Mild Traumatic Brain Injury, Post Concussion Syndrome, and Forensic Assessment

Presentation to National Academy of Neuropsychology, October 25, 2017
Glenn J. Larrabee, Ph.D., ABPP-Cn

Disclosures

I am the editor of *Forensic Neuropsychology: A Scientific Approach* (Oxford University Press, 2012) and receive royalties from the sales of this book.

I provide medicolegal evaluation and consultation to attorneys in litigated matters.
Plan of Talk

• Definition
• Typical Outcome
• Complicating Factors
• Post Concussion Syndrome
• Forensic Assessment

Definitions of mTBI and Concussion

• “Concussion” and “mTBI” refer to acute effects defined by circumscribed loss of consciousness, confusion, and post-traumatic amnesia (PTA)
• “Postconcussion syndrome” refers to non-specific symptoms persisting after mTBI
• Various definitions of mTBI have been offered in recent years
American Congress of Rehabilitation Medicine (ACRM; JHTR, 1993, 86-87)

- A traumatically induced physiological disruption of brain functioning characterized by at least one of the following:
  - Any loss of consciousness (LOC)
  - Any loss of memory (anterograde/retrograde)
  - Any alteration in mental state at the time of trauma (feeling dazed, disoriented or confused)
  - Focal neurologic deficits that may or may not be transient
  - LOC ≤30 min
  - After 30 min Glasgow Coma Scale (GCS) is 13-15
  - PTA ≤24 hours

Problems with ACRM Definition

- Persistent focal deficits may indicate a more severe TBI
- Patient reports of feeling dazed, disoriented or confused are non-specific
- Other injury (no TBI) and mTBI did not differ in “feeling dazed” (52% vs. 71%), “disoriented” (42% vs. 33%), or “confused” (65% vs. 67%)
  see Lees-Haley et al., 2001, ACN, 689-695)
World Health Organization
(Kristman et al., ACRM, 2014, 95, (3 Suppl 2) 265-77)

- mTBI is an acute brain injury resulting from mechanical injury to the head resulting in one or more of the following:
  - Confusion or disorientation
  - LOC ≤30 minutes
  - PTA ≤24 hours
  - Transient abnormalities, e.g. focal signs, seizures, intracranial lesions not requiring surgery
  - GCS of 13-15 >30 minutes post injury
  - Above criteria cannot be due to drugs, alcohol, medications or caused by other injuries

Problem with WHO Criteria

- Allowing presence of intracranial lesion includes a category of mTBI referred to as “complicated mTBI” that sometimes has outcome more similar to that associated with moderate TBI; i.e. these persons may or may not make complete recovery

- A traumatically induced structural injury and/or physiological disruption of brain function as a result of an external force that is indicated by new onset or worsening of at least one of the following clinical signs, immediately following the event
- Any period of loss of or a decreased level of consciousness (LOC)
- Any loss of memory for events immediately before or after the injury (post-traumatic amnesia [PTA])
- Any alteration in mental state at the time of the injury (confusion, disorientation, slowed thinking, etc.) (Alteration of consciousness/mental state [AOC])
- Neurological deficits (weakness, loss of balance, change in vision, praxis, paresis/plegia, sensory loss, aphasia, etc.) that may or may not be transient
- Intracranial lesion.

Definition of External Forces VA/DOD

- External forces may include any of the following events: the head being struck by an object, the head striking an object, the brain undergoing an acceleration/deceleration movement without direct external trauma to the head, a foreign body penetrating the brain, forces generated from events such as a blast or explosion, or other forces yet to be defined.
- The above criteria define the event of a TBI. Not all individuals exposed to an external force will sustain a TBI, but any person who has a history of such an event with immediate manifestation of any of the above signs and symptoms can be said to have had a TBI.
### Severity of TBI

**VA/DOD**

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Structural Imaging</td>
<td>Normal</td>
<td>Normal or Abnormal</td>
<td>Normal or Abnormal</td>
</tr>
<tr>
<td>Loss of Consciousness (LOC)</td>
<td>0-30 minutes</td>
<td>&gt; 30 min or &lt;24 hours</td>
<td>&gt;24 hours</td>
</tr>
<tr>
<td>Alteration of Consciousness/Mental State (AOC)</td>
<td>A moment up to 24 hours</td>
<td>&gt;24 hours</td>
<td>&gt; 24 hours</td>
</tr>
<tr>
<td>Post Traumatic Amnesia (PTA)</td>
<td>0 to 1 day</td>
<td>&gt;1 day and &lt;7 days</td>
<td>&gt;7 days</td>
</tr>
<tr>
<td>Glasgow Coma Scale (best available score in first 24 hours)</td>
<td>13-15</td>
<td>9-12</td>
<td>&lt;9</td>
</tr>
</tbody>
</table>

### Alerts/Warnings

**VA/DOD**

- Alteration of mental status must be *immediately* related to the trauma to the head.
- Typical symptoms would be: looking and feeling dazed and uncertain of what is happening, confusion, difficulty thinking clearly or responding appropriately to mental status questions, and being unable to describe events immediately before or after the trauma event.
- The terms concussion and mTBI can be used interchangeably.
Alerts/Warnings
VA/DOD

- The use of the term concussion or history of mild TBI may be preferred when communicating with the patient, indicating a transient condition, avoiding the use of the terms "brain damage" or "brain injury" that may inadvertently reinforce misperceptions of symptoms or insecurities about recovery.
- The patient who is told s/he has "brain damage" based on vague symptoms complaints and no clear indication of significant head trauma may develop a long-term perception of disability that is difficult to undo.

Additional Criteria for mTBI
VA/DOD

- A diagnosis of mTBI should be made when there is an injury to the head as a result of blunt trauma, acceleration or deceleration forces or exposure to blast that result in one or more of the following conditions:
  a. Any period of observed or self-reported:
     Transient confusion, disorientation, or impaired consciousness
     Dysfunction of memory immediately before or after the time of injury
     Loss of consciousness (LOC) lasting less than 30 minutes.
  b. Observed signs of neurological or neuropsychological dysfunction, such as:
     Headache, dizziness, irritability, fatigue or poor concentration, when identified soon after injury, can be used to support the diagnosis of mild TBI, but cannot be used to make the diagnosis in the absence of loss of consciousness or altered consciousness.
- The severity of TBI must be defined by the acute injury characteristics and not by the severity of symptoms at random points after trauma.
Symptoms Associated with mTBI
VA/DOD

• Concussion/mTBI is associated with a variety of symptoms that will manifest immediately following the event, and may resolve quickly, within minutes to hours after the injury event, or they may persist longer.
• The most typical signs and symptoms after concussion fall into one or more of the following three categories:
  a. Physical: headache, nausea, vomiting, dizziness, fatigue, blurred vision, sleep disturbance, sensitivity to light/noise, balance problems, transient neurological abnormalities
  b. Cognitive: attention, concentration, memory, speed of processing, judgment, executive function

Meaning of Signs and Symptoms
VA/DOD

• Signs and symptoms may occur alone or in varying combinations and may result in functional impairment.
• Although a variety of symptoms can occur in association with TBI, they are not part of the definition of TBI, and there are no pathognomonic symptoms or signs. The term “mild TBI” refers only to the initial injury severity and should not be interpreted referring to the level of the severity of the symptoms.
Signs and Symptoms Continued

- Signs and symptoms, following the concussion, should not be attributed to concussion/mTBI if they are better explained by pre-existing conditions or other medical, neurological, or psychological causes except in cases of an immediate exacerbation of a pre-existing condition.
- Symptoms associated with concussion/mTBI are not unique. These symptoms occur frequently in day-to-day life among healthy individuals and are often found in persons with other conditions such as chronic pain, depression or other traumatic injuries. These symptoms are also common to any number of pre-existing/pre-morbid conditions the patient may have had.

VA/DOD Risk Factors for Persistent Symptoms and/or Poorer Overall Outcomes
(bold face are most salient)

<table>
<thead>
<tr>
<th>Pre-Injury</th>
<th>Peri-Injury</th>
<th>Post-Injury</th>
</tr>
</thead>
<tbody>
<tr>
<td>-Age (older)</td>
<td>-Lack of support system</td>
<td>-Compensation</td>
</tr>
<tr>
<td>-Gender (female)</td>
<td>-Acute symptom presentation (headaches, dizziness or nausea in the ER)</td>
<td>-Litigation (malingering/delayed resolution)</td>
</tr>
<tr>
<td>-Low SES</td>
<td>-Context of injury (stress, combat-related, traumatic)</td>
<td>-Co-occurrence of psychiatric disorders</td>
</tr>
<tr>
<td>-Less Education/Lower level of Intelligence</td>
<td>-Pre-neurological conditions</td>
<td>-Co-occurrence of chronic pain conditions</td>
</tr>
<tr>
<td>-Pre-neurological conditions</td>
<td>-Pre-or co-occurrence of mental health disorders (depression, anxiety, traumatic stress, substance abuse)</td>
<td>-Lack of support system</td>
</tr>
<tr>
<td>-Compensation</td>
<td></td>
<td>-Low education</td>
</tr>
</tbody>
</table>
VA/DOD 2016 Update

• The definition of TBI remains the same as in 2009
• The definition of the severity levels (mild, moderate and severe) remains the same as in 2009
• The majority of persons who sustain a single concussion recover within hours to days without residual deficits (page 26)
• Postconcussion symptoms are non-specific (page 26)
• Little evidence to suggest different treatment when symptoms are attributed to concussion vs. a different etiology, therefore symptom-focused evaluation and treatment is recommended (page 26)

Glasgow Coma Scale

• Range is 3 (unresponsive) to 15 (spontaneous eye opening, oriented times three, and following commands); is written GCS 15, or E = 4, V = 5, M = 6
• Eye opening (1 = none, 2 = to pain, 3 = to voice, 4 = spontaneous)
• Verbal (1 = none, 2 = makes unintelligible sounds, 3 = nonsensical speech, 4 = confused/disoriented, 5 = oriented times 3)
• Motor (1 = none, 2 = decerebrate posturing, 3 = decorticate posturing, 4 = withdraws from pain, 5 = localizes pain, 6 = follows commands)
Use of Motor Component of GCS to Assess Level of Consciousness

- A problem with assessment of coma in the acutely injured patient is that they may be intubated and consequently, cannot provide a verbal response
- Alternatively, investigators have used time-to-follow commands to measure duration of loss of consciousness (e.g. Dikmen et al., 1995, *Neuropsychology*, 80-90)

Post Traumatic Amnesia

- Post-traumatic amnesia (PTA), is the period of confusion, disorientation and inability to form day to day memories following emergence from coma
- As per the VA/DOD criteria, PTA and GCS are important day of injury measures for determining severity of TBI
Relationship of Coma and PTA

- Wilson et al. (1994; JNNP, 57, 198-201)
- Found close association between GCS and PTA for those patients who experienced 6 hours or more of coma after TBI
- Eight patients had coma < 6 hours with PTA > 7 days, and 3 of these 8 were only briefly unconscious
- Conclusion: both coma and PTA must be evaluated, as prolonged PTA can signal presence of a more severe TBI in the presence of brief LOC

Levin et al. *Neurobehavioral Consequences of Closed Head Injury* (1982, OUP)
Recovery of PTA

- High et al. (1990, *JCEN*, 703-714) found that for 70% of cases, orientation to person preceded orientation to place which preceded orientation to time
- Tate et al. (2005 *JNNP*, 178-185) found essentially the same sequence
- Tate et al. also found that amnesia (memory function directly measured) resolved in 94% of their cases, prior to resolution of disorientation differing from results reported by Stuss et al. (1999, *J. Neurosurgery*, 635-643)
Clinical Assessment of PTA

• Careful interview of patient regarding first memories post-trauma, including what details made the memories stand out
• Results of High et al. (1990) and Tate et al. (2005) suggest that orientation to time can serve as a marker of the end of PTA
• Thus medical records can be reviewed for statements of “A and O X 3” and/or GCS values of 15 (since the verbal score of GCS of 15 must represent O X 3)
• Presence of orientation to time often correlates with the patient’s own report of return of memory for day to day events

Effect Size and Meta-Analysis

• Effect size is obtained by dividing the mean difference between two groups by the pooled standard deviation of the groups, for Cohen’s d
• As such, effect size is a direct measurement of the magnitude of difference between two groups on a particular test
• Effect sizes of .20 are small, .50 are medium, and .80 or higher are large (Cohen, 1988)
• Meta-Analysis involves the aggregation of effect sizes over multiple completed investigations to obtain an overall effect size
Effect Size for Cohen $d$ of 1.60, a 26.9% Overlap

Percentage Overlap as a Function of Effect Size
(Cohen, 1988; Zakzanis, et al, 1999)

<table>
<thead>
<tr>
<th>Effect Size</th>
<th>Percent Overlap</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.00</td>
<td>100</td>
</tr>
<tr>
<td>.20</td>
<td>85.3</td>
</tr>
<tr>
<td>.50</td>
<td>66.6</td>
</tr>
<tr>
<td>.80</td>
<td>52.6</td>
</tr>
<tr>
<td>1.00</td>
<td>44.6</td>
</tr>
<tr>
<td>2.00</td>
<td>18.9</td>
</tr>
<tr>
<td>3.00</td>
<td>7.2</td>
</tr>
</tbody>
</table>
### Effect Sizes in mTBI
Rohling et al., TCN, 2011, 608-623

<table>
<thead>
<tr>
<th>Study</th>
<th>0-7 days</th>
<th>8-30 days</th>
<th>15-92 days</th>
<th>&gt;93 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Binder et al. ‘97</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>-0.07</td>
</tr>
<tr>
<td>Schretlen et al. ‘04</td>
<td>-0.41</td>
<td>-0.29</td>
<td>-0.08</td>
<td>0.04</td>
</tr>
<tr>
<td>Frencham et al. ‘05</td>
<td>---</td>
<td>-0.33</td>
<td>---</td>
<td>-0.11</td>
</tr>
<tr>
<td>Belanger et al. ‘07</td>
<td>---</td>
<td>-0.52</td>
<td>---</td>
<td>-0.04</td>
</tr>
<tr>
<td>Pertab et al. ‘09</td>
<td>-0.42</td>
<td>-0.42</td>
<td>-0.24</td>
<td>-0.08</td>
</tr>
</tbody>
</table>

### mTBI Effect Sizes for Combined Binder et al., ‘97 and Frencham et al. ’05 (see Rohling et al., 2011 TCN)

<table>
<thead>
<tr>
<th>Test Domain</th>
<th>0-7 days</th>
<th>8-30 days</th>
<th>15-92 days</th>
<th>≥93 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Verbal Memory</td>
<td>-0.56</td>
<td>-0.27</td>
<td>-0.27</td>
<td>-0.10</td>
</tr>
<tr>
<td>Working Memory</td>
<td>-0.37</td>
<td>-0.42</td>
<td>-0.34</td>
<td>-0.19</td>
</tr>
<tr>
<td>Visual Memory</td>
<td>-0.66</td>
<td>-0.29</td>
<td>-0.45</td>
<td>0.03</td>
</tr>
<tr>
<td>Executive Functioning</td>
<td>-0.30</td>
<td>-0.40</td>
<td>-0.32</td>
<td>0.07</td>
</tr>
<tr>
<td>Verbal Comprehen.</td>
<td>-0.67</td>
<td>-0.40</td>
<td>---</td>
<td>0.10</td>
</tr>
<tr>
<td>Perceptual Reasoning</td>
<td>-0.36</td>
<td>-0.28</td>
<td>---</td>
<td>-0.05</td>
</tr>
<tr>
<td>Processing Speed</td>
<td>-0.19</td>
<td>-0.16</td>
<td>0.00</td>
<td>-0.09</td>
</tr>
<tr>
<td>ALL DOMAINS</td>
<td>-0.39</td>
<td>-0.32</td>
<td>-0.14</td>
<td>-0.07</td>
</tr>
</tbody>
</table>
Acute Effects and Recovery Time Following Concussion in Collegiate Football Players
The NCAA Concussion Study

Michael McCrea, PhD
Kevin M. Guskiewicz, PhD, ATC
Stephen W. Marshall, PhD
William Barr, PhD
Christopher Randolph, PhD
Robert C. Cantu, MD
James A. Onate, PhD, ATC
Jingchen Yang, MPH
James P. Kelly, MD

Context Lack of empirical data on recovery time following sport-related concussion hampers clinical decision making about return to play after injury.
Objective To prospectively measure immediate effects and natural recovery course relating to symptoms, cognitive functioning, and postural stability following sport-related concussion.
Design, Setting, and Participants Prospective cohort study of 1631 football players from 15 US colleges. All players underwent preseason baseline testing on concussion assessment measures in 1999, 2000, and 2001. Ninety-four players with concussion (based on American Academy of Neurology criteria) and 56 noninjured controls underwent assessment of symptoms, cognitive functioning, and postural stability immediately, 3 hours, and 1, 2, 3, 5, 7, and 90 days after injury.

Recovery After Sport-Related Concussion

McCrean et al., JAMA 2003; 290:2556-2563
Wright et al. (February 25, 2016, PLOS One) Transient Reduction in Myelin Water Fraction due to mTBI

- Studied myelin water fraction (MWF) on MRI which yields the total brain water attributable to myelin
- Scanning done at baseline (n=11), 72 hrs (n=8), 2 weeks (n=10) and 2 months post-concussion (n = 9) with end of season scans for non-concussed Ss (n = 34)
- For concussed Ss, MWF was lower than baseline at 2 weeks but not at 2 months (differences approached significance at 72 hours)
- Significant changes were in splenium, right posterior thalamic radiation, left superior corona radiata, left superior longitudinal fasciculus, and left posterior limb of internal capsule
- For non-concussed, there were no MWF differences comparing pre to post season scans
- In mTBI, myelin damage is reversible with recovery in 2 months
- Repetitive contact without concussion does not result in myelin damage

Hammeke et al. (2013 JINS, 19, 863-872) Physiologic Compensation May Extend Beyond Neurobehavioral Recovery

- Compared 12 concussed athletes with 12 non-concussed at 13 hours and 7 weeks post trauma
- Balance, symptom complaint and cognitive performance were poorer in concussed vs non-concussed at 13 hours but not 7 weeks
- A working memory task (Sternberg) linked to fMRI showed poorer performance at 13 hours but not 7 weeks
- fMRI showed reduction in right inferior frontal gyrus BOLD acutely, but an increase relative to control Ss at 7 weeks despite no mTBI performance decrements on Sternberg
- The increase in fMRI signal at 7 weeks suggests possible continuing physiologic differences underlying compensatory activity
McCrea et al. 2010 JHTR, v. 25, 283-292
Physiologic Recovery May Extend beyond Clinical Recovery

- Studied 28 concussed athletes vs. 28 non-concussed athlete controls
- QEEG at injury, 8 days, and 45 days
- Symptom Report, balance testing and cognitive function assessed at injury, 5, 8 and 45 days post-concussion
- Symptom report, cognition and balance recovered by 5-8 days
- QEEG did not normalize until 45 days

Physiologic Time to Recovery After Concussion
(Kamins et al., Brit J Sports Med, April 28, 2017)

- Reviewed fMRI, DTI, MR Spectroscopy, CBF, electrophysiology, heart rate, exercise, fluid biomarkers, and TMS
- Due to differences in modalities, time course, study design and outcomes, it is not possible to define a single “physiologic time window” for Sport-related concussion (SRC)
- Multiple studies suggest that physiologic dysfunction may outlast current clinical measures of recovery
- Reliable studies of MRS and CBF show physiological disturbance for >15 but <30 days after injury
Kamins et al. (2017) Implications for Return to Play after SRC

• Currently there are no standard biomarker(s) for physiological dysfunction underlying vulnerability to repeat concussion in humans, so the stand-down time should be determined by thorough clinical assessment

• There is insufficient evidence to recommend a change in the current graded return to play progression

• Overall conclusion: Given limitations of available data, medical providers should continue to use clinical data to manage return to play while reserving physiological metrics for research until more conclusive data are obtained

Full Recovery from mTBI Extends to Psychological and Psychiatric Factors, and to Older Adults

• Panayiotou et al. (JCEN, 2010, 463-473) reported $d$ of 0.05 for measures of depression, anxiety, coping and psychosocial disability with no domain significantly different from zero

• Babikian et al. (JINS, 2011, 886-895) reported data consistent with full recovery from mTBI in children compared to an orthopedic trauma control group

• Goldstein & Levin (JCEN,2001, 739-753) reported good recovery in a geriatric sample with mTBI
Outcome in Older Adults Kinsella et al. 2014 (JINS, v. 20, 663-671)

- Studied 50 older adults with mTBI, 58 with orthopedic injury not involving head, and 123 normal elderly controls
- Both mTBI and orthopedic injury groups differed significantly from normal elderly but did not differ from one another
- There is risk of cognitive impairment following trauma (mTBI and orthopedic) which may reflect predisposition to injury and/or reaction to general multi-system trauma

Important Factors to Control in mTBI Research

- Research design must be prospective or quasi-prospective (i.e. Ss recruited for another purpose but known to have history of mTBI)
- Belanger et al. (JINS, 2005, 215-227) found that at 3 months, mTBI $d$ was 0.04 for unselected/prospective studies whereas mTBI $d$ was 0.74 for clinic-based samples, and 0.78 for litigating samples
- Litigation was associated with stable or worsening of cognitive functions over time
Important Factors to Control in mTBI Research: Orthopedic Trauma Controls

• Use of orthopedic trauma controls allows control for pre-injury neuropsychological differences as well as the experience of being in an accident causing injury sufficient to be transported to the hospital
• This allows for control of non-tbi neuropsychological and psychological factors
• For example, Bijur et al. 1996 found that what appeared to be an effect of multiple mTBIs disappeared when the mTBI Ss were compared to children with 1, 2 or 3 orthopedic injuries

Effect Sizes Suggest Lower Premorbid function in mTBI as a group

• In Dikmen et al. 1995, the orthopedic trauma controls scored approximately 0.50 SD below the mean of Heaton normative data for their age and education-peer group
• Heitger et al. (Brain Injury, 2009, 2850-70) reported WITAR scores for an mTBI group with persistent symptoms that were 0.75 SD below the mean of a recovered mTBI group
• Mathias & Coats (JCEN, 1999, 200-215) reported NART scores for an mTBI group that were 0.53 below the mean of a non-injured control group
Potential Factors Modifying Outcome of mTBI: Complicated mTBI

• Complicated mTBI: the patient otherwise meets criteria for mTBI, (loss of consciousness <30 minutes, PTA <24 hours), but has a structural intracranial lesion on CT scan

• Williams et al. (1990, Neurosurgery, 27, 422-428) found that such persons had outcomes more similar to those of persons suffering moderate TBI (GCS 9-12)

• Kashluba et al. (2008, Arch. PM & R, 89, 904-911) also found outcome of complicated mTBI was more similar to outcome of moderate TBI
Complicated mTBI: No differences in Outcome

- Hanlon et al. (1999, *Brain Injury, 13*, 873-887) found no differences in 6 month outcome between mTBI with and mTBI without CT abnormalities.
- Hughes et al. (2004, *Neuroradiology, 46*, 550-558) found neuropsychological differences at 72 hours between MRI positive and MRI negative mTBIs, but no differences at 6 months neuropsychologically, return to work or in PCS endorsement.

Effects of Multiple Concussions

- Belanger et al. (2010, *JINS, 16*, 215-227) meta-analysis (all athletes, 8 studies, 614 with ≥2 concussions vs. 926 controls sustaining a single concussion,), evaluated symptom complaints and 7 domains of neuropsychological performance.
- Overall effect size of .06, non-significant.
- Followup analyses showed significant effects for *Executive functions* (d = 0.24) and *Delayed Memory* (d = 0.16).
Effects of Multiple Concussions

- Cumulative effects NCAA Concussion study
- History of $\geq 3$ concussions 3 times more likely to have incident concussion than those with 0 prior concussions
- Slowed recovery was associated with history of multiple prior concussions
- Of 12 incident within-season concussions, 11 were within 10 days and 9 within 7 days of the first injury

History of Multiple Concussions in NFL Recruits

- 226 potential NFL draft picks
- Self reported history of 0, 1, and $\geq 2$ concussions
- There was *no* relationship of concussion history with performance on the Wonderlic or ImPACT
Potential Moderating Factors Regarding Effects of Multiple Concussions

• Bijur et al. (see earlier slide) found children with one, two or three prior concussions, who showed an apparent “dose effect” (poorer cognitive performance in association with increasing # of concussions)

• The apparent dose effect was not specific to concussion, as these children did not differ cognitively from children with one, two or three orthopedic injuries

Concussion History, ADHD and Learning Disability

• Nelson et al. (2016, Clin J Sport Med, 26, 120-127)

• Sample was 8,056 primarily male, primarily football players (49% high school, 51% collegiate), mean age of 18.00 years

• ADHD and LD had 2.93 and 2.08 times the prevalence, respectively, of ≥3 concussions (comorbid ADHD/LD had prevalence ratio of 3.38)

• Baseline testing in Ss without history of concussion showed greater symptom report in association with ADHD and poorer cognitive test performance on baseline in association with ADHD and LD
Concussion History, ADHD and LD
Nelson et al.

- Athletes with ADHD and/or LD are at increased risk for repetitive concussive injuries
- Caution is warranted in managing concussion in athletes with ADHD and LD given elevated history of repeat injury
- Possible explanations include premorbid neurocognitive substrates of ADHD and LD may lead to high-risk situations on the field
- Or underlying neurophysiologic substrates of ADHD/LD may create a lower threshold for the occurrence of concussion and clinical manifestation of concussive symptoms
- Baseline testing needs to take into account effects of ADHD/LD

Chronic Traumatic Encephalopathy (CTE)
McKee et al. Brain, 2013, Jan. 136 (Pt.1) 43-64

- CTE is a progressive tauopathy that occurs as a consequence of repetitive mild TBI, initially described in boxers as dementia pugilistica
- Cases in this report ranged from 17 to 98 years of age
- Pathology of CTE can be staged from I to IV
- CTE starts perivascularly in the depth of the cortical sulci, spreading to neocortex, temporal lobes, diencephalon, basal ganglia, brain stem and spinal cord
CTE Clinical Symptoms (McKee et al., 2013)

- Data derived from post-mortem semi-structured family interviews (not derived prospectively)
- Symptoms start 8-10 years after experiencing repetitive mTBI
- Symptoms can be correlated with the stages of CTE

CTE Symptoms by Stage of Disease

- Stage I: headache and loss of attention/concentration
- Stage II: additionally, depression, explosivity, short term memory loss
- Stage III: memory loss, executive dysfunction, explosivity and problems in attention/concentration, mood swings, visuospatial difficulty and aggression
- Stage IV: severe memory loss, dementia, profound loss of attention/concentration, executive dysfunction, language difficulties, explosiveness, aggression, paranoia, depression, gait and visuospatial difficulties
Other Features of CTE in Former Professional Football Players

- Only 1 of 35 former professional football players studied did not show CTE
- 31 of 34 former pros had stage III-IV CTE
- 94% were symptomatic; most commonly had STM loss, executive dysfunction, poor attention/concentration
- Mean age at onset 54.1 +/- 14.1 years
- Mean age at death 67.1 +/- 16.6 years
- Mean duration of play 11.9 +/- 6.5 years

Additional Features of CTE in Former Professional Football Players

- # years played, rho = .805 with CTE stage
- # years since retired, rho = .753 with CTE stage
- Age at death, rho = .806 with CTE stage
- # of family reported concussions, years of education, lifetime steroid use and position played did **not** correlate with CTE stage
- The frequency of at least 1 APOE4 allele was the same as in the general population
Subtypes of CTE by Age at onset
(Stern et al., 2013, Neurology, 81, 1122-1129)

• Studied 33 cases using retrospective post-mortem family interviews
• Found two reliably distinct clinical presentations
  • A cohort with onset at a younger age (n = 22) whose initial symptom presentation was changes in behavior and mood
  • An cohort with onset at an older age (n = 11) whose initial symptom presentation was cognitive impairment

Criticisms of CTE as a Chronic, Degenerative Disorder Caused by Repetitive Head Trauma in Contact Sports

• Randolph (Jan/Feb 2014, Head, Neck & Spine, 33-37), “Is Chronic Traumatic Encephalopathy a Real Disease?”
• Concluded there are no established clinical or pathological criteria for diagnosing CTE
• Recent studies of NFL retirees show an all-cause mortality rate about half of the expected rate and even lower suicide rates
• Recent clinical studies of cognitively impaired NFL retirees have failed to identify any unique syndrome (e.g. Randolph et al JINS, 2013, 873-880, MCI in retired NFL athletes)
High School Football and Risk of Neurodegeneration

- Studied high school footballers who played between 1946 and 1956 when headgear was less protective than today
- In 438 former players, there was no increased risk of dementia, PD, or ALS

Deshpande et al. (JAMA Neurology, July 3, 2017)
Association of Playing High School Football with Cognition and Mental Health Later in Life

- Ss who graduated high school in Wisconsin in 1957 were tested at age 65
- Those who played football were compared with a control group of non-athletes and Ss who played a non-contact sport
- Footballers did not differ cognitively (letter fluency, delayed word recall) or on a depression scale (Center for Epidemiologic Studies Depression Scale) compared to controls
- There was also no association of having played football with secondary outcome measures such as the likelihood of heavy alcohol use
Neurodegenerative Causes of Death Among Retired NFL Players

- Cohort mortality study of 3,439 NFL players with at least 5 pension-credited playing seasons from 1959-1988
- Overall mortality compared to that of the US population was reduced
- Neurodegenerative mortality was increased for both ALS and AD (4 times higher risk)
- Higher neurodegenerative mortality was associated with speed position vs non-speed position players

Neurodegeneration and Sport

- Davis et al. (Neurosurgery, 2015, v.76, 643-656)
- A direct causative link between concussion and CTE has not been established
- Many confounding variables can account for brain tau deposition including genetic mutations, drugs, normal aging, environmental factors, postmortem brain processing and toxins
- It is likely that many of the cases with neuropathological findings represent the normal aging process, effects of opiate abuse, or a variant of frontotemporal lobar degeneration
Is There Chronic Brain Damage in Retired NFL Players?

• Casson et al. (2014, Sports Health, Sep/Oct, 384-395)
• Studied 45 retired players (30 to 60 years old, mean = 45.6), 6.8 +/- 3.2 years play, 6.9 +/- 6.2 concussions (max = 25)
• Day-long exam including MRI (SWI and DTI), neurological and neuropsychological exams, interviews, blood tests and APOE genotyping

Is There Chronic Brain Damage in Retired NFL Players?

• The majority had normal clinical mental status exams and neurological examinations
• 4 (9%) had microbleeds on SWI and 3 (7%) had large cavum septum pellucidum with brain atrophy
• # of concussions/dings correlated with abnormal SWI and DTI findings, and with abnormal neurologic examination results
Is There Chronic Brain Damage in Retired NFL Players?

- Neuropsych testing demonstrated isolated impairments in 11 (24%) but none had dementia, dysarthria, parkinsonism, or cerebellar dysfunction
- 9 (20%) endorsed symptoms of moderate or severe depression on the BDI
- Conclusion: MRI lesions and neuropsychological impairments were found in some players but the majority of retired NFL players had no clinical signs of chronic brain damage

Summary Regarding CTE

- CTE research to date, has suffered from the absence of well-controlled prospective investigations
- There is still no evidence demonstrating a clear link between multiple concussions and CTE
- Several studies question the cause of the tauopathy allegedly associated with the presence of CTE
- Select studies do not show a significant prevalence of dementia or brain damage in retired former professional football players
- These issues suggest a critical need for prospective investigation of professional players, including in vivo assessment for presence of tauopathy using reliable biologic markers
Postconcussive Symptomatic Complaints (PCS)

- Complaints fall in three primary domains
- Physical Complaints (headache, dizziness)
- Cognitive Complaints (problems with attention, memory)
- Affective/Emotional Complaints (irritability, emotional lability)

Etiology of PCS

- Debate: physiogenesis vs. psychogenesis of complaints (Lishman, 1988, Br. J. Psychiatr, 460-469)
- Lishman: “... where mild-to-moderate injuries are concerned, organic factors are chiefly relevant in the earlier stages, whereas long-continued symptoms are perpetuated by secondary neurotic developments, often of a complex nature.”
- Physiogenic factors are evident in acute/subacute concussion, with PCS recovery paralleling normalization of balance and cognition over the first 7 days post-injury (McCrea et al. 2003)
Psychogenic Factors In PCS
“Expectation as Etiology”

• Mittenberg et al. (JNNP, 1992, v.55, 200-204): head trauma naïve Ss endorsed symptoms a) as they currently experienced them and b) as they imagined what they would have after reading a vignette describing experiencing a mTBI
• The non-injured Ss endorse the same complaints following imagined mTBI as a group who actually sustained mTBI
• Moreover, the mTBI Ss, when asked to endorse their symptom experience prior to their mTBI under- endorsed symptoms relative to the non-injured control Ss

Mittenberg Explanation of the
Psychogenic Basis of Results

• Patients with mTBI consistently underestimated the normal prevalence of these symptoms in their retrospective reports compared to base rates in normal controls
• Consequently they may reattribute benign emotional, physiological, and memory symptoms to their head injury
• “That an imaginary concussion will reliably elicit expectations of a coherent cluster of symptoms virtually identical to PCS implies that expectations share almost as much variance with the syndrome as head injury itself. A causative role is suggested.”
Mittenberg: Selective Attentional Bias and Misattribution of Symptoms

- Draws a parallel between the results of his study and “medical students disease” (students misattributing normal bodily phenomena, e.g. muscular twitches to some dread disease, e.g. ALS)
- Patients with mTBI selectively attend to these common, benign symptoms, and misattribute them to their mTBI
- “Symptom expectations, selective attention, and anxiety can, under certain circumstances, interact to produce syndromes that mimic essentially any pathological process.” (note Mechanic, N. Eng. J. Med., 1972, 1132-39, Social psychologic factors affecting the presentation of bodily complaints.)

Putnam and Millis (1994, Advances in Med Psychotherapy, 1-22) Chronic PCS as Somatoform Disorder

- Persons with chronic PCS have selective attentional biases to commonly occurring physical, cognitive and affective phenomena, and engage in misattribution of symptom origin
- Watson and Pennebaker (1989, Psych Rev, 234-254) discuss similar mechanisms in elevated health concerns
- Delis and Wetter (2007, ACN, 589-604) proposed a new subtype of somatoform disorder: Cogniform Disorder
Nelson et al. (2016, Neurology, 1856-1863)

• Analyzed recovery of athletes following sports concussion
• Pre-injury Somatization (Brief Symptom Inventory-18 Somatization Scale) was the only significant premorbid indicator of recovery
• 24-hour post injury acute symptom report was the strongest predictor of recovery
• Somatization indirectly mediated recovery through effects on 24-hour acute symptom burden

<table>
<thead>
<tr>
<th>Symptom</th>
<th>MTBI Mittenberg</th>
<th>Family Practice Lees-Haley</th>
<th>Psychiatric Litigation Lees-Haley</th>
<th>University &amp; Community Garden</th>
<th>U &amp; Comm De-pressed Garden</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>59.1</td>
<td>62</td>
<td>88</td>
<td>81</td>
<td>95.8</td>
</tr>
<tr>
<td>Irritibility</td>
<td>65.9</td>
<td>38</td>
<td>77</td>
<td>78</td>
<td>91.7</td>
</tr>
<tr>
<td>Memory Problems</td>
<td>50.6</td>
<td>20</td>
<td>53</td>
<td>56</td>
<td>75.0</td>
</tr>
</tbody>
</table>
Longitudinal Study of PCS
(Hiploylee et al., 2017, J. Neurotrauma, 1511-1523)

• 110 mTBI cases were studied (data collected, retrospectively, from 1997 to 2013; screened to exclude hemorrhage, litigation, failure of TOMM)
• 30 recovered with 80 reporting persistent PCS
• Of the 80 with persistent complaints, the most common complaints were headache, concentration problems, and fatigue
• There were no orthopedic trauma controls

Hiploylee Data compared to Mittenberg, Lees-Haley, and Garden and Sullivan

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Hiploylee mTBI</th>
<th>Mittenberg mTBI</th>
<th>Garden &amp; Sullivan all Ss</th>
<th>Garden &amp; Sullivan Depressed</th>
<th>Lees-Haley Med ptnts</th>
<th>Lees-Haley Personal Injury</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>69</td>
<td>80</td>
<td>81</td>
<td>96</td>
<td>62</td>
<td>88</td>
</tr>
<tr>
<td>Concentration</td>
<td>68</td>
<td>67</td>
<td>73</td>
<td>83</td>
<td>26</td>
<td>78</td>
</tr>
<tr>
<td>Fatigue</td>
<td>53</td>
<td>47</td>
<td>81</td>
<td>83</td>
<td>58</td>
<td>79</td>
</tr>
</tbody>
</table>
Percentage Immediate Post-Accident Subjective Experiences in mTBI vs Other Injury (Lees-Haley et al., 2001, ACN, 16, 689-695)

<table>
<thead>
<tr>
<th>Complaint</th>
<th>Other Injury</th>
<th>mTBI</th>
<th>Probability Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>77</td>
<td>75</td>
<td>.822</td>
</tr>
<tr>
<td>Concentration</td>
<td>65</td>
<td>63</td>
<td>.816</td>
</tr>
<tr>
<td>Confused</td>
<td>65</td>
<td>67</td>
<td>.894</td>
</tr>
<tr>
<td>Irritability</td>
<td>62</td>
<td>46</td>
<td>.167</td>
</tr>
<tr>
<td>Dazed</td>
<td>52</td>
<td>71</td>
<td>.102</td>
</tr>
<tr>
<td>Nausea</td>
<td>46</td>
<td>29</td>
<td>.165</td>
</tr>
<tr>
<td>Disoriented</td>
<td>42</td>
<td>33</td>
<td>.436</td>
</tr>
<tr>
<td>Balance</td>
<td>39</td>
<td>54</td>
<td>.211</td>
</tr>
<tr>
<td>Dizzy</td>
<td>44</td>
<td>54</td>
<td>.390</td>
</tr>
<tr>
<td>Memory Loss (for some of accident)</td>
<td>36</td>
<td>42</td>
<td>.646</td>
</tr>
</tbody>
</table>

Interim Conclusions About PCS

- PCS is acutely related to transient neurologic changes in the first week post-trauma
- PCS symptoms are common in other non-TBI conditions as well as in everyday life
- PCS symptoms are non-specific (to TBI)
- Chronic PCS symptoms are likely due to factors other than brain injury, with a primary factor propensity for somatization
Diagnosis Threat Suhr & Gunstad (2002, JCEN, 448-457; JINS, 23-29)

- Sampled from university undergraduates volunteering for psychology research
- All Ss selected had self-reported history of concussion
- One half of the group underwent testing for a reason other than their concussion history
- The other half were understood the examination was being conducted due to their history of concussion
- The group who linked the examination to history of concussion performed less well than the group who did not perceive this connection

Non-specificity of PCS Complaints and Diagnosis Threat Pose Risks for Iatrogenesis

- Iatrogenesis is defined as treatment-caused disorder
- The high base rate of PCS complaints in both normal life and non-TBI conditions, makes them both non-specific for diagnosis, and at risk for causal mis-attribution
- Mis-attribution of these common phenomena can lead to anxiety, and the stress from this can lead to increased frequency of these symptoms, with increased attentional bias to these events
Cognitive Behavioral Treatment of PCS
(Mittenberg et al., 1996, ACN, 139-145)

• mTBI treatment group, n = 29, met with therapist in hospital who provided them with a treatment manual, discussed cognitive behavioral treatment model (see next two slides on post-test)
• mTBI control group, received routine hospital treatment and discharge instructions
• 6 month follow-up, symptom duration shorter for treatment group (33 days) vs control (51 days) with lower average total symptoms (1.6 for treatment vs 3.1 for controls)

Mittenberg Hospital Post-Test Prior to Discharge

• 1. What are the most common symptoms after a head injury? (poor concentration, irritability, fatigue, depression, memory problems, headaches, anxiety, trouble thinking, dizziness, blurry vision, light sensitivity, sound sensitivity).

• 2. What will make the symptoms worse? (thinking or worrying about the symptoms, pushing yourself too hard, paying attention to the symptoms, thinking depressed or anxious thoughts, muscle tension).

• 3. What will make the symptoms better? (rest, graded resumption of activities, cognitive restructuring, thought stopping, relaxation exercises, reducing distractions, writing things down, problem solving skills).

• 4. What are some common causes of postconcussion symptoms? (worrying, stress, fatigue, tension, negative thoughts).

• 5. How long do symptoms of mild head injury typically last? (3-6 months).
Mittenberg Hospital Post-Test Prior to Discharge

- 6. What are the most common things people forget? (telephone numbers, people's names, where the car was parked, where the car keys are, what groceries you meant to buy, why you came into a room, directions, appointments).

- 7. What should you do if you become depressed or anxious? (make sure good things happen by scheduling pleasant activities, stop thinking negative thoughts, and see if what you are telling yourself is really true).

- 8. What should you do if you have headaches? (take a break and relax, shorter work and activity schedules, relaxation exercises to reduce tension).

- 9. What is the main cause of poor concentration and irritability? (tiredness and fatigue).

- 10. What does it mean if you experience new symptoms? (you are pushing yourself too hard and need rest).

Thomas et al. (2015, Pediatrics, 213-223) Strict Rest vs Resumption of Normal Activities

- Studied 45 concussed children prescribed strict rest for 5 days following concussion vs. 43 instructed to rest 1-2 days followed by step-wise return to activity
- No difference in neurocognitive or balance outcome
- The 45 Strict Rest Ss reported more daily PCS symptoms and slower symptom resolution
- Findings similar to older adult study (Relander et al., BMJ, 1972, 777-779) bedrest group took 14 days longer to return to work than active therapy group
Differential Diagnosis

• The material prior to this section provides important scientific and clinical information for a solid knowledge base for differential diagnosis of the individual forensic case
• It is important to know that the typical outcome for mTBI is full and complete recovery
• Important moderating factors include information suggesting that an injury is more severe (complicated mild, moderate),
• Also important is the potential impact of premorbid factors (ADHD, LD, multiple prior mTBIs)

The Evidentiary Tripod for Forensic Assessment: Record Review, Interview, and Neuropsychological Testing

Record Review

- EMS Run Record allows establishment of date and time of accident, and acute injury characteristics such as Glasgow Coma Scale (GCS), Orientation (times three: person, place and time; times four: person, place, time and situation/event), and presence/duration of loss of consciousness (LOC)
- ER also allows determination of GCS, orientation, as well as neurologic and psychiatric findings, presence/duration of LOC, and CT scan report
- If admitted to hospital inpatient stay, GCS and orientation can be monitored over time for establishing duration of PTA
- Review of subsequent medical records includes information pertaining to subsequent symptom development and serial radiologic or other neurodiagnostic records

Interview

- Careful and detailed interview about the traumatic event itself, including events leading up to, during and following the event (can take up to 30 min), allows determination of presence/absence of LOC and PTA (only ask direct questions about LOC or gaps in recall after completion of open ended questions)
- During this detailed interview of the event, monitor examinee for evidence of emotional distress, agitation, etc
Interview Continued

• Interview about continuing care since the trauma, including asking examinee’s understanding of what each doctor has diagnosed—allows cross-check of memory compared with actual records and allows check for potential iatrogenic factors
• Interview about current symptoms (in open-ended format, to be compared later with symptoms elicited on structured interview)

Interview Continued

• Background history including family history, educational history, work history and medical history (for examinee and for parents, siblings)
• Be alert to history of LD, ADHD, whether examinee was retained or skipped a grade, particularly easy or difficult subjects, and ultimate educational attainment
• Personal history is important to query for significant physical or emotional traumas in the past
Interview: Structured Interview

- A number are available; my own preference is the Levin et al. structured interview from their book on Neurobehavioral Consequences of Closed Head Injury
- Covers physical, cognitive and emotional symptoms, past involvement with legal system, past or current psychological or psychiatric treatment, history of substance abuse
- As noted previously, structured interview should always follow open-ended interview—be alert to increased symptom endorsement

Neuropsychological Testing

- Must include free-standing and embedded/derived PVTs and SVTs that are spaced throughout the examination
- Must cover major neurobehavioral domains of function with multiple, redundant measures of each domain for later evaluation of consistency of results
- Assessment with an omnibus personality inventory containing validity scales is essential (MMPI-2-RF or PAI—note that MMPI-2-RF is preferable, in my opinion, because it contains SVTs for somatic and cognitive complaints that are not available in the PAI)
- Since chronic pain is a common co-morbidity, pain scales are also important to include, such as the McGill Pain Questionnaire, Pain Disability Index and Modified Somatic Perception Questionnaire
Integration of Information from the Evidentiary Tripod

• Interpretation of test data integrates information from record review, interview and direct examination


Four Part Consistency Analysis

• Are test data consistent within and between domains (e.g., within domain, does the examinee do less well on easier compared to more difficult tasks, e.g. poorer Finger Tapping than Grooved Pegboard) between domains (e.g. between domains, does the examinee show poor attention but normal memory)

• Are test data consistent with known neurobehavioral patterns (e.g. Digit Span is typically preserved in amnestic disorders and early AD; when impaired in AD, it is usually associated with presence of more advanced dementia that would also lower performance on WAIS Vocabulary)

• Are test data consistent with actual behavior (does the examinee perform at AD levels on memory testing yet show normal memory during the clinical interview, cross-checked with the actual medical records)

• Are test data consistent with history of injury severity (does an examinee with history of mTBI perform at a level associated with history of prolonged coma)
Everything Must Make Sense