MILD TRAUMATIC BRAIN INJURY AND SPORTS-RELATED CONCUSSION

Pennsylvania Childhood Injury Prevention Conference

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CONCUSSION DEFINITION

Consensus Statement from the 3rd International Conference on Concussions in Sport (Zurich 2008):

“Concussion is defined as a complex pathophysiological process affecting the brain, induced by biomechanical forces. Several common features that incorporate clinical, pathological, and biomechanical injury constructs that may be used in defining the nature of concussive head injury include the following 5 major features:

1. Concussion may be caused by a direct blow to the head, face, neck, or elsewhere on the body with an impulsive force transmitted to head
2. Typically results in a rapid onset of short-lived impairment of neurologic function that resolves spontaneously – stated differently, it is a temporary disruption of normal brain function
3. Concussion may result in neuropathological changes, but the acute clinical symptoms largely reflect a functional disturbance rather than structural injury
4. Concussion results in a graded set of clinical syndromes that may or may not involve LOC (90% occur WITHOUT LOC in sports) Resolution of clinical and cognitive symptoms typically follow a sequential course
5. Concussion is typically associated with grossly normal structural neuroimaging studies
QUICK TAKE HOME POINTS

- A concussion is a kind of brain injury and all brain injuries should be taken seriously
- It is largely a functional disturbance rather than a structural injury that we can see on CT scans or MRI
- Most athletic concussions do NOT involve loss of consciousness (LOC)
  - >90% do NOT involve LOC
- No athlete with post concussive signs/symptoms should be allowed to return to competition while symptomatic
- Grading scales are currently being reconsidered as the currently have little prognostic or predictive reliability

HOW BIG OF A PROBLEM IS IT?

- Difficult to know for sure. Some people don’t realize they had a concussion and many do not see a doctor after one
- Estimated 3.8 million sports-related concussions a year
- Only 1.5 million seek medical attention
MILD TRAUMATIC BRAIN INJURY AND CONCUSSIONS

- Brain injuries are classified as being SEVERE, MODERATE, and MILD depending on how a patient is doing when evaluated by a medical staff.
- A concussion is a form of Mild Traumatic Brain Injury (mTBI)
  - Although there are mTBI’s that cannot be classified as a concussion.

PATHOBIOLOGY OVERVIEW

- Biomechanical and Ultrastructural Injury (mechanoporation)
- Ionic Dysequilibrium
- Excitotoxicity: Excitatory Amino Acids (EAA) and NMDA receptors
- Na⁺/K⁺ pump Derangement
- Hypermetabolism
- Glycolysis
- Vascular Derangement
BRIEF SUMMARY OF PATHOPHYSIOLOGY

The pathobiology of concussion involves a mechanical ultrastructural injury with concommitant (and often synergistic) biochemical, cellular, and metabolic derangement

MECHANISM: ULTRASTRUCTURAL LEVEL

- Neurofilaments and microtubules, the framework for axonal transport, are disrupted (as are the molecular motors kinesin/dynein)
- This affects the anterograde and retrograde movement of membrane materials to/from the cell body
- Results in both mechanical damage and a progressive biochemical damage at the ultrastructural level via proteolysis
Rotational and angular forces associated with rapid acceleration/deceleration head motion are thought to be primarily responsible for concussions, rather than the forces of direct linear impact.

The rotational and angular forces impart tension force vectors on the neuronal membrane causing a transient perturbation in the permeability of the membrane.

Axonal stretching leads to mechanoporation and opening of voltage dependent K⁺ channels and increase of extracellular K⁺.

Glia cannot absorb excess K⁺

Extracellular K⁺ leads to depolarization and release of EAA (with widespread glutamate release)

Glutamate binds NMDA receptors (and AMPA, kainate) to elicit an increase in intracellular calcium (Ca²⁺) and greater K⁺ efflux

Ca²⁺ overload will cause mitochondrial injury

Excitotoxicity is followed by a wave of relative neuronal suppression (CORTICAL SPEADING DEPRESSION)
METABOLIC DYSFUNCTION AND ENERGY CRISIS

- There is often impaired mitochondria and cerebral oxidative metabolism after TBI
- Oxidative metabolism runs near is maximum ($V_{\text{max}}$), yet the metabolic demand after MTBI often challenges the brains ability to match energy requirments through increased glycolysis

METABOLIC DYSFUNCTION AND ENERGY CRISIS (cont)

- Impaired mitochondrial function
- Decreased ATP--- increased lactate
  - Lactate production increases in the face of decreased lactate metabolism
  - Elevated lactate → acidosis → neuronal dysfunction
  - Acidosis also alters BBB, therefore increases edema
  - Lactate may also increase susceptibility
VASCULAR RESPONSE

- Global decrease in cerebral blood flow
- Animal models: 50% reduction
- Hypermetabolism and hypoperfusion
- Cellular energy crisis
- After acute hypoperfusion → followed by hyperemia (peaking at 24 hours, lasting up to 14 days)

VASCULAR RESPONSE (cont)

- Blood flow changes in normal appearing white and grey matter
- Dissociated vasoparalysis is transient, contributes to susceptibility
- After repeated minor trauma, chronic hypoperfusion can occur
- SPECT of post-concussive patients with symptoms, 44% had hypoperfusion in structurally normal appearing brain
CORTICAL SPREADING DEPRESSION

- A depolarization wave in the gray matter that propagates across the brain at 2-5mm/min
- Associated with failures in ionic homeostasis, efflux of EAA’s, increased energy metabolism, and changes in cerebral blood flow

CORTICAL SPREADING DEPRESSION

- Early LOC, amnesia, and cognitive dysfunction may be manifestations of a post traumatic spreading depression like state
- Diffuse areas of brain are affected simultaneously in traumatic cortical spreading depression (CSD)
- Restoration of ionic homeostasis requires increased glucose (to fuel the Na⁺/K⁺ pump)
HOW CAN I RECOGNIZE A POSSIBLE CONCUSSION?

Watch for the following two things:

1) A forceful bump, blow, or jolt to the head or body that results in rapid movement of the head

AND

2) Any change in the athlete’s behavior, thinking, or physical functioning
### SYMPTOMS: 4 main categories

<table>
<thead>
<tr>
<th>COGNITIVE</th>
<th>PHYSICAL</th>
<th>EMOTIONAL/MOOD</th>
<th>SLEEP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Difficulty Thinking Clearly</td>
<td>Headache, Numbness/Tingling</td>
<td>Irritability</td>
<td>Sleeping More Than Usual</td>
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<tr>
<td></td>
<td>Fuzzy or Blurry Vision</td>
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</tr>
<tr>
<td>Feeling Slowed Down</td>
<td>Nausea or Vomiting (early on)</td>
<td>Sadness</td>
<td>Sleeping Less Than Usual</td>
</tr>
<tr>
<td></td>
<td>Sensitivity to Noise or Light</td>
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<tr>
<td>Difficulty Concentrating</td>
<td>Dizziness</td>
<td>More Emotional</td>
<td>Trouble Falling Asleep</td>
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<td></td>
<td>Balance Problems</td>
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<tr>
<td>Difficulty Remembering New Things</td>
<td>Feeling Tired, Having No Energy</td>
<td>Nervousness or Anxiety</td>
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### SYMPTOMS (cont)

- The signs and symptoms of a concussion can be subtle and/or vague. Early on, problems may be missed by the person with the concussion, family members, or doctors. People may look fine even though they are acting or feeling differently.
- Some symptoms may appear right away, while others can be delayed for days or months after the injury.
- Sometimes they are hidden by rest. They are not noticed until the person starts resuming their everyday life and more demands are placed upon them.
- Occasionally, symptoms are missed altogether. People do not recognize they are having problems. Or they may not understand why they are having problems, which can make them nervous and upset.
There are more than 25 different concussion grading scales but all have been difficult to standardize and none has proven to be effective at predicting severity, prognosis, or clinical course.

The current recommendation from the 2008 Zurich statement is to abandon the previous grading scales for a symptom-based approach for determination of return to play.

“EITHER YOU HAD ONE OR YOU DIDN’T”
CLASSIFICATION (CONT)

- The focus now is on documenting the number and severity of symptoms while carefully managing them as they resolve.
- Severity is better judged after observing the time and effort required for the resolution of symptoms (including the establishment of a normal neurological and cognitive examination).

CONCUSSION SEVERITY

- Loss of consciousness (LOC) does NOT relate to the severity of a concussion.
- Severity is more properly judged by the number, duration, and intensity of concussion symptoms.
- Severity of concussion should not be determined by loss of consciousness (LOC) alone.
**RISK FACTORS FOR LONGTERM SEQUELAE AFTER CONCUSSION**

- Multiple concussions
- A repeat concussion that occurs before the brain recovers from the first. In rare cases, repeat concussions can result in Second Impact Syndrome, resulting in malignant cerebral edema and even death
- There is still no “magic number” that predicts long-term difficulties. Each person probably has a different threshold
- For most: 3 major concussions can be considered a trigger

**CONSEQUENCES OF MULTIPLE CONCUSSIONS**

- Linked to later difficulties at multiple levels
- **HIGH-SCHOOL**: fMRI data suggests that adolescents have prolonged recovery of memory functioning
- **NCAA**: (JAMA) 3 concussions carry 3x the risk of future events and each concussion carries a longer recovery period (JAMA)
- **NFL**: If 3+ major concussion, then:
  - 5x the rate of mild cognitive impairment (MCI) [Guskiewicz, Neurosurgery 2005]
  - …AND MCI carries ~95% transition to Alzheimer’s within a decade
  - 3x the rate of being diagnosed and treated for depression (Guskiewicz Medicine and Science in Sports and Exercise 2007)
CHRONIC TRAUMATIC ENCEPHALOPATHY (CTE)

Characterized by:

1. Subconcussive blows
2. Prolonged latent period
3. Early behavioral personality changes with memory loss
4. Progressive dementia, Parkinsonism, gait and speech disorders
5. Mean survival of 18 years after diagnosis

…different than Dementia Pugilistica (CTE has more BG dysfunction and Parkinsonian expression of symptoms)

CTE Pathology

- Deposition of Hyperphosphorylated Tau
- These depositions aggregate into Neurofibrillary Tangles (NFT’s)
- Neutrophil threads
- Cell dropout
**TAU and NFT’s**

- Tau is a microtubule-associated-protein (MAP) that is abundant within neurons in the CNS and they stabilize microtubules (a major structural component of the cytoskeleton)
- Neurofibrillary Tangles:
  - Most commonly associated as the primary marker for Alzheimer’s Disease…
  - However, their presence is also seen in several other diseases classified as TAUOPATHIES
  - The relationship among the pathologies among these Tauopathies is still being investigated

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**CTE MECHANISM**

- One theory: **Immunoexcitotoxicity** (Maroon)
- MTBI elicits a neuroinflammatory response in the brain ⇒ activating the microglia (the resident macrophages of the brain) ⇒ this in turn activates macrophages
IMMUNOEXCITOTOXICITY: PROPOSED CASCADE

- **INFLAMMATORY MODE:** acute microglial activation after MTBI will release pro-inflammatory cytokines, chemokines, and excitotoxins

- **REPAIRATIVE MODE:** After a microglial switch, there is the release of neurotrophins, anti-inflammatory cytokines, metallomatrix proteins, and caspases

- **RESTING STATE:** microglia regress to resting state

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IMMUNOEXCITOTOXICITY

- With repetitive concussion, the switch to the Repairative Mode may be altered and the microglia remain chronically active leading to the deposition of Tau
THE UNKNOWN RE: CTE

- The exact incidence
- Does age at time of concussion make a difference?
- Is severity of concussions a factor?
- Is there a genetic link (Apo E4)?
- Do hormonal changes make a difference?
- Do illegal substances make a difference?

Before management comes....

PREVENTION
**HELMETS**

- NCAA 1939
- NFL 1940
- Single bar 1951
- Double bar 1958
- Increase in Head Injury and Fatalities
- NOCSAE 1969
- Standards 1973

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**PREVENTION: Historical Perspective**

- 1975-1979: Face tackling/spearing illegal
  - Brain injury fatality 42 decreased to 37
  - Brain injury fatalities 32
- 1985-1989: Brain Injury Education
  - 24 brain injury fatalities
- 1994-1999: Comparable to late 80’s 5-7/year
  - *Most deaths occur at high school level*
SPINE INJURIES

- Spinal injuries are the 2nd most common cause of Spinal Cord Injuries (SCI) in 1st 3 decades of life
- Team sports: football, gymnastics, ice hockey are highest risk of catastrophic SCI
- Past 25 years 223 football players w/ cervical SCI with no or incomplete recovery
  - 183 HS, 29 college, 7 pro, 4 sandlot
- Rule changes and Equipment standards lead to 270% reduction in SCI (20/year in 1971-75 to 7.2/year past 10-years).
  - * Vast majority (82%) at high school level

MANAGEMENT

- Management should be individualized to each specific patient
- A health care provider will do a comprehensive neurological evaluation to determine the right treatment for an uncomplicated concussion
- Relying on symptoms alone may not always be adequate
### MANAGEMENT (cont)

- Neuropsychological testing is important to better understanding subtle problems
- Physical and cognitive rest seems to be important in recovery
- The effects of concussion in children and adults are different
- Return to activity should be a gradual process

### RETURN TO PLAY REQUIREMENTS

- Absence of symptoms at rest
- Normalization to neuropsychological baseline (e.g. having ones ImPACT score return to normal, not just demonstrating an improvement)
- Clearance by a knowledgeable medical professional
- Absence of symptoms with exertion
Although most people recover fully after a concussion, how quickly they improve depends on many factors. These factors include how severe their injury was, their age, how healthy they were before the concussion, and how they take care of themselves after the injury.
WHAT SHOULD I DO IF CONCUSSION OCCURS

4-step action plan:

1) Remove the athlete from play
2) Get the athlete properly evaluated by a health care professional experienced in evaluating concussions
3) Inform the athlete’s caretakers about the possible concussion and give them the fact sheet on concussion
4) Keep the athlete out of play the day of the injury and until a health care professional has cleared them to return to play

A symptomatic athlete should NOT return to play

WHEN SHOULD I SEEK MEDICAL ATTENTION

- Changes in behavior or unusual behavior
- Changes in speech (slurred, difficult to understand, does not make sense)
- Difficulty waking up or becoming more sleepy
- Double vision or blurred vision
- Fever
- Fluid and blood leaking from your nose or ears
- Headache that is getting worse, lasts a long time, or is not relieved by over-the-counter pain relievers
- Problems thinking straight
- Problems walking or talking
- Seizures (jerking your arms or legs without control)
- Vomiting more than three times
- Symptoms that do not go away after 2-3 weeks
WHAT CAN YOU DO TO FEEL BETTER AFTER CONCUSSION

- **Rest** is very important after a concussion because it helps the brain to heal. Do not “tough it out”
- Be patient because healing takes time. You can slowly and gradually return to your daily activities when cleared by your health care professional
- If your symptoms come back or you get new symptoms as you become more active, this is a sign that you are pushing yourself too hard. Stop these activities and take more time to rest and recover. As the days go by, you can expect to gradually feel better.

TREATMENT BASICS

- You may use acetaminophen (Tylenol) for a headache. **Do NOT** use aspirin, ibuprofen (Motrin or Advil), naproxen, or other similar drugs
- **Eat a light diet.** Light activity around the home is okay. You do not need to stay in bed. However, avoid exercise, lifting weights, or other heavy activity
- **Have an adult stay with you for the first 12 - 24 hours after you are home from an emergency room**
Going to sleep is okay. For at least the first 12 hours, someone should wake you up every 2 or 3 hours. They can ask a simple question, such as your name, and then look for any changes in the way you look or act.

Do not drink alcohol until you have completely recovered. Alcohol may slow down your recovery, increase your risk for another injury, and make it even harder to make decisions.