Mild Traumatic Brain Injury and Post Traumatic Stress Disorder

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Disclosure

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TBI – Definition

• Traumatic Brain Injury - A bolt or jolt to the head or a penetrating head injury that disrupts the function of the brain

— Not all blows or jolts to the head result in a TBI. The severity of such an injury may range from “mild” (a brief change in mental status or consciousness) to “severe” (an extended period of unconsciousness or amnesia) after the injury.
# TBI Severity

<table>
<thead>
<tr>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Altered or LOC&lt;30 minutes with normal CT and/or MRI</td>
<td>LOC&lt;6 hours with abnormal CT and/or MRI</td>
<td>LOC&gt;6 hours with abnormal CT and/or MRI</td>
</tr>
<tr>
<td>GCS 13-15</td>
<td>GCS 9-12</td>
<td>GCS&lt;9</td>
</tr>
<tr>
<td>PTA&lt;24 hours</td>
<td>PTA&lt;7 days</td>
<td>PTA&gt;7 days</td>
</tr>
</tbody>
</table>

Department of Veterans Affairs 2004
Common Mild TBI Symptoms

**NOT** to be confused with the injury itself

TBI is a historical event
Common Mild TBI/Postconcussive Symptoms

- Headache
- Poor concentration
- Memory difficulty
- Irritability
- Fatigue
- Depression
- Anxiety
- Dizziness
- Light sensitivity
- Sound sensitivity

Immediately post-injury 80% to 100% describe one or more symptoms

Most individuals return to baseline functioning within a year

7% to 33% have persistent symptoms

Belanger et al., 2005, Ferguson et al. 1999, Carroll et al. 2004; Levin et al. 1987
Post-Deployment Data (n = 907)

Currently Symptomatic: Onset of Symptoms (n = 844)

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Persistent Sx since TBI</th>
<th>Post-deployment Onset (New Sx)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>200</td>
<td>150</td>
</tr>
<tr>
<td>Dizziness</td>
<td>50</td>
<td>30</td>
</tr>
<tr>
<td>Balance Problems</td>
<td>100</td>
<td>50</td>
</tr>
<tr>
<td>Irritability</td>
<td>200</td>
<td>150</td>
</tr>
<tr>
<td>Memory Problems</td>
<td>100</td>
<td>50</td>
</tr>
</tbody>
</table>

PTSD – A Review
DSM-IV Criteria – PTSD

Traumatic Event

The person has been exposed to a traumatic event in which both of the following have been present:

– (1) the person experienced, witnessed, or was confronted with an event or events that involved actual or threatened death or serious injury, or a threat to the physical integrity of self or others
– (2) the person's response involved intense fear, helplessness, or horror.
DSM-IV Criteria - PTSD

B. Re-experiencing symptoms (nightmares, intrusive thoughts)
C. Avoidance of trauma cues and Numbing/detachment from others
D. Hyperarousal (increased startle, hypervigilance)

Duration of the disturbance (symptoms in Criteria B, C, and D) is more than one month.

The disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.
PTSD
What Can We Expect?

• If we apply the range of prevalence estimates for PTSD (5 to 15 percent) and depression (2 to 10 percent) to the 1.64 million service members who have already been deployed, we can estimate that the number of service members returning home with PTSD will range from 75,000 to 225,000 and with depression, from 30,000 to 50,000.
Predisposing Factors

- Psychiatric Conditions
- Personality Traits
- Medical Conditions
- Intelligence Level
- Demographic Characteristics

Causative Factors

- Medical Iatrogenesis
- Litigation Iatrogenesis
- Self-Expectation

Perpetuating and Mitigating Factors

- Psychiatric Conditions
- Personality Traits
- Medical Conditions

Acute Symptoms

Chronic Symptoms

- Coping Abilities
- Social Support

Psychological Contributions

Rodney Vanderploeg, Ph.D.
Increased Rates of PTSD in those with Mild TBI

"Patients with mild TBI were twice as likely to develop PTSD [or other anxiety disorders]..."

"Mild traumatic brain injury (i.e., concussion) occurring among soldiers deployed in Iraq is strongly associated with PTSD..."
Increased Symptoms with TBI + PTSD

“In Soldiers with histories of physical injury, mTBI and PTSD were independently associated with PC symptom reporting. Those with both conditions were at greater risk for PC symptoms than those with either PTSD, mTBI, or neither.”
Symptom-Exposure:
Any Symptoms (n = 389)

- No mTBI & no PTSD: 1.00
- Had PTSD but no mTBI: 2.74
- Had mTBI but no PTSD: 4.03
- Had mTBI & PTSD: 6.27

Adjusted for age, gender, education, rank, and MOS

Total no. of soldiers (N = 1247)

Brenner et al., 2009
Treatment: Mild TBI and PTSD
Evidence Based Practice – Applying the best available research results (evidence) when making decisions about health care. Health care professionals who perform evidence-based practice use research evidence along with clinical expertise and patient preferences.
The Clinical Practice Guideline for the Management of Concussion/Mild Traumatic Brain Injury (mTBI) was developed under the auspices of the Veterans Health Administration (VHA) and the Department of Defense (DoD) pursuant to directives from the Department of Veterans Affairs (VA). VHA and DoD define clinical practice guidelines as:

“Recommendations for the performance or exclusion of specific procedures or services derived through a rigorous methodological approach that includes:

- Determination of appropriate criteria such as effectiveness, efficacy, population benefit, or patient satisfaction; and
- Literature review to determine the strength of the evidence in relation to these criteria.”

The intent of these guidelines is to:

- Reduce current practice variation and provide facilities with a structured framework to help improve patient outcomes
- Provide evidence-based recommendations to assist providers and their patients in the decision-making process related to the patient health care problems
- Identify outcome measures to support the development of practice-based evidence that can ultimately be used to improve clinical guidelines.

![Figure 1. Initial Stages following mTBI/Concussion](image)

**TABLE C-2 | Management of Persistent Physical Symptoms**

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Pharmacologic Treatment</th>
<th>Non-Pharmacologic Treatment</th>
<th>Referral After Failed Response to Initial Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headaches</td>
<td>Non-steroid pain meds, NSAIDs</td>
<td>Sleep education, Physical Therapy</td>
<td>Neurology, Pain clinic</td>
</tr>
<tr>
<td>Feeling dizzy</td>
<td>Antihistamines, decongestants</td>
<td>--</td>
<td>ENT/Neurology after ENT interventions</td>
</tr>
<tr>
<td>Loss of balance</td>
<td>--</td>
<td>Physical therapy</td>
<td>Neurology</td>
</tr>
<tr>
<td>Poor coordination</td>
<td>--</td>
<td>--</td>
<td>Gastrointestinal</td>
</tr>
<tr>
<td>Nausea</td>
<td>Antiemetics</td>
<td>Sleep education</td>
<td>Gastrointestinal</td>
</tr>
<tr>
<td>Change in appetite</td>
<td>--</td>
<td>--</td>
<td>Consider Mental Health</td>
</tr>
<tr>
<td>Sleep disturbances</td>
<td>Sleep medications</td>
<td>Sleep education</td>
<td>Mental Health, PM&amp;R, Neurology</td>
</tr>
<tr>
<td>- Difficulty falling</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Staying asleep (insomnia)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vision problems</td>
<td>--</td>
<td>Sleep education, Light desensitization</td>
<td>Ophthalmology **</td>
</tr>
<tr>
<td>- Blurring</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Trouble seeing</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Sensitivity to light</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hearing difficulty</td>
<td>--</td>
<td>Environmental modifications</td>
<td>Audiology, ENT</td>
</tr>
<tr>
<td>Sensitivity to noise</td>
<td>--</td>
<td>Environmental modifications</td>
<td>Speech and Language Pathology</td>
</tr>
</tbody>
</table>

** Depending on the local resources, impaired vision may be referred to some facilities to neuro-ophthalmologists. Note that the impaired vision may be due to problems with accommodation as well as due to disorders of the retina and visual pathways.

**TABLE C-3 | Management of Persistent Behavioral and Cognitive Symptoms**

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Job Review</th>
<th>Pharmacologic Treatment</th>
<th>Non-Pharmacologic Treatment</th>
<th>Referral After Failed Response to Initial Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td></td>
<td>Stimulant*</td>
<td>-</td>
<td>- Mental Health</td>
</tr>
<tr>
<td>- Loss of energy</td>
<td></td>
<td></td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>- Getting tired easily</td>
<td></td>
<td></td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Cognitive difficulties</td>
<td></td>
<td>SSRI, Stimulant*</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>- Concentration</td>
<td></td>
<td></td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>- Memory</td>
<td></td>
<td></td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>- Decision-making</td>
<td></td>
<td></td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Feeling anxious</td>
<td>Anaesthetic (short term) SSRI</td>
<td></td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Emotional difficulties</td>
<td>Antiepileptics</td>
<td></td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>- Feeling depressed</td>
<td></td>
<td></td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>- Irritability</td>
<td></td>
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<td>-</td>
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<tr>
<td>- Poor attention tolerance</td>
<td></td>
<td></td>
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<td>-</td>
</tr>
</tbody>
</table>

* Consider in the specialty care setting after ruling out a sleep disorder.
### Table 1.2.1 Psychotherapy Interventions for Treatment of PTSD

<table>
<thead>
<tr>
<th>SR</th>
<th>Significant Benefit</th>
<th>Some Benefit</th>
<th>Unknown Benefit</th>
<th>No Benefit</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>- EMDR</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>- Trauma-focused psychotherapy that includes components of exposure and/or cognitive restructuring, or,</td>
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<td></td>
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</tr>
<tr>
<td></td>
<td>- Stress inoculation training</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>- Patient Education</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>- Imagery Rehearsal Therapy</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>- Cognitive Therapy</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>- Hypnotherapy</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>- Relaxation Techniques</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>- Group Therapy</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>I</td>
<td>- Family Therapy</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<tr>
<td></td>
<td>- WEB-Based CBT</td>
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<tr>
<td></td>
<td>- Acceptance and Commitment Therapy</td>
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</tr>
<tr>
<td></td>
<td>- Dialectical Behavior Therapy</td>
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</tbody>
</table>

*SR = Strength of Recommendation (see Introduction)
“In summary, there was agreement that Veterans who experience mTBI and/or pain, along with PTSD, should have the opportunity to receive the two best evidence-based treatments in the VA/DoD practice guidelines for PTSD, prolonged exposure therapy or cognitive processing therapy.”
HBO$_2$ for PCS: State of the Science

Despite a series of favorable anecdotes and lobbying efforts by the hyperbaric industry, there remains no convincing medical evidence that HBO$_2$ has a therapeutic role in the relief of symptoms or brain dysfunction for warriors with post-concussion syndrome/mild TBI or PTSD.

DoD has partnered with the VA and academia to develop a coordinated research program to collect the data to allow evidence-based decision-making.
HBO$_2$ for TBI
Health System Perspectives

• HBO$_2$: a FDA-cleared product
  • can be prescribed ‘off-label’ per 10 USC 1107
  • problem is payment/reimbursement
  • no third party payers will cover acute TBI or TBI rehabilitation citing that lack of quality evidence
  • requires out-of-pocket payments (12-30K+ per patient)

• 2003 UMHS Position Statement – insufficient data for endorsement for acute or chronic brain injury
• 2003/2012 AHRQ – insufficient evidence for TBI, stroke and cerebral palsy
• 2008/2012 Cochrane Review – insufficient data for acute TBI
• 2009 VA Review – insufficient data to support use for TBI or PCS
Target Product Profile
Efficacy Claims being Evaluated

• Hyperbaric oxygen is being explored for the restorative treatment of post concussion syndrome. IND filed with FDA

• Relief of symptoms
  • post concussion symptom severity (NSI)
  • post traumatic stress disorder symptom severity in individuals with co-morbid PTSD and PCS (PCL)

• Improved cognitive functioning (neurocognitive battery)

• Improvement in quality of life for individuals with post concussion syndrome (PCS) – PGIC/WHOQoL

• Enhancement of other rehabilitation strategies?
HBO₂ for PCS
What We Don’t Know

**Under study currently**

• Are the observed effects due to hyperbaric oxygen?
• Are the improvements in cognitive function significant?
• What is the right dose of HBO₂?
• How many sessions are required?
• Are the effects durable?
• How does it work?
• How should this be used in TBI rehabilitation plans?

Is this a Leave/R&R Phenomenon or Indirect Study Effect?

- Month stay in New Orleans/San Antonio
- Interactions with Caring Staff/Placebo Effects
- HBO₂ Treatment
- We must conduct sham-controlled clinical trials
DoD/VA Clinical Trials Program

USAFSAM Pilot Study (n=50) - Completed

VA/VCU/USN Dose Ranging Study (n=60) - In Data Review

HOPPS IND Pilot Study (n=96) - In Data Review

NSI Outcome Validation Project

Phase II Confirmatory and Mechanisms of Action Study (BIMA) (n=72)

Outcomes in Normals Study (n=75)

Chambers Installation at 4 MTFs and Use of Existing Chambers

We must know these before we start a pivotal (Phase III) trial:
- sham method validated
- dose selection of HBO₂
- outcome measure validated to detect meaningful change after intervention
- establish range of placebo effects to determine sample size

TMA & UHMS Submission

Evaluation for future protocols?
USAF Study: Results
Symptom Scores – ImPACT and PCL

• Overall TBI symptom reduction noted over time (p=.001)
  • greatest change on sleep questions
• Aggregate 22% reduction in PCL-M Composite score 6 weeks after intervention compared to baseline (p<0.001)
• Neither PCS nor PTSD symptoms show benefit of HBO$_2$ 2.4 ATA over sham
Mission:
The mission of the VISN 19 MIRECC is to reduce suicidal ideation and behaviors among Veterans by focusing on promising clinical interventions. This work is advanced through research aimed at identifying the cognitive and neurobiological underpinnings of self-directed violence.

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http://www.mirecc.va.gov/visn19/