New Frontiers in Sports Concussion

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DISCLOSURES

• Royalties from Demo’s Publishing
Outline

- Definition
- Why do we care about concussions?
- Current concussion guidelines for hockey
- Future directions of concussion prevention, diagnosis, and treatment
- Conclusions
Definition

• Concussion is a brain injury defined as a complex pathophysiologic process affecting the brain, induced by biomechanical forces.
  • Rotational acceleration > linear acceleration
• Symptoms are short-lived, and resolve spontaneously
• +/- loss of consciousness
• Predominantly functional rather than structural (normal standard neuroimaging studies)

Neurometabolic Cascade Following Experimental Concussion

1. Depolarization
2. Neuro-transmitter release
3. Potassium efflux
4. Increased membrane pumping
5. Hyper-glycolysis
6. Lactate accumulation
7. Ca^{2+} sequestration/ mitochondrial dysfunction
8. Decreased energy (ATP) production
9. Enzyme activation/ initiation of apoptosis

Adapted from Gliza CC and Hovda DA. J Athletic Training 36:229, 2001
Pathophysiology

• Injured neurons remain extremely vulnerable to further injury for an unknown period of time.
Why do we care about Concussions?

• Increased risk of future concussion
  • 3-5 x increased risk
• Post-concussive syndrome
• Catastrophic injury
  • Second Impact Syndrome
• Chronic Traumatic Encephalopathy

Why do we care about Concussions?

- Chronic traumatic encephalopathy (CTE)
  - Begins with personality changes
    - mean age 42.8 years
  - Volatility, depression
  - Cognitive deficits (e.g., early onset Alzheimer’s)
  - Movement disorders
  - Motor neuron disease

*McKee et al.  J Neuropathol Exp Neurol 2009
Why do we care about Concussions?

- CTE Pathology
  - Cortical atrophy
  - Enlargement of ventricles
    - Prominent 3rd ventricle
  - Substantia nigra pallor
  - Tau protein deposition

*Mckee et al. J Neuopathol Exp Neurol 2009*
Why do we care about Concussions?

- CTE
  - Still a controversial diagnosis
    - Based upon post-mortem histopathologic analysis and retrospective information
  - Single cross-sectional study of 45 retired NFL players (30-60 y/o, mean 45.6)
    - MRI, DTI, neuropsych eval, interview, neurologic exam, APOE genotype
  - Results
    - Mean concussions during NFL career = 6.9
    - 9% microbleeds in brain parenchyma
    - 7% large cavum septum pellucidum & brain atrophy
    - Number of years pre-college football correlated with fractional anisotropy on DTI
    - Abnormal neuroimaging correlated with number of concussions
    - 24% had isolated neuropsych test abnormalities, but none had dementia, dysarthria, parkinsonism, or cerebellar dysfunction
    - Abnormal neuroimaging and number of concussions did not correlate with neuropsych abnormalities
    - 20% had depression (similar to general population)
    - 38% had APOE4 (normal population 23-26%)
  - Conclusion
    - Evidence of structural chronic brain injury likely related to football in 13% of retired NFL players
    - No evidence of increased incidence of abnormal neuro exam, neuropsych testing, or depression compared to general population

(Casson et al Sports Health 2014)
Current Concussion Guidelines in Hockey

• USA Hockey
  • Any athlete with a **suspected** concussion should be immediately removed from play
    • “When in doubt, sit them out”
  • Appropriate emergency treatments should be initiated, emergency transport if needed
  • Symptomatic athletes should be treated with physical and cognitive rest
  • Athlete may begin the functional return to play protocol when asymptomatic at rest and cleared by a qualified healthcare provider
• Functional Return to play protocol
  * Must successfully complete each phase before advancing to the next
  * Each phase requires a minimum of 1 day before advancing to the next phase
Current Concussion Guidelines in Hockey

- IIHF
  - Player with S & S of concussion = removed from play and evaluated by medical personnel
  - Team physician is solely responsible for determining if the player has a concussion
  - If (+) concussion, can’t return to play the same day
  - Return to play based upon 3 factors
    - No symptoms at rest
    - No symptoms with exertion at levels required for competitive play
    - Returned to neurocognitive baseline
  - Team physician has final say on when athlete returns to play
Current Concussion Guidelines in Hockey

• NHL
  • Requires baseline neuropsych testing
    • Testing supervised by neuropsychologist
  • Player with S & S of concussion = removed from ice and evaluated by team medical personnel with standardized, comprehensive acute concussion assessment tool (e.g., NHL SCAT2)
  • Team physician must assess athlete in person and is solely responsible for determining if the athlete has a concussion
  • (+) concussion = no return to same game/practice unless
    • Rapid and complete recovery of sx at rest and with exertion, and neuropsych assessment = athlete is at baseline function
  • Athletes returned to play on same day need neuropsych evaluation as soon as practicable after game to assess for delayed neuropsych deficits or symptoms
  • Other athletes should be seen by neuropsych after sx resolve at rest and with exertion and prior to return to play
  • May return to play when sx free at rest and with exertion and when achieve baseline neurocognitive function
Prevention

• Identify people at risk for concussion
  • History of concussion
    • 3-5 x higher risk for future concussion
  • High school > college > professional
  • Female > male
• Genetics
  • G219T polymorphism in the ApoE4 promoter region
  • Tau $^{\text{Ser}_{53}\text{Pro}}$ polymorphism

*Guskiewicz et al. J Athl Train 2001
*Finnoff J. PMR 2011
Prevention

- **Helmets**
  - 2 studies suggest that the new “anti-concussion” football helmets reduce the risk of concussion (Collins et al *Neurosurgery* 2006, Rowson et al *J Neurosurg* 2014)
  - Limited by their inability to dissipate rotational forces
  - No similar studies in hockey

- **Monitoring G-Forces**
  - Limited role due to inter-individual and inter-injury variability

- **Mouthguards**
  - Reduce maxillofacial/oral injury, but not concussions (Knapik et al *Sports Med* 2007)

- **Rules**
  - Enforce existing rules
  - Eliminate fighting and blows to the head

- **Legislation**

- **Education, pre-season conditioning, proper contact technique**
Identification and Management

• Pre-Season Preparation
  • Baseline testing
  • Sideline and “In Clinic” Tools
    • Concussion symptoms (e.g., Post-Concussion Symptom Scale, Concussion Symptom Inventory)
    • Visual and Oculomotor function (e.g., visual saccades, visual pursuit, convergence, King-Devick, near/far vision)
    • Balance (e.g., SOT, BESS, Wii Balance)
    • Neurocognitive function (e.g., ImPACT, AXON/CogSport, ANAM, CNS Vital Signs, Headminders)

• Must have access to baseline data in the clinic and on the sideline

• Have a pre-season plan regarding how to treat concussed athletes

• Practice!
Identification and Management

• Sideline assessment tools for concussion
  • King-Devick test
    • Assesses eye tracking, attention, concentration, and reaction time
    • Timed test, takes 1-2 minutes, rapid number naming on 3 successive cards
    • Lower time = better score
    • 4 studies have demonstrated decrements in King-Devick in concussed athletes relative to their baseline
    • 1 study demonstrated only a 20% sensitivity for King-Devick for concussion
    • King-Devick typically improves after baseline, even with fatigue (ie: decrement = very specific for concussion)
  • No ceiling effect
• Limitations
  • No standard difference in score that determines concussion
  • No standardized score based upon population matched controls (ie: need baseline)

Acute Imaging

- Typically not indicated
- No gold standard diagnostic imaging test for concussion
- Indications (ACEP-CDC joint practice guidelines)
  - Prolonged loss of consciousness (> 1 min)
  - Focal neurologic deficit
  - Declining neuro status
  - Severe HA
  - Coagulopathy
- If indicated, non-contrast CT is the appropriate study
  - Readily available, rapid, highly sensitive for fractures and acute intra-cranial hemorrhage

Increase Fractional Anisotropy Correlates with Symptom Severity in Mild TBI

- DTI changes also correlate with cognitive dysfunction and impaired reaction time
- Histological findings in animal models may correlate with DTI abnormalities

Kraus MS, et al. Brain 2007;130:2508-2519
Levin HS, et al. J Head Trauma Rehab 2008;23:197-208

Wilde EA, et al. Neurology 2008;70:948-955
1H-Magnetic Resonance Spectroscopy (MRS) May Provide Tool for Assessing Cerebral Metabolic Recovery

- NAA (N-acetylaspartate): neuronal marker and reflects mitochondrial related cerebral energy metabolism
- Myo-inositol: glial marker
- Choline: membrane marker
- Lactate: indirect marker for ischemic/hypoxia
- Creatine/phosphocreatine: energy metabolites
- Glutamate

NAA correlates with recovery of other metabolites
**1H-MRS-NAA Useful Tool to Monitor Full Recovery of Concussion-related Metabolic Brain Damage**

[Graph showing NAA/Cr ratio vs. days post injury for single concussion, double concussion, and controls.]

Acute Imaging

• Functional MRI
  • Measures blood oxygenation patterns
  • In concussed athletes:
    • Abnormal activation patterns while symptoms are present
    • Normalize when symptoms resolve
    • Correlate with neurocognitive abnormalities

Difiori JP 2010
Biomarkers

• Not indicated...yet
  • Goal to have an objective, serum test for concussion, similar to current testing for myocardial infarction
  • Potential markers
    • Cleaved-Tau (Specific, but not sensitive. Serum concentration 1 hour post injury can predict duration of symptoms.)
    • S-100B (highly sensitive, not very specific)
    • Neuron-specific enolase (NSE)
    • Calpain-cleaved alpha 2-spectrin N-terminal fragment (SNTF) (Specific, but not sensitive. Elevated concentration 1-36 hours post-injury is predictive of prolonged symptoms.)
  • Limitations
    • Variable sensitivity and specificity

Sideline EEG

- Halifax Consciousness Scan (HCS)
  - Headset with built in recording electrodes and earphones
  - Records EEG event related potentials (ERPs)
  - Provides quantitative data related to the processing of:
    - Sensation
    - Perception
    - Attention
    - Memory
    - Language
- Results compiled in diagnostic score, reliability score, validity score, and prognostic score
- Not validated in concussion at this time

(Arcy et al. IEEE Transactions on Biomedical Engineering 2011)
Identification and Management

- Acute treatments
  - Omega-3 Fatty Acids (e.g., fish oil)
    - 2 common omega-3 fatty acids are eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA)
    - Multiple mechanisms of action
      - Decreased inflammation
      - Decreased permeation of blood-brain barrier
      - Decreased apoptosis
    - DHA with or without EPA dosed either before (x 30 days) or after (x 30 days) experimentally induced mild brain injury in rat model = reduced brain injury
    - 40 mg/kg better than 20 mg/kg (i.e., roughly 3000 mg/day in 70 kg person)
    - Also decreases affective disorders commonly associated with concussion (e.g., depression, anxiety) and the development of dementia (e.g., Alzheimer’s disease)
  - N-acetylcysteine (possibly in amide form)
    - Preliminary animal studies suggest may reduce brain injury by maintaining normal mitochondrial bioenergetics, result in better functional outcome
    - Studies supplement within 15-30 minutes of injury
    - Single randomized, double blind, placebo controlled study in MTBI from blast injury
      - 4gm loading dose within 72 hours of injury, then 4 gm/day x 6 more days
      - 86% of NAC vs 42% placebo group treated within 24 hours of injury had complete sx resolution at 7 days ($p = 0.006$)

Delayed Recovery/Post-Concussion Syndrome

- Neuroimaging
  - T2 gradient echo or susceptibility weighted MRI (more sensitive of the two) sensitive for:
    - Hemorrhagic axonal shear injury
    - Contusions
    - Extra-axial fluid collections
  - Better at higher magnetic strength (3T > 1.5 T)
  - Evidence of brain contusion or hemorrhagic axonal injury at 12 days post injury = worse 3 month prognosis

(Barkovich AJ 2012, Yuh El 2014)
Complex Concussion

- UPMC Sports Concussion Program has identified 6 primary clinical trajectories for complex concussions
  - Cognitive/Fatigue
  - Vestibular
  - Oculomotor
  - Affective
  - Migrainous
  - Cervical spine

- Suggests specific treatment for each type of clinical trajectory

(Collins et al Knee Surg Sports Traumatol Arthrosc 2014)
Complex Concussion

- Clinical Trajectory Treatment - Cognitive/Fatigue
  - Structured, sub-symptom threshold exercise regimen
    - Some persistent symptoms may be due to autonomic dysfunction and impaired cerebral autoregulation
    - Exercise increases parasympathetic tone, reduces sympathetic activation, and improves cerebral blood flow
    - Exercise decreases depression and anxiety and improves neuroplasticity
    - Sx should be present > 4-6 weeks
      - Animal (and some human) data suggests that exercise < 7 days post injury impairs recovery, whereas 14-21 days post injury improves recovery
  - Graded exercise stress test to point of symptoms
    - Have athlete exercise at 80% of symptom threshold heart rate q day. Re-test every week and set new target heart rate
    - Improves activity tolerance significantly over 3-4 weeks
    - Improves function (ie: able to go to work or school)
    - Variable effect on resting symptoms

Retiring an Athlete

- Sometimes straightforward, but usually complicated
- No evidence based approach is currently available
- AMSSM position statement suggests considering the following:
  - Number of concussions
  - Decreased concussion threshold
  - Prolonged recovery
  - Structural abnormality
  - Persistent diminished brain function
- May fully disqualify athlete (ie; no competitive sports) or partially disqualify athlete (ie: no contact sports)

Conclusion

• Concussions are common among athletes

• There are significant potential risks associated with concussions including:
  • Increased risk of future concussion
  • Post-concussive syndrome
  • Catastrophic injury
  • Chronic Traumatic Encephalopathy
Conclusion

• A comprehensive program begins with prevention

• Identification starts before the season and should include tests for multiple different neurologic domains

• Game day return to play is still controversial, but when in doubt, sit them out

• Acute and chronic treatments beginning to extend beyond just physical and cognitive rest
Thank You