Curing Coma Campaign
Neurocritical Care Society

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CURING COMA
AWAKENING HOPE

NEUROCRITICAL
CARE SOCIETY

Disclosures: DSMB: Zoll

Neurocritical Care Society

- Multi-disciplinary medical society focused on the acute care of patients with neurological catastrophes (TBI, stroke, hypoxic-ischemic brain injury from cardiac arrest)
  - Emergency and intensive care unit management
  - 3206 members
  - Mission includes research, education, outreach

- Our role in acute TBI is to:
  - Save the patient's life
  - Prevent/limit secondary brain injury
  - Prepare patient for recovery/rehabilitation
  - Work with families when injury is too severe

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Why Curing Coma?

- What are the questions that patients (or most often their families) ask when in the ICU?
  - Are they going to die?
  - Are they going to wake up and be able to talk to and understand us?
  - Is there anything you can do to increase their chances of waking up and having good cognitive function?
- *These are the questions that matter most to patients, families, and to us*

- This cuts across most diseases we treat in neurocritical care (stroke, traumatic brain injury, hypoxic-ischemic brain injury, encephalitis/meningitis, status epilepticus, etc)

- What do we mean by “Curing Coma”?
  - *promoting recovery of consciousness through early intervention and long-term support*
  - Think coma “writ large”. Across the range of disordered consciousness; focus on recovery.

How We Prognosticate Coma Recovery – Current State

- Phenotype
  - Neurological exam at presentation and at the time we examine the patient (GCS, brainstem, motor)
- Demographics
  - Age, medical comorbidities
- Anatomic imaging of lesions
  - Hematoma location, thickness of subarachnoid hemorrhage, amount of midline shift, cisternal effacement
- Mathematical models based on this data

Prediction models for 6 month outcome after TBI

Admission Characteristics	Value
Core	
Age (14-99 years)	35
Motor Score	Abnormal Flexion
Pupils	Both reacting
Core+CT	
Hypoxia	No
Hypotension	No
CT Classification	Diffuse Injury IV
tSAH on CT	Yes
Epidural mass on CT	No
Core+CT+Lab	
Glucose (54-360 mg/dL)	100 mg/dL
Hb (6-17 g/dL)	12 g/dL

Calculate Reset

http://www.tbi-impact.org/

TABLE 3. Determination of the ICH Score

Component	ICH Score Points
GCS score	
3–4	2
5–12	1
13–15	0
ICH volume, cm^3	
≥30	1
<30	0
IVH	
Yes	1
No	0
Infratentorial origin of ICH	
Yes	1
No	0
Age, y	
≥80	1
<80	0
Total ICH Score	0–6

GCS score indicates GCS score on initial presentation (or after resuscitation); ICH volume, volume on initial CT calculated using *ABC*/2 method; and IVH, presence of any IVH on initial CT.

Hemphill *Stroke* 2001

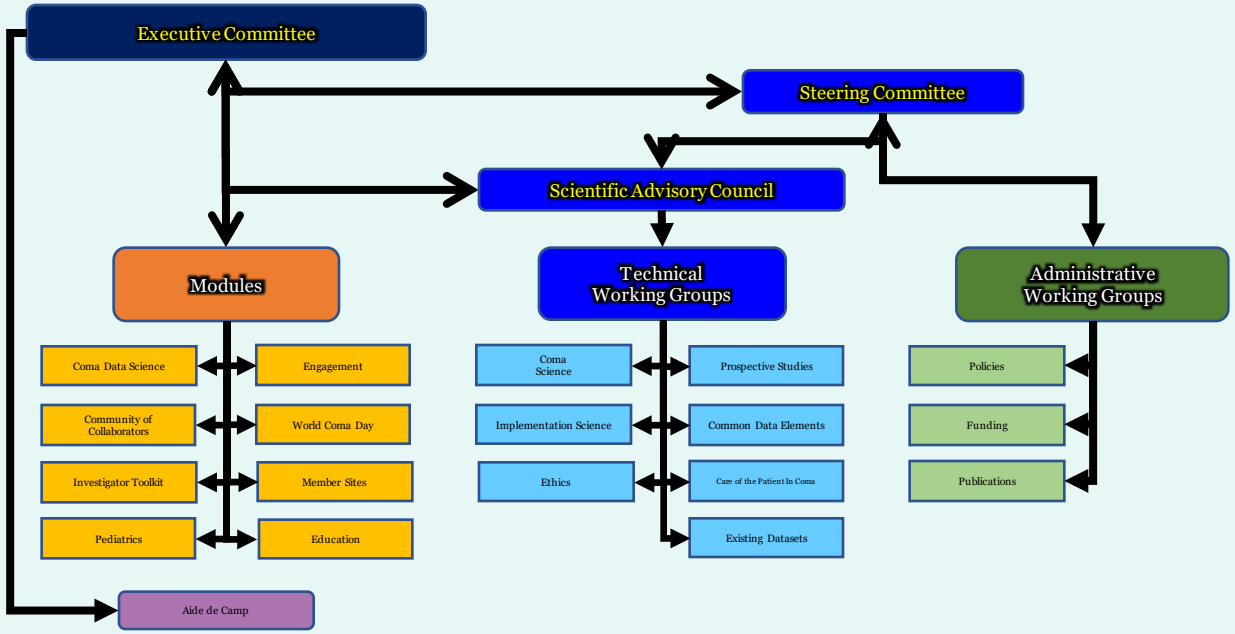
Self-fulfilling Prophecy

- Nihilism has been a common theme in the acute care of TBI patients (and other neurocritical care patients)
- Care limited due to "poor prognosis" in a patient that can (and would) recover
  - Heterogeneity in Canadian trauma centers and head injury (Turgeon *CMAJ* 2011)
  - Early do-not-resuscitate orders in intracerebral hemorrhage (Hemphill *Stroke* 2004)
  - Pervasive theme in neurocritical care across all conditions (TBI, ICH, SAH, cardiac arrest)

- Why aren't we better at this?
- We are currently assessing what the patient looks like "now" rather than assessing the true underlying mechanism of coma/impaired consciousness and the capacity of the brain to recover

What is the Curing Coma Campaign?

- Platform to enable two interrelated goals:
  1. Focus the **science** of acute disorders of consciousness (DoC) on identifying and testing therapeutic interventions
  2. Form an enduring **community** of medical providers, scientists, and advocates to test and implement these advances
     - Key takeaway – There is a role for *Everyone* in the Curing Coma Community
- Initial seed funding from the Neurocritical Care Society in 2019



- Currently ~260 active collaborators across various aspects of the CCC
- Intensivists, nurses, neurologists, neuroscientists, pharmacists, surgeons, rehabilitation specialists
- About half from outside Neurocritical Care Society

The NEW ENGLAND JOURNAL of MEDICINE

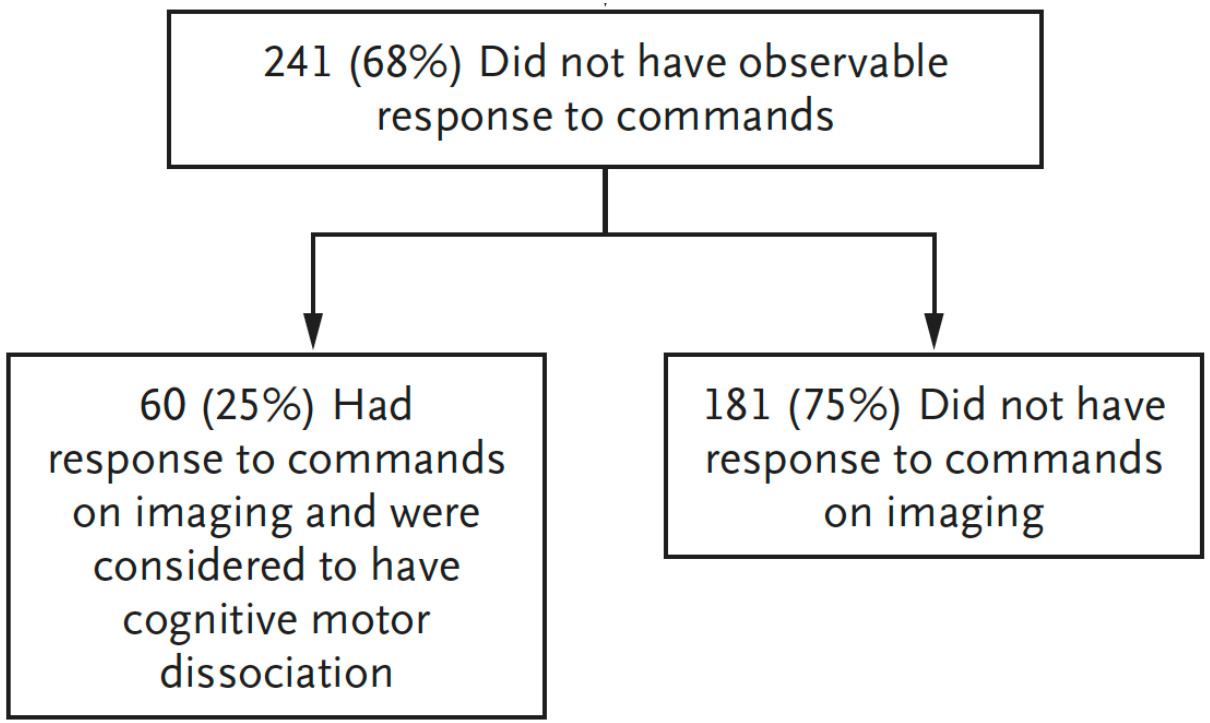
ORIGINAL ARTICLE

Cognitive Motor Dissociation in Disorders of Consciousness

Y.G. Bodien, J. Allanson, P. Cardone, A. Bonhomme, J. Carmona, C. Chatelle, S. Chennu, M. Conte, S. Dehaene, P. Finoia, G. Heinonen, J.E. Hersh, E. Kamau, P.K. Lawrence, V.C. Lupson, A. Meydan, B. Rohaut, W.R. Sanders, J.D. Sitt, A. Soddu, M. Valente, A. Velazquez, H.U. Voss, A. Vrosgou, J. Claassen, B.L. Edlow, J.J. Fins, O. Gosseries, S. Laureys, D. Menon, L. Naccache, A.M. Owen, J. Pickard, E.A. Stamatakis, A. Thibaut, J.D. Victor, J.T. Giacino, E. Bagiella, and N.D. Schiff

- Multi-center study (6 centers)
- 353 patients underwent Coma Recovery Scale-Revised (CRS-R) assessment and had "imaging" with fMRI or EEG
- Median 6.3 (0.6-16.9) months from injury
- 50% TBI

Patients with CMD are 3 times more likely to have significant recovery (Claassen NEJM 2019)



About ¼ of our patients who do not have clinically apparent (at least to us) command following, are following commands in their mind

Bodien *New England Journal of Medicine* 2024

Neurocrit Care
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NEUROCRITICAL CARE SOCIETY

PROCEEDINGS

The Curing Coma Campaign: Framing Initial Scientific Challenges—Proceedings of the First Curing Coma Campaign Scientific Advisory Council Meeting

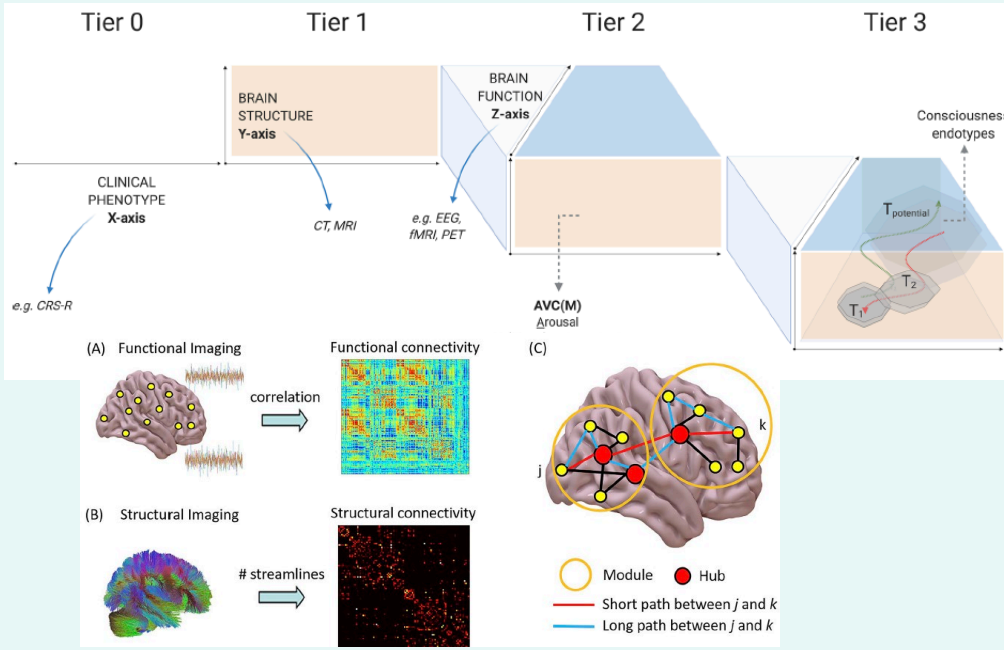
J. Javier Provencio[1], J. Claude Hemphill[2*], Jan Claassen[3], Brian L. Edlow[4], Raimund Helbok[5], Paul M. Vespa[6], Michael N. Diringer[7], Len Polizzotto[8], Lori Shutter[9], Jose I. Suarez[10], Robert D. Stevens[10], Daniel F. Hanley[11], Yama Akbari[12], Thomas P. Bleck[13], Melanie Boly[14], Brandon Foreman[15], Joseph T. Giacino[16], Jed A. Hartings[17], Theresa Human[18], Daniel Kondziella[19], Geoffrey S. F. Ling[20], Stephan A. Mayer[21], Molly McNett[22], David K. Menon[23], Geert Meyfroidt[24], Martin M. Monti[25], Soojin Park[3], Nader Pouratian[26], Louis Puybasset[27], Benjamin Rohaut[28], Eric S. Rosenthal[4], Nicholas D. Schiff[29], Tarek Sharshar[30,31], Amy Wagner[32], John Whyte[33] and DaiWai M. Olson[34] on behalf of on behalf of the Neurocritical Care Society Curing Coma Campaign

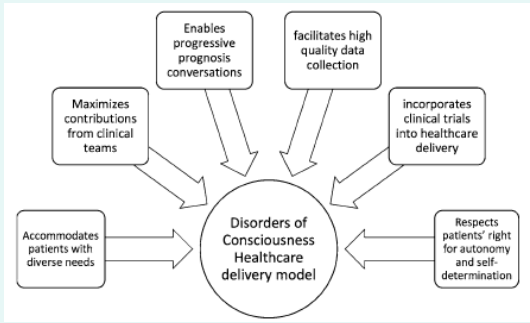
3 Scientific Pillars

1. Endotyping
2. Biomarkers
3. Proof-of-Concept Clinical Trials

- Multidisciplinary effort – grand challenge
- Emphasizing continuum from acute care to recovery
  - ICU providers and scientists should be working with post-acute and rehabilitation/recovery specialists and vice versa

Gap Analyses – Classification, Mechanisms, Trajectories, Therapies





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NEUROCRITICAL CARE SOCIETY

THE CURING COMA CAMPAIGN

Proceedings of the First Curing Coma Campaign NIH Symposium: Challenging the Future of Research for Coma and Disorders of Consciousness

Jan Claassen[1*], Yama Akbari[2], Sheila Alexander[3], Mary Kay Bader[4], Kathleen Bell[5], Thomas P. Bleck[6], Melanie Boly[7], Jeremy Brown[8], Sherry H.-Y. Chou[9], Michael N. Diringer[10], Brian L. Edlow[11], Brandon Foreman[12], Joseph T. Giacino[13], Olivia Gosseries[14], Theresa Green[15], David M. Greer[16], Daniel F. Hanley[17], Jed A. Hartings[18], Raimund Helbok[19], J. Claude Hemphill[20], H. E. Hinson[21], Karen Hirsch[22], Theresa Human[23], Michael L. James[24], Nerissa Ko[20], Daniel Kondziella[25,26], Sarah Livesay[27], Lori K. Madden[28], Shraddha Mainali[29], Stephan A. Mayer[30], Victoria McCredie[31], Molly M. McNett[32], Geert Meyfroidt[33], Martin M. Monti[34], Susanne Muehlschlegel[35], Santosh Murthy[36], Paul Nyquist[37], DaiWai M. Olson[38], J. Javier Provencio[39], Eric Rosenthal[40], Gisele Sampaio Silva[41], Simone Sarasso[42], Nicholas D. Schiff[43], Tarek Sharshar[44], Lori Shutter[9], Robert D. Stevens[37], Paul Vespa[45], Walter Videtta[46], Amy Wagner[47], Wendy Ziai[37], John Whyte[48], Elizabeth Zink[49] and Jose I. Suarez[37]the Curing Coma Campaign

Abstract

Coma and disorders of consciousness (DoC) are highly prevalent and constitute a burden for patients, families, and society worldwide. As part of the Curing Coma Campaign, the Neurocritical Care Society partnered with the National Institutes of Health to organize a symposium bringing together experts from all over the world to develop research targets for DoC. The conference was structured along six domains: (1) defining endotype/phenotypes, (2) biomarkers, (3) proof-of-concept clinical trials, (4) neuroprognostication, (5) long-term recovery, and (6) large datasets. This proceedings paper presents actionable research targets based on the presentations and discussions that occurred at the conference. We summarize the background, main research gaps, overall goals, the panel discussion of the approach, limitations and challenges, and deliverables that were identified.

Keywords: Coma, Consciousness, Electrophysiology, Magnetic resonance imaging, Biomarkers

CURING COMA *Virtual Symposium*

Challenging the Future of Research for Coma and Disorders of Consciousness

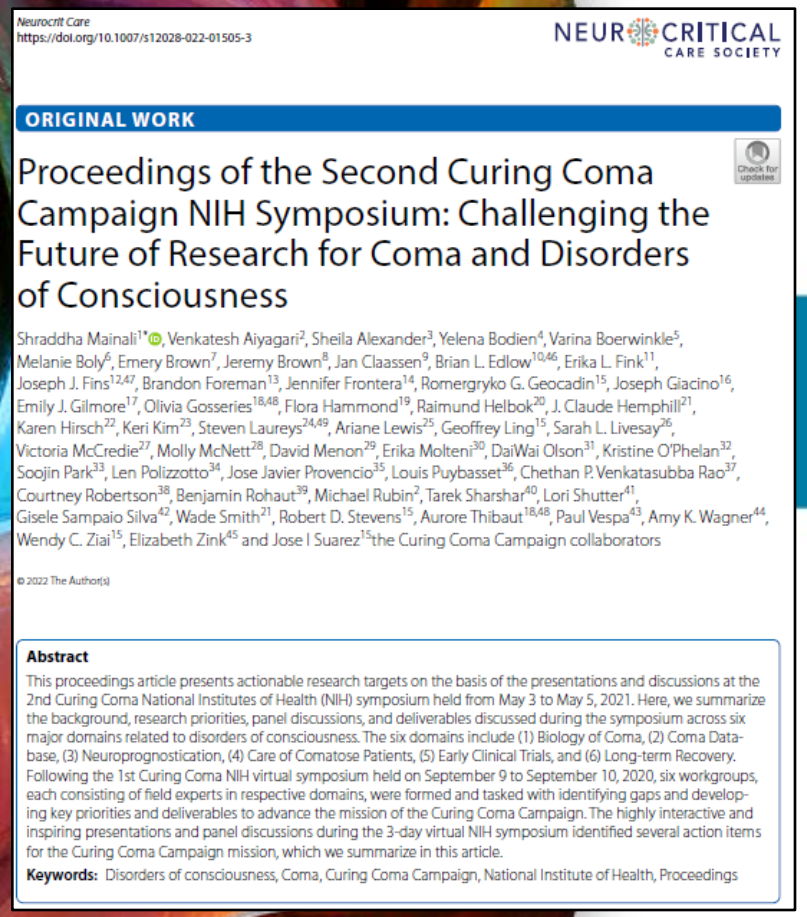
September 9–10, 2020

Co-sponsored by

NEUROCRITICAL CARE SOCIETY

CURING COMA AWAKENING HOPE

NIH National Institute of Neurological Disorders and Stroke



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NEUROCRITICAL CARE SOCIETY

ORIGINAL WORK

Proceedings of the Second Curing Coma Campaign NIH Symposium: Challenging the Future of Research for Coma and Disorders of Consciousness

Shraddha Mainali[1*], Venkatesh Aiyagari[2], Sheila Alexander[3], Yelena Bodien[4], Varina Boerwinkle[5], Melanie Boly[6], Emery Brown[7], Jeremy Brown[8], Jan Claassen[9], Brian L. Edlow[10,46], Erika L. Fink[11], Joseph J. Fins[12,47], Brandon Foreman[13], Jennifer Frontera[14], Romergryko G. Geocadin[15], Joseph Giacino[16], Emily J. Gilmore[17], Olivia Gosseries[18,48], Flora Hammond[19], Raimund Helbok[20], J. Claude Hemphill[21], Karen Hirsch[22], Keri Kim[23], Steven Laureys[24,49], Ariane Lewis[25], Geoffrey Ling[15], Sarah L. Livesay[26], Victoria McCredie[27], Molly McNett[28], David Menon[29], Erika Molteni[30], DaiWai Olson[31], Kristine O'Phelan[32], Soojin Park[33], Len Polizzotto[34], Jose Javier Provencio[35], Louis Puybasset[36], Chethan P. Venkatasubba Rao[37], Courtney Robertson[38], Benjamin Rohaut[39], Michael Rubin[2], Tarek Sharshar[40], Lori Shutter[41], Gisele Sampaio Silva[42], Wade Smith[21], Robert D. Stevens[15], Aurore Thibaut[18,48], Paul Vespa[43], Amy K. Wagner[44], Wendy C. Ziai[15], Elizabeth Zink[45] and Jose I Suarez[15]the Curing Coma Campaign collaborators

Abstract

This proceedings article presents actionable research targets on the basis of the presentations and discussions at the 2nd Curing Coma National Institutes of Health (NIH) symposium held from May 3 to May 5, 2021. Here, we summarize the background, research priorities, panel discussions, and deliverables discussed during the symposium across six major domains related to disorders of consciousness. The six domains include (1) Biology of Coma, (2) Coma Database, (3) Neuroprognostication, (4) Care of Comatose Patients, (5) Early Clinical Trials, and (6) Long-term Recovery. Following the 1st Curing Coma NIH virtual symposium held on September 9 to September 10, 2020, six workgroups, each consisting of field experts in respective domains, were formed and tasked with identifying gaps and developing key priorities and deliverables to advance the mission of the Curing Coma Campaign. The highly interactive and inspiring presentations and panel discussions during the 3-day virtual NIH symposium identified several action items for the Curing Coma Campaign mission, which we summarize in this article.

Keywords: Disorders of consciousness, Coma, Curing Coma Campaign, National Institute of Health, Proceedings

CURING COMA

Virtual Symposium

Challenging the Future of Research for Coma and Disorders of Consciousness

May 3 -4, 2021

Co-sponsored by

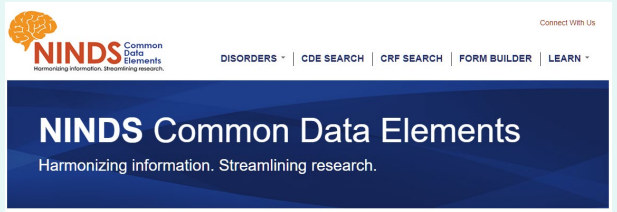
NEUROCRITICAL CARE SOCIETY

CURING COMA AWAKENING HOPE

NIH National Institute of Neurological Disorders and Stroke

Common Data Elements

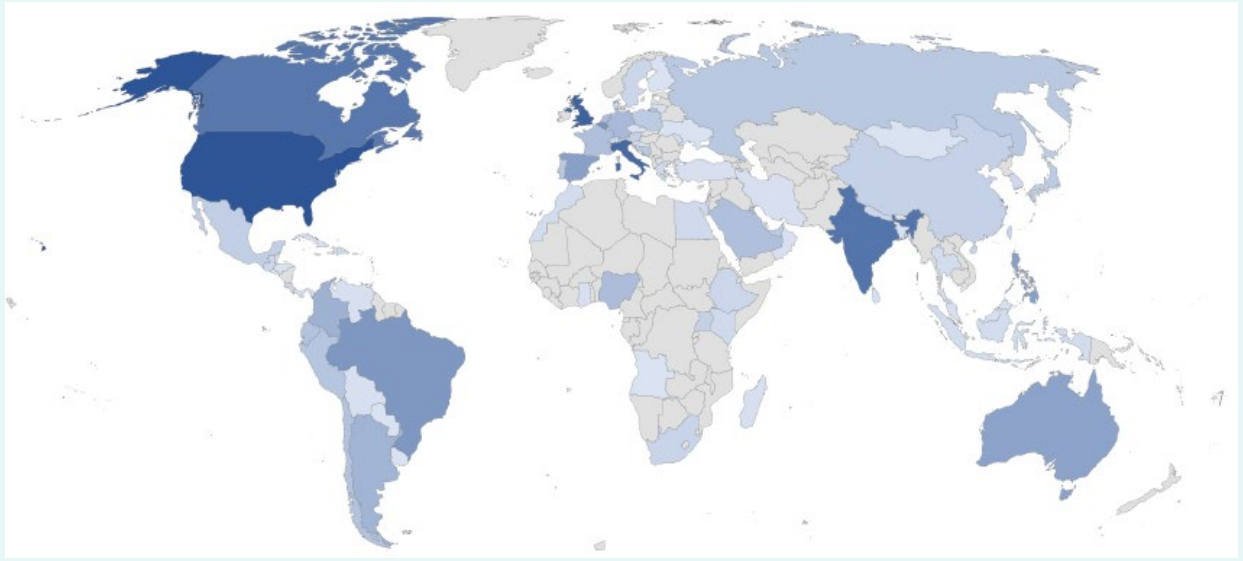
- CDEs are "content standards that enable clinical investigators to systematically collect, analyze, and share data across the research community"
- CCC developed the CDEs for Coma and DoC (Brian Edlow, Jan Claassen, Jose Suarez co-leads)
- 9 working groups including pediatrics
- Underwent public comment and multiple peer-reviewed publications https://link.springer.com/collections/cjhedaffbd
- Online archive https://zenodo.org/records/8172359 with goal of integration into NIH/NINDS CDE repository in 2025



World Coma Day

- **<u>Outreach</u>** for engagement of collaborators, public, and science community
- First WCD in 2021. Pandemic brought us together.
- 24 hour virtual event. Zoom platform.

- WCD 2023
  - 966 registrants
  - 56 speakers and moderators
  - 100 countries
  - ”Shoutouts” from ICUs, rehabilitation units, research labs arounds the world
  - “Stories of Hope” – patients & families
- WCD 2024 – YouTube format, >43,000 views



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NEUROCRITICAL CARE SOCIETY

ORIGINAL WORK

The Curing Coma Campaign International Survey on Coma Epidemiology, Evaluation, and Therapy (COME TOGETHER)

Raimund Helbok[1*†], Verena Rass[1†], Ettore Beghi[2], Yelena G. Bodien[3,4], Giuseppe Citerio[5,6], Joseph T. Giacino[3], Daniel Kondziella[7], Stephan A. Mayer[8], David Menon[9], Tarek Sharshar[10], Robert D. Stevens[11], Hanno Ulmer[12], Chethan P. Venkatasubba Rao[13], Paul Vespa[14], Molly McNett[15], Jennifer Frontera[16] and the Curing Coma Campaign and its Contributing Members

Abstract

Background: Although coma is commonly encountered in critical care, worldwide variability exists in diagnosis and management practices. We aimed to assess variability in coma definitions, etiologies, treatment strategies, and attitudes toward prognosis.

Methods: As part of the Neurocritical Care Society Curing Coma Campaign, between September 2020 and January 2021, we conducted an anonymous, international, cross-sectional global survey of health care professionals caring for patients with coma and disorders of consciousness in the acute, subacute, or chronic setting. Survey responses were solicited by sequential emails distributed by international neuroscience societies and social media. Fleiss κ values were calculated to assess agreement among respondents.

Results: The survey was completed by 258 health care professionals from 41 countries. Respondents predominantly were physicians ($n = 213$, 83%), were from the United States ($n = 141$, 55%), and represented academic centers ($n = 231$, 90%). Among eight predefined items, respondents identified the following cardinal features, in various combinations, that must be present to define coma: absence of wakefulness (81%, $\kappa = 0.764$); Glasgow Coma Score (GCS) ≤ 8 (64%, $\kappa = 0.588$); failure to respond purposefully to visual, verbal, or tactile stimuli (60%, $\kappa = 0.552$); and inability to follow commands (58%, $\kappa = 0.529$). Reported etiologies of coma encountered included medically induced coma (24%), traumatic brain injury (24%), intracerebral hemorrhage (21%), and cardiac arrest/hypoxic-ischemic encephalopathy (11%). The most common clinical assessment tools used for coma included the GCS (94%) and neurological examination (78%). Sixty-six percent of respondents routinely performed sedation interruption, in the absence of contraindications, for clinical coma assessments in the intensive care unit. Advanced neurological assessment techniques in comatose patients included quantitative electroencephalography (EEG)/connectivity analysis (16%), functional magnetic resonance imaging (7%), single-photon emission computerized tomography (6%), positron emission

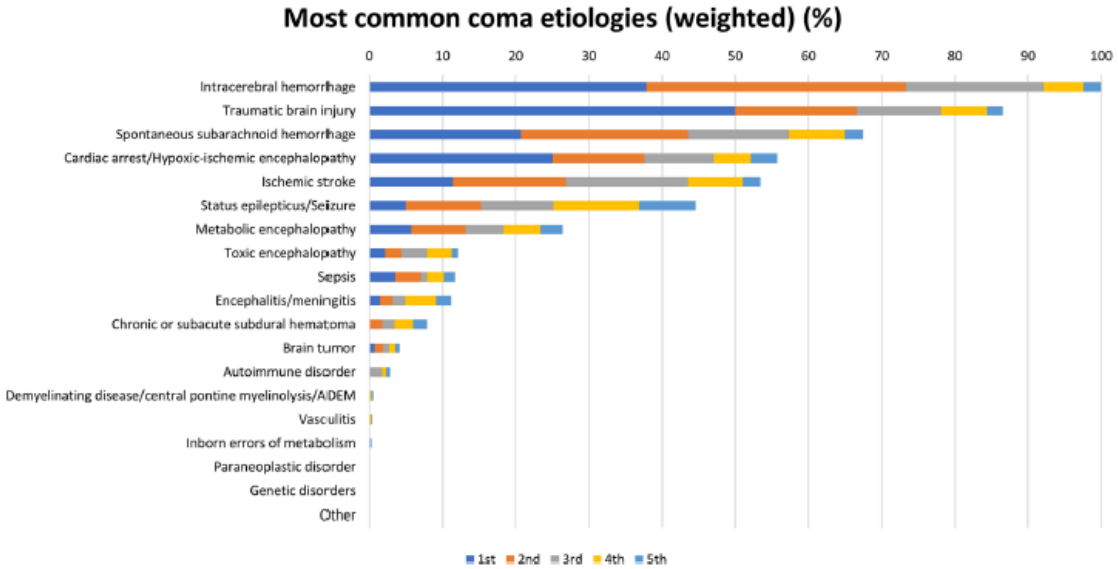

Fig. 3 Most common etiologies of coma weighted by the five most common causes. Survey question: Rank the top five most common etiologies of coma that you encounter in your institution based on the definition of coma provided above. Bars represent the selection of etiologies based on the most common (blue), second most common (orange), third most common (gray), fourth most common (yellow), fifth most common (light blue) etiology of coma. Data are given in percentage and weighted based on the grading of respondents, normalized to the most common etiology (intracerebral hemorrhage). The answers were weighted based on the most common (multiplied by 5), the second most common (multiplied by 4), the third most common (multiplied by 3), the fourth most common (multiplied by 2) and the 5th most common etiology (multiplied by 1)

TBI is an extremely common neurocritical care condition

This is where patients start, and it directs whether patients survive and where they go

Helbok *Neurocritical Care* 2022

Curing Coma

- "Curing coma" is mostly about *culture change*. Moving from pessimism and nihilism to "awakening hope" in a realistic and responsible manner
- Recognizing prognostic uncertainty – "prognostic humility"
- Recognizing the limits of the clinical neurological examination and the need for additional ways to assess consciousness
  - Imaging, electrophysiology, advanced/standardized neuro exam
- Treating patients in the acute care (ICU) setting and post-acute (rehabilitation) setting based on the potential for recovery, not just what they look like in the moment
  - Endotype versus phenotype
- Without rehabilitation for recovery, there is a negative feedback that reinforces nihilism in the ICU