SPORT-RELATED CONCUSSION –
THE EVOLVING ROADMAP

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WHAT IS A CONCUSSION?

• 42+ consensus-based definitions of a concussion

• Evidence-based definition- Concussion is:
  • Change in brain function
  • Following a force to the head or body
  • May be accompanied by temporary loss of consciousness, but is
  • Identified in wake individuals, with
  • Measures of neurologic and cognitive dysfunction
CHALLENGES

• Clinical diagnosis
• Physical and cognitive exams often normal
• Routine Imaging (CT/MRI) commonly normal
• Clinical effects often subtle and difficult to detect using current SRC tools
• Can be challenging to assess athlete with non-specific symptoms possibly related to other conditions
CHALLENGES

• May manifest with immediate or delayed-onset symptoms

• Symptoms can vary between individuals and in same individual with repeat concussion
  • If you’ve seen one concussion, you’ve seen one concussion

• Modifying factors and comorbidities should be considered in diagnosis, assessment and managing return to play/return to learn
  • ADHD, migraine/HA disorders, learning disability, mood disorders
CHALLENGES

• ‘signal-detection’ of clinical markers may quickly diminish in early recovery
• Under-reporting of symptoms
• …And inflation of level of recovery
NCAA-DOD CARE CONSORTIUM

• Prospective longitudinal multicenter, multisport investigation
• Better understand natural history of concussion in men and women
• Multidimensional assessment of:
  • standardized clinical measures of post-concussive symptomatology
  • Performance-based testing
  • Psychological health
IDENTIFY MULTIDISCIPLINARY TEAM AND DEFINE ROLES –

- ATC staff
- Team physician staff
- Emergency response
- Academic support staff
- Dietician
- Physical Therapist
- Psychology
- Neuropsychology
- Psychiatry
- Neuropsychiatry
- Neurology
- Neurosurgery
SO YOU DIAGNOSE A CONCUSSION...
NEUROMETABOLIC CASCADE FOLLOWING TRAUMATIC BRAIN INJURY

GIZA, HOVDA, NEUROSURGERY: OCTOBER 2014 - VOLUME 75 - ISSUE - P S24–S33

- Glutamate
- Glucose
- Calcium
- Cerebral Blood Flow

Graph showing changes in various metabolites and blood flow post-traumatic brain injury over time.
CONSIDERATIONS

• Concussions are characterized by diverse symptoms and impairments in function that may result in different recovery trajectories

• location(s) of change in brain function

• degree to which function is impaired

• other confounding variables
RETURN TO PLAY

• ‘vulnerable window’ for repeat injury
• Each concussion is unique
• Individualized treatment plan
• Decrease neurometabolic demands to shift resources for recovery
• Majority recover in a week or two
DETERMINING RETURN TO PLAY

• Symptom assessment
• Neurologic exam
• Balance testing
• Cognitive evaluation
PURPORTED RISKS OF PREMATURE RTP

- Second impact syndrome
- Repeat concussion – vulnerable window
- Chronic headaches
- Depression
- Long-term cognitive deficits
- Post-traumatic encephalopathy
2nd Impact Syndrome

- First described in 1973 by Schneider
- Diffuse cerebral swelling and increased ICP
- Associated with sustaining 2 concussive blows in close succession
- Rapid onset with high morbidity and mortality
- Controversial entity (McCrory 1998, 2001)
- Most likely malignant brain edema after TBI
THE VULNERABLE WINDOW
(LONGHI ET AL 2005)

• Mice in control (sham), single or repetitive CHI groups
• 2\textsuperscript{nd} CHI within 3-5 days of initial event showed significant cognitive impairment vs control, single CHI
• Greater axonal injury with 2\textsuperscript{nd} CHI within 3 days
• 2\textsuperscript{nd} CHI in 7 days → no difference in cognitive function vs single CHI
• Decrease in CMRglc associated w/vulnerable window in mice
• Single impact CMRglc recovers in 3d
• If 2nd impact occurs when CMRglc is depressed, recovery is prolonged
• If 2nd impact after CMRglc returns to baseline, recovery in 3d
RTP- SYMPTOM EVALUATION

- Document findings in a standardized form
- Allows for monitoring of findings on serial exams

<table>
<thead>
<tr>
<th>none</th>
<th>moderate</th>
<th>severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>0 1 2 3 4 5 6</td>
<td></td>
</tr>
<tr>
<td>“Pressure in head”</td>
<td>0 1 2 3 4 5 6</td>
<td></td>
</tr>
<tr>
<td>Neck Pain</td>
<td>0 1 2 3 4 5 6</td>
<td></td>
</tr>
<tr>
<td>Nausea or vomiting</td>
<td>0 1 2 3 4 5 6</td>
<td></td>
</tr>
<tr>
<td>Dizziness</td>
<td>0 1 2 3 4 5 6</td>
<td></td>
</tr>
<tr>
<td>Blurred vision</td>
<td>0 1 2 3 4 5 6</td>
<td></td>
</tr>
<tr>
<td>Balance problems</td>
<td>0 1 2 3 4 5 6</td>
<td></td>
</tr>
<tr>
<td>Sensitivity to light</td>
<td>0 1 2 3 4 5 6</td>
<td></td>
</tr>
<tr>
<td>Sensitivity to noise</td>
<td>0 1 2 3 4 5 6</td>
<td></td>
</tr>
<tr>
<td>Feeling slowed down</td>
<td>0 1 2 3 4 5 6</td>
<td></td>
</tr>
<tr>
<td>Feeling like &quot;in a fog&quot;</td>
<td>0 1 2 3 4 5 6</td>
<td></td>
</tr>
<tr>
<td>“Don’t feel right”</td>
<td>0 1 2 3 4 5 6</td>
<td></td>
</tr>
<tr>
<td>Difficulty concentrating</td>
<td>0 1 2 3 4 5 6</td>
<td></td>
</tr>
<tr>
<td>Difficulty remembering</td>
<td>0 1 2 3 4 5 6</td>
<td></td>
</tr>
<tr>
<td>Fatigue or low energy</td>
<td>0 1 2 3 4 5 6</td>
<td></td>
</tr>
<tr>
<td>Confusion</td>
<td>0 1 2 3 4 5 6</td>
<td></td>
</tr>
<tr>
<td>Drowsiness</td>
<td>0 1 2 3 4 5 6</td>
<td></td>
</tr>
</tbody>
</table>
| Trouble falling asleep | 0 1 2 3 4 5 6 | (if applicable)
| More emotional | 0 1 2 3 4 5 6 | |
| Irritability | 0 1 2 3 4 5 6 | |
| Sadness | 0 1 2 3 4 5 6 | |
| Nervous or Anxious | 0 1 2 3 4 5 6 | |
• Study in HS athletes with SRC following time to resolution

• Resolution <1wk, 70-75%

• Resolution<1mo, 90%
SYMPTOM CHECKLISTS

• Sensitivity 64-89%
• Specificity 91-100%
• No data in those younger than high school

• Typically resolve in 5-7 days (McCrea et al JAMA 2003)

• Deficits may be present after clinical symptoms have resolved (Maddocks DL 1996 Brain Inj; Broglio S 2007 J Ath Tr 42:504-508)
NP TESTING IN CONCUSSION

• Available computerized test packages:
  – Automated Neuropsychological Assessment Metrics (ANAM) – military
  – CNS Vital Signs
  – Axon Sports/CogSport
  – Headminder CRI
  – ImPACT (immediate post-concussion assessment and cognitive testing)

• Much less time required than paper: ≤20 min
• Baseline testing recommended ??
• Multiple forms to minimize practice effect
Test-Retest Reliability

- Reliability is not consistent between studies.
- Some specific indices may be more reliable than others.
- RCI - statistical concept used to correct for measured variability.
- Repeat baseline needed, but intervals not well established.

“Clinicians using the instruments evaluated here should adopt a cautious and conservative approach, with greater focus on those indexes with higher reliability.” Broglio 2007
OTHER ISSUES WITH NP TESTING

- “Gaming” the baseline
- Reaction time affected by mouse or other external factors (testing environment)
- pain, sleep, activity level
- Response errors

NONCREDIBLE EFFORT DURING PEDIATRIC NEUROPSYCHOLOGICAL EXAM: A CASE SERIES AND LITERATURE REVIEW

Michael W. Kirkwood, John W. Kirk, Robert Z. Blaha, and Pamela Wilson

Department of Physical Medicine & Rehabilitation, The Children’s Hospital, Aurora, Colorado and University of Colorado Denver School of Medicine, U.S.A.

Neuropsychological test interpretation rests upon the assumption that the examinee has exerted full effort. If an individual provides inadequate effort during exam, the resulting data will be invalid and represent an underestimate of the person’s true abilities. Although
CORRELATION OF NP W/ SX

• Many factors to consider in NP testing
• Not uncommon to see deficits in cognitive fxn by NP testing persist after symptoms have abated
• Opposite also true

Collins AJSM ’03, Collins CJSM ’03, Echemendia ’01, Lovell ’03, McCrory ’05, Broglio ’07, VanKampen ’06, Echemendia NAN 10/21/08
“Poor Signal Detection”
- Not all concussed athletes demonstrate cognitive dysfunction on available brief NP testing packages

- CNT testing most valuable as one component in assessing return to play

- If CNT testing does not detect deficits during acute period, its value in RTP decision making in that case is limited

- “CNTs have similar or superior psychometric properties compared to other practical tools used to detect concussion, such as balance testing”
COMPREHENSIVE NEUROPSYCHOLOGICAL ASSESSMENT

• Brief cognitive screening as sensitive to sport-related concussion as lengthier testing in the acute period

• Because most people recover quickly, comprehensive neuropsychological evaluation typically not indicated

• Can be valuable in subacute (5-30d) setting with persistent problems
  • relatively abbreviated neuropsychological evaluation could be appropriate
  • can help to identify reasons for problems
  • assist in creation of an appropriate clinical management plan
  • reduce risk of prolonged patient distress or secondary psychosocial problems
COMPREHENSIVE NEUROPSYCHOLOGICAL ASSESSMENT

• In the chronic setting, for patients who have apparently not returned to their baseline level of functioning, a neuropsychological evaluation is likely worthwhile
  • assist in identifying factors that may be producing problems
  • ensure accurate diagnostic decisions have been made
  • help develop an appropriate clinical management plan

• Some evidence of substantially reduced postconcussive symptomatology after neurospych consultation (Kirkwood, et al J Peds 2015)
Components of Concussion Management

- Symptoms
- Physical Exam
- Cognitive Eval
## RETURN TO ATHLETICS

<table>
<thead>
<tr>
<th>Rehabilitation stage</th>
<th>Functional exercise at each stage of rehabilitation</th>
<th>Objective of each stage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 1:</td>
<td>Symptom limited physical and cognitive rest.</td>
<td>Recovery</td>
</tr>
<tr>
<td>No activity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage 2:</td>
<td>Walking, swimming or stationary cycling keeping exercise intensity. &lt;70% maximum permitted heart rate. <strong>No resistance training.</strong></td>
<td>Increase HR</td>
</tr>
<tr>
<td>Light aerobic exercise</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage 3:</td>
<td>Skating drills in ice hockey, running drills in soccer. <strong>No head impact activities.</strong></td>
<td>Add movement</td>
</tr>
<tr>
<td>Sport-specific exercise</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage 4:</td>
<td>Progression to more complex training drills (eg: passing drills in football and ice hockey). May start progressive resistance training.</td>
<td>Exercise, coordination and cognitive load</td>
</tr>
<tr>
<td>Non-contact training drills</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage 5:</td>
<td><strong>Following medical clearance</strong>, participate in normal training activities.</td>
<td>Restore confidence and assess functional skills by coaching staff</td>
</tr>
<tr>
<td>Full-contact practice</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage 6:</td>
<td>Normal game play.</td>
<td></td>
</tr>
<tr>
<td>Return to play</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
TABLE 1. RISK FACTORS THAT MAY PROLONG OR COMPLICATE RECOVERY FROM CONCUSSION

<table>
<thead>
<tr>
<th>FACTORS</th>
<th>MODIFIER</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concussion History</td>
<td>Total number, proximity, severity (duration)</td>
</tr>
<tr>
<td>Symptoms</td>
<td>Total number, severity (intensity and especially duration)</td>
</tr>
<tr>
<td>Signs</td>
<td>Prolonged LOC (&gt;1 min)</td>
</tr>
<tr>
<td>Susceptibility</td>
<td>Concussions occurring with lower impact magnitude and/or requiring longer recovery.</td>
</tr>
<tr>
<td>Age</td>
<td>Youth and adolescent athletes may recover more slowly.</td>
</tr>
<tr>
<td>Pre-existing conditions</td>
<td>Migraine, depression, anxiety/panic attacks, attention deficit hyperactivity disorder (ADHD), learning disabilities (LD)</td>
</tr>
</tbody>
</table>
KEY CONSIDERATIONS IN RTP

• Should be off any medications started to treat concussion symptoms
  • Excludes previously taken meds such as ADHD meds, antidepressants
• Communication essential between healthcare team, athlete, parents, academic support, coaches
RTP SUMMARY

• Rest
• Exertional challenge
• Sport specific training
• Non-contact training
• Full contact practice
• Competition
**RTL- THE COLLEGE SETTING**

- Consideration should be given to avoiding the classroom for at least the same day as the sport-related concussion.

- Period of time needed to avoid class or homework should be individualized.

- Gradual return to academics should be based on the absence of concussion symptoms following cognitive exposure.

- Consensus to date includes:
  - If the student-athlete cannot tolerate light cognitive activity, he or she should remain at home or in the residence hall.
  - Once the student-athlete can tolerate cognitive activity without return of symptoms, he/she should return to the classroom, often in graduated increments.
RETURN TO LEARN RESOURCES

• On campus learning specialists
• Helpful to have ‘point person’
• should be managed in a stepwise program that fits the needs of the individual
• multi-disciplinary team: physicians, athletic trainers, coaches, psychologists/counselors, neuropsychologists, administrators as well as academic (e.g. professors, deans, academic advisors) and office of disability services representatives
RTP AND RTL

• If the athlete is well enough to play sports, they are well enough to attend school full-time and to take tests and do homework.
FRONTIERS...

- Blood biomarkers
- Accelerometers
- Cumulative head impact exposure
- Imaging biomarkers
- Rules of engagement in sports - safe play
**BLOOD BIOMARKERS**

- CARE Consortium (NCAA-DOD)

<table>
<thead>
<tr>
<th>Biomarker Assays</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Acute Biomarkers:</strong></td>
<td></td>
</tr>
<tr>
<td>UCH-L1 (ubiquitin C-terminal hydrolase L1; neuronal protein)</td>
<td></td>
</tr>
<tr>
<td>GFAP (glial fibrillary acid protein; astrocytic protein)</td>
<td></td>
</tr>
<tr>
<td>SBDP150 (calpain cleaved fragment of alpha II-spectrin breakdown product 150; a neural cell cytoskeleton structural protein)</td>
<td></td>
</tr>
<tr>
<td>S100B (S100 calcium binding protein B; astrocytic protein)</td>
<td></td>
</tr>
<tr>
<td>Micro RNA</td>
<td></td>
</tr>
<tr>
<td><strong>Chronic Biomarkers:</strong></td>
<td></td>
</tr>
<tr>
<td>MAP-2 (microtubule associated protein-2; marker of axonal damage)</td>
<td></td>
</tr>
<tr>
<td>CNPase (2',3'-Cyclic-nucleotide 3'-phosphodiesterase; marker of oligodendrocytes)</td>
<td></td>
</tr>
<tr>
<td>Micro RNA</td>
<td></td>
</tr>
</tbody>
</table>
BLOOD BIOMARKERS

- UCH-L1 peaks ~6-8hrs and may have role in acute setting
- GFAP may be a promising diagnostic tool for children with mTBI (Rhine et al, Brain Inj, Jul 16)
- S100B shows promise as marker for astrocytic damage
- All very preliminary but intriguing data
Brain Activation

- Exercise can upregulate BDNF and enhance recovery
- If begun too soon, recovery can be more prolonged
ACCELEROMETERS IN FB

• #Head impacts= game>full pad>shells>helmet only

• In practice-
  • equipment worn= number/cumulative burden of head impacts/event

• Can be utilized to assess group differences among types of football practices and competition

• Currently, accelerometers are unable to function as concussion detectors
  • No clear relationship between accelerometer data and clinical outcomes
EEG

• Background-
  • P300 ERP elicited in the process of decision-making
  • P300 amplitude and latency have been shown to be diminished following concussion

• Collaboration with WAVi
  • EEG at baseline, within 48hr after concussion, and after symptom-free and postseason
P300 CONCUSSION DATA
# Reference Groups

<table>
<thead>
<tr>
<th>Reference Groups</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Players Baselined</td>
<td>348</td>
</tr>
<tr>
<td><em>Men’s Football</em></td>
<td>300</td>
</tr>
<tr>
<td><em>Women’s Soccer</em></td>
<td>28</td>
</tr>
<tr>
<td><em>Men’s Hockey</em></td>
<td>20</td>
</tr>
<tr>
<td>Players Retested</td>
<td>56</td>
</tr>
<tr>
<td>Total Tests</td>
<td>470</td>
</tr>
</tbody>
</table>

# Concussion Group

<table>
<thead>
<tr>
<th>Concussion Group</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td># Events</td>
<td>49</td>
</tr>
<tr>
<td># Qualified Events</td>
<td>39</td>
</tr>
<tr>
<td># Players</td>
<td>30</td>
</tr>
<tr>
<td># Baseline Tests</td>
<td>28</td>
</tr>
<tr>
<td># Concussion Tests (1-2 days)</td>
<td>28</td>
</tr>
<tr>
<td># RTP Tests (7-12 days)</td>
<td>25</td>
</tr>
<tr>
<td># Post Season Tests (60-120d)</td>
<td>19</td>
</tr>
<tr>
<td># Next Season Base (160-340d)</td>
<td>10</td>
</tr>
</tbody>
</table>
**BETWEEN GROUP STATISTICS**

**Difference From Base:**
- Concussion: P<0.001
- RTP: P<0.001

**Note:** P300T No Difference from Base

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### P300V

- Baseline: 15.8
- Cn Group Base: 15.7
- Post Cn: 15.8
- RTP: 16.0
- Post Season: 16.0
- Next Baseline: 15.8

### Reaction Time

- Baseline: 16.0
- Cn Group Base: 16.0
- Post Cn: 16.0
- RTP: 16.0
- Post Season: 16.0
- Next Baseline: 16.0

**Difference From Base:**
- Concussion: P<0.001
- RTP: P>0.001

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DRAFT
INDIVIDUAL P300 TEST - RETEST VARIATION
**INDIVIDUAL P300 TEST-RETEST VARIATION**

### P300 and Recovery

<table>
<thead>
<tr>
<th>Indicator</th>
<th># Players</th>
<th># Players</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ref</td>
<td>RTP</td>
<td></td>
</tr>
<tr>
<td>( \Delta P300V &gt; 46% )</td>
<td>1/28</td>
<td>8/27</td>
</tr>
<tr>
<td># Expected by Chance</td>
<td>1/28</td>
<td>1/27</td>
</tr>
<tr>
<td>P300 Recovery (( \Delta RT \text{ norm} &amp; \Delta P300V &gt; 46% ))</td>
<td>-</td>
<td>6/27</td>
</tr>
<tr>
<td>RT Recovery (( \Delta RT &gt; 22% &amp; \Delta P300V \text{ norm} ))</td>
<td>-</td>
<td>0/27</td>
</tr>
</tbody>
</table>
IMAGING BIOMARKERS

• newer MRI methods have demonstrated the ability to detect and localize several pathologic and pathophysiologic consequences of concussion
  • susceptibility weighted imaging (SWI) to detect micro-hemorrhage
  • MR spectroscopy (MRS) to detect metabolic alterations
  • diffusion tensor imaging (DTI) to detect edema and axonal injury
  • perfusion weighted imaging (PWI) and arterial spin labeling (ASL) to measure cerebral blood flow in brain tissue
  • functional MRI (fMRI) to measure local changes in blood oxygen level in response to neuronal activity
Future Components of RTP Assessment

- Symptoms
- Exam
- Cognitive Eval
- Functional and Microstructural Neuroimaging?
- Biomarkers?
SUMMARY OF KEY POINTS

• Individualize management
• Understand limitations of components of management, including NP testing
• Consider subthreshold cognitive and exertional activity in the appropriate setting
• Return to play should not precede return to learn
• Establish overall management plan with staff in advance
• Evolving roadmap with new frontiers and testing on horizon
THANK YOU!