Predictors of Clinical Recovery Following Sport-Related Concussion

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Disclosures

Reimbursed by the government, professional scientific bodies, and commercial organizations for discussing or presenting research relating to mild TBI and sport-related concussion at meetings, scientific conferences, and symposiums.

Consulting practice in forensic neuropsychology involving individuals who have sustained mild TBIs, including former athletes.

Co-investigator, collaborator, or consultant on grants relating to mild TBI.

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Harvard Football Players Health Study (NFLPA)
Topics

• Observable Features and Acute Effects
• Predictors of Clinical Recovery
• The Promise of Precision Rehabilitation
Section I

Observable Features and Acute Effects
Basic Principles

- Concussion is a clinical diagnosis

- Tests do not diagnose concussion, they measure certain aspects of how a concussion affects a person

- There are tremendous individual differences in how people are affected by a concussion
Assessment Timeline

- Sideline
- Post-Game
- 24 Hours
- First Week
- Second Week
- Third Week
- At Risk!
Sideline and Post-Game

Observation and Examination
Observable Features

- Loss of Consciousness (uncommon)
- Balance Disturbance (e.g., “Bambi legs” on the ice)
- Amnesia (retrograde and/or anterograde; often very brief)
- Disorientation
- Confusion/Attentional Disturbance
  - Slowness to answer questions or follow directions
  - Easily distracted
  - Poor concentration
- Vacant Stare / “Glassy-Eyed”
- Inappropriate/confused Playing Behavior
Common Initially Reported Sideline Symptoms

- Headache
- Dizziness
- Some form of mental status disturbance, such as mental clouding, confusion, or feeling slowed down
Post-Concussion Scale: Symptoms Endorsed Acutely

- 260 acutely concussed high school and college athletes
- All assessed within 5 days
- Mean = 2.0 days; SD = 1.2 days
- 88% assessed within 3 days

(Lovell et al., 2006)
Most Common Symptoms

- Headaches (78.5%)
- Fatigue (69.2%)
- Feeling slowed down (66.9%)
- Drowsiness (64.2%)
- Difficulty concentrating (65.8%)
- Feeling mentally foggy (62.3%)
- Dizziness (61.2%)

(Lovell et al., 2006)
Least Common Symptoms

- Nervousness (21.2%)
- Feeling more emotional (17.7%)
- Sadness (15.0%)
- Numbness or tingling (14.6%)
- Vomiting (8.8%)

(Lovell et al., 2006)
Conceptualizing Symptoms Over Time
(individual differences in how symptoms change over time)

- Brain Injury
- Improving
- Improving

- Psychological Distress
- Unclear Progression
- Unclear Progression

- Life Stress
- Return to School
- Return to Sport
Acute and Subacute Concussion Symptoms

Remember:

Symptoms in the first two weeks following a concussion can be worsened by other factors, such as a neck injury, vestibular injury, psychological distress, and life stress.
Slow Recovery: Some Risk Factors

• Vestibular + Anxiety
• Stress, Worry, Depression
• Chronic Headaches
• Multiple Prior Concussions
Section II

Predictors of Clinical Recovery
Predictors of Clinical Recovery

• Results from a Systematic Review

• Preliminary Results from a Large Observational Study of High School Students and Division III Collegiate Athletes
Clinical Recovery

- For most concussed athletes, cognitive deficits (Williams et al., 2015; Kontos, et al., 2014), balance (McCrea et al., 2003; Nelson, LaRoche, et al., 2016), and symptoms (Nelson, Guskiewicz, et al., 2016) improve rapidly during the first two weeks following injury.

- Many past studies, particularly those published prior to 2005, concluded that most athletes recover from concussion and return to sports within 10 days (McCrea et al., 2003; Bleiberg, et al., 2004; Pellman, et al., 2004).
Studies over the past decade illustrate that the large majority of athletes appear to recover clinically within one month. Some have persistent symptoms beyond a month. There might be multiple underlying causes and contributors to those persistent symptoms.
Possible Predictors or Effect Modifiers of Clinical Outcome

- Pre-injury differences
  - Sex
  - Age
  - Genetics
  - Neurodevelopmental conditions (e.g., ADHD, LD)
  - Migraine history (personal or family)
  - Mental Health history (personal or family)
  - Concussion History

- Initial injury severity/acute symptoms (e.g., LOC, PTA, retrograde amnesia)

- Post-injury clinical differences
  - Severity of cognitive deficits
  - Development of headaches, migraines, depression
  - Dizziness and/or oculomotor functioning
Literature Review on Predictor Variables

• Examine factors that might be associated with, or influence, clinical recovery.
  – Clinical recovery is defined functionally as a return to normal activities, including school and sports, following injury.
  – Operationally it encompasses a resolution of symptoms and a return to clinically normal balance and cognitive functioning.

• Defining Predictors and Modifiers (a “Third Variable” in a disease model)
  – Effect modification
  – Intermediary (causal pathway)
  – Confounding (not on causal pathway)
Methodological differences in:

- Outcomes (e.g., symptom resolution, cognition, balance, return to sports, return to school)
- Time between injury and outcome (e.g., days to several months)
- Settings (e.g., high school, college, specialty clinic, emergency department)
- Number of modifiers examined in each study (e.g., 1-47)
  - Univariate
  - Multivariate
Considerations: Greater Pre-Injury/Baseline Symptom Reporting

• Females (Brown et al., 2015; Iverson et al., 2015)

• Athletes with a history of ADHD (Iverson et al., 2015; Nelson et al, 2015), learning disability (Zuckerman et al., 2013; Elbin et al., 2013), mental health treatment (Iverson, 2015), substance use treatment (Iverson et al., 2015), migraine treatment (Iverson et al., 2015), headache treatment (Brooks et al., 2016).

• Individuals with multiple prior concussions (Iverson et al., 2015; Brooks et al., 2016).

• Some athletes without any of these prior conditions report concussion-like symptoms in their daily lives (Iverson et al., 2015), potentially related to stress (Edman et al., 2012), depression (Covassin et al., 2012), or insufficient sleep (McClure et al., 2014).
Predictors of clinical recovery from concussion: a systematic review

Grant L Iverson,1,2 Andrew J Gardner,3 Douglas P Terry,1,2 Jennie L Ponsford,4 Allen K Sills,5 Donna K Broshek,6 Gary S Solomon7
Objective

Review the factors that might be associated with, or influence, clinical recovery from concussion.

Clinical Recovery – a return to normal activities, including school and sports, following injury. Encompasses resolution of symptoms and return to normal balance and cognitive functioning.
PRISMA

- 7,648 initially identified
- 4,777 after duplicate removals
- 101 full-text articles and 13 conference abstracts ultimately included

Study Inclusion Criteria
1. Published by June 2016
2. Examined clinical recovery from concussion
Caveats for Interpreting Results

• Results of all predictors were mixed.

• Many initial studies examined outcome during the first 2 weeks post-injury, while more recent studies examined those who are slow to recover (e.g., > 1 month).
## Mixed Evidence For All Potential Predictors

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Younger Age (Systematic Review)

Yes

No
Age

- There is some, but not definitive, support for a gradient age and level of play effect with clinical recovery being fastest in professional athletes, followed by college athletes, followed by high school athletes.

- No age effects in several studies, including some large-scale studies (Nelson, Guskiewicz, et al., 2016; Nelson, Tarima, et al., 2016).

- In the large multicenter Canadian study (Zemek et al., 2016), children presenting to the ED following injury, the rates of those having persistent symptoms > 4 weeks:
  - Ages 5-7=17.9%, ages 8-12=26.3%, ages 13-17=39.9%.
Preliminary Results from Prospective Observational Studies of Concussion Recovery in High School and Division III Student Athletes
Paul Berkner, D.O., Project Director

Recovery Curve Graphs Interspersed with Findings from the Systematic Review
Methods

• **Head Injury Tracker (HIT)**
  – Free online/smartphone application
  – Completed by athletic trainer or school nurse
  – Following a concussion, the following information is collected:
    • Demographics (e.g., age, sex, sport played)
    • Self-reported health history variables (e.g., pre-injury history of migraines, ADHD, depression, or concussion)
    • Scenario (e.g., practice vs. game; in season vs. out of season)
    • Injury date
    • 22-Item Post-Concussion Symptom Scale score at the time of the evaluation
    • Date of return to academics (full days, no accommodations).
    • Date of return to athletics (finished return to play protocol).
Methods

• 1,451 athletes sustained concussions
  • 183 were not sports-related injuries, 3 were 20-year-old high school students.

• Final sample N=1,265 sustained a sport-related concussion.
  – High School: 485 athletes (45.8% girls)
    • Boys: football (39.5%), soccer (22.4%), ice hockey (9.5%), lacrosse (7.2%), basketball (6.8%) and several other sports (14.6%).
    • Girls: soccer (45.0%), basketball (10.8%), spirit squad (cheerleading; 10.8%), field hockey (7.7%), and several other (25.7%).

  – College: 780 athletes (40.4% women)
    • Men: football (38.1%), rugby (15.7%), ice hockey (12.7%), lacrosse (12.3%), soccer (7.7%), and several other sports (13.5%).
    • Women: ice hockey (21.0%), rugby (21.0%), soccer (19.0%), basketball (6.3%), volleyball (6.3%), lacrosse (6.0%), and several other sports (20.4%).
Women took longer to return to academics (MW U=51529, p=.001).

7 days (63.9% vs. 72.4%, $\chi^2=5.84, p=.016$); 14 days (84.6% vs. 89.7%, $\chi^2=4.00, p=.045$); 21 days (93.6% vs. 95.6%, $\chi^2=1.28, p=.258$)
There were no group differences in recovery rates when examining return to athletics (ps > .05).
High School: Days to Return to School

Percentage Returned to School vs. Days Following Injury for Girls and Boys.

- Girls: Days to Return to School
- Boys: Days to Return to School

Days Following Injury:
- 0: 25.4%
- 6: 64.4%
- 12: 80.2%
- 18: 86.8%
- 24: 94.9%
- 30: 97.7%

Percentage Returned to School:
- 0: 16%
- 6: 65.4%
- 12: 74.6%
- 18: 83.4%
- 24: 88.8%
- 30: 94.1%

Graphs show percentage of days following injury when students returned to school for girls and boys.
High School: Days to Return to Sports

Days Following Injury vs. Percentage Returned to Athletics for Girls and Boys.
Female Sex
(Systematic Review)

Yes
Baker (2016) 26378093; Berz 2013 23703518; Henry 2016 26445375; Kostyun 2015 25553213; Bock 2015; 26243160; Zuckerman 2014 24206343; Covassin 2012 22539534; Covassin 2013 24197616; Covassin 2016 26950073; Majerske 2008 18523563; Colvin 2009 19460813; Eisenberg 2013 23753087; Ellis 2015 26359916; Miller 2016 26684762; Preiss-Farzenagan (2009) 19627902 (in adults); Heyer (2016) 27056449

No
Sex

• Comparable number of studies show positive and negative findings that worse outcomes are associated with female sex.

• Some large-scale and epidemiological studies indicate that girls and young women are at greater risk for having symptoms that persist for more than a month (e.g., Wasserman et al., 2016; Zemek, et al., 2016; Kostyun et al., 2016).

• The extent to which recovery is slower/outcomes are worse for females is still unclear.
Prior Concussions (Systematic Review)

Yes

No
Prior Concussions

• Many studies find an association between prior concussions and worse clinical outcomes.

• A greater number of studies have not found that prior concussions are associated with worse outcomes.

• Still likely a significant modifier because:
  • Prior history of concussion is a risk factor for future concussions (Abrahams et al., 2012)
  • Prior concussions are associated with greater pre-injury symptom reporting in some athletes (Abrahams et al., 2012; Iverson et al., 2015)
  • Some large-scale studies show an association between concussion history and increased risk for symptoms lasting more than four weeks (e.g., Castile et al., 2012; Miller et al., 2016; Wasserman et al., 2016)
High School and College Combined Days to Return to School
Stratified by Number of Prior Concussions

- No significant differences in return to school [$\chi^2(3) = 4.56, p = .21$].

Days post injury
Percentage returned to school

Days to Return to School
Stratified by Number of Prior Concussions
With regard to days to return to sports, the groups significantly differed, $X^2(3)=8.043, p = .045$. Follow-up KS tests showed that those 3+ prior concussions took longer to return to athletics compared to the groups with no prior concussions ($Z=2.080, < .001$) and 1 prior concussion ($Z=1.734, p = .005$).
• **Mental Health History**  
  – Almost all studies suggest worse outcome.

• **ADHD History**  
  – Almost all studies **do not** suggest worse outcome.

• **Learning Disability History**  
  – Almost all studies **do not** suggest worse outcome.

• **Personal Migraine History**  
  – Almost all studies **do not** suggest worse outcome.
  – One large well-designed study reported that a personal history of migraine is associated with risk for symptoms lasting more than four weeks (Zemek et al., 2016).
Pre-Injury ADHD: Days to Return to School
(High School and College Combined)
Pre-Injury ADHD: Days to Return to Sports
(High School and College Combined)
Pre-Injury **Migraine**: Days to Return to School
(High School and College Combined)
Pre-Injury Migraine: Days to Return to Sports

Days Post Injury

Percentage Returned to Athletics

No History of Migraine

History of Migraine
Injury Severity (Systematic Review)

- **Loss of consciousness**
  - Some studies report positive findings that LOC is associated with worse outcomes, but most do not find an association with LOC.

- **Post-traumatic amnesia/“amnesia”**
  - Mixed, but more studies do not find association with worse outcomes.

- **Retrograde amnesia**
  - Less frequently studied.
  - Consistently associated with worse outcome in the first 10 days following injury.
Greater Acute Symptoms
(Systematic Review)

Yes

No
Barlow (2011) 21904694; Moor (2015) 25883871; Morgan (2015) 25745949
Acute Clinical Findings (Systematic Review)

- Acute/sub-acute symptom burden
  - Associated with worse outcome
  - Of all possible predictors, it was the most consistently associated with worse outcome.

- Acute/Subacute Post-injury Headaches
  - Almost all studies suggest worse outcome.
Conclusions

• Strongest/most consistent predictor of slow recovery: more severe acute/subacute symptoms after injury.

• Those with preinjury mental health problems or migraines seem to be at a slightly increased risk for persistent symptoms.

• Those with ADHD/learning disabilities do not seem to be at an increased risk for persistent symptoms.

• Teenagers may be at the highest risk for persistent symptoms.

• Girls have a higher likelihood of prolonged recovery.
Section III

The Promise of Precision Rehabilitation
Resources for Treatment and Rehabilitation
Future Directions

- Determining the optimal or preferred amount of rest (including defining rest, activity restrictions, and activity resumption)

- Determining the role of exercise as a component of active rehabilitation (including when to begin, frequency, intensity, and other parameters)

- Tailoring specific treatment and rehabilitation strategies for specific problems (including when to initiate, frequency, and duration)
The Promise of Precision Rehabilitation

**Personal History**
- ADHD
- Learning Problems
- Headache/Migraine
- Family History of Migraine
- Prior Concussions
- Mental Health Problems
- Life Stress

**Acute Symptoms**
Type and Severity of Symptoms in the first 12-72 Hours Strongly Predict Later Clinical Outcome

**Injury Severity**
- Concussion severity
- Neck injury
- Vestibular injury
- Other bodily injuries

**Current Functioning**
- Headaches
- Vestibular Problems
- Visual-Oculomotor Issues
- Cognitive Difficulties
- Sleep Disturbance
- Fatigue
- Anxiety and Depression
Precision Rehabilitation

**Personal History**
- ADHD
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Conclusions
Concussions disrupt normal brain functioning.
## Mixed Evidence For All Potential Predictors of Outcome

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• Those with preinjury mental health problems or migraines seem to be at a slightly increased risk for persistent symptoms.

• Those with ADHD/learning disabilities do not seem to be at an increased risk for persistent symptoms, although emerging research might identify modest increased risks.

• Teenagers may be at the highest risk for persistent symptoms.

• Girls have a higher likelihood of prolonged recovery.
Resources for Treatment and Rehabilitation

Guideline for Concussion/Mild Traumatic Brain Injury & Persistent Symptoms
Healthcare Professional Version
Third Edition
Adults (18+ years of age)

Guidelines for Diagnosing and Managing Pediatric Concussion
First edition, June 2014

American Medical Society for Sports Medicine position statement: concussion in sport

Kimberly G Harmon,¹ Jonathan A Drezner,¹ Matthew Gammons,² Kevin M Guskiewicz,³ Mark Halstead,⁴ Stanley A Herring,¹ Jeffrey S Kutcher,⁵ Andrea Pana,⁶ Margot Putukian,⁷ William O Roberts⁸

Endorsed by the National Trainers’ Athletic Association and the American College of Sports Medicine
Precision Rehabilitation

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- Vestibular injury
- Other bodily injuries

**Acute Symptoms**
- Type and Severity of Symptoms in the first 12-72 Hours Relate to Clinical Outcome Days and Weeks Later

**Current Functioning**
- Headaches
- Vestibular Problems
- Visual-Oculomotor Issues
- Cognitive Difficulties
- Sleep Disturbance
- Fatigue
- Anxiety and Depression