The Neuro-Ophthalmology of Concussion
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Disclosure Statement:
Dr. Leong is employed by the King-Devick Test as the Director of Research. Other lecturers have no disclosures.

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Concussion by the Numbers
• Epidemiology: 1.6 – 3.8 million annually
• Estimated 85% go undiagnosed
• Concussions drawing national attention
• NFL interest in Chronic Traumatic Encephalopathy (CTE)
• 20-30% of Alzheimer’s patients report head trauma vs. 8-10% of controls

What is a Concussion?
• A complex pathophysiological process affecting the brain, induced by traumatic biomechanical forces
• Functional rather than Structural Injury
• Mild traumatic Brain Injury (mTBI) – Diffuse axonal injury
• Loss of Consciousness in less than 10%

Epidemiology
• 300,000 to nearly 4 million per year
• Problem of under-reporting and debate regarding definition
• Multiple studies suggest rate on rise
• Girls have a higher rate of concussion
• High school football followed by girl’s soccer lead the list

JAMA, October 27, 2010
High School Concussions (per 100,000)

- Football: Between 60 and 76
- Girl's soccer: Between 33 and 35
- Boys' lacrosse: Between 30 and 46
- Girls' lacrosse: Between 20 and 31
- Boys' soccer: Between 17 and 19
- Boys' wrestling: Between 17 and 23
- Girls' basketball: Between 16 and 18
- Softball: Between 11 and 16
- Boys' basketball: Between 11 and 21
- Girls' field hockey: Between 10 and 24
- Cheerleading: 11
- Girls' volleyball: Between 5 and 8
- Boys' baseball: Between 4 and 6


Hockey Concussion Education Project (HCEP)

- 67 male hockey players (ages 16-21)
- Prospective, physician-observed surveillance for concussion (2009-2010)
- 17 players sustained 21 concussions (25%)
- 5/17 (29%) sustained a second concussion
- 15/17 (88%) players admitted to prior concussion
- Concussion by position:
  - 71% forwards
  - 29% defensemen

Neurological Focus 2010

Youth Sports & Concussion

Children are more susceptible to head injury than adults and require a longer period of recovery


Cognitive Impairment in Children with TBI (Impaired Neuroplasticity and Brain Development)

- Metabolic vs. structural changes


Challenges: Recognition and Management of Concussion

1. Wide variety of symptoms – easily “missed” by coaches, medical staff
2. Denial of symptoms (“I feel fine”)
   - Metabolically-mediated euphoria (McKee 2010)
3. Current management protocols not evidence-based
4. Traditional neurological / radiological studies (CT, MRI, EEG) normal with mTBI
   - Metabolic vs. structural changes

“Structure vs. Function”

- Concussion is a metabolic rather than a structural abnormality
  - Detectable abnormalities (N-acetylaspartate (NAA)) on MR spectroscopy

**Advent of trench warfare and continuous shelling**
- 10% overall fatalities – most due to shrapnel/indirect trauma
- Term “shell shock” used to describe psychiatric findings

**Major Frederick Mott**
- British neuropathologist who proposed studying brains of deceased WWI soldiers
- Questioned link between “shell shock” and organic brain disease
- In 1917, British Army bans further use of term “shell shock”

**Battle of Ypres - 1917**
- Finnish psychiatrist Dr. Harry Federley adopts term LMF (Lacks Moral Fibre) for combat-related neuroses
- German psychiatrist Dr. Rudolph Brickenstein: “…that if a soldier did break down and could not continue fighting, it was a leadership problem, not one for medical personnel or psychiatrists. Breakdown (he said) usually took the form of unwillingness to fight or cowardice.”

**Combat-Related TBI**
- Most deployed soldiers report one or more blast injuries
- TBI proposed as “signature injury” of modern combat
- Limited data on prevalence
- Potential link to post-traumatic stress disorder (PTSD)

**mTBI in Soldiers Returning from Iraq**
- Survey of 2525 Army soldiers 3-4 mos after return from deployment
  - 4.9% reported injury with LOC
  - 43.9% with PTSD
  - 10.3% injury with altered mental status
  - 27.3% with PTSD

Neurology of Concussion

- Many symptoms not captured by cognitive testing
- Photophobia: occipital lobe, brainstem
- Blurred vision: frontal, temporal lobes
- Diplopia and vertigo: brainstem, cerebellar paths

Vision/Oculo-Motor

Biomechanics of Concussion …
“Brain in a Box”

- Direct injury to brain at point of contact (coup)
- Injury opposite the point of impact (contrecoup)
- Rotational forces with shearing/stretching of axons
  “wash-over” effect (blast injuries)


Neuronal Injury Following Concussion

from ‘Head Games: The Film’ 2012
Neuronal Injury: Key Steps

- Axonal stretching
- Release of excitatory amino acids (glutamate)
- Glutamate binding to NMDA receptors
- Efflux of K+
- Influx of Ca+

Massive depolarization

Timeline of Neurometabolic Instability – “Window of Vulnerability”


Longitudinal Changes in Brain Volume Following TBI

- Longitudinal, segmentation analysis of TBI patients (one concussion)
- Post hoc analysis @ 1 year
- Atrophy of cingulate gyrus, ishmus of cingulate gyrus and pre-cuneus
- Correlation with neuro-cognitive and behavioral abnormalities


Concussion Signs and Symptoms (May be Delayed Minutes to Days)

- Physical: headache, dizziness, vision changes
- Cognitive: memory impairment, concentration
- Emotional: irritability, sadness
- Sleep disorder

Complications of Concussion

- Second-impact syndrome (SIS)
- Postconcussion syndrome (PCS)
- Chronic traumatic encephalopathy (CTE)

Second-Impact Syndrome

- Sustaining a second concussion before "recovery" from first concussion
- Majority in pediatric/adolescent populations (< 20 yrs.)
- Enhancement of cerebrovascular congestion
  - Diffuse cerebral edema
  - Death (within minutes!)


Post-Concussion Syndrome

3 months duration of three or more of following:
- Fatigue
- Disordered sleep
- Irritability / aggressiveness
- Anxiety / depression
- Personality changes / apathy
- Impaired attention / memory
- Impaired eye tracking

Diagnostic and Statistical Manual of Mental Disorders. Fourth Edition
Heitger MH et al. Brain 2009 #aaoptom13

Chronic Traumatic Encephalopathy (CTE)

- Historical evidence of progressive neurologic disability in boxers:
  - “punch drunk” (Martland 1928)
  - “dementia pugilistica” (Millspaugh 1937)
- Signs & symptoms:
  - Memory disturbance, confusion, behavioral/personality changes, Parkinsonism and speech/gait abnormalities
- Average age of diagnosis = 43 yrs.
- Average age of death = 54 yrs.

Neuropathology of CTE

- Atrophy of cerebral hemispheres, temporal lobe, mammillary bodies & brainstem
- Ventricular dilatation
- Fenestration of septum pelucium
- Marked accumulation of tau-immunoreactive astrocytes


Mr. Duerson’s Clinical History

- Long-standing complaints of headaches since NFL and onward.
- Over the ~5 years prior to death, he had worsening short-term memory difficulties, as well as problems with language and “vision”
- Increasingly out of control:
  - Short fuse
  - Hot tempered
  - Physically abusive
  - Verbally abusive
Comparison with other former NFL players

- **Owen Thomas**
  - Co-Captain of 2010 Penn Football Team
  - Began playing football at 9 years old
  - Committed suicide April 26, 2010, at the age of 21
  - No history of concussion
  - No history of mental illness
  - Mentioned doing poorly in two classes to his parents the day before hanging himself in his off-campus apartment

- 18 y/o male with CTE
Stage 1: headache and loss of attention and concentration

Stage 2: depression, explosivity and short-term memory loss

Stage 3: loss of executive function and cognitive impairment

Stage 4: dementia, word-finding difficulty and aggression


CTE is a disease of progressive neurologic dysfunction with increasing CNS deposition of tau related to repetitive head blows over time.

CTE Masquerades

- Alzheimer disease
- Progressive Supranuclear Palsy
- Parkinsonism
- Amyotrophic lateral sclerosis (Lou Gehrig's Disease)

The Search for Surrogate Biomarkers

- PET scans of retired NFL players reveals FDDNP signals in areas of histopathologic documentation of Tau (Small GW, et al. Am J Geriatr Psychiatry 2013)
- OCT abnormalities in veterans with TBI vs. age-matched controls (Kardon R, et al. ARVO 2013)
DETECT (Diagnosing and Evaluating Traumatic Encephalopathy Using Clinical Tests)

- Joint funding by NIH, NINDS, NIA & NICHD
- The ultimate goal of this study is to develop methods of diagnosing CTE during life through the use of a variety of tests, including MRI scans (such as diffusion tensor imaging), MRS scans (also known as a “virtual biopsy”), blood tests, and measures of proteins in spinal fluid.
- The study will include 150 former NFL players (ages 40-69) and 50 same-age “control” athletes who played non-contact sports.

New Rapid Sideline Tests

Concussion Tests: 2 Types

- Testing for screening/diagnosis: King-Devick (K-D) test, Standardized Assessment of Concussion (SAC), SCAT2, MACE
- Testing for management: ImPACT, other computerized testing

Why Do We Need a Rapid Sideline Test for Concussion?

- Detecting early signs of concussion may improve outcomes in athletes with mild closed head trauma
- Possible devastating long-term disability
- Following a concussion, you are 3 times more likely to have another one
- Need an easy objective test since qualified personnel not always available

What is the Evidence?

- Management is largely guided by expert opinion or retrospective data
- Levels of evidence in medicine: 5 levels
  - Highest: prospective study, established criteria
  - Lowest: expert opinion
- Formal research testing is the only way to get evidence that a test works!
**SCAT3 for Sideline Testing?**
- Evaluation of symptoms, orientation, memory & balance
- Takes 20 minutes
- Not all components validated
- Validation of SAC using prior definitions of concussion / only tests cognitive domain
- Requires medical professionals

**Concussion Anatomy**
- Cerebral cortex, brainstem, cerebellum
- All pathways vulnerable in concussion

**Why Test Eye Movements?**
- Many symptoms not captured by cognitive testing
- Vision accounts for >50% of the brain’s pathways
- Planning and execution of saccades involves wide network of anatomical structures in the brain:
  - Frontal eye field (Frontal Cortex)
  - Dorsal lateral prefrontal cortex
  - Supplementary motor area
  - Posterior parietal cortex
  - Middle temporal area
- Impaired eye movements are an indicator of suboptimal brain function

**Remove from Play**
- King-Devick Test for Concussions
  - Test of rapid number naming & eye movements
  - Speed & error compared to baseline time
  - Two trials to determine Baseline Time
  - Retest after suspected head injury: INCREASED time or ERRORS ➔ Concussion
  - Can be administered by coaches/parents (non-medical professional)
  - May help coaches/trainers with game time decisions

**King-Devick Test in Scientific Literature**
"The King-Devick Test is an accurate and reliable method for identifying athletes with head trauma, and is a strong candidate rapid sideline screening test for concussion."

"...addresses the need for a quick, reliable test that can accurately identify concussion and thus reduces the potentially devastating effects of second impact syndrome and recurrent neurological injury."

"Because the K-D test does not require a medical professional and can be administered in 1-2min, it is practical for sideline use at all levels of sports. The K-D test has the potential to capture brain impairment not observed in standard neurocognitive testing."

"...able to identify players with a suspected concussion, players with a concussion that was not reported or witnessed..."

"...the ease-of-use made it more acceptable to team management and players and, as it provided immediate feedback to the player and coach."

"...the K-D test served to provide support for the decision made by the team medical staff to rule out the player from further match participation."

**King-Devick Test in Scientific Literature**
"...able to identify players that had not shown, or reported, any signs or symptoms of a concussion but who had meaningful head injury."

"...suitable for rapid assessment in a limited time frame on the sideline such as a five-minute window to assess and review suspected concussed players in rugby union."

"Three football players whose concussion diagnosis was confirmed by a neurologist did in fact demonstrate diminished KD test performances."

"Two players tested rink-side immediately following concussion had KD scores worsened from baseline. These athletes had no differences found for SCAT2 SAC components, but reported symptoms of concussion."

"The K-D test was associated with reductions in Immediate Memory Scores and the overall SAC score."

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**Figures and Images**

- SCAT3 for Sideline Testing?
- Concussion Anatomy
- Why Test Eye Movements?
- Remove from Play
- King-Devick Test in Scientific Literature
King-Devick Test: Boxers & MMA Fighters Study

- K-D scores worse after head trauma
- K-D scores worse with loss of consciousness

Galetta et al. Neurology. 2011

K-D Boxing/ MMA Study: Other Findings

- Minimal improvement pre- to post-fight for K-D, consistent with learning effects
- Worse post-fight K-D scores ($r_s = -0.79$) and greater worsening ($r_s = -0.90$) correlated with post-fight MACE scores
- Worsening of K-D score by $\geq$5 seconds noted only in participants with head trauma


King-Devick Test: Penn Collegiate Athlete Study

- K-D scores worse after concussion
- K-D scores not worse after exercise


Penn Collegiate Athlete Cohort

<table>
<thead>
<tr>
<th></th>
<th>All Participants (n = 219)</th>
<th>No Concussion (n = 206)</th>
<th>Concussion In Season (n = 13)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), years</td>
<td>20.3 ±1.4</td>
<td>20.3 ±1.4</td>
<td>20.4 ±1.0</td>
</tr>
<tr>
<td>Best pre-season baseline K-D, sec</td>
<td>(23.5-63.4)</td>
<td>(23.4-58.0)</td>
<td>(23.4-58.0)</td>
</tr>
<tr>
<td>Post-concussion K-D (sideline n=10), sec</td>
<td>47.0 (32.7-64.1)</td>
<td>36.0 (32.5-63.4)</td>
<td>47.0 (32.7-64.1)</td>
</tr>
<tr>
<td>K-D change from baseline to sideline at time of concussion, median (range), sec</td>
<td>5.9 (0.5-38.1)</td>
<td>-</td>
<td>-</td>
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</tbody>
</table>

* P-value vs. baseline, sign-rank test


King-Devick Test: Amateur Rugby Studies

- New Zealand
- Pilot Study:
  - Participants: 50 athletes over 12 matches
  - Concussions: 5
  - 3 witnessed/self reported
  - 2 incidental, un-witnessed
  (detected on post-game assessment with King-Devick test)

Follow-up Study:

- Participants: 37 athletes over 24 matches
- Concussions: 22
  - 5 witnessed/self reported
  - 17 incidental, un-witnessed
  (detected on post-game assessment with King-Devick test)
Concussions in High School Football

- Participants: 47 high school football players, 2012 season
- Concussions: 3
  - Concussion confirmed by neurologist
  - ALL abnormal KD scores
    - Student 1: 41% worse
    - Student 2: 100% worse
    - Student 3: 143% worse
- Test-retest Reliability: ICC = 0.873 (p<0.05)

King-Devick Test: Wheaton College Football

- Wheaton, IL
- Participants: 102 athletes
- Concussions: 11 (no LOC)
  - 9/11 abnormal K-D test & SCAT2/physician examination
  - 1/11 "symptom free" and returned to play since K-D was only slightly slower; Developed headache after next play, was removed from play and did not return for remainder of season.
  - 1/11 "symptom free" and removed from play as K-D was significantly slower.

Saccades & Memory

Professional Ice Hockey: Philadelphia Flyers

- 27 athletes, 2011-2012 pre-season
- Worse KD scores associated with:
  - Lower SCAT2 SAC Memory score
  - Lower overall SAC score
- For every 1 point reduction in SAC Immediate Memory Score, corresponding worsening of KD by 7.3s

Working memory and saccades share closely related anatomical structures, including the dorsolateral prefrontal cortex (DLPFC)


Concussion Sideline Assessment: Composite Measure?

- Standardized Assessment of Concussion (SAC)
- Balance Error Scoring System (BESS)
- King-Devick (K-D) Test
When is it acceptable for an athlete to return to play following a concussion?

Concussion Management
- The only proven treatment for concussion is REST (both physical and cognitive REST)
- No drug, nutritional supplement, or treatment that has been proven to accelerate recovery
- Follow graduated Return to Play and Return to School protocol guidelines
  - School considerations
  - Home restrictions

Graduated Return to Play Protocol

<table>
<thead>
<tr>
<th>Rehabilitation Stage</th>
<th>Functional Exercise at Each Stage of Rehabilitation</th>
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<tbody>
<tr>
<td>(1) No activity</td>
<td>Complete physical, cognitive rest</td>
</tr>
<tr>
<td>(2) Light aerobic exercise</td>
<td>Walking, swimming, stationary bike</td>
</tr>
<tr>
<td>(3) Sport-specific exercise</td>
<td>Running drills in soccer, skating drills in hockey, etc.</td>
</tr>
<tr>
<td>(4) Noncontact drills</td>
<td>More complex training drills, may start resistance training</td>
</tr>
<tr>
<td>(5) Full-contact practice</td>
<td>With medical clearance, participate in normal training activities</td>
</tr>
<tr>
<td>(6) Return to play</td>
<td>Normal game play</td>
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Concussion Prevention
- Reduce exposure, reduce hits
  - 75% of head trauma occurs during practice
- The role of helmets
  - Helmets originally designed to prevent skull fractures, not concussion
  - Helmets can also make the game more dangerous
  - Accelerometers in helmets to measure G force of hits
- Education
  - Athletes, coaches, parents, teachers, medical personnel all involved in the management team
  - 40% of concussed athletes return to play prematurely

Questions to be Answered
- What are the best tests to diagnose and manage concussions?
- How can we best develop evidence to support the use of current and new tests?
- In what ways can we lead the effort to reduce effects of concussion?

There’s No Such Thing as a Tough Brain

NFL Hall of Fame-Class of 1997
Mike Haynes, far left
King-Davis Test Representative
Mike Webster (1952-2002), far right
Suffered from Dementia, Amnesia and Depression