Disclosures

• None

• Funding: Washington University Institute of Clinical and Translational Sciences NIH grant UL1TR002345
Outline

• Introduction
  • Epidemiology, mechanisms and pathophysiology of injury

• Factors that predict and influence outcome
  • Moderate-severe TBI
    • Secondary injuries
  • Mild TBI/concussion
    • Diagnosis and management

• Chronic Traumatic Encephalopathy
Epidemiology

- 2013:
  - 2.5 million ED visits
  - 282,000 TBI-related hospitalizations
  - 56,000 TBI-related deaths

- 80 hospitalizations & 6 deaths per 100,000 kids

Mechanism varies by age
Mortality varies by age
GCS: Morbidity and Survival

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<thead>
<tr>
<th>Best eye opening</th>
<th>Spontaneously</th>
<th>4</th>
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<td>To verbal stimuli</td>
<td>3</td>
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<td>To painful stimuli</td>
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<td>No eye opening</td>
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<td>Best verbal response</td>
<td>Appropriate coo/cry</td>
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<td>Irritable Cry</td>
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<td>Inconsolable</td>
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<td>Grunts</td>
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<td>No verbal response</td>
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<td>Best motor response</td>
<td>Normal spontaneous</td>
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<td>Withdraws to touch</td>
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<td>Withdraws to pain</td>
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<td>Flexion to pain</td>
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<td>Extension to pain</td>
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<td>No motor response</td>
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Story

- Jack, 19 years old and his sister Jill, 16 years old were driving too fast down a hill when the car went off the road and hit a tree.

- Jack (the unrestrained driver) sustained moderate TBI with a contusion and diffuse axonal injury.

- Jill (restrained passenger) sustained a whiplash injury.
Moderate TBI: Jack
Acute Injury

- Direct tissue damage
  - Swelling, ischemia, hemorrhage
- Glutamate increases
  - Cell membrane rupture
  - Failure of Na/K pump
  - Activation of post-synaptic neurons & Ca++ toxicity

Diffuse Axonal Injury (DAI)

- Spectrum of MRI negative to profound
- Shearing injury to axons with local swelling
- Microhemorrhages
Primary versus Secondary Factors

Injury Factors

GCS
Mechanism

ED
ICU
Floor

ICP
Hypotension
Hypoxia
Seizures
Dose of ICP influences outcome


Blood Pressure

CPP = MAP – ICP

MAP = \[\frac{2}{3}\ \text{diastolic}\] + \[\frac{1}{3}\ \text{systolic}\]
Hypoxia worsens outcomes

Hypoxia worsens outcomes

Hx = Hypoxia
Nx = Normoxia

Seizures

• Adults: 94 patients
  • 22 % had seizures, 6/94 with SE
  • 52 % with nonconvulsive seizures
• Kids: 189 patients
  • 30 & 43 % had seizures
  • 7 & 40 % with subclinical only seizures
• Risk factors
  • Younger age
  • AHT
  • Intraaxial blood

How is Jack going to do?
Age impacts neurocognitive outcome

Injury severity impacts outcome

- DAI and IPH leads to reduced processing speed, but not IQ and other domains

Guerriero, Dodd, Pineda in preparation
Outcomes

• Post-traumatic epilepsy: 10 – 20 %
  • Risk: Younger age and severity of injury


• Sleep disturbance associated with increased depression, anxiety and apathy 12 months post-injury


• Affective disorders, ADHD and Anxiety
  • Mild: Anxiety decreases
  • Severe: Anxiety increases

  Keenan, et al. *J Neurotrauma*, 2018
Therapeutic options

• Cognitive
• Headache
• Affective
• Sleep dysfunction
• Motor
  • Gross Motor -> PT
  • Fine Motor -> OT
  • Speech/communication -> Speech
What happened to Jill?

- In the ED, Jill complains of a headache and dizziness
Concussion

• Transient neurologic symptoms
• Complex pathophysiologic process
• No traditional brain imaging correlate

History

• Hit to the head or body with transient neurologic symptoms
• Mechanism of injury
• Additional history
Recovery

Injury

Full Recovery

Course -> 7 - 28 days
Symptoms

• General

• Neurologic

• Cognitive

• Emotional
Symptoms

• **General**
  – Headache
  – Dizziness
  – Nausea
  – Vomiting
  – Fatigue
  – Sleep difficulties

• **Cognitive**
  – Disorientation
  – Memory loss
  – Feeling “foggy”, “dazed”
  – Attention problems
  – Difficulty concentrating
  – Slow to respond

• **Neurologic**
  – LOC
  – Balance problems
  – Visual disturbances
  – Sensitivity to light or noise
  – Seizures

• **Emotional**
  – Irritability
  – Emotional lability
  – Sadness
  – Anxiety
Physical Exam

• General and Neurologic Exams
• Mental Status Exam
• Focal findings = Red Flag

• And some specifics -
Physical Exam

- General appearance
- Saccadic intrusions or difficulties with visual pursuit
- Balance problems

Neuroanatomy

• Frontal Eye Fields
  – Guide attention and saccades
Physical Exam

• General appearance
• Saccadic intrusions or difficulties with visual pursuit
• Balance problems

BESS
Double leg stance Single (non-dom)
Tandem (non-dom in back)
20 secs & Record errors
What’s Jill’s course going to be?
Recovery

Injury

Susceptibility & Risk

Full Recovery

Course -> 7 - 28 days

Post-concussive syndrome
Outcomes

- Kids: 13–29% of mild TBI have persistent somatic, cognitive, sleep, and psychological symptoms 3 months following injury

- Adults: Litigation status and disability seeking status were significant predictors of prolonged concussion

Psychological and behavioral outcomes

- Higher rates of ADHD in:
  - Hospitalized vs not hospitalized
  - Injured vs noninjured (healthy) controls

- **Depression**: Children 6 months post-mTBI 9.3 x more likely vs orthopedic injury

- **Anxiety**: Higher rates 0-6 months after injury, but not by 1 year

Will Jill have prolonged symptoms?

• Premorbid factors
• Number of injuries
• Genetic predisposition
• Resiliency factors
• Recovery strategy
Risk factors for prolonged recovery

• Symptom severity
• Multiple concussions
• Female sex
• Preexisting conditions:
  • Anxiety
  • Mood disorders
  • ADHD
  • Migraine

Giza, Kutcher and Ashwal, Neurology 2013.
Premorbidities

- Children < 12 with premorbid conditions
- Adolescents +/- premorbid conditions
- Life stressors

- Family history:
  - Mood disorders
  - Psychiatric history
  - Migraines

Cycle

- Trouble concentrating
- Light headed
- Sleep dysregulation
- Injury

Avoid activities
Feeling down
Headache
Anxiety
Decreased exercise
Premorbid conditions
How do we break the cycle?
Rest

• **Benefit of 5 days of strict rest over conventional recommendations (1-2 days rest, graded return to activities)**

• **Outcome**: Neurocognitive performance and balance at 10 days.

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**Figure 4**
Proportion of patients reporting symptom resolution (PCSS ≤7) over time. It took longer for 50% of the intervention group to report symptom resolution. However, the difference in overall proportion of patient reporting symptom resolution did not meet statistical significance (P = .08).

How much screen time is too much?

- Individuals with greatest cognitive activity had longest symptom duration.

Does exercise help or hurt?

- Subthreshold exercise
- 80% of heart rate threshold for symptoms

Pharmacologic treatments

• Post-traumatic headache
  • Acute: ibuprofen or naproxen
  • If migraine: triptans
  • Preventive: amitriptyline > topiramate/zonisamide

• Nausea
  • ondansetron, prochlorperazine, metoclopramide

• Attention

• Depression/Anxiety

• Sleep dysfunction
Can Jill go home from the ER?
When to suspect more than a concussion

• Differentiating:
Signs of Increased ICP

• Progressively decreasing mental status
• Papilledema (although may be normal early)
Signs of Increased ICP

• Worsening headaches
• Focal neurologic deficits
• Cushings triad
  - Hypertension
  - Bradycardia
  - Decreased respiratory rate
Lucid interval

• Typically 5 – 60 mins
• More often in younger kids (< 24 months)
• Can be as long as a 3 hours
• Case reports only of 12 hours and 48 hours (with arterial dissection)

If concerned..

• Observe for some period of time
...6 months later

- Jill and parents come into you office
- Soccer season is coming up and Jill is working towards a possible Division 1 scholarship
- Jill's parents don't want her to play, because they're afraid she will develop CTE

CTE found in former soccer players, study shows

By Meera Senthilingam and Nadia Kounang, CNN
Updated 9:58 AM ET, Wed February 15, 2017
Chronic Traumatic Encephalopathy (CTE)

• **Neuropathologically**
  – Atrophy of the cerebral hemispheres, medial temporal lobe, thalamus, mammillary bodies, and brainstem

• **Microscopically**
  – Tau-immunoreactive neurofibrillary tangles
  – Preferential involvement of superficial cortical layers, patchy distribution in frontal and temporal cortices, sulcal depths and perivascular regions
A new study by Boston University researcher Dr. Mez found that 110 of 111 of NFL players who donated their brains had chronic traumatic encephalopathy (CTE), and the results were published in the Journal of the American Medical Association (JAMA).

- 110 of 111 of NFL players
- Brains donated by concerned family members

Mez, J, et al. *JAMA*, 2017; 318(4)
Case series

- 14 retired soccer players with dementia
  - 4 had CTE
  - 6 had Alzheimer’s disease
  - 5 cerebral amyloid angiopathy
  - 5 other (Lewy body, vascular pathology)

Clinical features of CTE?

- Memory disturbances, behavioral & personality changes, speech & gait abnormalities.

Clinical features of CTE?

• CTE in the brains of 21 of 66 former contact sports athletes, but not in the brains of 198 without contact sports exposure
• No difference in premortem clinical characteristics

Are contact sports bad for your health?

- 3,400 NFL retirees
- Mortality rates due to cardiovascular disease, suicide, and cancer are dramatically reduced
- Suicide rate: 41% of expected
- Death rates due to AD and ALS were higher than expected, but only in "skill/speed" positions

“Speed” position players were found to be generally healthier and live longer, therefore they would be at increased risk of late life neurodegenerative disease

For review see: Randolph, Arch of Clin Neuropsy, 2018; 33; 644–648
Suicide rates in retired NFL players

- 1920–2015
- 26,702 athletes
- 26 suicides
  - 46% of those occurred since 2009

Webner & Iverson. *Brain Injury*, 2016: 30, 1718–1721
Annual Pubmed articles on CTE
Some conclusions

• TBI is an environmental risk factor for cognitive decline or dementia

• So is:
  • Alcohol abuse
  • Anabolic steroid use
  • Drug use
  • Marijuana

• And - air pollution, aluminum, silicon, selenium, pesticides, vitamin D deficiency, and electric and magnetic fields

Schwarzinger, et al. The Lancet Public Health, 2018
Kaufman, et al. Drug & Alcohol Depend, 2015; 152
Hulse, et al. Int Psychogeriatr, 2005; 27
Auer, et al. JAMA int Med, 2016; 176(3)
Killin, et al. BMC Geriatrics, 2016; 16, 175
Summary

- Moderate TBI – Avoid secondary injuries
- Mild TBI
  - ~ 75% will be recover by 28 days
  - Early rehabilitation, particularly for those with premorbid conditions
- To date there is no causal relationship between head impacts and CTE
Collaborators

**Neurology:** Chris Smyser, Chris Gurnett, Jon Zempel, Mike Morrisey, Stuart Tomko, Jen Griffith, Sarah Bauer-Huang, Susan Hibits, Mike Noetzel, Brad Schlaggar

**Critical Care:** Julie Bubeck-Wardenburg, Mary Hartman, Jose Pineda, Stuart Friess, Erin Murphy

**Neurosurgery:** Dave Limbrick, Jen Strahle, Sean Mcvoy

**NCFP:** Jon Dodd, Chris Bosworth Sara Small, Celine Zidar

- r.guerriero@wustl.edu