Sports Concussion: From Behavior to Biochemistry

Tennessee Psychological Association
November 5, 2011
Nashville, TN

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Overview

- Definition (CIS)
- Epidemiology
- TBI Biomechanics

- Signs and Symptoms
- Balance Testing
- Mental Status Examinations
- Neuropsychological Testing

A representative study regarding:

- Functional neuroimaging
- Neurophysiology
- Biochemistry
- TBI biomarkers and genetics
- Animal studies

- Clinical Management Overview
Epidemiology of Concussion

- 1.5-3.8 million reported cases of TBI per year (CDC)
- 20% (300,000-760,000) are sports-related (822 per day based on 1.5m; 2,082 based on 3.8m)
- 53,000 deaths; 70-90,000 permanently disabled
- Highest incidence: ages 15-24
- Cost estimated at > $60 billion annually ($25b for mTBI)
- CDC: “Epidemic”

“...a complex pathophysiological process affecting the brain, induced by traumatic 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:

1. Concussion may be caused either by a direct blow to the head, face, neck or elsewhere on the body with an “impulsive” force transmitted to the brain.
CIS: Definition of Concussion

2. Concussion typically results in the rapid onset of short-lived impairment of neurological function that resolves spontaneously.

3. Concussion may result in neuropathological changes, but the acute clinical symptoms largely reflect a functional disturbance rather than a structural injury.

4. Concussion results in a graded set of clinical syndromes that may or may not involve loss of consciousness. Resolution of the clinical and cognitive symptoms typically follow a sequential course.

5. Concussion is typically associated with grossly normal neuroimaging studies.
Concussion: Physical Signs

- Loss of or altered consciousness
- Poor coordination or balance; gait unsteadiness
- Convulsions/seizure
- Poor concentration; distractible
- Slow to follow directions or answer questions
- Nausea/vomiting

- Unusual or inappropriate emotions (crying, giddy)
- Vacant stare or glassy eyed
- Slurred speech
- Personality change
- Inappropriate playing behavior
- Decreased playing ability
Type of biomechanical impact and concussive symptoms: Loss of consciousness (LOC)

- Linear impacts rarely cause LOC
- Rotational impacts typically cause LOC
Biomechanics: g force

- Measure of acceleration
- Sitting, standing, lying down = 1 g
- Human Sneeze = 3 g
- Roller Coaster = 5-7 g
- Woodpecker pecking = 10 g
- Auto crash tests at 30 mph = 40-50 g
G forces in sport-related concussion

First used in Indy automobile racing but studied mostly in football

Laboratory and clinical studies (football and soccer)

Accelerometers embedded in helmets with sideline telemetry systems

Average g force for concussive injury in NFL studies was 98g

Football studies have revealed concussion-causing impacts ranging from 60 to 160 g
Concussion: Typical Symptoms

- Headache
- Dizziness
- Nausea
- Unsteadiness/Loss of Balance
- Feeling “dinged”, stunned, or dazed
- “Bell rung”
- “Just don’t feel right”
- Seeing stars_FLASHING LIGHTS
- Ringing in the ears
- Double/blurry vision
- Sleepiness
- Feeling of slowness or “fogginess”
- Sensitive to light or noise
Balance Testing (Posturography)
Maddocks’ Questions

*Clinical Journal of Sport Medicine, 1995*

- Which ground (field) are we at?
- Which team are we playing today?
- Who is your opponent at present?
- Which quarter (period) is it?
- How far into the quarter (period) is it?
- Which side scored the last goal (points)?
- Which team did we play last week?
- Did we win last week?
Standardized Assessment of Concussion (SAC)

- McCrea, Kelly, & Randolph, 1997 (with BIA of America)
- Brief 5” scale based on AAN Practice Parameter
- Assesses neurologic function (strength, sensation, and coordination), exertional maneuvers, and cognition (orientation, immediate memory, concentration, and delayed recall)
- Equivalent forms A, B, and C
- Maximum = 30 points
- 1 point drop between baseline and post-concussion score has 94% sensitivity and 76% specificity for concussion
SCAT2: Sport Concussion Assessment Tool-2

- CIS Group: Prague, 2004; updated Zurich, 2009 SCAT-2

- Used rink side in NHL and will be used sideline in NFL in 2011

- Derived from the SAC, Colorado Head Injury Foundation’s Sideline Evaluation for Concussion, the AAN’s Management of Concussion in Sports Palm Card, UPMC, ThinkFirst, and Sports Medicine New Zealand’s Sideline Concussion Check, the McGill ACE, and the NHL Physician Evaluation Form

- Completed by the athlete and a sports medicine professional

- Assesses symptoms (PCS-R), Glasgow Coma Scale (GCS), cognition (SAC), balance (BESS), and neurological screening

- Available in April, 2009 editions of *Clinical Journal of Sport Medicine*, *British Journal of Sports Medicine*, and the *Physician and Sportsmedicine*
**Symptom Evaluation**

**How do you feel?**

You should score yourself on the following symptoms, based on how you feel now.

<table>
<thead>
<tr>
<th>Symptom</th>
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<td>Headache</td>
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<td>Neck pain</td>
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<td>Nausea or vomiting</td>
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<td>Dizziness</td>
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<td>Blurred vision</td>
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<td>Balance problems</td>
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<td>Sensitivity to light</td>
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<td>Sensitivity to sound</td>
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<td>Feeling slowed down</td>
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<td>Feeling like a &quot;fog&quot;</td>
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<td>&quot;Don’t feel right&quot;</td>
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<td>Difficulty concentrating</td>
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<td>Difficulty remembering</td>
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<td>Difficulty focusing</td>
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<td>Fatigue low energy</td>
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<td>Troubled falling asleep (if applicable)</td>
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<td>More emotional</td>
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<td>Irritability</td>
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<td>Badness</td>
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<td>Troubled making decisions (if applicable)</td>
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<td>Total number of symptoms (max score possible)</td>
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</table>

**Symptom severity score**

(Add all scores in Table, maximum possible: 22 x 6 = 132)

- Do the symptoms get worse with physical activity? [Y/N]
- Do the symptoms get worse with mental activity? [Y/N]

**Overall rating**

If you know the athlete will prior to the injury, how different is the athlete acting compared to his/her usual self? In order, from no different to very different.

<table>
<thead>
<tr>
<th>Rating</th>
<th>0</th>
<th>1</th>
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<tbody>
<tr>
<td>No different</td>
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<tr>
<td>Very different</td>
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<tr>
<td>Unrecognizable</td>
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</table>

**Physical signs score**

- Were there any symptoms or impairments? [Y/N]
- If yes, how long? (in minutes)
- Were there a balance problem/unsteadiness? [Y/N]
- Physical signs score (point for each negative response)

**Glasgow coma scale (GCS)**

- Best eye response [1-4]
- Eye opening to pain [1-4]
- Eye opening to speech [1-4]
- Eye opening spontaneously [1-4]
- Best verbal response [1-5]
- Incomprehensible sounds [2]
- Incoherent words [2]
- Confused [2]
- Oriented [5]

**Best motor response (MM)**

- No motor response [1]
- Extension to pain [1]
- Abnormal reflex to pain [1]
- Motor withdrawal to pain [1]
- Stupor/tetanus [5]
- Obeying commands [6]

**Glasgow coma score (E + V + MM)**

GCS should be recorded for all athletes in case of subsequent deterioration.

**Cognitive & Physical Evaluation**

1. **Symptom score** (from page 1)
   - 0-22: moderate number of symptoms
   - 0: asymptomatic

2. **Physical signs score**
   - 0-8: moderate number of symptoms
   - 0: asymptomatic

3. **Glasgow coma scale (GCS)**
   - 3-15: moderate number of symptoms
   - 3: asymptomatic

4. **Sideline Assessment – Maddock Score**
   - "I am going to ask you a few questions, please listen carefully and give your best effort." [Written in all caps]
   - "What are you wearing today?"
   - "What is the date today?"
   - "What is the day of the week?"
   - "What time is it?"
   - Maddock score [0-5]

5. **Cognitive assessment**
   - Standardized Assessment of Concussion (SAC) (Orientation is paid for each correct answer)
   - Orientation score [0-15]

**Immediate memory**

If the athlete has memory loss, they will be read a list of words and when they are done, the athlete's repetition back with as many words as you can remember is "any order".

**Try these 2 & 3:**

- "I am going to repeat the same list again. Repeat back as many words as you can remember in any order even if you did the list the same way.

**Completion of the task**

Complete all 4 tasks regardless of score on the 1st & 2nd task. Read the words at a rate of one word at a time. Each trial consists of a list of words. Three trials per session are across all 3 trials. Do not inform the athlete that stage 2 will be tested.

**List 1**

- Dull spider
- Cold cat
- Olive
- Cedar
- Straw
- Cowboy
- Broom
- Barn

**List 2**

- Dull spider
- Cold cat
- Olive
- Cedar
- Straw
- Cowboy
- Broom
- Barn

**List 3**

- Dull spider
- Cold cat
- Olive
- Cedar
- Straw
- Cowboy
- Broom
- Barn

**List 4**

- Dull spider
- Cold cat
- Olive
- Cedar
- Straw
- Cowboy
- Broom
- Barn

**Test 1 & 2 score**

- 1 point per word recalled.
- 0 points per word not recalled.
- 0 points for not recalling any words.

**Test 3 & 4 score**

- 2 points per word recalled.
- 0 points per word not recalled.
- 0 points for not recalling any words.

**Total score**

- 1 point for each correct response.

**Concentration**

- 0-15 points

**References**

Athlete Information

Any athlete suspected of having a concussion should be removed from play, and then seek medical evaluation.

**Signs to watch for**

- Problems could arise over the 24-48 hour period. You should not be left alone and must go to a hospital at once if you:
  - Have a headache that gets worse
  - Are very dizzy or can't be awakened (excepted for a short period of being drowsy)
  - Can't recognize people or places
  - Have repeated vomiting
  - Believe normally or seem confused, are very irritable
  - Have seizures (arms and legs jerk uncontrollably)
  - Have weak or numb arms or legs
  - Are unsteady on your feet, have slurred speech

**Return to play**

- Athletes should be returned to the same day of injury when returning to play.
- They should follow a stepwise symptom-limited program, with stages of progression:
  1. Walk until asymptomatic (physical and mental rest)
  2. Light aerobic exercise (e.g., stationary cycle)
  3. Sports-specific exercise
  4. Non-contact training drills (start light resistance training)
  5. Full contact training after medical clearance
  6. Return to competition (game play)

- There should be approximately 24 hours (or longer) for each stage and the athlete should return to stage 1 if symptoms recur. Resistance training should only be added in the later stages.

**Medical clearance should be given before return to play.**

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**Cognitive assessment**

**Standardized Assessment of Concussion (SAC)**

**Delayed recall**

- "Do you remember that list of words I read a few times earlier? Tell me as many words from the list as you can remember in any order.

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**Concussion injury advice (to be given to concussed athlete)**

This patient has received an injury to the head. A careful medical examination has been carried out and no sign of any serious complications has been found. It is expected that recovery will be rapid, but the patient will need monitoring for a further period by a responsible adult. Your treating physician will provide guidance as to this timeframe.

If you notice any change in behaviour, vomiting, dizziness, worsening headache, double vision or excessive drowsiness, please telephone the clinic or the nearest hospital emergency department immediately.

**Important points:**

- Rest and avoid strenuous activity for at least 24 hours
- No alcohol
- No sleeping tablets
- Use paracetamol or ibuprofen for headache. Do not use any other pharmaceuticals
- Do not drive until medically cleared
- Do not train or play sport until medically cleared

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**Clinic phone number**

**SCAT2 sport concussion assessment tool:**

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**Vanderbilt Sports Concussion Center**
Bottom Line Conclusions: Formal Sideline Tests

The SAC has the best psychometric data. It does not have a review of symptoms built in. It does assess balance. It produces a quantitative score, but works best when a baseline score is available for comparison. Alternate forms are available. It has a low ceiling.

The SCAT2 is the more comprehensive, assesses cognition, balance, and symptoms, is the most labor intensive, and has good individual normative data for the SAC, GCS, and BESS. However, the SCAT2 has little to no normative data for the instrument as a whole. Its sensitivity to concussion has not been demonstrated empirically.
Neuropsychological Testing

• “...one of the cornerstones of concussion evaluation...” (CIS, 2002, 2005, 2009)

• Paper and Pencil (NHL, NFL)
• Computer-based tests (ImPACT, CogSport, ANAM, HeadMinder)

• Cognitive domains assessed include Attention and Concentration, Verbal and Visual Memory (Immediate and Delayed Recall), Reaction Time, and Speed of Information Processing, the brain functions most vulnerable to the effects of concussion
The neuropsychological impact of sports-related concussion: A meta-analysis

*JINS*, 2005, 11, 345-357

Drs. Heather Belanger and Rodney Vanderploeg

- Based on 21 studies involving 790 concussed athletes and 2,014 controls

- 9 cognitive domains: orientation, global cognitive ability, attention, executive functioning, memory acquisition (learning), delayed memory, language, visuospatial ability, motor abilities

- Overall effect of concussion: $d^* = 0.49$, which is comparable to the effect size of $d = 0.54$ in non-sports related mTBI (about $\frac{1}{2}$ Standard Deviation or 7.5 IQ points)

- Acute effects (within 24 hrs.) were greatest for delayed memory ($d = 1.00$), learning ($d = 1.03$), and global cognitive functioning ($d = 1.42$)

- Acute effects generally dissipate by Day 7 post-concussion (and by Day 10 for delayed memory)

- $d =$ control group mean minus the concussed group mean divided by the pooled standard deviation
“Nobody in football should be called a genius. A genius is a guy like Norman Einstein.”

Joe Theismann, Commentator and former professional quarterback
In assessing 288 potential draft picks for the Tennessee Titans over the past 10 years, a 2 subtest short form of the Wechsler Adult Intelligence Scale-III yielded estimated IQ scores ranging from 78-119 (scores are truncated by range restrictions of the regression equation).

Scores on the Wonderlic have ranged from 6-47; statistical transformation based on data in the Wonderlic manual yields estimated IQ scores ranging from 72-130.

Athletes vary in terms of baseline cognitive abilities.
Bottom Line Conclusions: Neurocognitive Testing

Although there remains active debate as to the utility of neurocognitive testing in sports concussion, the evolving standard of care in high school, collegiate, and professional sports is to conduct baseline cognitive testing with some objective measure (paper and pencil or computerized), and to use the cognitive testing as a guide in concussion management. This is reflected in new NCAA policy, as well as in the NFL and NHL and in nearly all published practice parameters (e.g., NAN, NATA, CIS). AOSSM recommends “some evaluation of cognitive function” and the new AAN practice parameter does not address cognitive assessment.
Structural Neuroimaging for Sport Concussion

- Computerized Axial Tomography (CT)
- Magnetic Resonance Imaging (MRI)

- In sport-related concussion, structural neuroimaging results are normal >97% of the time: CIS Group did not recommend routine imaging.
Structural Injury in Sports Concussion

- Diffuse Axonal Injury (DAI) (Traumatic Axonal Injury)
- Subdural Hematoma
- Epidural hematoma
- Second Impact Syndrome
Second Impact Syndrome (SIS)

“SIS occurs when an athlete who has sustained an initial head injury, most often a concussion, sustains a second head injury before symptoms associated with the first have fully cleared.”

(Cantu & Voy, 1995)

The brain’s autoregulatory system is disrupted. Vascular engorgement in the cranium increases ICP, leading to brain herniation. Massive edema is the primary finding on autopsy.
PET Scans in Head Injury

Marvin Bergsneider, M.D., and David Hovda, Ph.D.
UCLA School of Medicine
A Validation of the Post Concussion Symptom Scale in the Assessment of Complex Concussion Using Cognitive Testing and Functional MRI


- Assessed 18 athletes with PCS and 10 controls via Concussion Sentinel, a Concussion Symptom Scale, and fMRI

- Athletes with a PCS score of > 21 (Moderate PCS severity) showed slower reaction times than controls on aspects of the cognitive test

- Athletes with PCS had a virtual absence of activation in prefrontal regions of interest on the working memory tasks (verbal and non-verbal)
Are other cortical areas recruited for compensatory functioning post-concussion?

Figure 2  Additional activation in the posterior brain region. Both mild and moderate post concussive symptom (PCS) groups showed additional activation peaks in the left temporal lobe (circled in red) during the verbal working memory task. These peaks were not present in the normal control group.
Postconcussive Symptoms Are Associated With Compensatory Cortical Recruitment During a Working Memory Task

FIGURE 1. Neural response for the 2-back vs 0-back contrast overlaid with significant associations between the neural response and symptom severity. Pictures represent different axial slices with Z coordinates representing vertical location based on the Talairach atlas. Positive levels of the blood oxygenation level-dependent response (BOLD) are shown in yellow/red and negative levels are shown in blue for the 2-back vs 0-back contrast. Voxel values are thresholded at a Z score of \( \pm 2 \), with color saturation at a Z score of \( \pm 7 \) or more. Regions where the BOLD response for the 2-back vs 0-back contrast increases with concussion severity are shown in black, and regions where the BOLD response decreases with concussion severity are shown in white. Regions of interest have been projected to the nearest slice from slabs 6 mm thick, for a maximum projection distance of 3 mm.

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**Bottom Line Conclusions: Neuroimaging**

- If indicated, CT scan remains the test of choice in the emergency department for ruling out a structural injury post-concussion.

- Concussion in Sport Group did not recommend routine imaging in the assessment of sports-related concussion.

- Structural injury occurs less than 3% of the time in sports-related concussion.

- Functional neuroimaging (PET and fMRI, as well as DTI) holds great potential for identifying the functional metabolic impairments seen after sports-related concussion.
Long Term and Cumulative Effects of Sports Concussion on Motor Cortex Inhibition


- 45 University of Montreal Football players
- No history of psychiatric illness, LD, substance abuse, or non-sports related TBI
- Group 1: 15 asymptomatic athletes with 2 or more (<6) concussions (at least 9 months post), with all concussions diagnosed by the Team Physician and graded according to AAN criteria
- Group 2: 15 athletes with one sports concussion
- Group 3: 15 athletes with no history of concussion
De Beaumont et al., 2007

- Administered neuropsychological tests (NFL paper and pencil battery), with no significant differences among the three groups on any test
- Administered Transcranial Magnetic Stimulation (TMS) with EMG recordings, assessing motor evoked potentials

RESULTS

- The duration of the Cortical Silent Period (CSP; the pause between the administration of the TMS and the resumption of the EMG) was significantly prolonged in athletes with a history of concussion(s)
- CSP duration was significantly correlated with severity of concussion (graded according to AAN criteria)
- Five athletes with a history of multiple concussions later sustained concussions and were retested
- The CSP abnormality was exacerbated in this group
“Findings from this study show that sports concussions result in long-term motor system dysfunctions that seem to be attributable to subclinical intracortical inhibitory system abnormalities. This study also shows that sustaining subsequent concussions exacerbates this deficit, thus providing support for the contention that the adverse effects of concussions on intracortical inhibitory systems are cumulative” (p. 7).
Bottom Line Conclusions: Electrophysiology

- There is accumulating evidence that electrophysiological changes (especially a decrement in visual and auditory P300 amplitude) persist well beyond symptom resolution and return to baseline cognitive functioning in concussed athletes. qEEG changes may also be evident in the acute recovery phases, but resolve.

- The electrophysiological changes may be a function of concussion severity and frequency.

- The duration of the P300 changes could be months or years.

- The clinical significance of these changes is unknown.
The “Chemical Cascade” of Concussion

David Hovda, Ph.D., UCLA

- Glutamate released up to 50% > normal
- Potassium exits cells up to 400% above normal
- Loss of consciousness occurs when K+ level exceeds 40-50 mmol/L
- Calcium enters cells up to 500% above normal
- Cerebral blood flow decreases by 50% within 2 minutes
- Hypermetabolism: “Energy Crisis”
- Hypometabolism: 6-10 days post (may be age dependent)
The Chemical Cascade of Concussion

- Na-K pump works overtime trying to restore neuronal membrane potential
- Na-K pump uses ATP, triggering a jump in glucose metabolism
- Hypermetabolism occurs in context of decreased cerebral blood flow (< or = 50%)
- Disparity between glucose supply and demand triggers energy crisis
- Cells are in a vulnerable state
Chemical Cascade

Leads to Lactic Acid accumulation, loss of Mg, and Ca+ accumulation

Can lead to cellular death and/or axon bulb formation

Alterations in systems modulating glutamate, norepinephrine, and acetylcholine

Recovery may be age-dependent (caution with younger athletes)
Animal models (and to a lesser extent, data from humans with severe TBI) support the hypothesis of biochemical changes in the brain post-concussion. These changes persist, on average, for 7-10 days post-trauma. Current evidence suggests that age, gender, genetic factors, activity level during the recovery period, and prior headache and concussion history are some of the major moderating variables.
Serum Biomarkers for Concussion

- **S-100B**: secreted from brain astrocytes (summed concentration of S-100B monomers in S-100A1B and S-100BB); typically clears from serum within 4-6 hours post trauma

- **Neuron-Specific Enolase (NSE)**: Marker of cell regeneration

- **Glial Fibrillary Acidic Protein (GFAP)**: Found in Glial cells (astrocytes), and helps to maintain mechanical strength and cell shape
S-100B and NSE


- Pre- and post-game blood samples
- Both S-100B and NSE levels were elevated
- S-100B levels were correlated with number of headers and the number of “other trauma” events
Clinical Policy: Neuroimaging and Decisionmaking in Adult Mild Traumatic Brain Injury in the Acute Setting
Approved by the ACEP Board of Directors, August 13, 2008

From the American College of Emergency Physicians (ACEP)/Centers for Disease Control and Prevention (CDC) Panel to Revise the 2002 Clinical Policy: Neuroimaging and Decisionmaking in Adult Mild Traumatic Brain Injury in the Acute Setting:

Level C recommendations. In mild TBI patients without significant extracranial injuries and a serum S-100B level less than 0.1 μg/L measured within 4 hours of injury, consideration can be given to not performing a CT.*

*This test has not yet received Food and Drug Administration approval for clinical use in the United States.
Genetic typing for concussion/head injury


CACNA1A calcium channel subunit gene (??-SIS) (Kors et al., *Annals of Neurology*, 2001)

Interleukin 1RN allele 2 and cerebral hemorrhage after TBI (Hadjigeorgiou et al., *Neurology*, 2005)
ApoE e4 as a risk factor for concussion in collegiate athletes: 3 studies

APOE, APOE Promoter, and Tau Genotypes and Risk for Concussion in College Athletes

Thomas Roland Terrell, MD, MPhil,* Robert M. Bostick, MD, MPH,† Ruth Abramson, PhD,‡
Dawen Xie, MD, PhD,§ William Barfield, PhD,¶ Robert Cantu, MD,‖
Michele Sianek, MSH,*** and Trina Ewing, MS**

Clin J Sport Med • Volume 18, Number 1, January 2008

Does the Apolipoprotein e4 Allele Predispose Varsity Athletes to Concussion? A Prospective Cohort Study

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Clin J Sport Med • Volume 18, Number 4, July 2008

Apolipoprotein E Genotype and Concussion in College Athletes

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Clin J Sport Med • Volume 20, Number 6, November 2010
ApoE e4 and professional athletes: 2 studies

Apolipoprotein E ε4 Associated With Chronic Traumatic Brain Injury in Boxing
Barry D. Jordan, MD, MPH; Norman R. Relkin, MD, PhD; Lisa D. Ravdin, PhD; Alan R. Jacobs, MD; Alexandre Bennett, PhD; Sam Gandy, MD, PhD

JAMA. 1997;278:136-140

Lower Cognitive Performance of Older Football Players Possessing Apolipoprotein E ε4
Kenneth C. Kutner, Ph.D., David M. Erlanger, Ph.D., Julia Tsai, B.S., Barry Jordan, M.D., M.P.H., Norman R. Relkin, M.D., Ph.D.

Neurosurgery, Vol. 47, No. 3, September 2000
ApoE and Boxers


- 30 professional boxers, ages 23-76 years
- ApoE genotyping and CTBI (0-9) Scale
- CTBI Scale: motor, cognitive, neuropsychiatric symptoms

<table>
<thead>
<tr>
<th>CTBI Score</th>
<th>No Symptoms</th>
<th>Mild Symptoms</th>
<th>Moderate Symptoms</th>
<th>Severe Symptoms</th>
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</thead>
<tbody>
<tr>
<td>0</td>
<td>11</td>
<td>12</td>
<td>4</td>
<td>3</td>
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- ApoE genotype frequency paralleled the general population
Jordan: ApoE and Boxers

- High Exposure Boxers (>12 professional bouts) had higher CTBI scores than Low Exposure Boxers
- High Exposure Boxers with positive ApoE had greater CTBI scores vs. High Exposure Boxers who were ApoE negative
- Low Exposure Boxers had Normal CTBI scores, whether positive or negative ApoE
- All Boxers with Severe CTBI scores were ApoE positive
- Conclusion: *ApoE status interacts with exposure in professional boxing to produce CTBI*
Bottom Line Conclusions: Biomarkers and Genes

S-100B may be the most robust biochemical marker immediately post-concussion

ApoE and its promoter polymorphisms have the most evidence to date as a genetic marker
Hypothesis of the Postconcussive Vulnerable Brain: Experimental Evidence of its Metabolic Occurrence

Vagnozzi et al., Neurosurgery, 2005, 57, 164-171

- Assessed the temporal effects of successive concussive injuries (via fluid percussion methodology) in rats; 6 animals per group
- Group 1: Single mTBI
- Group 2: Single mTBI with next mTBI 3 days later
- Group 3: Single mTBI with next mTBI 5 days later
- Group 4: Single Severe TBI
- Group 5: Sham
- Animals sacrificed 48 hours post
- Assessed NAA (N-Acetylaspartate, a brain specific indicator of metabolic activity), Adenosine 5-Triphosphate (ATP), and Adenosine Biphosphate via high performance liquid chromatography

Single mTBI animals’ brain metabolic indicators were equal to Controls by Day 5

Animals receiving the second concussive injury 3 days after the first had brain metabolic indicators similar to those with a Severe TBI
• In the rats who received the second mTBI within 3 days of the first and sacrificed up to 7 days post-impact, there was no evidence of cerebral recovery, suggesting that this type of damage is difficult to reverse.

• The metabolic pattern noted in control rats was similar to those concussed rats receiving mTBIs 5 days apart.
Conclusion: “This study shows that the existence of a temporal window of brain vulnerability after mTBI. A second concussive event falling within this time range had profound consequences on mitochondrial-related metabolism. Furthermore, because NAA recovery coincided with normalization of all other metabolites, it is conceivable to hypothesize that NAA measurement by 1-H-NMR spectroscopy might be a valid tool in assessing full cerebral metabolic activity in the clinical setting and with particular reference to sports medicine in establishing when to return mTBI-affected athletes to play”.
Clinical Management of Sports Related Concussion: Overview

- Remove from contest; observe for acute signs and symptoms, perform sideline examination serially and monitor frequently. The standard is no RTP in the same contest if a concussion is diagnosed
- “When in doubt, sit them out”
- Give instructions to family or friends for observation
- Transport to ED if neurological status worsens or if acute signs/symptoms emerge (e.g., vomiting, deteriorating mental status)
- Rest; no cognitive or physical exertion
- May need to request academic accommodations/excuse from gym class
- Criteria for readiness for rehab: 1) asymptomatic at rest, 2) normal neurological exam by a physician, 3) normal neuroimaging (if done), and 4) cognitive test scores have returned to baseline or are considered WNL
- Begin rehab under supervision of ATC or PT, involving graduated, stepwise levels of physical exertion. Completion of one step with asymptomatic status is a prerequisite for progression to the next step
- Return to play after completion of physical rehab and clearance by licensed health care professional
16. Voted to approve the addition of a clinical neuro-psychologist with concussion training as one of the individuals who are allowed to sign off on our “Return to Play” form.
Thanks to all of you for your attention.

Questions?

A CONCUSSION IS A BRAIN INJURY
TAKE IT SERIOUSLY!