BRAIN INJURY: DISORDERS OF CONSCIOUSNESS 101

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Coma

- No eye opening at any time.
- No meaningful interaction with the environment.
- No purposeful movement.
- No command following at any time.
- No sleep-wake cycles are observed.

Coma is typically a self-limited condition that evolves to vegetative state or a higher level of consciousness within a matter of weeks.
VEGETATIVE STATE

- Also known as Unresponsive Wakefulness Syndrome.

- Devoid of cognitive content.
- Eyes open & sleep wake cycles are observed
- Absence of purposeful responses.

One of the first signs of emergence from vegetative state is sustained visual pursuit.
PERSISTENT VS. PERMANENT VEGETATIVE STATE

PERSISTENT = VS longer than 30 days

PERMANENT = VS longer than 1 year after TBI or more than 3 months after Anoxic BI

The terms Persistent Vegetative State and Permanent Vegetative State are less useful than describing:

- cause of the brain injury,
- duration of unconsciousness,
- age,
- GCS, and
- anatomic lesion(s)
MINIMALLY CONSCIOUS STATE (MCS)

Inconsistent but unequivocally meaningful responses indicative of conscious awareness. Observe any one of the following:

- sustained visual tracking, +/or
- simple command following, +/or
- reaching toward an object, +/or
- intelligible verbalization (not vocalization), +/or
- use of gestures to communicate, +/or
- contingent emotional response.

Standardized Neurobehavioral Scales in the Diagnosis of DOC (PVS vs MCS)

- JFK Coma Recovery Scale – Revised (CRS-R)
- Western Neuro Sensory Stimulation Profile (WNSSP)
- Coma/Near-Coma Scale (C/NC)

Correct diagnosis is useful in determining prognosis → decisions re: aggressive treatment vs withdrawal of care.

Establish a baseline of neurologic function against which the impact of treatment (activating drugs) can be measured.

Sensitive enough to document neurologic improvement/change.

Misdiagnosis = 30-40%
WHEN IS VEGETATIVE STATE NOT VEGETATIVE STATE?

Willful Activation of Brain Activity in Disorders of Consciousness

- N = 54 Patient in total were studied
- 23 in Vegetative State
- 31 Minimally Conscious State

How many patients were able to show evidence of willful activation of brain?

Willful Activation of Brain Activity in Disorders of Consciousness

- Only 5/54 could willfully activate appropriate brain activity.
- Of these, 4/5 had been diagnosed as vegetative.
- Only 1/31 patients in MCS demonstrated willful activation of brain activity.
- All responders were TBI patients. None had anoxic BI.
USING BEHAVIORAL CRITERIA, MCS MAY BE MISDIAGNOSED AS VEGETATIVE STATE

- Severe dystonia (spasticity/rigidity)
- Paralysis
- Contractures
- Cortical blindness
- Apraxia
- Abulia
- Aphasia
FUNCTIONAL LOCKED IN SYNDROME

• This includes individuals with NO detectable behavioral signs of meaningful interaction who nevertheless demonstrate preserved cognitive processes (willful cognitive intent) using technology, such as fMRI, PET, or electrophysiologic studies.

• These technologies are likely to play a more prominent role in the future.
PM&R Input for spasticity management:

- Botox
- Oral medications (Dantrium, Baclofen)
- Nerve blocks
- Intrathecal Baclofen trials
INTERDISCIPLINARY TEAM

Identify and remove barriers to the patient’s ability to demonstrate observable behavioral responses:

- Treat spasticity with appropriate least sedating medication, nerve blocks, Botox, splinting, &/or casting.
- Measure tone with Modified Ashworth Scale.
- Treat contractures.
- Be aware of signs of heterotopic ossification.
- Augment concise verbal requests with repetition, demonstration, and contextual cues.
PROGNOSIS

What factors impact a patient’s potential to recover from a severe BI?
PROGNOSTIC FACTORS

- Glasgow Coma Score (Depth of coma → Severity of brain injury)
- Duration of Coma or Vegetative State
- Duration of Post-Traumatic Amnesia
- Cause (Traumatic vs. Anoxic)
- Genetics
- Age
- Imaging studies (neuroanatomy)

- General Health and h/o prior TBI
- Pre-injury Personality
- Pre-injury Intelligence
- Psychosocial Characteristics
- Family Support
- Therapeutic Environment/Opportunity for Rehabilitative Therapies.
PROGNOSIS

Traumatic BI:

- Over 50% of pts still in VS at 1 month → conscious at 1 year.
- 35% pts in VS at 3 months → regained consciousness at 1 year.
- 16% of those in VS at 6 months → conscious at 1 year.

Non-traumatic (Anoxic)

- Non-traumatic (anoxic) BI: 15% of pts in VS at 1 month → conscious at 1 year.
- 7% in VS at 3 months → conscious at 1 year.

NEJM 330 (22), 1994
PROGNOSIS IN MCS

- 38% of patients in MCS at 1 month progressed to moderate or no disability on the Glasgow Outcome Scale at 1 year compared to < 5% of patients in VS.

(Moderate disability = No need for assistance in everyday life. Employment is possible with accommodations.)

- Outcomes are best when patients recover to MCS within 8 weeks of injury.

- More favorable outcomes after TBI than non-traumatic BI.

- Up to 30% of patients still in MCS at 1 year can emerge from this condition, though most are left severely disabled.

BEFORE Pharmacologic Treatment of Disorders of Consciousness

1. ESTABLISH A BASELINE OF NEUROLOGIC FUNCTION.

2. RULE OUT TREATABLE CAUSES OF FAILURE TO IMPROVE BEFORE PRESCRIBING ACTIVATING MEDICATION.
All patients with mod-severe TBI should undergo neuroendocrine screening on discharge from ICU or acute care, again at 3 months, and at 1 year post-injury. Labs include morning Cortisol levels, TSH, free Thyroxine, LH, FSH Prolactin, Insulin-like Growth Factor (IGF-1), Testosterone (males only) and Estradiol (Females only).
NEUROLOGIC CAUSES OF FAILURE TO IMPROVE

INTRACRANIAL COMPLICATIONS

- Recurrent bleeding
- Hydrocephalus
- Shunt Malfunction

Screening test of choice: Non-contrast CT Head
Post-traumatic HYDROCEPHALUS

Hydro = Water
Cephalus = Brain

The abnormal accumulation of CSF in the ventricles stalls recovery and causes a progressive decline in neurologic function.
TREATMENT of HYDROCEPHALUS

Ventriculoperitoneal Shunt Placement

Enlarged Left Ventricle

Entry into Cranium

Valve (Behind Ear)

Extra Tubing in Peritoneal Cavity for Growth

Underneath Skin
VP SHUNT MALFUNCTION occurs in up to 25% of patients in a lifetime.

A shunt study is an easy way to evaluate shunt continuity.
Nuclear Medicine Shunt Study

NORMAL SHUNT STUDY

OBSTRUCTED SHUNT
SUBCLINICAL SEIZURES

A screening EEG is mandatory for patients with disorders of consciousness or fluctuating levels of alertness to R/O subclinical seizures.

Not all seizures are apparent on clinical exam. Seizures can interfere with recovery from DOC.
TREATABLE CAUSES OF FAILURE TO IMPROVE

- Altered Sleep-Wake Cycles
- Malnutrition
ELIMINATE OR REDUCE SEDATING MEDICATIONS

Clonidine
Neuroleptics e.g. Haldol
Metoclopramide (Reglan)
Compazine
Prazosin
Benzos

Avoid Polypharmacy
Neuropharmacology

- First, know your patient’s **neurologic baseline** and address treatable causes of the patient’s failure to improve.

- Then consider the judicious prescription of **activating medications**. Use a team approach where family, nursing, MDs, and therapists know what target behaviors to expect.
Pharmacologic Neuromodulation in Disorders of Consciousness

Neural plasticity & recovery can be modulated by drugs → affect neurotransmitter systems.

**WAKE PROMOTING**
- Dopamine
- Norepinephrine
- Glutamate
- Serotonin
- Acetylcholine
- Histamine
- Hypocretins-orexins

**CNS DEPRESSANT**
- Zolpidem (Ambien) facilitates gamma aminobutyric acid (GABA) neurotransmission. However, in select patients Zolpidem may promote increases in LOA.
AMANTADINE (Symmetrel)

Enhances **Dopaminergic** transmission pre- and post-synaptically.

- Facilitates Dopamine (DA) release and blocks its reuptake pre-synaptically.

- Increases the number of post-synaptic receptors.

- May also exert its effect by restoring the balance between Glutaminergic and Dopaminergic neurotransmitter systems.
N = 184 patients in either VS or MCS
   All patients were 1-4 months post-TBI
   All patients were enrolled in inpatient acute rehab

Randomly assigned to take Amantadine or a placebo for 4 weeks, and then followed for an additional 2 weeks after drug treatment was terminated. The Disability Rating Scale (DRS) was used to assess each patient’s clinical status during the 4 week trial and the 2 week washout period.

DRS ranges from 0-29. Higher scores indicate greater disability.
Mean Disability Rating Scale (DRS) Scores during the 6-Week Assessment Period, According to Study Group.

Amantadine group recovered faster until the drug was stopped. Then the rate of improvement became slower in the Amantadine group compared to the placebo group in weeks 5 & 6. The overall change in DRS scores at week 6 was similar in the two groups. In a subgroup analysis, Amantadine worked equally well for patients in VS and those in MCS as well as for those 1 month and 4 months out from injury.

ZOLPIDEM (AMBIEN)

- Facilitates gamma aminobutyric acid (GABA) neurotransmission.
- Normally functions to promote sleep.

About 5-6% of patients respond with measurable improvements in LOC and do so within 1 hour of drug administration. May transiently follow commands and communicate for up to 4 hours, then return to reduced LOC thereafter. Effect evident on day #1.
DOC CASE STUDY - HISTORY

27 y.o. male S/P bicycle vs. MVA on his way to work 6 months ago. 
**Initial GCS 3.** CT head - R SDH w 9 mm MLS, uncal herniation. High ICP → R decompression craniectomy D#1. Subsequent cranioplasty. Unresponsive for 6 months when referred for evaluation.
On exam 6 months post-injury:

- No command following.
- Nonverbal and unable to communicate.
- Immobile with tetraplegia & spasticity in all 4 extremities.
- Trach has been weaned. Snores.
- Nutrition, hydration, & meds via Gastrostomy tube (GT).
- No neuro-activating med trials.
CASE STUDY - HISTORY

- Left gaze preference. Tracking to midline when alert but fluctuating levels of alertness (LOA).

- Significant daytime fatigue. Not on AED. No recent EEGs.

- CT imaging last performed 3 months ago but not compared with prior studies. It had shown mild ventriculomegaly slightly out of proportion to encephalomalacia.

CASE STUDY WORK-UP OF FAILURE TO IMPROVE & INTERVENTION

- Persistent emesis with high gastric residuals → IR change from GT to JGT. Emesis resolved. Reglan D/C’d.

- We order a screening non-contrast CT head → Post-traumatic communicating hydrocephalus superimposed on mild ex-vacuo hydrocephalus →

Therefore, a high volume lumbar tap test was performed. Hydrocephalus confirmed → VPS placement → Follows commands and patient speaks for 1st time since injury. Spasticity 50% improved and can now move his right leg as well as right arm > left arm.
CASE STUDY & INTERVENTION

• EEG + for seizures. AED Rx → Consistent commands and no longer fluctuating performance.

• Snoring and daytime fatigue assessed with polysomnography → + for central and obstructive sleep apnea. BIPAP titrated for control. Family notes great improvement in daytime alertness. Be aware of a nearly 50% incidence of sleep D/O after TBI.

• Activating medication trial with Amantadine in progress. Consider boost with addition of low-dose Sinemet if necessary.

This patient is now able to participate in PT, OT, and Speech Therapy. The future is looking much brighter.
Every 13 seconds someone in America suffers a brain injury.

And together we can help.
Thank you!

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