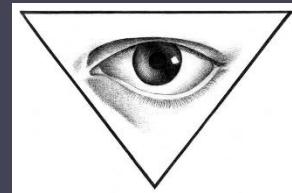


Diagnosing Mild Traumatic Brain Injury; More than meets the



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Learning Objectives

- Understand the challenges and necessary elements of a valid mild TBI (mTBI) diagnosis
- Differentiate between the diagnosis of mTBI and post-concussion syndrome or other residual effect of mTBI
- Describe the Chronic Effects of Neurotrauma Consortium (CENC) standardized method of diagnosing lifetime mTBI and learn to apply elements to research and clinical practice

Poll Question #1

- What is your primary role in VA?
 - a) student, trainee, or fellow
 - b) clinician
 - c) researcher
 - d) Administrator, manager or policy-maker
 - e) Other

Poll Question #2

- Which best describes your clinical role with regards to mild TBI?
 - a) First responder or emergency department
 - b) Primary care
 - c) Neurology or Rehabilitation
 - d) Neuropsychologic care or assessments
 - e) Other

TBI Incidence in U.S.

- All severities incidence
 - almost 2 million injuries/year
- Mild TBI (mTBI) incidence
 - >80% of all TBI's are “mild”
 - estimated 1.5 million injuries/year
 - 30% of all high school football players
 - >10% of all OIF/OEF warriors



Why is mild TBI a concern?

- Most common TBI severity level by a factor of 20x.
- Although “mild”, chronic difficulties may exist
 - Up to 20% may not fully recover within 3 months.
 - Post-concussion syndrome (PCS) = persistence of \geq TBI-like symptoms \geq 3 months post-event
 - Focal problems may also persist in the absence of full-blown PCS
 - When present, these difficulties are similar to moderate and severe TBI and may be as or more bothersome, and have major impact on life functioning.
- Elevates risk for CTE?
 - Zero rigorous evidence that a single mTBI leads to CTE
 - ? evidence for link to repetitive mTBI is under active study by CENC and others

Why is diagnosing mTBI challenging?

- TBI is entirely a “Clinical” diagnosis
- Criteria not precisely defined in terms of differential diagnosis (e.g. arrest, shock, syncope, toxicity, fear)
- No confirmatory tests exist
- Diagnosis may be entirely based on self-reported information
- Systematic or idiosyncratic clinical judgment issues
- In mTBI research, inclusion criteria often differ

DoD/VA Common Definition of TBI

A traumatically induced structural injury &/or physiologic disruption of brain function resulting from external force

Indicated by new onset or worsening of at least one of the following immediately following the event:

Loss of consciousness (LOC)

- Any period of LOC or decreased level of consciousness

Post-traumatic amnesia (PTA)

- Any loss of memory for events immediately before or after injury

Alteration of consciousness (AOC)

- Any change in mental state at the time of injury such as confused, disoriented, or slow thinking

Neurological deficits that may or may not be temporary

- Weakness, loss of balance, change in vision, paralysis etc

Intracranial lesion

- A demonstrated structural change to the brain

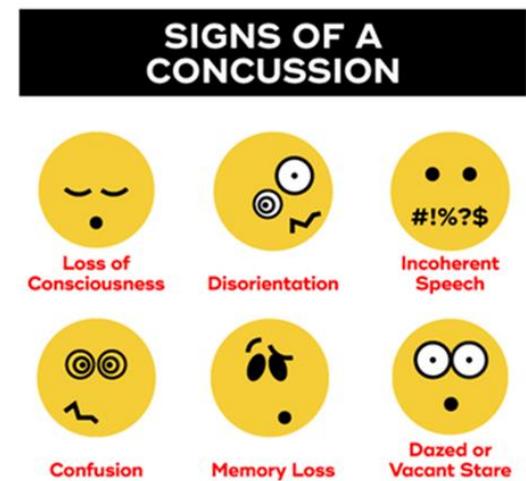
The severity category of Mild TBI

Mild TBI or mTBI = Concussion

- Abnormal Initial Glasgow Coma Score ≥ 13 , &/or
- Loss of consciousness (LOC) ≤ 30 minutes, &/or
- Post-traumatic Amnesia (PTA) ≤ 24 hours, &/or
- Other evidence of immediate AOC consistent with TBI causality, &/or
- Immediate neurologic deficit c/w TBI causality*
- Provision: No intracranial abnormalities on head computerized tomography (CT)

AOC footnote in DoD/VA CPG on TBI diagnosis

- Alteration of mental status must be immediately related to the trauma to the head.
- Typical AOC exam findings:
 - Looking dazed and uncertain of what is happening
 - Being confused or disorientated
 - Difficulty responding appropriately to mental status questions
 - Being unable to describe events immediately before or after the trauma event
- Typical AOC symptoms:
 - Feeling dazed and uncertain of what is happening
 - Feeling confused
 - Having difficulty thinking clearly

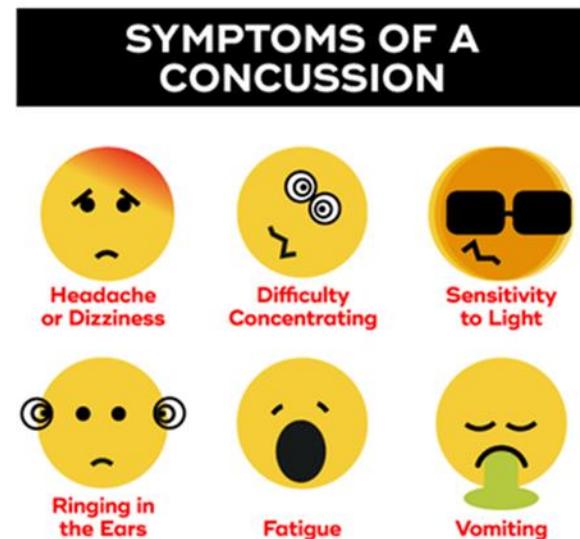


TBI AOC has overlap with fear and acute stress responses

- Fear response
 - Driven by autonomic nervous system overdrive.
 - The ability to think and reason decreases as time goes on.
- Acute stress reaction can include:
 - Withdrawal
 - Narrowing of attention
 - Disorientation
 - Despair
 - Hopelessness
 - Grief
 - Anger
 - Heightened arousal

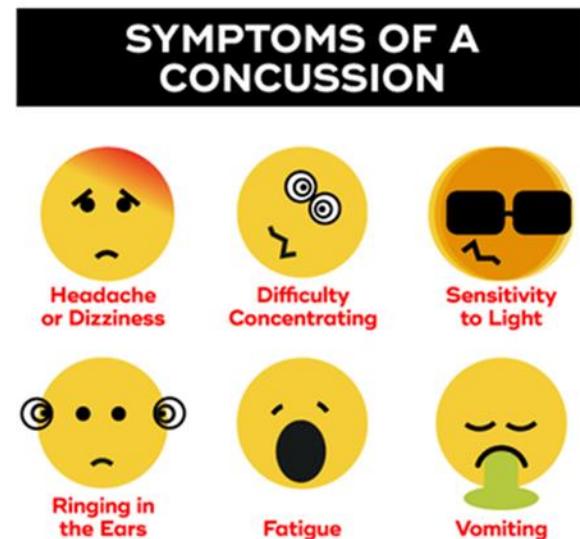
Early Effects of TBI

- Symptoms
 - Somatic
 - Cognitive
 - Emotional
- Exam Findings
 - Subtle if any
 - Vestibular-Oculomotor
- Role in Diagnosis:
 - Not necessary
 - Can be used as supportive evidence only
 - Immediate AOC is still required



Late Effects of mild TBI

- Symptoms
 - Somatic
 - Cognitive
 - Emotional
- Exam Findings
 - Rare and subtle if any
 - Vestibular-Oculomotor
- Role in Diagnosis:
 - None
- Postconcussion Syndrome
 - Positive mild TBI diagnosis
 - Persistence of ≥ 3 TBI-like symptoms for > 3 months



Diagnosis of mTBI versus late effects of mTBI (e.g. Post-concussion Syndrome)

- VA TBI screen
 - 4 elements:
 1. Traumatic event
 2. LOC/PTA/AOC immediately after event (e.g. TBI diagnosis)
 3. Early effects of TBI (TBI like symptoms right after event)
 4. Persisting effects of TBI (TBI like symptoms ongoing)
- Positive VA screen requires all 4 elements; thus:
 - Not intended to screen for any past TBI
 - If no active symptoms, historical TBI(s) will screen “negative”
 - Instead, screens for possible late effects of possible TBI
- Limiting to 1st 2 elements does screen for any past TBI

Screening for mTBI: DoD PDHRA (January 2008)

9.a. During this deployment, did you experience any of the following events? **(Mark all that apply)**

- (1) Blast or explosion (IED, RPG, land mine, grenade, etc.)**
- (2) Vehicular accident/crash (any vehicle, including aircraft)**
- (3) Fragment wound or bullet wound above your shoulders**
- (4) Fall**
- (5) Other event (for example, a sports injury to your head). Describe:**

9.c. Did any of the following problems begin or get worse after the event(s) you noted in question 9.a.? (Mark all that apply)

- (1) Memory problems or lapses**
- (2) Balance problems or dizziness**
- (3) Ringing in the ears**
- (4) Sensitivity to bright light**
- (5) Irritability**
- (6) Headaches**
- (7) Sleep problems**

9.b. Did any of the following happen to you, or were you told happened to you, IMMEDIATELY after any of the event(s) you just noted in question 9.a.? **(Mark all that apply)**

- (1) Lost consciousness or got “knocked out”**
- (2) Felt dazed, confused, or “saw stars”**
- (3) Didn’t remember the event**
- (4) Had a concussion**
- (5) Had a head injury**

9.d. In the past week, have you had any of the symptoms you indicated in 9.c.? (Mark all that apply)

- (1) Memory problems or lapses**
- (2) Balance problems or dizziness**
- (3) Ringing in the ears**
- (4) Sensitivity to bright light**
- (5) Irritability**
- (6) Headaches**
- (7) Sleep problems**

Positive screen = concurrence to all four questions

Positive screen ≠ concussion diagnosis

Need clinician confirmation to diagnose concussion

Poll Question #3

- Along with a sufficiently traumatic force to head, which of the following symptoms can alone be diagnostic for a mild TBI (select all that apply):
 - a) Memory gap of impact and immediate aftermath
 - b) Headache immediately after impact
 - c) Traumatic intracranial hemorrhage on head CT
 - d) Dazed and confused for several minutes after impact
 - e) Memory gap for the week before the event

Immediate vs Delayed Evaluation

Immediate Eval (during AOC)

- Validated, structured symptom measures and mental status examinations exist to assist the acute diagnosis



Delayed Eval (after AOC)

- Identifying now resolved immediate AOC relies primarily or solely on self-report



Alteration of Consciousness (AOC)

- AOC is the **clinical hallmark** of diffuse axonal injury, the primary pathology in TBI
- **PTA & LOC** are discrete clinical phenomena of the AOC spectrum
- Longer PTA (or LOC) = more severe TBI = worse outcome
- Identifying AOC is rarely a diagnostic challenge in Severe TBI
- **In Mild TBI identifying presence of AOC can be difficult**

Delayed Eval: Sources for Evidence for Immediate AOC

- **Documentation** of History or Exam from First Responders & Urgent Care Providers
- **Witness** report
- **Self-report**, options:
 - Questionnaire format (e.g. VA TBI screen)
 - Unstructured Interview (e.g. typical clinical interview)
 - Structured Interview
 - Semi-structured Interview

Early Documentation

- Advantages:
 - Relatively “objective”, especially when performed during AOC period
- Disadvantages:
 - Unless LOC or frank confusion is directly observed may not capture information needed to make diagnosis
 - Heavily dependent on skill, expertise, bias and diligence of assessor (witness report could be considered a type of early assessor)

Powell JM, et al. Accuracy of mild TBI diagnosis. Arch Phys Med Rehabil 2008;89:1550-5.

Self Report: Questionnaire Format

- Advantages
 - Efficient
 - Can be done remotely
 - Standardized
 - Unbiased
- Disadvantages
 - Sensitivity/specificity depends on instrument and prevalence
 - Contradictory or illogical responses can not be vetted

Self Report: Unstructured Interview

- Advantages
 - Can be individualized
 - Real time vetting of responses and tailoring of f/u questions
- Disadvantages
 - Heavily dependent on interviewer skill/experience
 - Interviewer bias even if skilled
 - Lack of standardization of content
 - Lack of transparency for reproducibility

Self Report: Structured Interview

- Fully structured Interview
 - Advantages
 - Complete standardization
 - Unbiased
 - Maximal reliability (both inter-rater and test-retest)
 - Disadvantages
 - Efficiency
 - Availability
- Semi-structured Interview
 - Compromise between Un- and Fully Structured

Evidence for Validity of Methods for diagnosing Mild TBI

- Emergency Department documentation of diagnosis
 - False negative rate of 56% in one study (Powell, 2008)
 - False positives not uncommon (anecdotal)
- Witness Report (if witnessed)
 - No psychometric data available
 - Often have only what the patient was “told” since rarely is the witness available during eval

Validity of Self-Report

- Questionnaire
 - Scant psychometric data exists despite being primary tool in most published mild TBI identification studies of OIF/OEF population
 - Most are “screening” tools
 - What is gold standard to compare?
- Interview
 - Limited psychometric data
 - Which interview method is best?

The Brief Traumatic Brain Injury Screen (BTBIS)

- self-report **questionnaire tool** for “probable” TBI
- **compared to semi-structured interview** in a military sample.
- Interview consisted of a series of **primarily open ended questions** with vetting of responses left up to judgment of the interviewer (Masters’ level psychologist or trained staff member)
- **15% of BTBIS pos were false pos** on interview
- False negatives were not sought since only screen positive soldiers were contacted for interview.
- Schwab KA 2007

OSU TBI-ID (structured interview)

- Designed for retrospective identification of TBI
- Very High inter-rater reliability for TBI with LOC ($r=0.9$) and # early effects ($r=0.92$) in a Substance Abuse sample (Corrigan 2007); not assessed for mTBI without LOC
- Mod high test-retest reliability for # early symptoms ($r=0.74$) and # early fxl effects ($r=0.72$) in a Prisoner sample (Bogner 2009)
- Reliability of individual items or profiles not reported
- Poor predictive validity (late TBI effects)

Traumatic Brain Injury Questionnaire (TBIQ)

- **Semi-structured interview** with 12 Y/N response items assessing for a possible TBI incident followed by open-ended interview of the incident(s) identified to determine dx
- **Test-retest reliability had moderate dx agreement ($k=0.56$)** with trained research assistants conducting the interviews in a prison offender sample. (Diamond 2007)
- How open ended question responses were vetted was not reported and inter-rater reliability was not reported

How CENC multicenter study is addressing these challenges

- Screening for all lifetime potential concussion events (PCEs)
 - Based on OSU TBI-ID
- Validated structured interview for each PCE that generates an algorithm diagnosis
 - VCU retrospective Concussion Diagnostic Interview (VCU rCDI)
 - Walker WC, et al. J Neurotrauma 2015;32(7):464-73.
- Open ended interview component to cross check structured interview along with any early/subacute documentation
- If doubt exists, additional unstructured interview may occur, then Site PI either:
 - confirms algorithm, or
 - overrides algorithm, or
 - refers to central diagnosis committee

How structured interview addresses each component of DoD/VA Common Definition of TBI

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Traumatic Force

- Ask patient to describe event
 - If not divulged, ask what they were doing at time of the traumatic impact
 - If not divulged, ask what caused the event
 - If blast, ask about type and distance
 - If combat, motorcycle, or non-motorized transportation (bicycle, ski, skate, etc.) event, ask: Were you wearing a helmet at the time of the impact or sporting event?
- Ask: To your knowledge, was your head struck or did your head hit something?
 - If yes, ask: What struck your head? Or What did your head hit?

VCU rCDI; open-ended interview component

- Please tell me in as much detail as possible what happened to you and what you felt during and right after this _____ (MVA, fall, assault, or etc. type of event)
- Instructions: *Make sure to get a clear narrative about events leading up to the _____ (traumatic event), information about the event, and information about what happened after the event including what he/she experienced physically and emotionally.*

Post-traumatic Amnesia (PTA)

1. First probe recall of event, in particular the traumatic force/insult (e.g. blast, collision)
2. Second, probe for retrograde amnesia (missing memory for immediate beforemath)
3. Third, probe for antegrade amnesia (missing memory for immediate aftermath)

Structured Interview of PTA

- Do you have personal memory of the impact (collision, fall, assault, or whatever type of traumatic impact was reported) itself?
- Is there a period of time just BEFORE the impact for which you have no personal memory of at all?
 - If Yes:
 - What is the last thing that you personally remember occurring just BEFORE the impact?
 - How long was the period of time between [the above thing] and the impact?
 - Is there a period of time just AFTER the impact for which you have no personal memory of at all?
 - If Yes:
 - What is the first thing that you personally remember occurring just AFTER the impact?
 - How long was the period of time between the impact and [the above thing]?

Sensitivity Check for False Negative PTA

- Review the prior answers: Does the pattern of responses show continuous memory of immediate fore math, event, and aftermath? (i.e. are responses Yes, No, and No?)
- If No: depending on pattern may have PTA
- If Yes, ask: It sounds like there are no holes or gaps in your memory from that day, is that correct?
 - If Yes, then PTA is ruled out by interview.
 - If No, inform patient: "I need to understand how this fits with the earlier questions," then re-administer questions PTA questions and repeat process. If this leads to identical responses then add unstructured interview to help sort out.

Loss of Consciousness (LOC)

- Patients may not understand concept, so give definition
- LOC is a state that can't be remembered, so ask how they determined
- Structured interview for LOC:
 - Right after the impact did you become unconscious, that is, you could not see, speak, and move for any period of time?
 - If yes: Were you told this by a witness, or is this based upon your experience?
 - If not witness based: How did you determine this?
 - If yes: How long were you unconscious?
- Caveats:
 - Self determined LOC usually indicates a gap in memory (PTA)
 - Witnessed verified immediate LOC in context of traumatic force to head almost always rules in TBI
 - In CDI, algorithm handles self-determined versus witnessed LOC differently

Structured Interview for other AOC symptoms

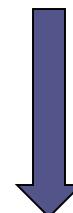
- Did you feel dazed?
- Did you feel confused?
- Did you “see stars”?
- If Yes for any also ask:
 - Did you feel dazed/confused/see stars immediately after the impact or was there a delay?
 - If Immediate, ask how long it lasted
 - If delayed, also ask how long after the impact did it start?

mTBI diagnosis Must Have: Evidence of immediate AOC

- MSE during AOC window c/w AOC (or seizure)
- Patient Interview **after** AOC window
 - Witness corroborated LOC (or seizure)
 - Memory gap pattern c/w TBI physiology
 - AOC symptoms c/w TBI physiology

Least specific

- Dazed
- Confused
- Saw Stars



Most specific

Walker WC et al,
J Neurotrauma 2015

Poll Question #4

- Immediately after a traumatic event, feeling dazed for a minute or less could be due to:
 - a) TBI
 - b) Acute stress reaction
 - c) Fear response
 - d) All of the above

CDC criteria for Mild TBI diagnosis

- Furthermore stipulates:

Post-injury symptoms (e.g., headache, dizziness, irritability, fatigue, or poor concentration) can be used to support, but **cannot be used to make**, a diagnosis of mild TBI in adults

Structured Interview for symptoms supportive of TBI diagnosis

- Did your head ache?
- If Yes,
 - Did your head ache begin immediately after the impact or was there a delay?
 - If Delayed, did it start:
 - Within 2 weeks
 - More than 2 weeks after
- Did you have any other feelings or symptoms that you noticed right after or soon after the impact?
- If Yes, complete table below.
 - Other symptom:_
 - Other symptom:_

Poll Question #5

- Headache after a traumatic event may be due to:
 - a) TBI
 - b) PTSD
 - c) Cervical whiplash
 - d) None of the above
 - e) All of the above

Structured Interview for early medical evaluation

- Were you medically evacuated or treated immediately after the impact at an aid station or other medical center?
- If Yes,
 - Ask for treatment location.
 - Ask if admitted to hospital and for how long
- Importance:
 - is there potentially discoverable immediate or early documentation
 - If records not obtainable, moderate or severe TBI highly unlikely if not admitted to medical facility for a least 2 days

Poll Question #6

- Along with a sufficiently traumatic force to head, which of the following symptom can be diagnostic for a mild TBI by itself (select all that apply):
 - a) Memory gap of impact and immediate aftermath
 - b) Dizziness & Tinnitus immediately after impact
 - c) Traumatic intracranial hemorrhage on head CT
 - d) Dazed and confused for several minutes after impact
 - e) Memory gap for the week before the event

Summary VCU retrospective Concussion Diagnostic Interview

1. Cause of event
2. Open-ended query of what happened and what felt
3. Memory of impact
4. Memory gap of immediate beforemath
5. Memory gap of immediate aftermath
6. If 3=Y, 4=N, 5=N, confirm continuous memory
7. Loss of consciousness and how determined
8. Dazed, confused, or saw stars immediately after event
9. Headache or other symptoms immediately after event
10. If/where medically evaluated

CENC experience with CDI algorithm

- Only 3% of diagnoses overturned
- Most common confounders:
 - Syncope
 - Intoxication
 - Asleep at time of event



