Concussion: diagnosis and treatment

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Disclosure

Relevant Financial Relationships

None

Off Label Usage
Disclosure

Personal disclosure

Being “concussed” many times
Learning Objectives

• To highlight the clinical diagnosis of concussion

• To analyze the diagnostic management of acute and chronic concussion

• To review the available treatment for concussion
Overview

• Definition of concussion
• Clinical characteristics of concussions
• Diagnostic tools
• Updates on current and future research
Incidence of traumatic brain injury (concussions)

- From 1987-2000
- 1257 identified with > 80 codes
- 558 per 100,000 person/years
- Male (56%); symptoms (53%)
- Young: recreational/sports
- Adults: vehicle accidents
- Elderly: Falls

Leibson et al. Epidemiology 2011
Definition of concussion

• complex pathophysiological response to biomedical forces imparted to the brain

• constellation of symptoms reflecting functional rather than structural injury

(Continuum Vol 20, December 2014)
Pathophysiology

- Cascade of metabolic events
- Direct trauma with external object
- Skull-brain contact
- Acceleration-deceleration
Pathophysiology

- Heterogeneous symptoms
- Lack of anatomical correspondence
Clinical Scenario

• 18 ys, male
• Backflips with wakeboard
• Football linebacker

• Transient unilateral blindness
• Confusion
• Complete recovery
Clinical Scenario: MRI brain
Symptoms of Concussion

Cognitive
• Amnesia
• Disorientation
• Inability to focus
• Delayed response
• Slurred speech
• Drowsiness

Non-cognitive
• Dizziness
• Balance disturbances
• Photophobia
• Blurred vision
• Double vision
• Phonophobia
• Headache
Symptoms of Concussion

Affective
- Emotional lability
- Depression
- Anxiety
- Mania
- Irritability

Sleep
- Increased latency
- Awakenings
- Increased sleep time
- Decreased sleep time
- RBD
- Nightmares
Symptoms of concussion

- Loss of consciousness: <10%
- Amnesia: 30-50%
- Acute migraine
- Review videotapes
- Review the dynamic of the injury
- Multiple sources
Aggravating factors

• Repetitive concussions
• Severity
• Duration of loss of consciousness
• Younger age
• Sex
• Pre-existing migraine, ADHD, learning disabilities, anxiety, depression
Contributing factors

• Sleep deprivation
• Fatigue
• Dehydration
• Illness
• Medications
• Illicit drugs
• Recovering from previous concussion
Concussions Clinical Timeline

- **Concussion**: transient alteration of brain function as the direct result of a biomechanical force. *Days to weeks*

- **Post-concussion syndrome**: complex pathophysiology, both biological and psychological, that occurs after the concussion is over. *Months to years*

- **Chronic effects**: unknown pathophysiology, unclear epidemiology. Chronic Traumatic Encephalopathy (CTE), depression, parkinsonism, cognitive decrement. *Lifetime*
Post-concussion syndrome

- No reliable tests for diagnosis
- Clinical history: detailed concussions history
- Review videotapes
- Review the dynamic of the injury
- Multiple sources
Chronic Effects

• Multiple concurrent diseases
• Mild cognitive impairment
• Parkinsonism
• Chronic migraine
• Dementias
• ALS
World Cup Final 2014 
Argentina-Germany

• [https://www.youtube.com/watch?v=HlwY69oVL8l](https://www.youtube.com/watch?v=HlwY69oVL8l)

• [https://www.youtube.com/watch?v=v4utKcINpkI](https://www.youtube.com/watch?v=v4utKcINpkI)
Diagnosis of concussion

• No reliable tests for diagnosis
• Clinical history: detailed concussions history
• Review videotapes
• Review the dynamic of the injury
• Multiple sources
Biomarkers

• Indicator of presence or severity of a disease:
  Specific
  Sensitive
  Predictive
  Robust
  Non invasive
  Non expensive
Biomarkers: neuroimaging

Structural
- Xray
- CT
- MRI
- DTI
- Amyloid PET
- Tau PET

Functional
- Functional MRI
- FDG PET
Neuroimaging: Xray/CT scan

- Xray: fractures
- CT: use is controversial
- Not good for subtle changes
- Use in the acute phase?
Neuroimaging: MRI

• Serial scans for subtle changes
• Look at the areas of the trauma
• GRE sequences: microbleeds
• Hippocampal atrophy (High Res coronal)
• Midbrain atrophy
• Cortical atrophy
• White matter changes
• Look is symptoms match the MRI
Neuroimaging: GRE Sequences

Greenberg et al. Lancet 2009

Vernoij et al. Radiology 2008
Neuroimaging: Hippocampal Atrophy

Normal

normal hippocampi

AD

hippocampal atrophy
Cavus septum pellucidum
Neuroimaging: DTI

- White matter changes
- Metanalysis: WM in posterior corpus callosum
- Cognitive scores reduced with lower FA

Aoki et al. JNNP 2012; Wada et al AJNR 2012
Neuroimaging: DTI

- 49/42 normal DTI
- None had symptoms
Neuroimaging: Amyloid PET

- Amyloid present in many conditions
- Reader dependent
- Clinical interpretation unclear
- Amyloid also labels white matter

Yang et al. NEJM 2012; Moghbel et al EurJNuclMedMolImaging 2012
Neuroimaging: TAU PET

MRI

[11C]PBB3

B-Amyloid

[11C]PIB

AD

Normal control
Neuroimaging: FDG PET SCAN

Normal
Neuroimaging: FDG PET SCAN

AD

Posterior cingulate
Temporoparietal
Frontal

DLB

Occipital

Kantarci et al, Neurobiol Aging 2011
Clinical Case

Courtesy of Dr. Drubach
Neuroimaging: FMRI

<table>
<thead>
<tr>
<th>No Clinically-Observed Impairment (COI-)</th>
<th>Change in Neurological Behavior (FOI+)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-Season</td>
<td>In-Season</td>
</tr>
<tr>
<td>![Brain Image]</td>
<td>![Brain Image]</td>
</tr>
</tbody>
</table>

**No Change in Neurological Behavior (FOI-)**
- Pre-Season and In-Season fMRI studies show no change

**Change in Neurological Behavior (FOI+)**
- Newly discovered category: 50% of players with no clinically-observable symptoms still show significant alterations during In-Season fMRI

**Clinically-Observed Impairment (COI+)**
- Not Observed

**All players with concussion show significant alteration during In-Season fMRI**
Biomarkers: body fluids

Serum/blood
- ApoE
- Presenilin
- Amyloid
- Tau
- C-reactive
- TNF

CSF
- Abeta-42
- tau

Small et al. 2008
Head Trauma and ALS

• First description in 1897 (Erb W. 1897)

• 3 fold increase in subjects with previous HT (Chen et al Am J Epidemiol 2007)

• Increased risk of ALS in soccer players (Chiò et al. Neurology 2005)

• 40 fold increase of prevalence in football players (Abel E. Perceptual Motor Skills 2007)
Head trauma and AD

- Pooled analysis of 11 case-control studies that investigated HT and AD
- The relative risk for dementia was 1.82
- Stronger association in cases with family hx of dementia and males (Mortimer et al. Int J Epidemiol 1991)
Head trauma and PD

• Head trauma and future risk of PD: Lag-time between HT and PD: 21 years; OR = 4.3  \((\text{Bower et al. Neurology 2003})\)

• HT injury with amnesia/loss of consciousness increased the risk for PD: OR = 3.8  \((\text{Goldman et al. Ann Neurol 2006})\)
Head trauma and genetic predisposition

- FAME and SEARCH: 476 (89+387) cases and 576 controls (387+189)
- Rep 1: a promoter increasing a-synuclein
- HT not associated with increased risk of PD
- HT was associated with PD and Rep1
  FAME: OR, 5.4; 95% CI, 1.5-19;
  SEARCH OR, 2.3; 95% CI, 0.6-9.2
  pooled OR, 3.5; 95% CI 1.4-9.2, (p interaction = 0.02).
- 4.9 years earlier (p = 0.03).

Ann of Neurology 2012
Genetic and head trauma

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Neurology 2014
Cluster Analysis of risk factors of PD in Olmsted County

Men only

- Coffee consumption
  - No: 119 / 103
  - Yes: 2 / 18
    - 90.0% Cases

- Head trauma
  - No: 117 / 93
  - Yes: 2 / 10
    - 83.3% Cases

- Pesticide use
  - No: 108 / 74
  - Yes: 9 / 19
    - 67.9% Cases

- Immunologic diseases
  - No: 91 / 53
    - 63.2% Controls
  - Yes: 17 / 21
    - 69.2% Controls

- Family history of dementia
  - No: 9 / 4
    - 68.0% Cases
  - Yes: 8 / 17
    - 68.0% Cases

(Savica et al., Hormones and Behavior 2013)
Chronic Traumatic Encephalopathy

• Progressive degenerative disorder
• Onset in midlife, many years after retirement from professional sport
• 3 stages: behavioral/cognitive changes, parkinsonism, dementia

(Gavett et al. 2011 Clin Sports Med)
Dementia Pugilistica

- Described in 1928 by Dr. Harrison Martland
CTE Diagnosis

• It is not possible to diagnose CTE without pathological confirmation

• Signs and symptoms are identical to PD, Fronto-temporal Dementia, AD, and ALS (Gavett et al. 2011 Clin Sports Med)
Concussion vs Post Concussion syndrome

- 7 days to 3 months after concussion
- Age
- Sex (female)
- Trauma
Second impact syndrome

- Repetitive injuries
- Second trauma
- Sex (female)
- Boxers? Football players?
Management of symptoms

- Headache
- Sleep
- Mood
- Attention
- Balance
Post-traumatic headache (PTH) is just headache?

- Headache in athletes: 58%
- Triggers: sleep deprivation, emotional stress, skipping meals, exercise, travel, altitude, etc…
- Benign exertional headache
- Airplane headache
- Altitude headache
- Swimmer/diver headache

NCAA Task Force
Post-traumatic headache (PTH) is just headache?

- Most common symptom after trauma (90%)
- Exclude intracranial and secondary causes
- Exclude primary headache
- Rule out concussion
- Excacerbation of primary headache

*Kirc et al 2008;*
Mimickers of PTH

- Dehydration
- Hypoglicemia
- Hypertension
- Hypertermia
- Drugs (prescription and not prescription)
Drugs causing headache in athletes

- Alcohol
- NSAIDs
- Anabolic Steroids
- Nicotine
- Antibiotics
- Nitrazepam
- Antihypertensives
- Oral Contraceptives
- Caffeine
- Sympathomimetics
- Corticosteroids
- Theophylline
- Dipyridamole
- Vasodilator Agents
- Analgesics
Management of Headache

• 24 hours: nothing, acetaminophen
• Concussion: naproxen
• Persistent: prednisisone
• Post-concussion: migraine profilaxis

• Treat PTH as primary migrain disorder
Management of Sleep

• 24 hours: nothing
• Concussion: melatonin
• Persistent: zolpidem
• Post-concussion: tricyclic

• Quietapine
Management of Mood

- 24 hours: nothing
- Concussion: nothing
- Persistent: nothing
- Post-concussion: tricyclic, SSRI, SNRI
Management of Attention

- 24 hours: nothing
- Concussion: nothing
- Persistent: nothing
- Post-concussion: like ADD
Management of Neurodegeneration

- Parkinsonism
- Dementias
- ALS

Use the current state of the art treatment
High school football form 1946-1956 and risk of neurodegeneration

Savica et al 2013
High school football form 1946-1956 and risk of neurodegeneration

**Ascertainment via high schools yearbooks, 1946-1956**

- 512 football players
- 203 non-football players (band, glee club, choir)

Rochester Epidemiology Project (REP) Browser

- Tracked in the REP: 438 (85%) football players
- Tracked in the REP: 140 (69%) non-football players

Review of the medical records

- Dementia: 13/438 cases
- PD: 10/438 cases
- ALS: 2/438 cases
- Dementia: 2/140 cases
- PD: 5/140 cases
- ALS: 1/140 cases

Savica et al 2013
# High school football form 1946-1956 and risk of neurodegeneration

## Table 1. Historical cohort study of football players vs non-football players and risk of neurodegenerative diseases.

<table>
<thead>
<tr>
<th></th>
<th>Football players</th>
<th>Band/glee/choir members</th>
<th>HR</th>
<th>(95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N = 438</td>
<td>N = 140</td>
<td></td>
<td></td>
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<tr>
<td><strong>Descriptive Information</strong></td>
<td></td>
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</tr>
<tr>
<td>Years of follow-up*</td>
<td>50.2 (13.7, 57.5)</td>
<td>42.7 (8.8, 55.4)</td>
<td>--</td>
<td>--</td>
<td>0.03</td>
</tr>
<tr>
<td>Age at follow-up*</td>
<td>68.4 (31.5, 75.6)</td>
<td>59.1 (26.7, 73.4)</td>
<td>--</td>
<td>--</td>
<td>0.01</td>
</tr>
<tr>
<td><strong>Outcomes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dementia</td>
<td>13 (3.0%)</td>
<td>2 (1.4%)</td>
<td>1.58</td>
<td>(0.36-7.01)</td>
<td>0.55</td>
</tr>
<tr>
<td>Parkinson’s Disease</td>
<td>10 (2.3%)</td>
<td>5 (3.6%)</td>
<td>0.48</td>
<td>(0.17-1.42)</td>
<td>0.19</td>
</tr>
<tr>
<td>Amyotrophic Lateral Sclerosis</td>
<td>2 (0.5%)</td>
<td>1 (0.7%)</td>
<td>0.52</td>
<td>(0.05-5.68)</td>
<td>0.59</td>
</tr>
</tbody>
</table>

* Values are median (25th percentile, 75th percentile). P-values are for the Wilcoxon rank-sum test. HR = hazards ratio; CI = confidence interval.
Table 2. Historical cohort study of football players and non-football players vs. general population and risk of neurodegenerative diseases.

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<td>Observed</td>
<td>13 (3.0%)</td>
<td>2 (1.4%)</td>
<td></td>
</tr>
<tr>
<td>Expected*</td>
<td>18.1 (4.1%)</td>
<td>4.3 (3.1%)</td>
<td></td>
</tr>
<tr>
<td>SIR vs. Expected†</td>
<td>0.72 (0.38-1.23)</td>
<td>0.47 (0.05-1.68)</td>
<td></td>
</tr>
<tr>
<td>Years after index‡</td>
<td>55.3 (51.5, 59.4)</td>
<td>57.8 (57.2, 58.5)</td>
<td>0.44</td>
</tr>
<tr>
<td>Age at outcome‡</td>
<td>72.4 (69.3, 77.0)</td>
<td>76.0 (75.0, 77.0)</td>
<td>0.35</td>
</tr>
<tr>
<td><strong>Parkinson Disease</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Observed</td>
<td>10 (2.3%)</td>
<td>5 (3.6%)</td>
<td></td>
</tr>
<tr>
<td>Expected*</td>
<td>4.2 (0.9%)</td>
<td>1.0 (0.7%)</td>
<td></td>
</tr>
<tr>
<td>SIR vs. Expected†</td>
<td>2.36 (1.13-4.34)</td>
<td>4.94 (1.61-11.51)</td>
<td></td>
</tr>
<tr>
<td>Years after index‡</td>
<td>52.4 (42.4, 59.6)</td>
<td>49.8 (37.4, 60.2)</td>
<td>0.95</td>
</tr>
<tr>
<td>Age at outcome‡</td>
<td>70.5 (58.9, 77.4)</td>
<td>67.7 (55.5, 78.1)</td>
<td>0.95</td>
</tr>
<tr>
<td><strong>ALS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Observed</td>
<td>2 (0.5%)</td>
<td>1 (0.7%)</td>
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</tr>
<tr>
<td>Expected*</td>
<td>0.64 (0.1%)</td>
<td>0.16 (0.1%)</td>
<td></td>
</tr>
<tr>
<td>SIR vs. Expected†</td>
<td>3.15 (0.38-11.33)</td>
<td>6.44 (0.16-35.7)</td>
<td></td>
</tr>
<tr>
<td>Years after index‡</td>
<td>47.6 (46.3, 48.8)</td>
<td>42.8 (42.8, 42.8)</td>
<td>0.67</td>
</tr>
<tr>
<td>Age at outcome‡</td>
<td>65.9 (64.8, 66.9)</td>
<td>61.0 (61.0, 61.0)</td>
<td>0.67</td>
</tr>
</tbody>
</table>

* Expected number of cases are calculated from age-specific person years and previously published incidence rates in the Olmsted County population.
† Standardized incidence ratios (SIRs) are calculated based on observed number of cases and expected number of cases.
‡ Values are median (25th percentile, 75th percentile). P-values are for the Wilcoxon rank-sum test.
Conclusions

- Concussion is a complex and heterogenous syndrome
- No certain diagnosis…in vivo
- Desperate need of good science

- In practice: use the available evidence and treat the symptoms regardless of concussion
Thank You

Messina, Italy
Rochester, MN
Questions?