Mild Traumatic Brain Injury In U.S. Troops Returning from Iraq and Afghanistan:

Public Health Considerations

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Mild Traumatic Brain Injury (mTBI) Definition

• Blow or jolt to the head that causes physiological disruption of brain function:
  – Brief loss of consciousness (<30 min)
  – Transient alteration in consciousness
  – Post-traumatic amnesia of <24 hours
• “Mild TBI” is synonymous with “concussion”.
• Distinct from moderate / severe TBI
• Acute symptoms may be followed by persistent post-concussion symptoms / syndrome (PCS)
  – e.g. headaches, sleep disturbance, fatigue, irritability, dizziness, concentration problems, cognitive problems balance problems, ringing in ears, blurred vision, reduced ability to tolerate stress / alcohol / emotions
The mTBI Express Train

- Incidence reported to be 20% among troops deployed to Iraq/Afghanistan; often “blast” related
  - As many as half continue to report symptoms post-deployment
- Labeled “signature injury” of this war
- Subject of various Commissions/Boards
  - AFEB memo to DoD Health Affairs, Aug ’06
  - Independent Review Group (West, Marsh), April ’07
  - DoD Mental Health Task Force Report, June ’07
  - President’s Commission (Dole, Shalala), July ’07
  - Army TBI Task Force Report, May 2007 (released Jan ’08)
- $900M FY07 Congressional appropriation
- Key recommendations: population-wide screening post-deployment and neurocognitive assessments
What DoD Has Done So Far

• Established common DoD-VA definition of TBI (Dec ’06; Oct ’07)
• Published in theater CPG (MACE) (Dec ’06)
• Published clinical guidance for garrison settings (Oct ’07)
• Initiated population-wide screening/assessments for mTBI as part of PDHA/PDHRA (phased in)
• Mandated baseline neurocognitive assessment testing for deploying population using NCAT (ANAM) (Jan ’08)
• TBI specialty clinics (various forms)
• Education efforts
Assumptions That Are Driving DoD Policies

• Mild TBI is on same continuum as moderate / severe TBI.
• Mild TBI caused by blast may have unique health effects.
• Case definitions for mTBI and PCS are sufficiently valid.
• Symptoms usually resolve in 1-3 months, but persistent post-concussive symptoms are not uncommon (~15%).
• Mild TBI “overlaps” with and may be confused with PTSD.
• A careful clinical history (perhaps with the help of cognitive testing) can distinguish symptoms due to mild TBI.
• The “silent” epidemic; requires “high index of suspicion”.
• It doesn’t matter what label we use, since “mild TBI” means the same thing as “concussion”.
• Screening for mTBI is imperative for appropriate care.
• There is specific treatment available for mild TBI.
mTBI is **Not** on Same Continuum as Mod / Severe TBI

Adapted from McCrea, Oxford Univ Press, 2008 and Iverson. In: Brain Injury Medicine 2008

<table>
<thead>
<tr>
<th>Focal neurological signs</th>
<th>Mild TBI (concussion)</th>
<th>Mod/Severe TBI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Natural History / Recovery</td>
<td>Full recovery is expected; No consensus on post-concussive symptoms / syndrome</td>
<td>Directly related to injury severity and functional neuroanatomy</td>
</tr>
<tr>
<td>Case definitions and specificity of physical, behavioral, cognitive symptoms / sequelae</td>
<td>Very poor, low validity (e.g. low kappa b/w ICD-10 &amp; DSM-4; high baseline rates and with other injuries)</td>
<td>High</td>
</tr>
<tr>
<td>CT / MRI</td>
<td>Usually negative / equivocal</td>
<td>Diagnostic</td>
</tr>
<tr>
<td>Neurocognitive testing</td>
<td>Inconclusive; evidence for clinical utility lacking</td>
<td>Diagnostic</td>
</tr>
<tr>
<td>Neuronal cell damage</td>
<td>Twisting / Stretching</td>
<td>Shearing / Death</td>
</tr>
<tr>
<td>Predictors of Persistent Symptoms / Disability</td>
<td>Debated: neurological vs. psychological</td>
<td>Based directly on injury characteristics</td>
</tr>
<tr>
<td>Epi. evidence of causation</td>
<td>Inconsistent</td>
<td>Consistent</td>
</tr>
</tbody>
</table>
mTBI: What the Evidence Indicates

- Blast physics and casualty data suggest that primary blast overpressure injuries are very rare.
- Neither mTBI or PCS case definitions have been validated using clinical interviews and adequate control groups.\(^1\)-\(^3\)
- Incidence of mTBI during deployment is unknown:
  - Only 5% of OIF/OEF Soldiers report injury with LOC, usually very brief (<3 min).
  - It is impossible to know how many of the other Soldiers with “altered mental status” actually had physiological disruption of brain function.
- Acute concussion symptoms usually resolve within a few hours to a few days, not 1-3 months\(^1\),\(^4\)
- A re-analysis of the classic studies indicate that persistent PCS occur in about 3-5% of concussion cases, not 15+%.\(^1\)

mTBI/PTSD “Overlap”: The Evidence

• Concussion (mTBI), by definition, does not “overlap” with PTSD, because it is the injury event itself.
• However concussion in combat is strongly associated with subsequent PTSD, likely because of the high threat context.¹
• PTSD, in turn, is strongly associated with somatoform and post-concussive symptoms due to neuroendocrine, autonomic nervous system, and immune system dysregulation; as well as altered perception of symptoms.²
• Post-concussive symptoms overlap with hundreds of medical conditions, and all historical post-war syndromes.
• Two studies have found that PTSD explains the majority of symptoms categorized as “post-concussive” in Soldiers who have had concussions during Iraq deployment.¹,³

PCS and NC Testing: **What The Evidence Indicates**

- A careful clinical history is *not* sufficient to attribute persistent symptoms to mTBI (especially months after injury).\(^1\)\(^-\)\(^4\)
  - ICD-10 and DSM-4 definitions correlate poorly.
  - High baseline rates of symptoms in normal populations
  - Several studies have shown that the PCS symptoms occur just as frequently after non-head traumas as after mTBI.
- The available data indicate that neurocognitive assessment testing in concussion lacks reliability, validity, and clinical utility.\(^5\)\(^-\)\(^8\)

New DoD mTBI Post-Deployment Screening Revised PDHA/ PDHRA

Problems with this include the lack of validation and:

a. “experience” of a blast is not the same thing as an injury, blow or jolt to the head. b. “IMMEDIATELY after” is confusing. “Felt dazed, confused, or saw stars” may not correlate with physiological disruption of brain function, and had low specificity in NEJM study. c. and d. are not independent from the injury questions.
Foundations of Population Screening

• **Understand Risk Factors:**

• What do we know about the risk factors for developing persistent post-concussive symptoms after concussion?
Risk Factors for Persistent PCSs

• 4 principal risk factors have been associated with persistent post-concussive symptoms:
  – Repeated concussive events (e.g. recovery mean 14 days vs. <1-7 days in NCAA Concussion Study)
    • Guskiewicz K, et. al., JAMA 2003;
  – Depression, anxiety, PTSD
    • Bryant RA, Harvey AG. J Nerv and Mental Disorder 1999;
  – Presence of medical disability and legal processes
    • Carroll LJ, et. al. (WHO Task Force). J Rehabil Med 2004
  – Expectations and beliefs that patients have about the seriousness of their condition
    • Carroll LJ, et. al. (WHO Task Force). J Rehabil Med 2004
    • Ferguson RJ. Neuropsychology 1999
Foundations for Population Screening

- **Effective interventions:**
- What evidence-based treatments are available for mTBI identified through post-deployment screening assessments?
Evidence-Based mTBI Treatment

- None, …except cognitive education to normalize symptoms and provide the expectation of rapid recovery.\textsuperscript{1-4}

1. Peloso PM, et. al. (WHO Task Force); J Rehab Med 2004;
2. Borg J, et. al. (WHO Task Force); J Rehab Med 2004;
Necessary Criteria for Population-Level Screening Have Not Been Met

- Rona, et al. JAMA 2005

• Screening test should be simple, precise, and validated.

• High-quality research evidence demonstrates the effectiveness of screening in reducing morbidity.

• Adequate staffing and facilities are critical.

• Potential benefits from the screening program outweigh risks.
Screening: First Do No Harm

Possible iatrogenic Effects*

Acute Period
- mTBI / Other Combat Trauma
- PDHA
- PDHRA
- PHA

Persistent Symptoms
- MEBs
- Screening in VA

*Iatrogenic pathways: labeling, inconclusive cognitive or neuroimaging studies, unproven interventions, medication side effects, failure to provide effective treatment for real problems, use of rehabilitation services designed for mod/severe TBI, poor risk communication, disability seeking, cost.

Expectation as etiology. The belief that one is sick is well known to amplify symptoms (e.g. mTBI, hypertension, whiplash, chronic fatigue, irritable bowel, chest pain, herpes zoster, lactose intolerance). Perceptions are reinforced by the number of tests performed that legitimizes symptoms as “medical”.

NEJM Study (Jan 31, 2008)

- Cross-sectional survey of 2525 Soldiers from 2 BCTs studied 3-4 months post-deployment
- Measures: Combat experiences, injuries, concussion history (using DVBIC questions); validated clinical scales for PTSD, depression, somatic/physical symptoms
- Soldiers with other injuries served as control group for all comparisons
- Clinical scales were independent from injury and combat experience measures
- Analyses controlled for demographics, combat intensity, injury mechanism, and multiple blast exposures.
- 60% availability, 98% participation rate
Mild TBI Prevalence (NEJM 2008)

<table>
<thead>
<tr>
<th>Injury Type*</th>
<th>(N=2525)</th>
<th>* Blast was the most common mechanism for mTBI (75%), whereas falls were the most common mechanism of other injuries.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Soldiers with mTBI**</td>
<td>124 (4.9%)</td>
<td>** LOC usually lasted &lt;3 minutes. Of the 260 with altered MS, 253 reported being “dazed, confused, or seeing stars.”</td>
</tr>
<tr>
<td>Loss of Consciousness</td>
<td>260 (10.3%)</td>
<td></td>
</tr>
<tr>
<td>Altered Mental Status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(“dazed, confused, or seeing stars”)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Soldiers with Other Injuries</td>
<td>435 (17.2%)</td>
<td></td>
</tr>
</tbody>
</table>
Mild TBI and Mental / Physical Health

<table>
<thead>
<tr>
<th>Health Measures Past-Month</th>
<th>mTBI with LOC (n=124) (%)</th>
<th>mTBI with Altered MS (n=260) (%)</th>
<th>Other Injuries (n=435)(%)</th>
<th>No Injury (n=1706) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mental Disorders</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PTSD</td>
<td>43.9*</td>
<td>27.3*</td>
<td>16.2</td>
<td>9.1</td>
</tr>
<tr>
<td>Major Depression</td>
<td>22.9*</td>
<td>8.4</td>
<td>6.6</td>
<td>3.3</td>
</tr>
<tr>
<td>Physical Health</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poor General Health</td>
<td>12.6*</td>
<td>6.6</td>
<td>6.9</td>
<td>2.3</td>
</tr>
<tr>
<td>Sick-call ≥ 2</td>
<td>42.5*</td>
<td>32.8</td>
<td>28.9</td>
<td>19.7</td>
</tr>
<tr>
<td>Missed work ≥ 2 days</td>
<td>23.3*</td>
<td>15.6</td>
<td>14.6</td>
<td>7.3</td>
</tr>
<tr>
<td>High Physical Symptoms (Score ≥ 15)</td>
<td>24.8*</td>
<td>16.1</td>
<td>11.3</td>
<td>5.1</td>
</tr>
</tbody>
</table>

Soldiers who reported mTBI, particularly with loss of consciousness (LOC), were much more likely to have PTSD and physical health problems post-deployment than Soldiers with other injuries.
However, That Was Not the Whole Story

### Injury Type

<table>
<thead>
<tr>
<th></th>
<th>Overall % with High PHQ-15</th>
<th>Stratified Analysis</th>
<th>Statistics</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>PTSD</td>
<td>No PTSD</td>
</tr>
<tr>
<td>PTSD</td>
<td></td>
<td>% High</td>
<td>% High</td>
</tr>
<tr>
<td>No PTSD</td>
<td></td>
<td>PHQ-15</td>
<td>PHQ-15*</td>
</tr>
<tr>
<td>LOC</td>
<td>24.8</td>
<td>50.9</td>
<td>4.5</td>
</tr>
<tr>
<td>Altered MS</td>
<td>16.1</td>
<td>41.8</td>
<td>7.0</td>
</tr>
<tr>
<td>Other Injury</td>
<td>11.3</td>
<td>42.0</td>
<td>5.3</td>
</tr>
</tbody>
</table>

- High physical symptoms (PHQ-15 score ≥ 15) occurred almost exclusively among Soldiers with PTSD.
- Similar relationship observed for all outcomes, including PCSs.

N for all injuries = 801; N for PTSD = 189

N's for LOC = 123;54;69; Altered MS = 260;71;189; Other Injury = 433;79;363
## Health Symptoms Stratified by PTSD

(analysis does not control for depression or other variables)

<table>
<thead>
<tr>
<th>Health Symptoms</th>
<th>LOC (n=124)</th>
<th>Altered MS (n=260)</th>
<th>Oth Injury (n=435)</th>
<th>PTSD LOC (n=54)</th>
<th>Altered MS (n=71)</th>
<th>Oth Injury (n=70)</th>
<th>No PTSD LOC (n=69)</th>
<th>Altered MS (n=189)</th>
<th>Oth Injury (n=363)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High PHQ-15 (≥15)</td>
<td>24.8*</td>
<td>16.1</td>
<td>11.3</td>
<td>50.9</td>
<td>41.8</td>
<td>42.0</td>
<td>4.5</td>
<td>7.0</td>
<td>5.3</td>
</tr>
<tr>
<td>Headaches</td>
<td>32.2*</td>
<td>17.7*</td>
<td>12.1</td>
<td>49.1*</td>
<td>31.3</td>
<td>29.9</td>
<td>19.4*</td>
<td>12.8</td>
<td>8.8</td>
</tr>
<tr>
<td>Sleep disturbance</td>
<td>53.8*</td>
<td>44.9*</td>
<td>37.2</td>
<td>80.4</td>
<td>75.0</td>
<td>73.5</td>
<td>33.3</td>
<td>34.4</td>
<td>30.2</td>
</tr>
<tr>
<td>Concentration prob</td>
<td>31.4*</td>
<td>26.0*</td>
<td>18.1</td>
<td>58.8</td>
<td>61.5</td>
<td>54.4</td>
<td>10.4</td>
<td>13.5</td>
<td>11.1</td>
</tr>
<tr>
<td>Irritability</td>
<td>56.8*</td>
<td>47.6*</td>
<td>36.8</td>
<td>80.4</td>
<td>86.2</td>
<td>82.4</td>
<td>38.8</td>
<td>33.9</td>
<td>27.9</td>
</tr>
<tr>
<td>Memory problems</td>
<td>24.6*</td>
<td>16.2</td>
<td>13.7</td>
<td>42.3</td>
<td>37.9</td>
<td>35.8</td>
<td>10.8</td>
<td>8.6</td>
<td>9.6</td>
</tr>
</tbody>
</table>
PTSD as Mediator

- A combat event associated with LOC reflects intense traumatic event with high threat to loss of life (near miss on one’s life). This leads to PTSD.
- PTSD in turn leads host of health symptoms by well known mechanisms involving neuroendocrine, autonomic NS, and immune system dysregulation.
Clinical Implications

• Screening for mTBI months after injury will result in large numbers of service members being unnecessarily referred for evaluation and treatment of non-specific symptoms attributed to “brain injuries”.
  – “Brain injury” label likely to amplify symptoms. 1-8
  – Unintended iatrogenic consequences will occur. 5-8

• For sleep disturbance related to mTBI:
  – 14 day trial of trazodone / ambien
  – If comorbid nightmares or other PTSD symptoms, give trial of quetiapine (seroquel) (an atypical antipsychotic with metabolic side effects such as weight gain and hyperglycemia)

• For irritability related to mTBI:
  – Six week trial of SSRI or SNRI (e.g. sertraline, venlafaxine) (SSRIs commonly cause sexual side effects. Venlafaxine has significant risk of hypertension.)
There Are Some Simple Answers to This Problem: Recommendations

– Modify post-deployment screening assessments immediately (e.g. PDHA, PDHRA, PHA) to minimize risks.

– Build the structure of care for mild TBI on evidence-based step-care and collaborative care approaches centered in primary care, not TBI specialty clinics (or de-facto TBI clinics).

– Disseminate effective risk communication.
Modify Post-Deployment Screening for mTBI

• Focus on point of injury evaluation. Modify post-deployment assessments to minimize risks:
  – Screen for all injuries at the PDHA time point only.
  – Do not rescreen for mTBI at PDHRA or subsequently.
  – Screen for depression and PTSD.
  – Increase specificity of mTBI questions:
    • Focus on LOC. Remove or change non-specific “dazed or confused” question.
    • De-couple symptom questions from injury questions.
Treat Symptoms in **Primary Care**

- **Build foundation of mTBI care on evidence-based models centered in primary care:**
  - Step-care approaches in primary care have been proven to be effective in treating physical symptoms, while minimizing unnecessary and costly diagnostic evaluations, procedures, and referrals\(^1\)\(^-\)\(^3\) (e.g. DoD-VA Post-Deployment Health CPG)
  - Collaborative care models in primary care, have been proven to be effective in reducing the medical morbidity associated with co-morbid mental disorders (depression, PTSD)\(^4\),\(^5\)

- **Educate providers about mTBI.**
Always convey reassurance and promote the expectation for rapid and full recovery:

- Utilize proven cognitive behavioral techniques\textsuperscript{1-4}
- Throw out “mild TBI” label. Use “concussion” instead.
  - Lower stigma
  - Better understood term; more reassuring
  - Less likely to be confused with moderate / severe TBI
- Reserve “brain injury” label for moderate and severe TBI
- Draw on sports concussion analogies
- Minimize speculation about possible blast effects. Instead talk about brain plasticity.
  - There is no evidence that being knocked unconscious for 30 seconds from a blast is any different clinically than being knocked unconscious for 30 sec. by another mechanism.

1. Peloso PM, et. al. (WHO Task Force); J Rehab Med 2004; 2. Borg J, et. al. (WHO TF; J Rehab Med 2004;
Thank You!

The views are those of the author(s) only and do not reflect the official position of the Army or DoD.

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Backups
ANAM Recommendations (Based on Literature Review)

- Discontinue routine or population-wide use of ANAM until there are clear guidelines for how test data should be utilized clinically.
- Continue to make ANAM available to neuropsychologists who want to use it, as part of their “tool kit”, but establish systematic program evaluation of clinical utility.
- Establish policy that ANAM test data should be interpreted only by neuropsychologists.
- Ensure that research portfolio includes an adequate number of NC studies that evaluate clinical utility.
- Insure scientific review of all guidelines and policies by independent experts (e.g. Defense Health Board).
Additional Recommendations to Primary Care Clinicians

- Post-concussion symptoms are like other unexplained symptom-based conditions.
- Develop a plan in collaboration with patient to evaluate and treat each symptom in step-wise manner.
- Acknowledge health concerns, but avoid attribution errors & potential iatrogenic harm:
  - The belief that one is sick amplifies symptoms
  - Belief is reinforced by number of medical tests / referrals
  - May lead to failure to provide effective treatment for the real problems
- Trust your clinical judgment.
- Screen for mental health problems, but don’t label symptoms as “mental”.