➞ Clinicians should be cautious about suggesting high probability of poor outcome (and WOLST) within the first month post-injury in patients with severe TBI.

Recovery During the First Year Post-Injury

Research

JAMA Neurology | Original Investigation

Functional Outcomes Over the First Year After Moderate to Severe Traumatic Brain Injury in the Prospective, Longitudinal TRACK-TBI Study

Michael A. McCrea, PhD; Joseph T. Giacino, PhD; Jason Barber, MS; Nancy R. Temkin, PhD; Lindsay D. Nelson, PhD; Harvey S. Levin, PhD; Sureyya Dikmen, PhD; Murray Stein, MD, PhD; Yelena G. Bodien, PhD; Kim Boase, BA; Sabrina R. Taylor, PhD; Mary Vassar, RN, MS; Pratik Mukherjee, MD, PhD; Claudia Robertson, MD; Ramon Diaz-Arrastia, MD, PhD; David O. Okonkwo, MD, PhD; Amy J. Markowitz, JD; Geoffrey T. Manley, MD, PhD; and the TRACK-TBI Investigators

Supplemental content

IMPORTANCE Moderate to severe traumatic brain injury (msTBI) is a major cause of death and disability in the US and worldwide. Few studies have enabled prospective, longitudinal outcome data collection from the acute to chronic phases of recovery after msTBI.

OBJECTIVE To prospectively assess outcomes in major areas of life function at 2 weeks and 3, 6, and 12 months after msTBI.

DESIGN, SETTING, AND PARTICIPANTS This cohort study, as part of the Transforming Research and Clinical Knowledge in TBI (TRACK-TBI) study, was conducted at 18 level 1 trauma centers in the US from February 2014 to August 2018 and prospectively assessed longitudinal outcomes, with follow-up to 12 months postinjury. Participants were patients with msTBI (Glasgow Coma Scale scores 3-12) extracted from a larger group of patients with mild, moderate, or severe TBI who were enrolled in TRACK-TBI. Data analysis took place from October 2019 to April 2021.

EXPOSURES Moderate or severe TBI.

MAIN OUTCOMES AND MEASURES The Glasgow Outcome Scale–Extended (GOSE) and Disability Rating Scale (DRS) were used to assess global functional status 2 weeks and 3, 6, and 12 months postinjury. Scores on the GOSE were dichotomized to determine favorable (scores 4-8) vs unfavorable (scores 1-3) outcomes. Neurocognitive testing and patient reported outcomes at 12 months postinjury were analyzed.

RESULTS A total of 484 eligible patients were included from the 2679 individuals in the TRACK-TBI study. Participants with severe TBI (n = 362; 283 men [78.2%]; median [interquartile range] age, 35.5 [25-53] years) and moderate TBI (n = 122; 98 men [80.3%]; median [interquartile range] age, 38 [25-53] years) were comparable on demographic and premorbid variables. At 2 weeks postinjury, 36 of 290 participants with severe TBI (12.4%) and 38 of 93 participants with moderate TBI (41%) had favorable outcomes (GOSE scores 4-8); 301 of 322 in the severe TBI group (93.5%) and 81 of 103 in the moderate TBI group (78.6%) had moderate disability or worse on the DRS (total score ≥4). By 12 months postinjury, 142 of 271 with severe TBI (52.4%) and 54 of 72 with moderate TBI (75%) achieved favorable outcomes. Nearly 1 in 5 participants with severe TBI (52 of 270 [19.3%]) and 1 in 3 with moderate TBI (23 of 71 [32%]) reported no disability (DRS score 0) at 12 months. Among participants in a vegetative state at 2 weeks, 62 of 79 (78%) regained consciousness and 14 of 56 with available data (25%) regained orientation by 12 months.

CONCLUSIONS AND RELEVANCE In this study, patients with msTBI frequently demonstrated major functional gains, including recovery of independence, between 2 weeks and 12 months postinjury. Severe impairment in the short term did not portend poor outcomes in a substantial minority of patients with msTBI. When discussing prognosis during the first 2 weeks after injury, clinicians should be particularly cautious about making early, definitive prognostic statements suggesting poor outcomes and withdrawal of life-sustaining treatment in patients with msTBI.

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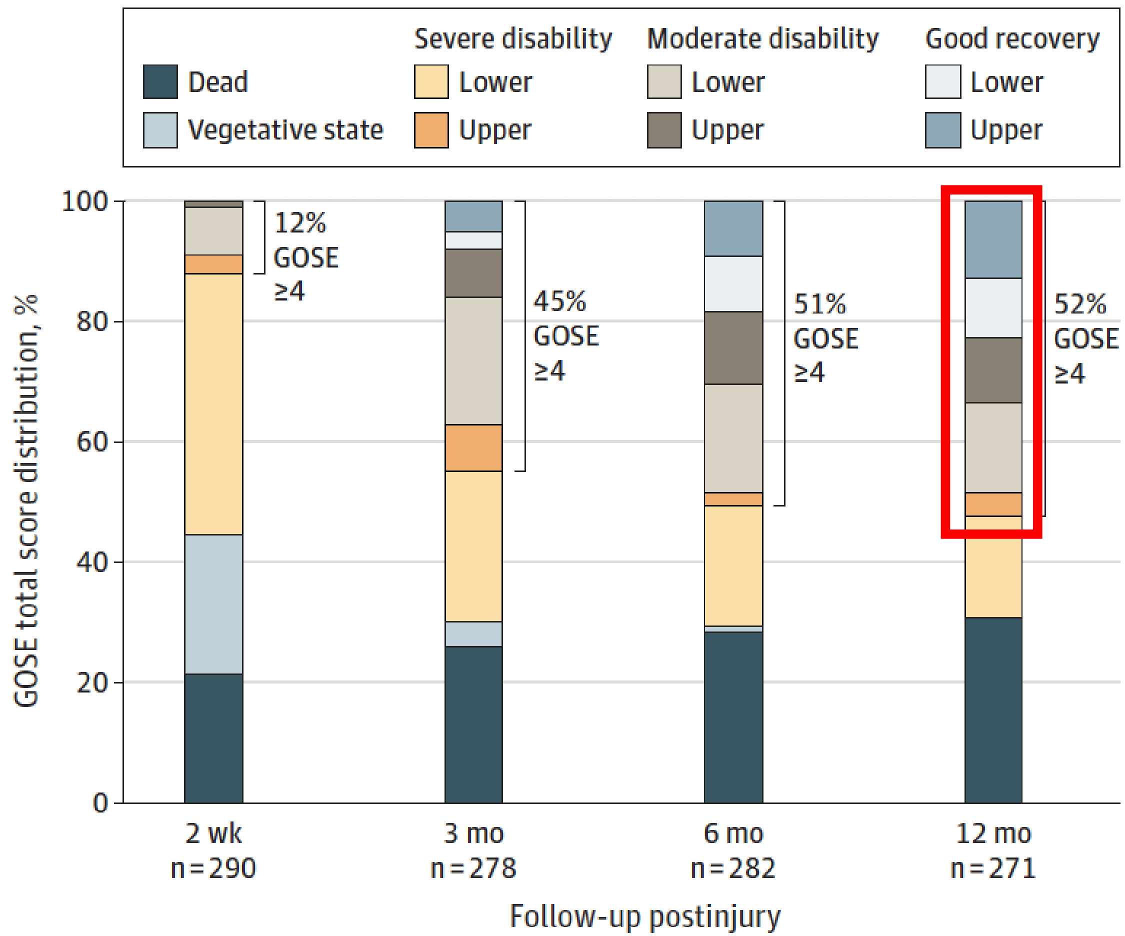
- **Aim:** To prospectively assess outcomes in major areas of life function at 2 weeks and 3, 6, and 12 months after moderate to severe TBI (msTBI).
- **Sample:** 362 patients with severe TBI (GCS=3-8) enrolled in Track-TBI between February 2014 and August 2018.
- **Outcomes:**
  - Primary:
    - Glasgow Outcome Scale- Extended (brain + peripheral injury scoring system)
  - Secondary:
    - Disability Rating Scale (DRS)
    - Rivermead PCS, BSI-18, Satisfaction with Life, Rey Auditory Verbal Learning Test, Trail Making Test, WAIS Processing Speed Index (not covered here)

TRACK-TBI
Transforming Research and Clinical Knowledge in Traumatic Brain Injury
International Traumatic Brain Injury Research Initiative

Key Findings

- > 50% of those with severe TBI recovered the ability to function independently at home for at least 8 hours per day.

Figure 1. Glasgow Outcome Scale–Extended (GOSE) Total Score Distribution for Patients With Severe Traumatic Brain Injury at 2 Weeks and 3, 6, and 12 Months Postinjury

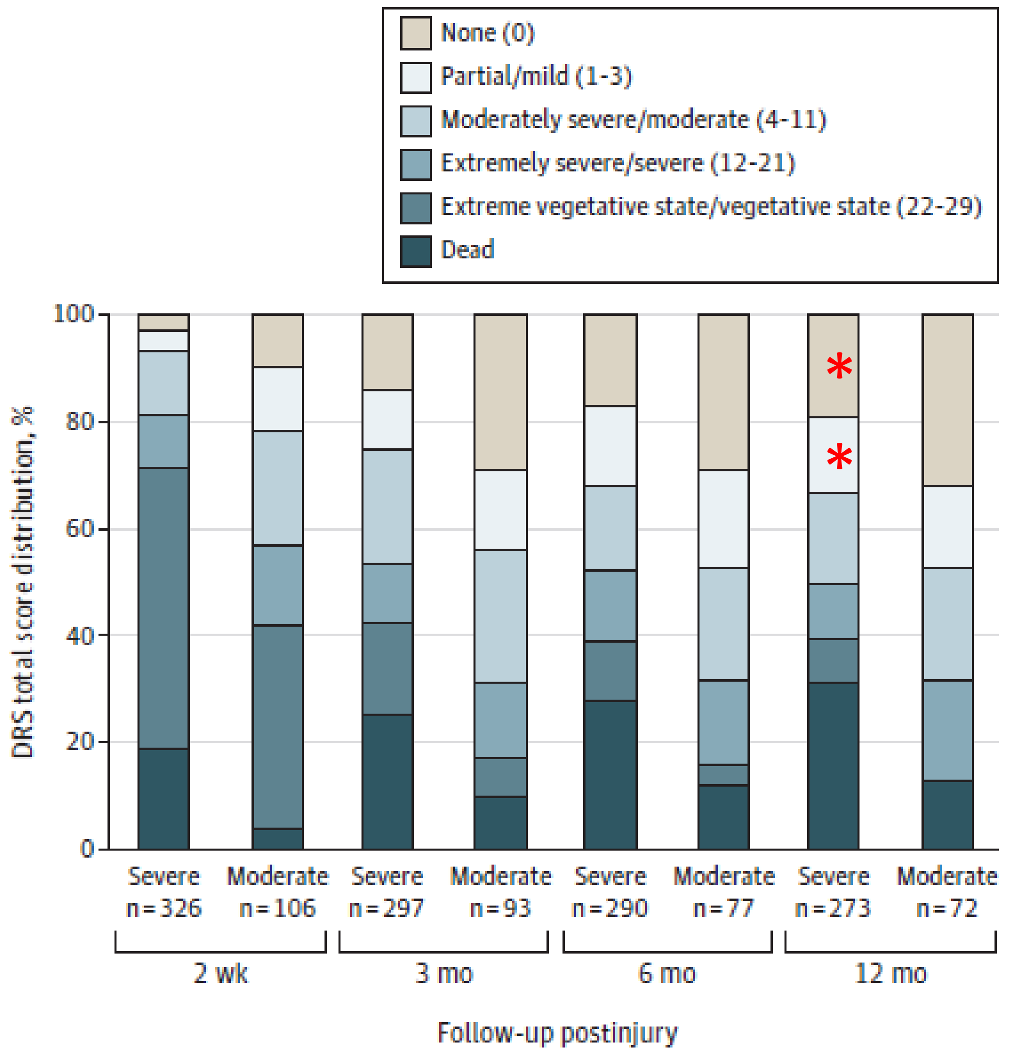


GCS 3-8

Key Findings

- Nearly 1 in 5 patients with severe TBI reported no disability (DRS score 0) at 12 months.

Figure 3. Disability Rating Scale (DRS) Total Score Distribution for Patients With Moderate or Severe Traumatic Brain Injury at 2 Weeks and 3, 6, and 12 Months Postinjury



Key Findings

Table 2. Frequencies Within Each Glasgow Outcome Scale–Extended (GOSE) Domain for Severe and Moderate Traumatic Brain Injury (TBI) Groups at 2 Weeks and 3, 6, and 12 Months Postinjury

GOSE domain severity in unweighted analyses	No. (%)[a] 2 wk Severe (n = 290)	2 wk Moderate (n = 93)	3 mo Severe (n = 278)	3 mo Moderate (n = 84)	6 mo Severe (n = 282)	6 mo Moderate (n = 75)	12 mo Severe (n = 271)	12 mo Moderate (n = 72)
Vegetative state and death								
Vegetative state	68 (23.4)	11 (12)	10 (3.6)	0	4 (1.4)	0	1 (0.4)	0
Died	60 (20.7)	4 (4)	73 (26.3)	9 (11)	78 (27.7)	9 (12)	83 (30.6)	9 (13)
Independence in the home								
No assistance	31 (10.7)	36 (39)	115 (41.4)	55 (65)	139 (49.3)	51 (68)	137 (50.6)	50 (69)
Infrequent assistance	5 (1.7)	2 (2)	9 (3.2)	3 (4)	6 (2.1)	2 (3)	5 (1.8)	4 (6)
Frequent assistance	126 (43.4)	40 (43)	71 (25.5)	17 (20)	55 (19.5)	13 (17)	45 (16.6)	9 (13)
Independence in shopping								
No assistance	33 (11.4)	36 (39)	115 (41.4)	54 (64)	140 (49.6)	48 (64)	135 (49.8)	47 (65)
Assistance	128 (44.3)	42 (45)	80 (28.8)	21 (25)	60 (21.3)	18 (24)	52 (19.2)	16 (22)
Independence in traveling								
No assistance	33 (11.4)	34 (37)	110 (39.6)	54 (64)	139 (49.3)	47 (63)	133 (49.1)	46 (64)
Assistance	128 (44.1)	44 (47)	85 (30.6)	21 (25)	61 (21.6)	19 (25)	54 (19.9)	17 (24)
Work[b]								
No deficit	2 (1.0)	8 (10)	25 (11.8)	21 (29)	57 (26.9)	23 (37)	70 (34.0)	30 (49)
Reduced capacity	3 (1.4)	4 (5)	25 (11.8)	12 (17)	26 (12.3)	12 (19)	20 (9.7)	7 (11)
Limited or unable to work	133 (63.3)	55 (70)	125 (59.2)	34 (47)	94 (44.3)	22 (35)	79 (38.3)	19 (31)

- All but 1 of the surviving patients who were in VS at 2 weeks recovered consciousness and 25% regained functional independence by 12 months

Why These Findings Matter

- Understanding of recovery from severe TBI is fraught with nihilism.

  ➞ Percentage of participants with severe TBI and a favorable outcome nearly quadrupled from 2 weeks to 12 months.

- Vegetative state diagnosis generally viewed as static condition incompatible with subsequent functional recovery.

  ➞ Great majority of those who survive VS recover consciousness and 1 in 4 regain functional independence over the first year post-injury.

Recovery Between 1-10 Years Post-Injury

ACRM AMERICAN CONGRESS OF REHABILITATION MEDICINE
Archives of Physical Medicine and Rehabilitation
journal homepage: www.archives-pmr.org
Archives of Physical Medicine and Rehabilitation 2013;94:1855-60

ORIGINAL ARTICLE

Functional Outcomes in Traumatic Disorders of Consciousness: 5-Year Outcomes From the National Institute on Disability and Rehabilitation Research Traumatic Brain Injury Model Systems

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Abstract
Objective: To characterize the 5-year outcomes of patients with traumatic brain injury (TBI) not following commands when admitted to acute inpatient rehabilitation.
Design: Secondary analysis of prospectively collected data from the National Institute on Disability and Rehabilitation Research–funded Traumatic Brain Injury Model Systems (TBIMS).
Setting: Inpatient rehabilitation hospitals participating in the TBIMS program.
Participants: Patients (N=108) with TBI not following commands at admission to acute inpatient rehabilitation were divided into 2 groups (early recovery: followed commands before discharge [n=72]; late recovery: did not follow commands before discharge [n=36]).
Interventions: Not applicable.
Main Outcome Measures: FIM items.
Results: For the early recovery group, depending on the FIM item, 8% to 21% of patients were functioning independently at discharge, increasing to 56% to 85% by 5 years postinjury. The proportion functioning independently increased from discharge to 1 year, 1 to 2 years, and 2 to 5 years. In the late recovery group, depending on the FIM item, 19% to 36% of patients were functioning independently by 5 years postinjury. The proportion of independent patients increased significantly from discharge to 1 year and from 1 to 2 years, but not from 2 to 5 years.
Conclusions: Substantial proportions of patients admitted to acute inpatient rehabilitation before following commands recover independent functioning over as long as 5 years, particularly if they begin to follow commands before hospital discharge.
Archives of Physical Medicine and Rehabilitation 2013;94:1855-60

0003-9993/13/$36 - see front matter © 2013 by the American Congress of Rehabilitation Medicine
http://dx.doi.org/10.1016/j.apmr.2012.10.041

JOURNAL OF NEUROTRAUMA 36:1136–1146 (April 1, 2019)
Mary Ann Liebert, Inc.
DOI: 10.1089/neu.2018.5954

Disorders of Consciousness due to Traumatic Brain Injury: Functional Status Ten Years Post-Injury

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Abstract
Few studies have assessed the long-term functional outcomes of patients with a disorder of consciousness due to traumatic brain injury (TBI). This study examined functional status during the first 10 years after TBI among a cohort with disorders of consciousness (i.e., coma, vegetative state, minimally conscious state). The study sample included 110 individuals with TBI who were unable to follow commands prior to inpatient rehabilitation and for whom follow-up data were available at 1, 2, 5, and 10 years post-injury. The sample was subdivided into those who demonstrated command-following early (before 28 days post-injury) versus late (≥ 28 days post-injury or never). Functional Independence Measure (FIM) at 1, 2, 5, and 10 years following TBI was used to measure functional outcomes. Measureable functional recovery occurred throughout the 10-year period, with more than two thirds of the sample achieving independence in mobility and self-care, and about one quarter achieving independent cognitive function by 10 years. Following commands prior to 28 days was associated with greater functional independence at all outcome time-points. Multi-trajectory modeling of recovery of three FIM subscales (self-care, mobility, cognition) revealed four distinct prognostic groups with different temporal patterns of change on these subscales. More than half the sample achieved near-maximal recovery by 1 year post-injury, while the later command-following subgroups recovered over longer periods of time. Significant late functional decline was not observed in this cohort. Among a cohort of patients unable to follow commands at the time of inpatient rehabilitation, a substantial proportion achieved functional independence in self-care, mobility, and cognition. The proportion of participants achieving functional independence increased between 5 and 10 years post-injury. These findings suggest that individuals with disorders of consciousness may benefit from ongoing functional monitoring and updated care plans for at least the first decade after TBI.

Keywords: brain injuries; cognition; consciousness disorders; minimally conscious state; prognosis; rehabilitation outcome; vegetative state

Introduction

Few studies have assessed the long-term functional outcomes of patients with disorders of consciousness (DOC) due to traumatic brain injury (TBI). In addition, many utilized broad, non-specific outcome measures with variable samples at follow-up intervals. There is consequently a lack of data to guide families, providers, and payers in trying to plan for future needs, compare outcomes, and assess quality of interventions. Given the lack of knowledge regarding meaningful long-term outcomes, it is not

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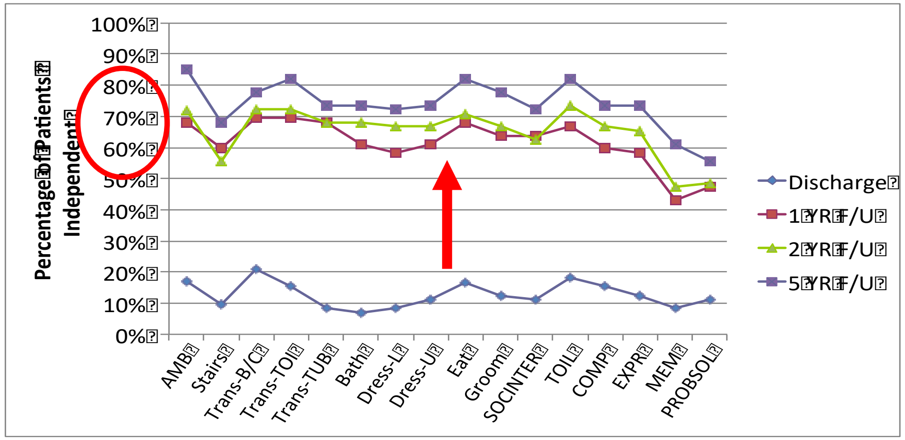
- **Aim:** To monitor long-term outcomes in patients not following commands when admitted to acute inpatient rehabilitation.
- **Sample:** 110 rehabilitation inpatients prospectively enrolled in the TBIMS with no evidence of command-following prior to rehabilitation admission and followed at 1, 2, 5 *and* 10 years post-injury.
- **Outcomes:**
  - Functional Independence Measure
    - Self-care domain score
    - Mobility domain score
    - Cognition domain score

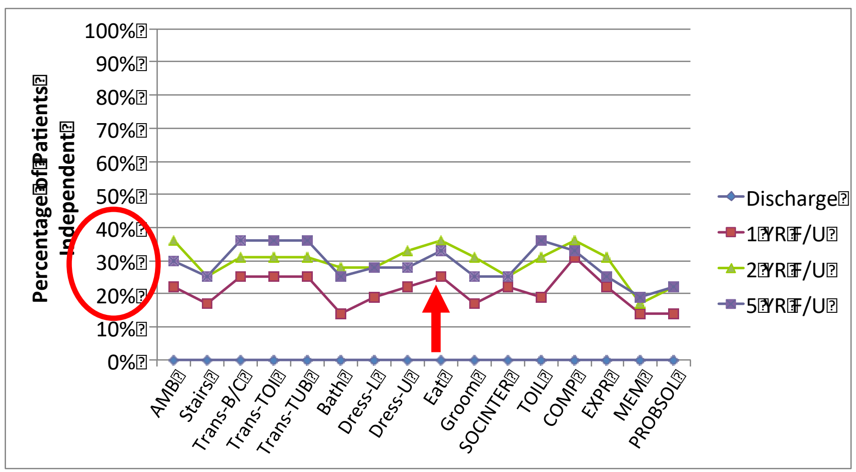
TBIMS
Traumatic Brain Injury Model System
Since 1987

Key Findings

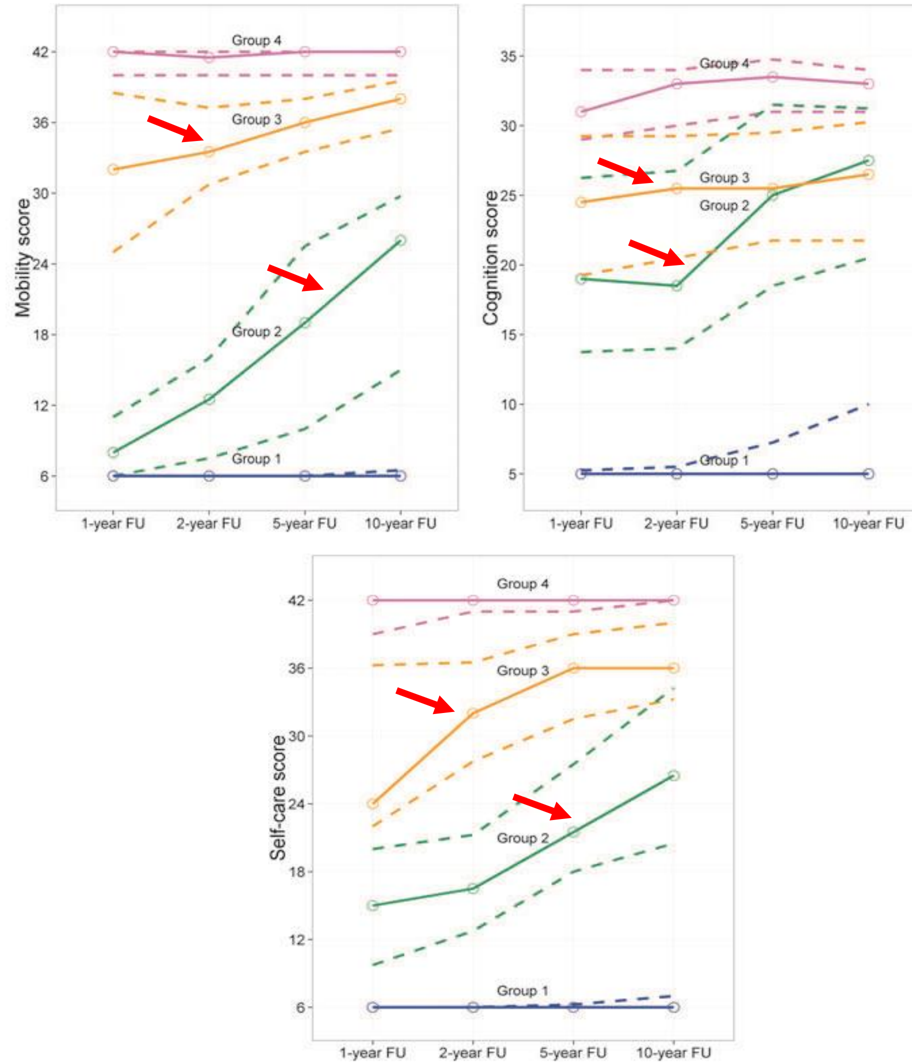
Recovered command-following during inpatient rehab



Did not recover command-following during inpatient rehab



All patients during inpatient rehab



(Whyte, et al, 2013)

(Hammond, et al, 2019)

Why These Findings Matter

- Many healthcare providers and insurers in the U.S. deem patients with DOC who lack command-following as inappropriate for acute inpatient rehabilitation.

  ➞ Many patients in this study who were unable to follow commands on admission to inpatient rehabilitation eventually achieved independence in self-care, mobility and cognitive domains.

- Prior studies of patients with moderate to severe TBI indicate that approximately 30% show decline in function over time in the years following TBI.

  ➞ No evidence of a pattern of deterioration up to 10 years in any functional domain or subgroup.

Prognostication

Recommendations for Prognostic Assessment

Recommendation Statement 3

- When discussing prognosis with caregivers of patients with a DoC during the first 28 days post injury, clinicians ***must avoid statements that suggest these patients have a universally poor prognosis (Level A)***.

(Giacino et al., DoC Practice Guideline Update, Neurol 2018)

DoC Outcome Predictors

Table 3 Prognostic features in disorders of consciousness (DoC) ≥28 days

Type of DoC	Prognostic factors associated with better prognosis: Moderate confidence	Prognostic factors associated with better prognosis: Low confidence	Prognostic factors associated with worse prognosis: Moderate confidence	Prognostic factors associated with worse prognosis: Low confidence
Adult traumatic VS/UWS	Higher-level activation of the associated auditory cortex using BOLD fMRI in response to a familiar voice speaking the patient's name	Normal SPECT scan 1–2 months postinjury	Hydrocephalus in the late phase	Corpus callosum lesions, dorsolateral upper brainstem injury, or corona radiata injury on MRI performed 6–8 weeks postinjury
	DRS scores of <26, 2–3 months postinjury	Lower scores on the DRS in general 2–3 months postinjury		Fever of central origin in the acute phase
	Detectable P300 at 2–3 months postinjury	The presence of P300 after controlling for DRS and EEG reactivity		Diffuse body sweating in the acute phase
	Reactive EEG at 2–3 months postinjury			Epilepsy in the late phase
				Respiratory disturbance
				Flaccidity in the acute phase
Adult traumatic mixed (VS/UWS and MCS)		Faster improvements in DRS scores	Longer time post injury at study enrollment	
		Amantadine use	Worse DRS score at study enrollment	
			Dantrolene use	
		Left temporal lobe lesions, contusions/mass lesions, or subarachnoid hemorrhage on imaging	Left frontal or bilateral lesions on imaging	

(Giacino, et al, Neurol, 2018)

DoC Outcome Predictors

Table 3 Prognostic features in disorders of consciousness (DoC) ≥28 days

Type of DoC	Prognostic factors associated with better prognosis		Prognostic factors associated with worse prognosis	
	Moderate confidence	**Low confidence**	**Moderate confidence**	**Low confidence**
Adult nontraumatic VS/UWS	CRS-R scores of ≥6 more than 1 mo after onset			
	Presence of SEPs			
Adult mixed traumatic and nontraumatic populations[a]	Approximate entropy value of ≥0.8 (vs <0.8)	Higher baseline composite score combining the CRS-R score plus points for DoC subtype		Older age
	Presence of MMN on EEG	Mental imagery fMRI		Longer length of time postinjury
		Increasing complexity of sleep architecture on PSG performed 3.5 ± 2 months postinjury		Abnormal early MLAEPs
				Presence of 3 or more medical complications during inpatient rehabilitation
Pediatric traumatic VS/UWS		Absence of posttraumatic autonomic dysfunction		Posttraumatic hyperthermia at any time

Prognostication in the first 72 hours and WLST

Table 4: Deaths and percentage of deaths following withdrawal of life-sustaining therapy within the first three days of care

			Among all deaths within the first 3 d of care, deaths following withdrawal of life-sustaining therapy		Among deaths following withdrawal of life-sustaining therapy, deaths occurring within the first 3 d of care	
Centre	No. of admissions	Deaths within first 3 d of care, no.	No.	% (95% CI)	No.	% (95% CI)
A	120	15	11/15	73.3 (48.1–89.1)	11/26	42.3 (25.5–61.1)
B	120	28	26/28	92.9 (77.4–98.0)	26/46	56.5 (42.3–69.8)
C	120	4	2/4	50.0 (15.0–85.0)	2/9	22.2 (6.3–54.7)
D	120	22	14/22	63.6 (43.0–80.3)	14/39	35.9 (22.7–51.6)
E	120	23	7/23	30.4 (15.6–50.9)	7/18	38.9 (20.3–61.4)
F	120	22	13/22	59.1 (38.7–76.7)	13/22	59.1 (38.7–76.7)
Total	720	114	73/114	64.0 (54.9–72.3)	73/160	45.6 (38.1–53.4)

Note: CI = confidence interval.

Turgeon, et al., CMAJ, 2011

Table 3. Length of Stay and Disposition by Withdrawal of Life-Supporting Treatment

Characteristic	No withdrawal of LST	Withdrawal of LST	Total
No. of persons included	30 080	7869	37 949
Total LOS			
No. with data	30 040	7868	37 908
Mean (SD), d	15.4 (17.4)	5.3 (7.3)	13.3 (16.4)
Median (Q1-Q3), d	10.0 (3.5-21.0)	3.0 (1.0-7.0)	8.0 (2.0-19.0)
(Range), d	(1.0-357.0)	(1.0-179.0)	(1.0-357.0)
Total ICU LOS			
No. with data	27 542	7909	34 751
Mean (SD), d	9.7 (10.0)	5.2 (6.3)	8.8 (9.5)
Median (Q1-Q3), d	6.0 (3.0-14.0)	3.0 (1.0-7.0)	5.0 (2.0-13.0)
(Range), d	(1.0-178.0)	(1.0-180.0)	(1.0-180.0)
Total ventilator days			
No. with data	25 960	7327	33 987
Mean (SD), d	7.5 (9.0)	4.8 (6.0)	6.9 (8.5)
Median (Q1-Q3), d	4.0 (2.0-11.0)	2.0 (1.0-6.0)	3.0 (2.0-10.0)
Range, d	1.0-207.0	1.0-180.0	1.0-207.0
Discharge disposition, No. (%)			
Deceased/expired	5961 (18.3)	7026 (93.7)	12 987 (33.9)
Discharged/transferred to home	8572 (29.8)	28 (0.4)	8600 (23.7)
Discharged/transferred to hospital	13 562 (47.1)	74 (1.0)	13 636 (37.6)
Discharged/transferred to hospice	395 (1.4)	359 (4.8)	754 (2.1)
Other	987 (3.4)	10 (0.1)	997 (2.7)

Williamson, et al, JAMA Surg, 2020

Recommendations for Prognostic Assessment

Recommendation Statement 7

- Given the frequency of recovery of consciousness after 3 months in patients in nontraumatic VS/UWS, and after 12 months in patients with traumatic VS/UWS (including some cases emerging from MCS) ***use of the term permanent VS should be discontinued***.
- After these time points, ***the term chronic VS (UWS) should be applied, accompanied by the duration of the VS/UWS*** (Level B).

(Giacino et al., DoC Practice Guideline Update, Neurol 2018)

Conclusions

- Diagnostic accuracy may be optimized through:
  - Serial, systematic, standardized evaluation approach
  - Maximizing arousal level
  - Identifying factors that can mask conscious awareness
  - Supplementing behavioral assessment with functional imaging and/or electrophysiological studies, where indicated
- Prognostic accuracy may be improved by:
  - Accurate diagnostic assessment
  - Awareness of the confidence limits around outcome predictors and models
  - Recognizing that severe impairment early in recovery (first 2 weeks post-injury) is NOT a definitive indicator of unfavorable long-term outcome (return to independence possible).

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Discussion