Traumatic Brain Injury: An Overview in Pediatric and Adult Populations

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Objectives

- Learn methods to assess traumatic brain injury (TBI) severity
- Discuss recovery patterns in pediatric and adult populations with TBIs of varying severities
- Develop a general understanding of the current state of knowledge related to chronic traumatic encephalopathy (CTE)

Assessing injury severity

- Mild TBI (aka Concussion)- 71-77%
- Moderate TBI- 7-11%
- Severe TBI- 8-12%

Langlois et al., 2003

- Glasgow Coma Scale (Pediatric Coma Scale)
- Duration of Post-traumatic Amnesia
- Duration of Coma

Assessing injury severity: GCS and PCS

GCS

Eyes Open
Spontanteously-4
To speech-3
To pain-2
None-1

Best Motor Response
Obeys commands 6**
Localizes pain-5
Withdraws-4
Flexion to pain-3
Extension to pain-2
None-1

Best Verbal Response
Oriented-5
Confused-4
Words-3
Sounds-2
None-1

PCS

Eyes Open: Same as adults

Best Motor Response: Same as adults
6: Maximum Score for >2
5: Maximum Score for 6 months- 2 yrs
4: Maximum Score for <6 months

Best Verbal Response
Oriented-5 (Maximum for >5 yrs)
Words-4 (Maximum for 1-5 yrs)
Vocal Sounds-3 (Maximum for 26-52 wks)
Cries-2 (Maximum for 0-26 wks)
None-1

Assessing injury severity: Post-traumatic amnesia (PTA)

- PTA: Period of confusion/disorientation following TBI or emergence from coma

Duration	Injury Severity
<5 minutes	Very Mild
5 minutes-1 hour	Mild
1 to 24 hours	Moderate
1 to 7 days	Severe
>1 week	Very Severe
>4 weeks	Extremely Severe

Jennett (1976)

- Children's Orientation and Amnesia Test (Ewing-Cobbs et al., 1990)
- Galveston Orientation & Amnesia Test (Levin et al., 1979)
- Oxford Test (Artiola et a., 1980)
- Westmead Post-Traumatic Amnesia Scale (Shores, 1989)

Assessing injury severity: Duration of coma

Classification	Coma Duration
Mild	<20 minutes
Moderate	No longer than within 6 hours of admission
Severe	>6 hours after admission

Bond, 1986

Patients with GCS< 8 are considered to be in a coma

TBI Recoveries: What to expect

Concussion recovery: Symptoms

Early Symptoms (Minutes to Hours)

- Headaches
- Dizziness
- Nausea
- Vomiting
- Lack of awareness

Later Symptoms (Days to Weeks)

- Persistent headaches
- Sleep disturbance
- Diminished concentration
- Memory dysfunction
- Irritability

Concussion recovery

- Concussions **not** typically associated with identifiable cell death or other structural changes.
- When attempting to return to its normal state, brain has to temporarily operate using less efficient anabolic metabolism.
- Additional activity during this recovery period (physical or cognitive) is a source of additional neurometabolic demand. If the activity is excessive, the cycle is perpetuated causing exacerbation of symptoms.

This is why rest is recommended in the recovery period

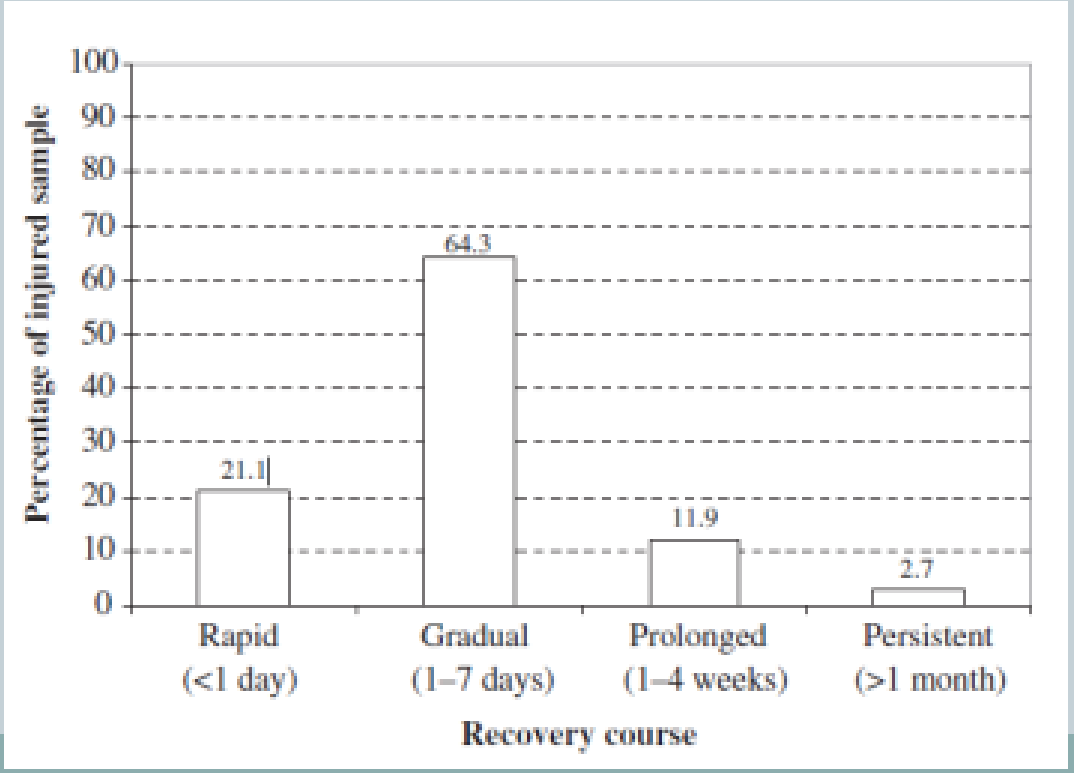
How long should you rest?

- Some studies of high school athletes indicate recovery of symptoms and neurocognitive functioning within about 7 to 10 days.

- Others have shown more prolonged recovery period.

What does the data suggest?

Based on 635 prospectively enrolled concussed high school and college athletes. From McCrea, Iverson, McAllister, Hammeke, Powell, Barr, & Kelly (2009).



Current slide and next slide are data discussed during 2015 INS meeting presentation:

Pediatric Mild TBI: Who Gets Better, Who Doesn't, and What's Neuropsychology Got To Do With It by Michael Kirkwood, Ph.D., ABPP-CN

What does the data suggest?

Risk factors for concussive symptoms 1 week or longer in high school athletes

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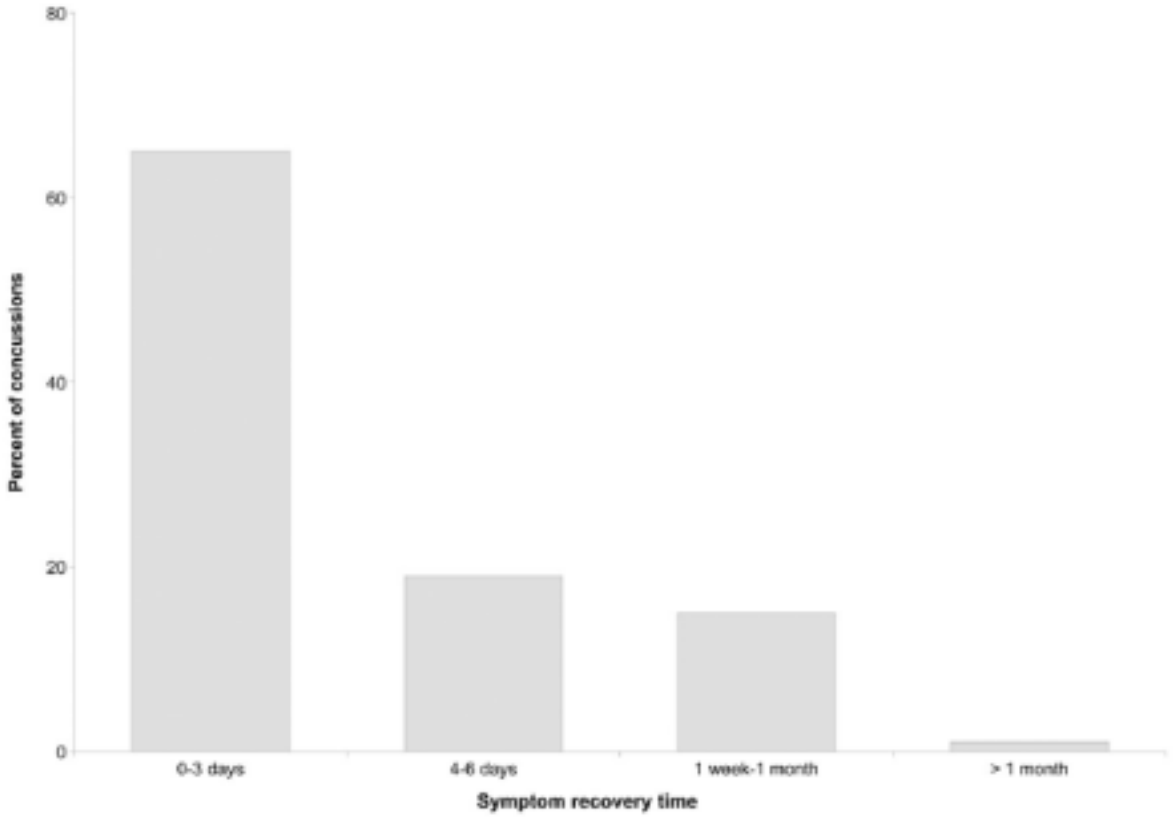


Figure 1. Concussive symptom recovery time in the National High School Sports-Related Injury Surveillance System Reporting Information Online database (RIO™) 2006–2009.

Post-concussive syndrome (PCS)

What predicts a longer recovery?

- Loss of consciousness or neuroimaging abnormalities (CMTBI)
- Post-injury reports of acute or chronic pain (particularly if associated with bodily injuries)
- PTSD (which varies depending on the mechanism of injury)
- Pre-injury learning problems, psychiatric problems, cognitive ability
- Coping strategies
- Psychosocial factors (e.g. family functioning, parental psychological adjustment and availability of resources and stressors)
- **When evaluating and treating persistent PCS, clinicians should consider factors that may elicit symptoms for reasons other than an underlying brain injury.**

McNally et al., 2013

Neuropathology of severe TBI

Type of Insult	Neuropathology
Primary	Skull fracture
	Intracranial contusions and hemorrhage
	Shear-strain injury
Secondary	Brain swelling
	Cerebral edema
	Elevated intracranial pressure
	Hypoxia-ischemia
	Mass lesions (hematoma)
Neurochemical	Excessive production of free radicals
	Excessive release of excitatory neurotransmitters
	Alterations in glucose metabolism
	Decreased cerebral blood flow
Late/delayed	White matter degeneration and cerebral atrophy
	Posttraumatic hydrocephalus
	Posttraumatic seizures

Severe TBI

Can produce deficits in:

- IQ
- Attention
- Executive Functioning
- Memory
- Language/Communication
- Nonverbal Skills
- Sensory/Motor Skills
- Academics
- Social Functioning
- Behavior
- Psychological Functioning
- Adaptive Skills

Severe TBI: Predictors of Outcome

Poorer Outcomes Associated with…

- More severe injury
- More structural or functional abnormalities on imaging
- Younger age at injury (particularly in infancy or preschool age)
- Weaker premorbid cognitive functioning
- Lower socioeconomic status
- More dysfunctional family environments
- Poorer quality of acute care or rehabilitation services

What About Age at Insult?

Plasticity vs. Early Vulnerability

Plasticity refers to the notion that a young child's brain is "plastic" and reorganization of function is more likely to occur (resulting in a better outcome than in the mature brain).

Early Vulnerability argues that brain damage during childhood (especially early childhood) disrupts development, resulting in greater impairments.

What About Age at Insult?

- The literature largely supports the early vulnerability argument, with deficits observed in nearly all cognitive domains following early severe childhood brain insults.
- Children with more severe injuries are at greatest risk, supporting a "double-hazard" effect (Escalona, 1982).
- Consider the notion of "growing into deficits."

Adults

mTBI and the Postconcussive Syndrome in Adults

- Adult patients frequently present in primary care settings with vague, nonspecific functional complaints, which they may attribute to a past "head injury"
  - Often, these injuries are remote, the person may not have sought medical care at the time or is unable to report on where they received care, or they are poor personal historians broadly speaking
    - Due to these limitations, primary care providers must often rely on retrospective patient self-report to gauge the potential contribution of the patient's "head injury" to their current clinical presentation.
    - Thus, clinical history taking is crucial in deciding how to manage these patients and address their symptoms

mTBI and the Postconcussive Syndrome in Adults

Table 1. VHA/DoD clinical practice guideline for management of concussion/MTBI: TBI classification scheme

	Severity level		
Criteria	Mild	Moderate	Severe
Structural imaging	Normal	Normal or abnormal	Normal or abnormal
Loss of consciousness (LOC)	0–30 min	>30 min and <24 hours	>24 hours
Alteration of consciousness/ mental state	a moment up to 24 hours	>24 hours. Severity based on other criteria	>24 hours. Severity based on other criteria
Post-traumatic amnesia (PTA)	0–1 day	>1 day and <7 days	>7 days
Glasgow Coma Scale (GCS)	13–15	9–12	<9

Alteration of consciousness/mental state must be immediately related to trauma to the head.
VHA/DoD = Veterans Health Administration and Department of Defense.

mTBI and the Postconcussive Syndrome in Adults

- mTBI/concussion is by definition a transient disruption in brain functioning, with no associated structural sequelae
  - ACRM Definition: Requires a single criterion consisting of either loss of consciousness, posttraumatic amnesia, or altered mental status for diagnosis (using the time frames presented previously)
  - Pathophysiology: Sudden application of force to the head results in ionic shifts, altered neuronal metabolism, transient alterations in neuronal connectivity, and/or transient changes in neurotransmission.
    - However, this does NOT typically result in measurable cell death or structural alterations, rather, these transient changes cause neurons and axons to become temporarily dysfunctional

mTBI and the Postconcussive Syndrome in Adults

- Disruptions in brain physiological functioning are considered to parallel clinical symptoms and recovery time
  - Natural history of mTBI/Concussion
    - Within first few day post-injury, patients may experience headaches, blurred vision, dizziness/balance changes, concentration problems, forgetfulness, cognitive slowing, sleep disturbances, and/or irritability
      - For the VAST majority of individuals, these symptoms subside and eventually resolve within a few weeks of the injury
      - The term postconcussive disorder has been proposed to describe individuals that do not follow this modal trajectory of recovery, which has been operationalized by some as postconcussive symptoms that persist for three months or more post-injury (although this construct is controversial and disagreement exists in the field) (Iverson, et al., 2007).

mTBI and the Postconcussive Syndrome in Adults

- Postconcussive Disorder
  - These patients often present to PCP's, physiatrists, or neurologists seeking relief for lingering concussive symptoms
    - Some will have likely received medical evaluation in the acute phase to rule out more devastating injuries or neurological emergencies (e.g., an intracranial bleed); however, many will have had no prior contact with a medical professional (McCrea, 2008).
  - Assessment
    - Medical workup for PCD in the outpatient setting is typically unremarkable and fails to identify a neurological cause for the patient's symptoms

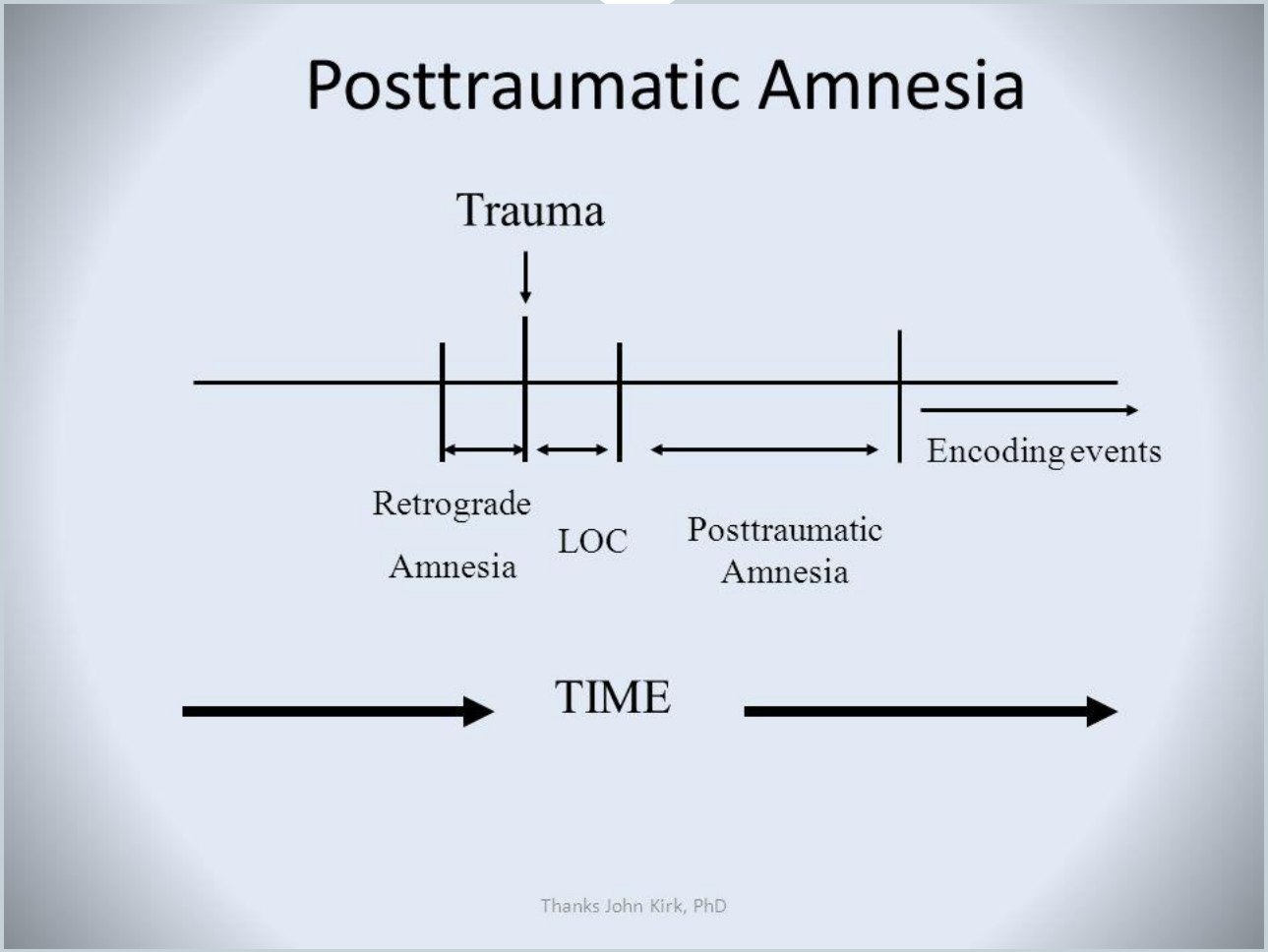
mTBI and the Postconcussive Syndrome in Adults

- Assessment, cont. and tips for use during patient evaluation
  - A patient cannot ascertain whether they have had a LOC. Therefore, unless a witness is available to verify a positive LOC, a patient's report most likely represents an interval of PTA (some of which may have been LOC). Therefore, PTA ranges and NOT LOC ranges should be use to determine injury severity in these cases
  - PTA is a marker of TBI severity that begins with the application of impact forces to the head. Thus, if the patient can describe personal memories of the circumstances of the injury (particularly the injury event itself), it is likely that any brain injury from the event is trivial or mild at worst
    - Also, delayed onset amnesia would suggest that factors other than the head impact are responsible for said amnesia (e.g., neurologic deterioration due to intracranial bleed, shock from fluid loss, hypoxia from respiratory distress, effects of medication, emotional distress, etc.)

mTBI and the Postconcussive Syndrome in Adults

- The end of PTA is signaled when the individual is reliably able to form new memories (e.g., is able to recall numerous details of a scene, retains information expressed to them, or can reliably stay oriented to time and place)
  - "Islands of memory" are not uncommon when recovering from the confusional state associated with PTA and these should therefore not be used to signal the end of a PTA period
- When ascertaining length of PTA from retrospective self-report, it is important to tell the patient that you are interested in THEIR memory of the event and not what they have been told by others or what their understanding of the event is. Also, avoid leading questions
  - Ask the patient what they remember about the injurious event
  - Carefully probe what the patient's last memory was prior to the injury and what their first memory after it was (focusing on obtaining as detailed a timeline as possible)
- Structural abnormalities on neuroimaging are likely to result in a more prolonged or otherwise complicated course of recovery, even when injury characteristics are consistent with mTBI (these are sometimes referred to as "complicated" mTBI's in the literature).

mTBI and the Postconcussive Syndrome in Adults



mTBI and the Postconcussive Syndrome in Adults

- Recovery is the norm, so why do some develop PCD?
  - Orthopedic injuries sustained along with the concussion can cause chronic pain, which can result in cognitive inefficiency, distraction, and changes in behavior (e.g., irritability, reduced frustration tolerance, etc.)
  - Likewise, chronic headaches can result from intracranial events (e.g., a bleed in complicated mTBI's), as well as scalp, neck, or musculoskeletal injuries. These are likewise distracting, functionally impairing, and may result in behavior change.
  - Concussions can result in vestibular changes and dizziness/balance problems. These too are distracting and potentially functionally impairing

mTBI and the Postconcussive Syndrome in Adults

- Recovery is the norm, so why do some develop PCD?
  - Psychiatric distress/illness: Psychiatric conditions can serve as both risk-factor for or underlying driver of PCD.
    - Premorbid ADHD/LD has been associated with protracted recovery from mTBI in the research literature
    - PTSD, depression, and anxiety disorders may develop in response to psychological trauma suffered during the injury itself or in response to functional difficulties experienced during the acute recovery period
    - Patients who tend to somaticize emotional distress are at higher risk for PCD and protracted recovery from mTBI
  - "Litigation neurosis", secondary gain, and/or frank malingering

mTBI and the Postconcussive Syndrome in Adults

- Summary: PCD is a multifactorial clinical entity that may be due to a variety of underlying, comorbid etiologies, which can include physical injuries, vestibular disturbances, psychiatric difficulties (both premorbid or in reaction to the injury), and in some cases, an individual's personal motivations. However, the research is clear, concussion/mTBI is NOT associated with lasting changes in brain function or structure, and therefore, alternate etiologies should be suspected when a patient fails to recover fully after 3 months.
- Clinical Management
  - A thorough review of the clinical history to obtain injury characteristics and identify treatment targets should be performed during the first patient contact
  - Subsequent management is contingent on the treatment targets identified and the complexity of an individual case; referral to specialists may be helpful in some cases
    - Headaches: neurology; vestibular complaints: physical medicine; behavioral/emotional disturbances: behavioral health, etc.

Moderate-Severe TBI

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Moderate-Severe TBI

- Unlike mTBI, moderate to severe TBI typically results in significant structural damage to the brain, which is usually identifiable in neuroimaging (even when the injury is remote in nature)
  - Neuroimaging findings can include focal brain injuries (skull fractures, cerebral contusions, intracranial bleeds, etc.) and diffuse axonal injuries secondary to acceleration/deceleration forces
  - Secondary brain injuries such as those caused by increased intracranial pressure, hypoxia, focal/diffuse cerebral edema, seizures secondary to brain trauma, or communicating hydrocephalus can also occur depending on the mechanism of injury
  - Persisting neurocognitive and functional decline is expected following these injuries, with increased impairment occurring as a function of injury severity

Moderate-Severe TBI

- Trajectories of recovery and clinical presentations are highly heterogenous and dependent on individual injury characteristics
  - Typical sequelae, however, include changes in personality (behavioral apathy/disinhibition), significant cognitive slowing (secondary to DAI), disturbances in attention, memory, and frontal systems functioning, social cognition deficits, loss of insight, alexithymia, etc.
  - Generally speaking, moderate TBI's are associated with lesser functional impairment. These individuals may be able to live a fairly independent life with structured and routinized activities being most manageable for them, but they may have a harder time engaging in spontaneous behavior or in adapting to sudden unexpected situations (Lezak, et al., 2012).

Moderate-Severe TBI

- However, severe TBI is associated with much poorer functional outcomes and significant, life long, functional impairment (Lezak, et al., 2012)
- Severe TBI's are also associated with a more protracted course of recovery
  - Individuals may be in a confused, agitated state for days (or more rarely) weeks after emerging from a post TBI coma
  - Spontaneous recovery tends to occur most robustly in the first three to six months post severe TBI and tends to level off at about a year post TBI
    - Additional, functional improvements tend to occur from subsequent learning and implementation of compensatory strategies; however, significant neurocognitive impairments and functional deficits typically remain at 5-year follow-up (Lezak, et al., 2012).
      - Rehabilitation to promote recovery of lost skills and help the patient develop compensatory techniques are therefore of paramount importance in the post-acute period

Moderate-Severe TBI

- Patients with this type of injury are far more likely to have received medical intervention in the acute period
  - Therefore, corroborating medical records confirming the nature of the injury and their post-injury course of recovery should, in theory, be easier to obtain
- Intervention/clinical management should focus on providing these individuals with supportive resources as needed in the chronic stage or ensuring access to adequate rehabilitative services during the post-acute stage
  - Speech, physical, and occupational therapies
  - Social work or case management services to assist them in applying for Medicaid waiver programs or SSDI
  - Psychiatric medication management for behavioral and emotional disturbances
  - Psychotherapy to promote successful adjustment to their new functional limitations

CTE: Current Controversies

- Overall, current data supporting CTE as a novel clinical entity is quite limited and marred by significant selection bias
- As conceptualized currently, CTE is a tauopathy putatively associated with repetitive brain trauma (RBT)
  - Major area of research interest in the field of sports concussion and mTBI
  - However, there are many limitations currently with regard to epidemiology, mechanisms of CTE development, and clinicopathological correlations of CTE, which are due to the reliance on postmortem case series investigations
  - Postmortem case investigation approach is subject to confirmation bias and circular reasoning (i.e., repetitive head trauma->behavioral/cognitive disturbances->CTE pathology at autopsy; etiology must be CTE)
  - What about the many contact sport athletes who age normally and do not go on to develop CTE symptoms, despite histories of repetitive head trauma? Studies examining these athletes are extremely limited (only one such study was identified in a review by Asken, et al. published in 2017 in JAMA Neurology)

CTE: State of Research and Future Directions

- Current data suggests that repetitive brain trauma is the best established risk-factor for CTE neuropathology at autopsy
  - However, in the one postmortem study that examined individuals with RBT histories and that included those that were not clinically symptomatic in life, only 21 out of 66 examined brains (31.8%) evidenced CTE neuropathology
    - A separate brain bank study examining brains affected by multiple system atrophy found that 8 out of 139 (5.8%) evidenced CTE pathological findings, only 4 of which had a documented history of head trauma
  - Moderating and mediating factors have not been adequately explored. Causal relationships are sometimes conflated (e.g., substance abuse as a product of CTE rather than a possible contributory factor to its neuropathology)
    - Areas in need of further research exploration include premorbid cognitive reserve, quality and quantity of education, lifestyle factors (such as substance abuse), clinicopathological correlates, progression (or lack thereof) of clinical symptoms, and operational definition of the CTE clinical syndrome (if future research indicates CTE is a distinct clinical entity)

CTE: Conclusion

- Considering the preponderance of the available data, RBT is the most well-established risk-factor for developing CTE neuropathology; however, in one of the only studies that examined both asymptomatic and symptomatic individuals with documented RBT histories, over two thirds showed no CTE pathology at autopsy.
- Recently developed pathological diagnostic criteria for CTE should serve to advance research in this field; however, at present, CTE mediators and moderators, clinicopathological correlates, and the nature of CTE clinical symptom onset and progression (if any) remain largely unknown.

Questions?