

Neuro-ICU Myths: We Can Accurately Predict Prognosis From Coma

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Nicholas D. Schiff, M.D.
Director, Laboratory of Cognitive Neuromodulation
Associate Professor of Neurology and Neuroscience
Department of Neurology and Neuroscience
Weill Medical College of Cornell University
New York, New York

Overview

- Classical Statistics
- Nosology Matters
- Why we really should worry...

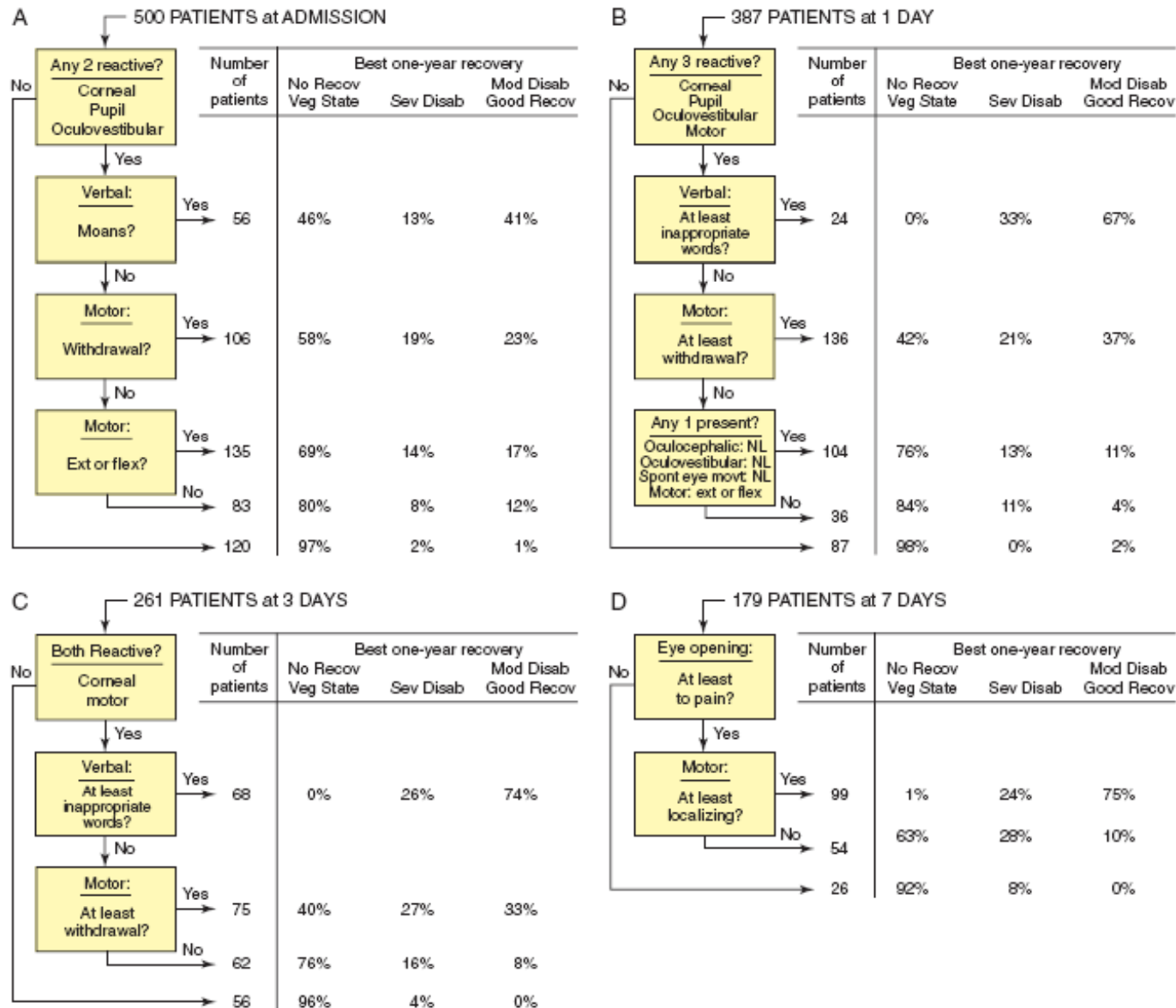


Figure 9-3. (A-D) The best 1-year outcome for 500 conventionally treated patients in coma from nontraumatic causes. For each time period following onset, the diagram correlates the degree of recovery with clinical signs. The numbers are, in most instances, sufficiently large to provide a basis for estimating prognosis among similarly affected patients in the future. (From Levy et al.,⁴ with permission.)

Posner
et al. 2007

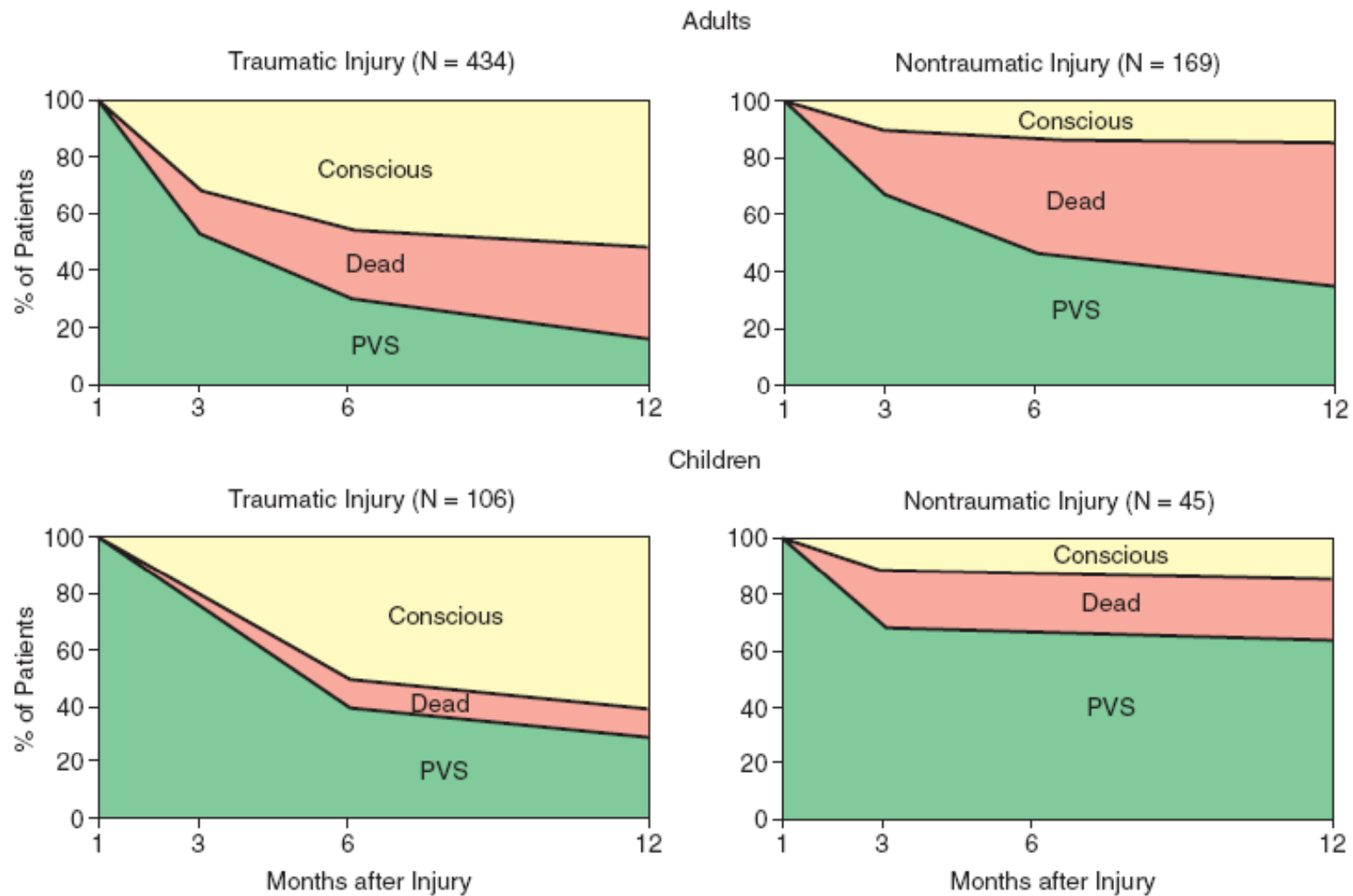


Figure 9–4. Outcome for patients in a persistent vegetative state after a traumatic or nontraumatic injury. See also Table 9–11. (From the Multisociety Task Force,⁶⁴ with permission.)

Table 4. Useful Clinical Findings in the Prognosis of Post-Cardiac Arrest Coma Organized by Time After Onset of Coma (Not Pooled)*

Clinical Finding	Study	LR of Poor Neurological Outcome (95% Confidence Interval)	
		Positive	Negative
At Time of Coma Onset			
Absent pupillary reflex	Earnest et al ³⁵	7.2 (1.9-28.0)	0.5 (0.4-0.6)
Absent motor response	Levy et al ³⁹	3.5 (1.4-8.6)	0.6 (0.4-0.7)
Absent corneal reflex	Levy et al ³⁹	3.2 (1.1-9.5)	0.7 (0.6-0.8)
Absent oculocephalic reflex	Earnest et al ³⁵	2.5 (1.3-4.8)	0.4 (0.3-0.6)
Absent spontaneous eye movement	Levy et al ³⁹	2.2 (1.3-4.0)	0.4 (0.3-0.6)
ICS <4	Berek et al ³³	2.2 (1.1-4.5)	0.2 (0.1-0.6)
GCS <5	Madl et al ⁴⁰	1.4 (1.1-1.6)	0.3 (0.2-0.5)
Absent verbal effort	Levy et al ³⁹	1.2 (0.9-1.6)	0.1 (0.0-0.7)
At 12 Hours			
Absent cough reflex	Sasser ⁴²	13.4 (4.4-40.3)	0.3 (0.2-0.4)
Absent corneal reflex	Sasser ⁴²	9.1 (3.9-21.1)	0.3 (0.2-0.4)
Absent gag reflex	Sasser ⁴²	8.7 (4.0-18.9)	0.4 (0.4-0.5)
Absent pupillary reflex	Sasser ⁴²	4.0 (2.5-6.6)	0.5 (0.5-0.6)
GCS <5	Sasser ⁴²	3.5 (2.4-5.2)	0.4 (0.3-0.4)
Absent motor response	Sasser ⁴²	3.2 (2.2-4.6)	0.4 (0.3-0.5)
Absent withdrawal to pain	Sasser ⁴²	2.4 (1.9-3.1)	0.2 (0.1-0.2)
Absent verbal effort	Sasser ⁴²	1.6 (1.4-1.9)	0.1 (0.0-0.1)
At 24 Hours			
Absent cough reflex	Sasser ⁴²	84.6 (5.3-1342.0)	0.4 (0.3-0.5)
Absent gag reflex	Sasser ⁴²	24.9 (6.3-98.3)	0.5 (0.4-0.5)
GCS <5	Sasser ⁴²	8.8 (5.1-15.1)	0.4 (0.3-0.4)
Absent eye opening to pain	Sasser ⁴²	5.9 (3.9-9.0)	0.3 (0.3-0.4)
Absent spontaneous eye movement	Levy et al ³⁹	3.5 (1.4-8.8)	0.5 (0.4-0.7)
Absent eye opening to pain	Levy et al ³⁹	3.0 (1.5-6.2)	0.4 (0.3-0.5)
Absent oculocephalic reflex	Sasser ⁴²	2.9 (1.8-4.6)	0.5 (0.5-0.6)
Absent spontaneous eye movement	Sasser ⁴²	2.7 (2.1-3.4)	0.3 (0.2-0.3)
Absent verbal effort	Sasser ⁴²	2.4 (2.0-2.9)	0.1 (0.0-0.1)
At 48 Hours			
GCS <6	Madl et al ⁴¹	2.8 (1.3-5.9)	0.3 (0.1-0.5)
GCS <10	Madl et al ⁴¹	1.3 (1.0-1.7)	0.0 (0.0-0.7)
At 72 Hours			
Absent withdrawal to pain	Levy et al ³⁹	36.5 (2.3-569.9)	0.3 (0.2-0.4)
Absent spontaneous eye movement	Levy et al ³⁹	11.5 (1.7-79.0)	0.6 (0.5-0.7)
Absent verbal effort	Levy et al ³⁹	7.4 (2.0-28.0)	0.3 (0.2-0.5)
Absent eye opening to pain	Levy et al ³⁹	6.9 (1.8-27.0)	0.5 (0.4-0.6)
At 7 Days			
Absent withdrawal to pain	Levy et al ³⁹	29.7 (1.9-466.0)	0.4 (0.3-0.6)
Absent verbal effort	Levy et al ³⁹	14.1 (2.0-97.7)	0.4 (0.2-0.6)

From: Booth et al. (2004) “Is this Patient dead, vegetative, or severely Neurologically impaired?” JAMA 291:870-879

Abbreviations: GCS, Glasgow Coma Scale; ICS, Innsbruck Coma Scale³³; LR, likelihood ratio.
*Clinical findings that have a positive LR greater than 2 and lower confidence interval boundary greater than 1 are presented with the corresponding negative LR.

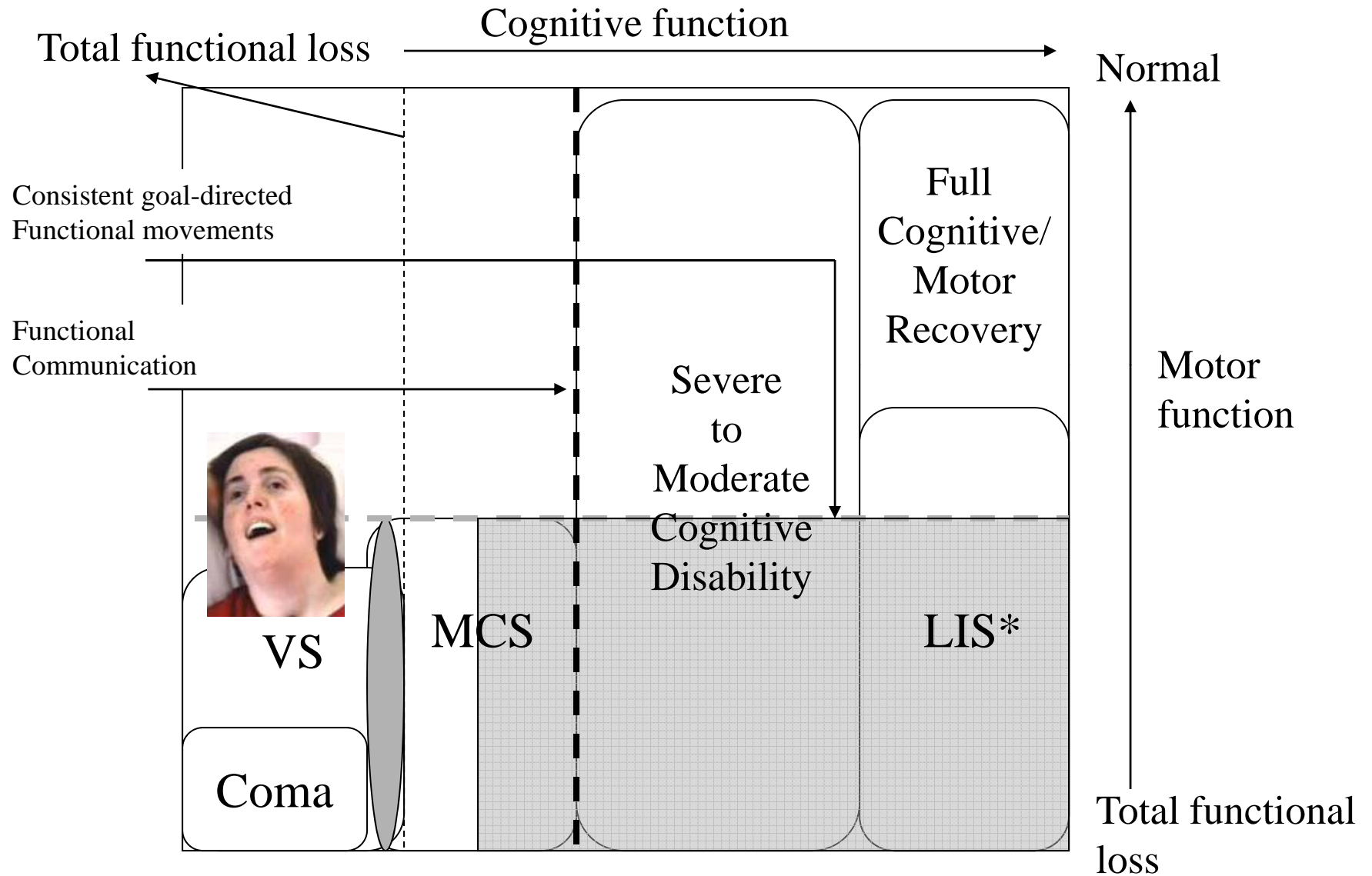
Table 5. Pooled Clinical Signs in the Prognosis of Post-Cardiac Arrest Coma

Source	LR of Poor Neurological Outcome (95% Confidence Interval)	
	Positive	Negative
At Time of Coma Onset*		
Absent Withdrawal to Pain		
Summary LR	1.7 (0.7-4.2)	0.4 (0.1-1.1)
Earnest et al ³⁵	3.7 (1.6-8.2)	0.4 (0.3-0.6)
Levy et al ³⁹	1.4 (1.0-1.9)	0.4 (0.2-0.7)
Snyder et al ⁴³	1.4 (0.9-2.1)	0.5 (0.2-1.2)
At 24 Hours		
Absent Withdrawal to Pain		
Summary LR	4.7 (2.2-9.8)	0.2 (0.1-0.6)
Edgren et al ³⁶	3.9 (1.1-14)	0.4 (0.2-0.8)
Levy et al ³⁹	6.8 (2.3-19.8)	0.2 (0.2-0.3)
Sasser ⁴²	5.1 (3.6-7.3)	0.2 (0.1-0.2)
Snyder et al ⁴³	6.5 (1.0-42.0)	0.3 (0.1-0.7)
Absent Pupil Response		
Summary LR	10.2 (1.8-48.6)	0.8 (0.4-1.4)
Chen et al ³⁴	0.9 (0.0-19.1)	1.0 (0.8-1.2)
Edgren et al ³⁶	5.6 (0.3-95.0)	0.8 (0.6-1.1)
Levy et al ³⁹	10.7 (0.7-170.0)	0.8 (0.7-0.9)
Sasser ⁴²	39.2 (5.6-276.6)	0.6 (0.6-0.7)
Absent Motor Response		
Summary LR	4.9 (1.6-13.0)	0.6 (0.3-1.3)
Chen et al ³⁴	3.7 (0.2-59.1)	0.8 (0.6-1.1)
Levy et al ³⁹	5.5 (1.4-21.0)	0.6 (0.5-0.8)
Sasser ⁴²	7.6 (4.6-12.6)	0.4 (0.3-0.4)
Snyder et al ⁴³	3.5 (0.5-24.3)	0.7 (0.5-1.1)
Absent Corneal Reflex		
Summary LR	12.9 (2.0-68.7)	0.6 (0.2-1.9)
Edgren et al ³⁶	1.8 (0.2-15.4)	0.9 (0.7-1.2)
Levy et al ³⁹	14.8 (0.9-233.0)	0.7 (0.7-0.8)
Sasser ⁴²	90.9 (5.7-1442.9)	0.4 (0.4-0.5)
At 72 Hours		
Absent Pupil Response		
Summary LR	3.4 (0.5-23.6)	0.9 (0.4-2.1)
Chen et al ³⁴	0.9 (0.0-19.1)	1.0 (0.8-1.2)
Edgren et al ³⁷	5.3 (0.3-84.0)	0.8 (0.7-1.0)
Levy et al ³⁹	5.8 (0.4-94.0)	0.9 (0.8-1.0)
Absent Motor Response		
Summary LR	9.2 (2.1-49.4)	0.7 (0.3-1.3)
Chen et al ³⁴	2.0 (0.1-34.8)	0.9 (0.7-1.2)
Edgren et al ³⁷	12.6 (0.8-193.0)	0.6 (0.5-0.7)
Levy et al ³⁹	16.5 (1.1-261.0)	0.7 (0.6-0.8)
Snyder et al ⁴³	3.0 (0.2-38.8)	0.6 (0.3-1.1)
Seizure or Myoclonus†		
Summary LR	1.4 (0.5-3.9)	0.8 (0.3-2.1)
Krumholz et al ³⁸	1.7 (0.8-3.4)	0.7 (0.5-1.0)
Levy et al ³⁹	1.1 (0.5-2.3)	1.0 (0.8-1.2)
Snyder et al ⁴⁴	1.7 (0.7-4.2)	0.8 (0.6-1.1)

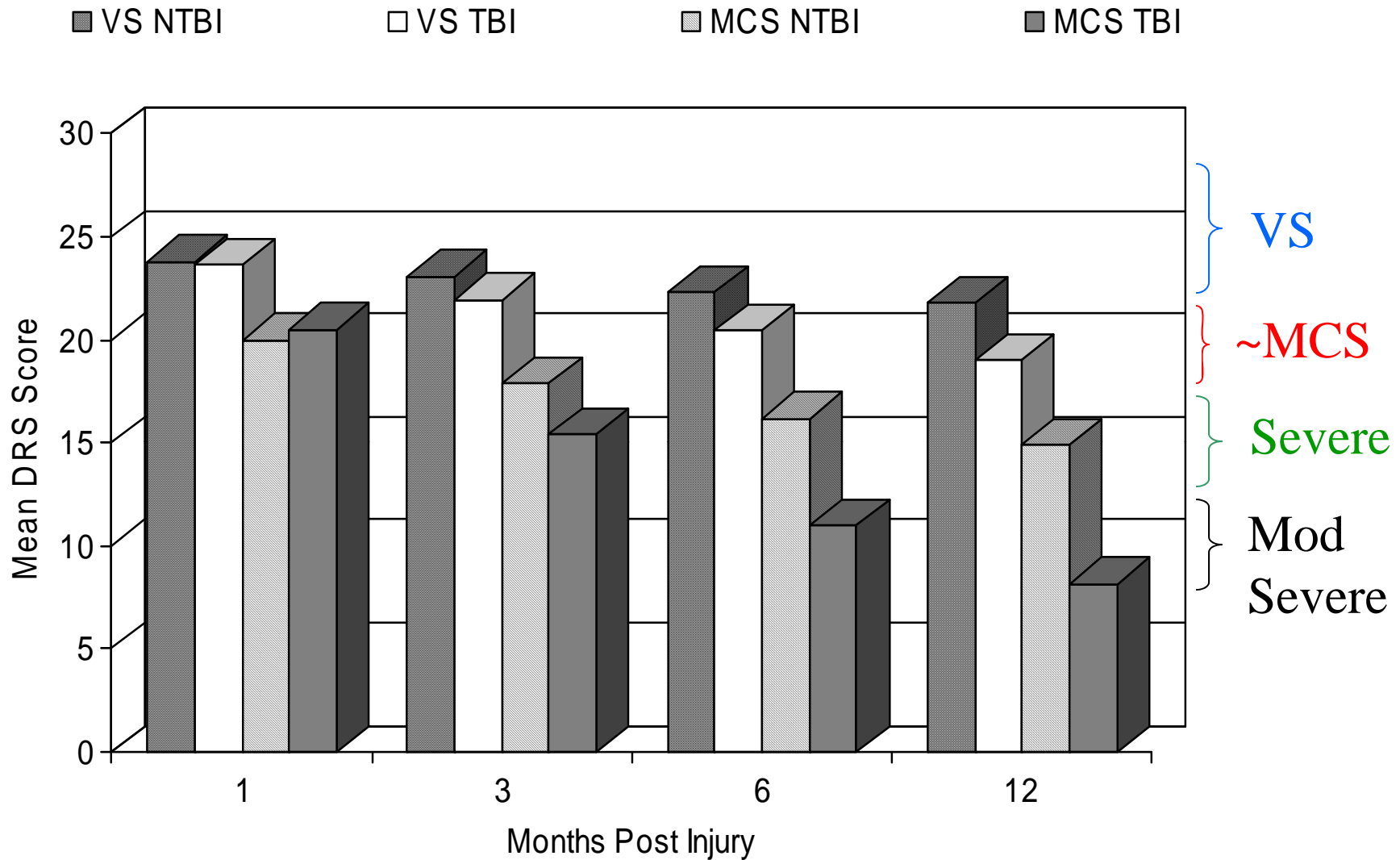
From: Booth et al. (2004) “Is this Patient dead, vegetative, or severely Neurologically impaired?”
JAMA 291:870-879

Abbreviation: LR, likelihood ratio.
 *Times reflect number of hours since cardiac arrest.
 †These figures refer to the presence of seizures or myoclonus at any time after cardiac arrest.

Correspondence of cognitive and motor impairment across human disorders of consciousness



(Adapted from Schiff, (2009) Recovery of Consciousness after Brain Injury, In: The Cognitive Neurosciences IV, MIT Press)



N=104 (55 VS, 49 MCS)

From “The vegetative and minimally conscious states: A comparison of clinical features and functional outcome, “ J.T. Giacino and K. Kalmar, 1997, Journal of Head Trauma Rehabilitation 12 (4), p. 42.

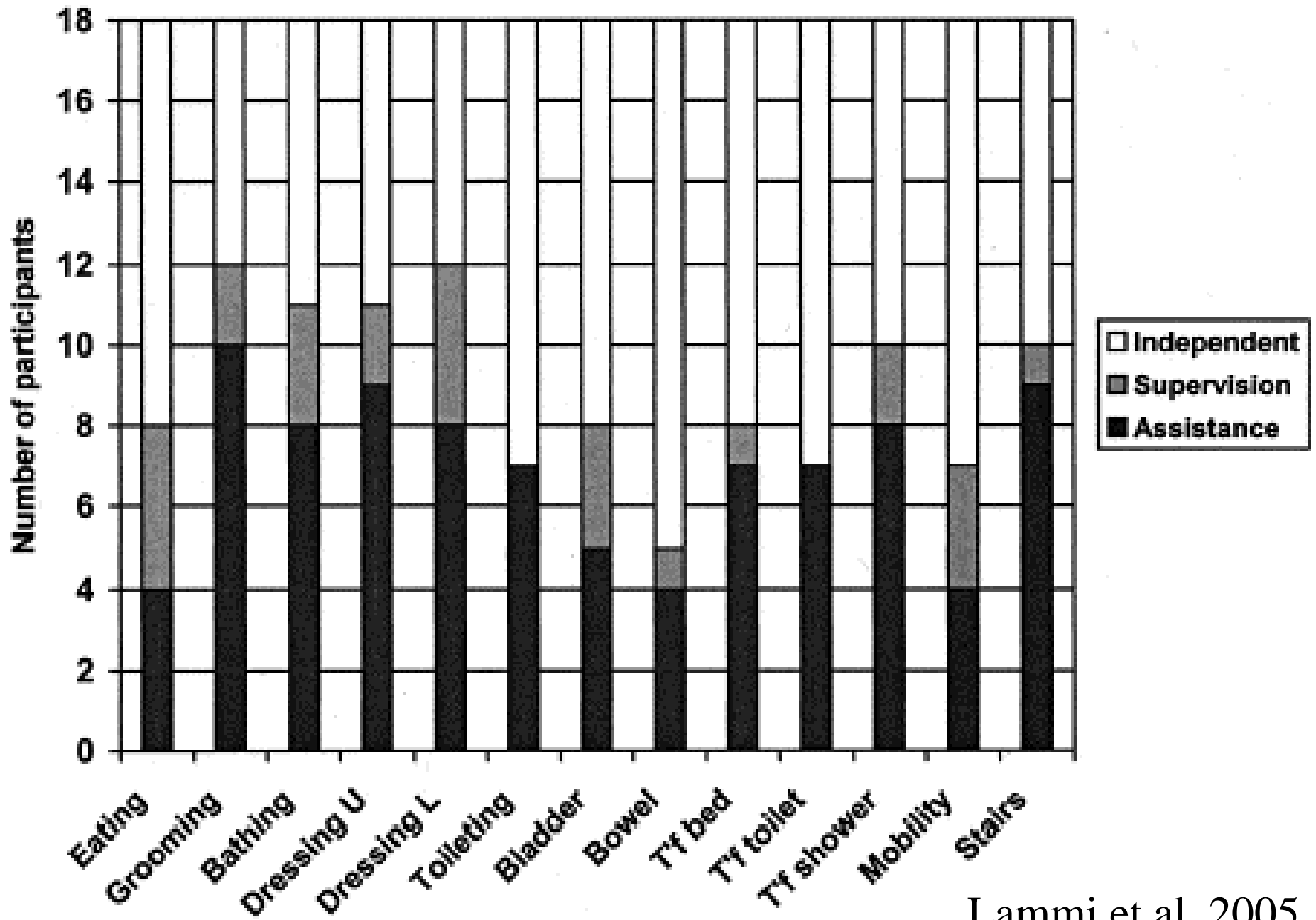
The Minimally Conscious State and Recovery Potential: A Follow-Up Study 2 to 5 Years After Traumatic Brain Injury

Michele H. Lammi, BAppSc, Vanessa H. Smith, BAppSc, Robyn L. Tate, MPsychol, PhD, Christine M. Taylor, BAppSc

Table 1: Demographic and Injury Data (N=18)

Variables	Mean ± SD (Median)
Age at injury (y)	37.89 ± 14.76 (37.0)
Age at follow-up (y)	41.67 ± 15.06 (40.5)
Time posttrauma (mo)	43.36 ± 8.86 (43.88)
Lowest GCS score (n=14)	4.29 ± 1.49 (4.0)
Length of MCS (d) (n=16)*	98.94 ± 141.15 (56.0)
Initial WNSSP score	35.56 ± 22.43 (32.5)
FIM score at rehabilitation admission	18.06 ± 0.24 (18.0)
FIM score at rehabilitation discharge	63.17 ± 33.78 (67.5)
	N (%)
Sex	
Men	14 (77.8)
Women	4 (22.2)
Type of injury	
Closed	7 (38.9)
Open/neurosurgery	11 (61.1)
Cause of injury	
Road traffic collision	10 (55.6)
Fall	8 (44.4)
Initial RLAS level	
I: no response	1 (5.6)
II: generalized response	10 (55.5)
III: localized response	3 (16.7)
IV: confused-agitated	4 (22.2)

Abbreviations: GCS, Glasgow Coma Scale; SD, standard deviation.
 *Data from 2 participants who were still in the MCS at follow-up at 1610 and 1460 days posttrauma are excluded.



Lammi et al. 2005

The neuropathology of the vegetative state after an acute brain insult.

Adams JH, Graham DI, Jennett B. *Brain*. 2000; 123:1327-38.

- Specific patterns of neuronal loss in 49 patients remaining in a vegetative state.
- Non-traumatic injuries associated with VS showed severe bilateral thalamic damage (98%), associated with diffuse cortical damage (64% of cases).
- Traumatic etiologies showed severe thalamic degeneration in the majority of VS patients (96% of patients who survived for 3 months before death).
- That the most consistent and severe pathologies arising from both types of injuries are in the thalamus, is not widely appreciated.

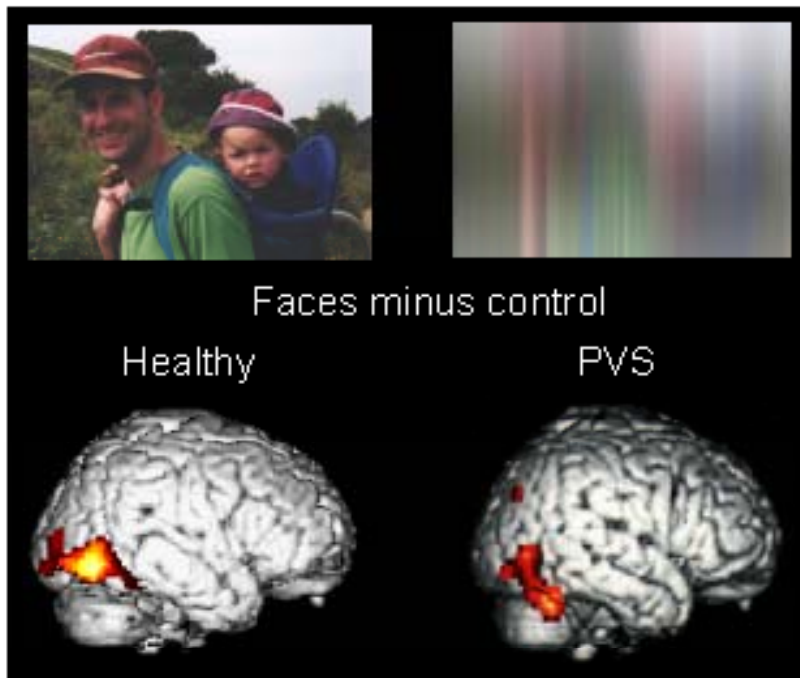
Neuropathology in vegetative and severely disabled patients after head injury.

Jennett, B, Adams, JH, Murray, LS, and Graham, DI.

Neurology 2001, 56: 486-490

- Autopsy studies comparing 35 VS and 30 severely disabled patients.
- In 50% of the severely disabled group no evidence of thalamic injury—pattern not identified in any VS case.
- Outcomes in the severely disabled group included MCS patients (including 2 MCS patients without thalamic injury or evidence of moderate or severe diffuse axonal injury).
- Findings suggest potential anatomical substrates for residual cognitive capacity in some severely brain injured persons.

Menon DK, Owen AM, Williams EJ, Minhas PS, Allen CM, Boniface SJ, Pickard JD.
(1998) **Cortical processing in persistent vegetative state.** *Lancet* 352:1148-9



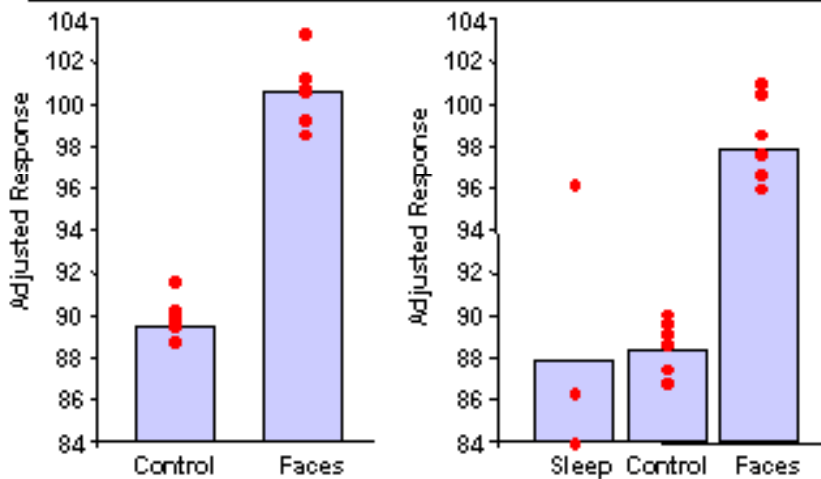
26 year-old woman with acute disseminated encephalomyelitis (ADEM):

-- Initial CT with diffuse cerebral edema

-- Bilateral thalamic and medullary lesions

-- Remained in VS/MCS until 6 months
(imaged at 4 months)

Three years after injury:



“Thank you so much for the assessments, they treated me as if I was stupid in the (hospital). My stay there was absolute hell they never told me anything. They used to suction me through my mouth and they never told me why or what it was called, they had never told me about my (tracheostomy). I am lucky that I am with it and have a good memory so I could work it out.....”