Evidence for Concussion Subtypes

Angela Lumba-Brown, MD
Co-Director, Stanford Concussion and Brain Performance Center
Assistant Professor of Emergency Medicine, Stanford University
Disclosures

• No conflicts of interest to disclose
• Co-investigator on the U.S. Department of Defense-funded Brain Trauma Evidence Based Consortium (B-TEC)
Brain Trauma Evidence-Based Consortium
PI: Jamshid Ghajar, MD, PhD

• 1. Establish evidence for concussion subtypes by describing their prevalence and informing recovery trends -- to direct targeted strategies effecting better care.

• 2. Maximize the utility of scientific efforts to-date that address the epidemic of concussion and brain trauma, for the purpose of deriving a clinically useful classification system and evidence-based guidelines for diagnosis, prognosis, treatment, and outcomes.

• 3. Create a consortium among the neurotrauma community that will inspire a commitment to the principles of evidence-based medicine in the design and conduct of brain trauma research.

• 4. Continue updating the Brain Trauma Foundation traumatic brain injury guidelines.
STANFORD CONCUSSION AND BRAIN PERFORMANCE CENTER

Pushing the limits of brain performance

Advancing the science of injury recovery in children, adults, and athletes

Delivering state-of-the-science care

https://med.stanford.edu/braincenter.html
Objectives

<table>
<thead>
<tr>
<th>Describe</th>
<th>Summarize</th>
<th>Recognize</th>
</tr>
</thead>
<tbody>
<tr>
<td>Describe the prevalence of concussion subtypes</td>
<td>Summarize a model for subtype clustering</td>
<td>Recognize how stratification by concussion subtype may influence prognosis and recovery</td>
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</tbody>
</table>
Background

Variability in concussion recovery

- Pre-injury factors
- Post-injury factors

Clinical presentations post-injury may predict recovery

Establishing evidence: concussion subtypes

- Aid diagnosis
- Prognostic counseling
- Target therapies and rehabilitation
- Direct future research
Expert Workgroup and Panel of Observers

Josh Bloom – Duke University
David Brody – Uniformed Services University
Jim Chesnutt – Oregon Health and Science University
Jay Clugston – University of Florida
Micky Collins – University of Pittsburgh
Jam Ghajar – Stanford University
Gerry Gioia – George Washington University
Anthony Kontos – University of Pittsburgh
Angela Lumba-Brown – Stanford University
Allen Sills – Vanderbilt University
Masaru Teramoto – University of Utah

Observing Organizations
• CDC
• DoD
• NCAA
• TBI Endpoints Development
• Zurich Consensus Group
• AANS/CNS
• ACSM
• NATA
Concussion Subtypes

Cognitive

Headache/Migraine

Anxiety/Mood

Vestibular

Ocular-motor

*Associated condition: Sleep Disturbance and Cervical Strain
Clinical Questions

1. What is the prevalence of concussion subtypes and associated conditions compared with controls within the first 3 months post injury?
2. What is the severity of symptoms reported compared to control populations?
3. What is the temporal recovery trajectory by concussion subtype and associated conditions over the first 3 months post injury?
4. How do subtypes cluster?
Methods

Expert Workgroup of 11 participants

Panel of Observers

Literature search
1980 – July 1st, 2017

AAN methodology of systematic review

Data-extraction and meta-analysis
Preliminary Results
Results

- Literature search: 3,029 applicable studies
- Full text review: 1,024 studies
- Inclusion for subtype classification: 427 studies
Study Inclusion by Subtype*

- Vestibular: 129 (30%)**
- Ocular-motor: 84 (20%)
- Anxiety/Mood: 160 (37%)
- Cognitive: 236 (55%)
- Headache/Migraine: 141 (33%)
- Sleep Disturbance: 94 (22%)
- Cervical Strain: 18 (4%)

*Subtype inclusion is not mutually exclusive
**Percentage of studies
Time points of Diagnostic Measures Post-Injury

- 0 to 3 days
- 4 to 10 days
- 11 days to 1 month
- > 1 month to 3 months
Symptom Scales Used By Extracted Literature

- Rivermead 32%
- Post concussive symptom scale (PCSS) 26%
  - Post traumatic checklist (PTC) 6%
  - SCAT 2/3 6%
- High School Reporting Information Online injury surveillance system (HS RIS)
- General symptom reports (other surveys and checklists) 13%
- Neuropsychological batteries 6%
- Neurobehavioral Symptom Inventory
- Military acute concussion evaluation (MACE) 2%
- Brief Symptom Inventory-18
- Abbreviated Concussion Symptom Inventory 3%
- Concussion Symptom Inventory
- Patient Health Questionnaire (PHQ-15)
- Patient Health Questionnaire (PHQ-9)
- British Columbia Post-Concussion Symptom Inventory (BC-PSI) 6%
<table>
<thead>
<tr>
<th>Subtype Categorization</th>
<th>Symptom Reported</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vestibular</td>
<td>Balance difficulty, Dizziness, Coordination difficulty, Disoriented, Gait problem, Lightheadedness, Nausea, Vomiting</td>
</tr>
<tr>
<td>Ocular-motor</td>
<td>Visual problem, Double vision, Blurred vision, Eye strain, Sensitivity to light, Reading issue, Strabismus, Accommodation issue, Nystagmus, Flashing lights, Vergence</td>
</tr>
<tr>
<td>Anxiety/Mood</td>
<td>Anxiety, Depression, Irritability, Fatigue, Loss of energy, Frustration, Sad, Nervousness, Restlessness, Emotional, Personality change, Confusion, Impatient, Agitated, Anger</td>
</tr>
<tr>
<td>Cognitive</td>
<td>Memory difficulty, Remembering/Memory problems, Feeling slow, Mentally foggy, Forgetfulness, Concentration, Attention, Confusion, Longer to think</td>
</tr>
<tr>
<td>Headache/Migraine</td>
<td>Headache, Nausea, Vomiting, Sensitivity to light, Sensitivity to noise, Migraine</td>
</tr>
<tr>
<td>Associated Condition: Sleep Disturbance</td>
<td>Drowsiness, Sleeping more, Sleeping less, Insomnia, Trouble falling asleep, Trouble sleeping through the night, Sleep Disturbance</td>
</tr>
<tr>
<td>Associated Condition: Cervical Strain</td>
<td>Neck pain, Neck stiffness, Cervicogenic headache</td>
</tr>
</tbody>
</table>
Concussion Subtype Symptom Scale

01
Current Symptom Scales do not capture key aspects of subtype symptom reports

02
Workgroup examples
• Headache upon awakening
• Unease in crowds or busy settings
• Feeling unstable
• Motion sickness
• Worried
• Fearful
• Short-tempered
• Neck spasm
• Neck tightness

03
Future directions – development of subtype-directed symptom scale
<table>
<thead>
<tr>
<th>Concussion Subtype or Associated Condition</th>
<th>Concussion</th>
<th>Control</th>
<th>n(N)</th>
<th>OR [95% CI]</th>
<th>$I^2$</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Vestibular Subtype</strong></td>
<td></td>
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<tr>
<td>Dizziness*; Balance problems; Tinnitus; Fogginess; Vomiting; Nausea</td>
<td>60%</td>
<td>8%</td>
<td>5(1015)</td>
<td>16.68 [11.63, 23.93]</td>
<td>74%</td>
<td>&lt;0.00001</td>
</tr>
<tr>
<td><strong>Ocular-Motor Subtype</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Visual problems*; Sensitivity to light</td>
<td>36%</td>
<td>3%</td>
<td>5(1015)</td>
<td>16.34 [4.00, 66.67]</td>
<td>81%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td><strong>Headache/ Migraine Subtype</strong></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headache*; Migraine; Sensitivity to light; Sensitivity to noise; Vomiting; Nausea</td>
<td>81%</td>
<td>14%</td>
<td>5(1015)</td>
<td>33.67 [13.52, 83.85]</td>
<td>83%</td>
<td>&lt;0.00001</td>
</tr>
<tr>
<td><strong>Anxiety/Mood Subtype</strong></td>
<td></td>
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<tr>
<td>Depression*; Anxiety; Sadness; Irritability; Emotional problem; Confusion; Slowed down; Nervousness</td>
<td>61%</td>
<td>30%</td>
<td>2(310)</td>
<td>4.30 [2.56, 7.24]</td>
<td>0%</td>
<td>&lt;0.00001</td>
</tr>
<tr>
<td><strong>Cognitive Subtype</strong></td>
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</tr>
<tr>
<td>Concentration*; Problems remembering; Longer to think; Cognitive problems; Fogginess; Feeling slow</td>
<td>49%</td>
<td>15%</td>
<td>4(801)</td>
<td>5.55 [3.94, 7.82]</td>
<td>0%</td>
<td>&lt;0.00001</td>
</tr>
<tr>
<td><strong>Sleep Disturbance</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sleep disturbance*; Drowsiness; Sleeping more; Sleeping less; Trouble falling asleep; Trouble sleeping through</td>
<td>34%</td>
<td>10%</td>
<td>1(696)</td>
<td>4.74 [3.12, 7.19]</td>
<td>NA</td>
<td>&lt;0.00001</td>
</tr>
<tr>
<td><strong>Cervical Strain</strong></td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>--</td>
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</tr>
</tbody>
</table>
Concussion as a Disorientation Disorder

Disorientation Deficits: A spatial-temporal disorientation of self interacting with the world
- Ocular-motor
- Vestibular

Trigger Disorders: Sequelae of disorientation and/or in isolation
- Headache/Migraine
- Anxiety/Mood
- Cognitive
# Targeted Treatments

<table>
<thead>
<tr>
<th>Targeted Treatments</th>
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<tbody>
<tr>
<td><strong>Headache/Migraine</strong></td>
<td><strong>Anxiety/Mood</strong></td>
<td><strong>Vestibular</strong></td>
<td><strong>Cognitive</strong></td>
</tr>
<tr>
<td>Medication</td>
<td>CBT</td>
<td>Vestibular rehabilitation</td>
<td>Medication</td>
</tr>
<tr>
<td>Exercise</td>
<td>Meditation</td>
<td>Exercise</td>
<td>Exercise</td>
</tr>
<tr>
<td></td>
<td>Psychotherapy</td>
<td>Sleepy hygiene</td>
<td>Sleepy hygiene</td>
</tr>
</tbody>
</table>
Keys to Recovery

- Cardio-type Exercise
- Sleep (REM)
- Patient Education
  - Supporting expectations of recovery and symptom control
- Vestibular-ocular motor Training
Key Takeaways

- Concussion subtypes are prevalent with varying degrees of presentation in heterogeneous populations
- Headache/Migraine and Anxiety/Mood subtype presentations are the most common
- Subtype presentations are not mutually exclusive
- 1 out of 4 patients exhibit aspects of symptomatology inclusive of all domains
Current Work

- Concussion subtype symptom scale pilot testing
- Subtype-specific recovery trajectory characterization
- Prospective dataset applications for validation with imaging and biomarkers
Thank you

• Questions?

Angela Lumba-Brown, MD
Assistant Professor of Emergency Medicine
Assistant Professor of Pediatrics
Stanford University School of Medicine

Co-Director Stanford Concussion and Brain Performance Center
alumba@stanford.edu
