The Paradox of Predicting Persistent Concussion Symptoms in Children and Adolescents

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Objectives

• Systematically review the current literature for concussion prognosis in children
• Prove physicians poorly predict concussion symptom duration
• Demonstrate the vital need for concussion prognosis research in the ED
What we know:

- We are here
- 5 years from now
Concussion Definition

• **Concussion** is defined as:

  “a complex pathophysiological process affecting the brain, induced by traumatic biomechanical forces”

• 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 head

• Due to acceleration/deceleration forces

• **Note:** LOC is NOT required

Neuron Following Concussion

Metabolic dysfunction results in ENERGY CRISIS

Massive release of neurotransmitters interferes with cell communications

It may take many days for the nerve cells to return to their normal condition.
EPIDEMIOLOGY:

According to the CDC, it is a “silent epidemic”
Epidemiology

• Up to 3.8 million of concussions occur annually
  – Many do not seek medical care

• 700,000+ ED visits/ year (USA) pediatric concussion

• An accurate number is difficult to estimate
Top Causes of Concussions

**Females**
- Soccer
- Horseback Riding
- Cycling
- Ice Hockey
- Snowboarding

**Males**
- Ice hockey
- Cycling
- Football
- Soccer
- Snowboarding
Signs/Symptoms

- Amnesia, retrograde or antegrade
- Disorientation
- Appearing dazed
- Acting confused
- Forgetting game rules or play assignments
- Inability to recall score or opponent
- Inappropriate emotionality
- Physical incoordination
- Imbalance
- Seizure
- Slow verbal responses
- Personality changes

- Headache
- Dizziness
- Nausea or vomiting
- Difficulty balancing
- Vision changes
- Photophobia
- Phonophobia
- Feeling “out of it”
- Difficulty concentrating
- Tinnitus
- Drowsiness
- Sadness
- Hallucinations
- None initially
Persistent Post-Concussive Symptoms
Background: Persistent Post-Concussive Symptoms

• “Prolonged concussion”
• Post-concussion syndrome
  – Ongoing/recurrent headache
  – Psychological/behavioral change
  – Missed school and lower QOL
• 58% 1-month, 11% 3-month
• “PCS”

Who is at risk for PCS?

• Clinicians cannot identify who is at highest risk
  – No validated, easy-to-use prognosticators

• What are the key prognosticators of PCS?

• Which children will get PCS?

• How severe? Time to symptom resolution?
Systematic Review

- Searched MEDLINE, Ovid Embase, Cochrane Library
- 1950 to April 16, 2012
- Peer-reviewed search (PRESS)
- Age 2 to 18 years
- Patients must have PCS
- Excluded moderate traumatic brain injury
Records identified through database searching (n = 824)

Records after duplicates removed (n = 561)

Records screened (n = 561)

Full-text articles assessed for eligibility (n = 25)

Studies included in qualitative synthesis (n = 15)

Records excluded (n = 538)
Reasons:
- 365 not pediatric
- 129 no PCS
- 41 no original or useable data
- 3 published before 1980

Articles excluded, with reasons (n = 10)
Reason:
- Duplication of patient level data (n=10)
Results: Systematic Review

- 824 records identified; 561 after duplicates removed
- 15 relevant studies included in descriptive analysis
  - 7 observational trials
  - 2 retrospective chart reviews
  - 6 case-control design
    - matched non-injured athletes
    - orthopedic injured patient
    - non-head-injury trauma patients
    - abdominal pain patients
- Most excluded preschool and primary-school aged
- Heterogeneity precluded meta-analysis

Zemek, et al. Archives of Pediatric Adol Med. (Accepted, in press)
Qualitative Summary

- Risk of developing PCS was increased in:
  - Older children
  - History of loss of consciousness
  - Presenting with headache or nausea/vomiting
  - Initial dizziness
  - History of previous head injury
  - Learning difficulties
  - Behavioral problems

Zemek, Farion, Archives of Pediatric Adol Med. (In press)
How do we predict PCS?
Pilot Study

Identify and quantify clinically available factors associated with prolonged symptoms in children presenting to the ED following concussion.
Study Design

• Prospective cohort study
• ED presentation with concussion
• Parent and physician data collection:
  – patient demographics
  – past medical history
  – mechanism and time of injury
  – initial symptoms
  – current signs and symptoms
  – physical examination
Follow-up Design

• Follow-up phone (or online) survey
  – 3 day, 7 day, 2 week, 4 week, 3 month
  – STAI-S (Spielberger State-Trait Anxiety Inventory State Anxiety scale)

• ImPACT test at 3 months
Parental Anxiety/STAI-S

• Parental anxiety associated chronic pain
  – Persistent pediatric headache (Emiroglu, 2004)
  – Recurrent abdominal pain in children (Garber, 1990; Campo 2007)

• Elevated baseline anxiety/stress levels are predictive of PCS in adults (Wood 2011; Edmed 2012)

• No evidence examining if parental anxiety is associated with PCS in children.
STAI-S

• Validated self-report measure
• 20 brief statements related state anxiety:
  – Apprehension, tension, nervousness, and worry
• Respondents rank on 4-point Likert scale
• Scored from 20 to 80
• Published means:
  – 35.7 (SD=10.4) male; 35.2 (SD=10.61) females
  – Normal conditions.
**ImPACT Test**

- Immediate Post-Concussion Assessment and Cognitive Testing
- *Computerized concussion evaluation system*
- Takes approximately 20 minutes to complete
- Measures multiple aspects of cognitive functioning:
  - Attention span
  - Working memory
  - Sustained and selective attention time
  - Response variability
  - Non-verbal problem solving
  - Reaction time
Inclusion Criteria

Patients were eligible if they:
(1) are aged 5 to 17 years
(2) have a concussion, defined as:
   injury to the head, neck or body resulting
   in one or more of the symptoms delineated
   in the screening form
(3) had the initial injury in the previous 48 hours
(4) are proficient in English or French
Exclusion Criteria

Patients were excluded if:

1. present with traumatic brain injuries
   - GCS ≤13, open head injury, positive CT finding, neurosurgical intervention required, intubation, PICU
2. multi-system injuries (admission, OR, procedural sedation)
3. significant developmental delay
4. intoxication
5. no clear history of trauma as the primary event (e.g., seizure, syncope or migraine)
6. previously enrolled in the study
Types of Outcomes

Primary outcome: which variables are strongly associated with persistence of symptoms at 1 month

Secondary outcomes:
• Derive Clinical Prediction Rule
• Delineate which components best predict time until full symptom resolution
• Association with Parental Anxiety
CONSORT Diagram

Eligible
N = 317

Not eligible  N = 194

- Research Assistant unavailable;  N = 46
- Patient under five years of age;  N = 105
- Unable to obtain informed consent;  N = 7
  - Language barrier;  N = 6
     - No parental guardian present;  N = 1
- Injury occurring over 48 hours from time of triage;  N = 21
- No concussion symptoms present;  N = 10
- No clear history of direct/indirect blow to head as cause of symptoms;  N = 5

Eligible
N = 123

Initially enrolled
N = 100

Declined participation
N = 23

Excluded by physician post-enrollment
N = 2

Total participants
N = 98

Completed 1-week follow-up
N = 76

Completed 2-week follow-up
N = 77

Completed 1-month follow-up
N = 77

Completed 3-month follow-up
N = 70
## Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex (N = 98)</td>
<td>57 (58.2)</td>
</tr>
<tr>
<td>Age (N = 98); Mean (S.D.)</td>
<td>12.1 (3.4)</td>
</tr>
<tr>
<td>Grade of School Currently Enrolled In (N = 98)</td>
<td></td>
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<tr>
<td>Kindergarten to Grade 4</td>
<td>21 (21.4)</td>
</tr>
<tr>
<td>Grade 5 to 8</td>
<td>33 (33.7)</td>
</tr>
<tr>
<td>Grade 9 to 13</td>
<td>44 (44.9)</td>
</tr>
<tr>
<td>Average Prior Academic Achievement (N = 97)</td>
<td></td>
</tr>
<tr>
<td>Straight A Student</td>
<td>15 (15.5)</td>
</tr>
<tr>
<td>A and B Grades</td>
<td>44 (45.4)</td>
</tr>
<tr>
<td>Straight B Grades</td>
<td>15 (15.5)</td>
</tr>
<tr>
<td>B and C Grades</td>
<td>22 (22.7)</td>
</tr>
<tr>
<td>Below C Grades</td>
<td>1 (1.0)</td>
</tr>
<tr>
<td>Average Number of School Days Missed Over Last 6 Months (N = 98)</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>28 (28.6)</td>
</tr>
<tr>
<td>1-2 Days</td>
<td>42 (42.9)</td>
</tr>
<tr>
<td>3-6 Days</td>
<td>22 (22.4)</td>
</tr>
<tr>
<td>7+ Days</td>
<td>6 (6.1)</td>
</tr>
<tr>
<td>Characteristic</td>
<td>N (%)</td>
</tr>
<tr>
<td>-------------------------------------------------------------------------------</td>
<td>---------------</td>
</tr>
<tr>
<td><strong>Baseline Characteristics (cont)</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Headache History</strong></td>
<td></td>
</tr>
<tr>
<td>Prior Treatments (N = 87)</td>
<td>22 (25.3)</td>
</tr>
<tr>
<td>History of Migraine (N = 87)</td>
<td>21 (24.1)</td>
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<tr>
<td>Personal History (N = 87)</td>
<td>21 (24.1)</td>
</tr>
<tr>
<td>Family History (N = 82)</td>
<td>33 (40.2)</td>
</tr>
<tr>
<td><strong>Developmental History</strong></td>
<td></td>
</tr>
<tr>
<td>Learning Disabilities (N = 88)</td>
<td>8 (9.1)</td>
</tr>
<tr>
<td>ADHD (N = 88)</td>
<td>11 (12.5)</td>
</tr>
<tr>
<td>Other Developmental Disorder (N = 88)</td>
<td>4 (4.5)</td>
</tr>
<tr>
<td><strong>Sleep/Mood History</strong></td>
<td></td>
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<tr>
<td>Anxiety (N = 88)</td>
<td>8 (9.1)</td>
</tr>
<tr>
<td>Depression (N = 88)</td>
<td>4 (4.5)</td>
</tr>
<tr>
<td>Sleep Disorder (N = 88)</td>
<td>5 (5.7)</td>
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<tr>
<td>Other Psychiatric Disorder (N = 87)</td>
<td>1 (1.1)</td>
</tr>
<tr>
<td><strong>Number of Previous Concussions (N = 88)</strong></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>57 (64.8)</td>
</tr>
<tr>
<td>1</td>
<td>21 (23.9)</td>
</tr>
<tr>
<td>2</td>
<td>5 (5.7)</td>
</tr>
<tr>
<td>3</td>
<td>3 (3.4)</td>
</tr>
<tr>
<td>4+</td>
<td>2 (2.2)</td>
</tr>
<tr>
<td><strong>Event Caused by Less Forceful Blow Than Previous Concussions (N = 28)</strong></td>
<td>13 (46.4)</td>
</tr>
<tr>
<td>Signs and Symptoms (N=98)</td>
<td>N (%)</td>
</tr>
<tr>
<td>--------------------------</td>
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</tr>
<tr>
<td><strong>Physical Symptoms</strong></td>
<td></td>
</tr>
<tr>
<td>Nausea or Vomiting</td>
<td>59 (60.2)</td>
</tr>
<tr>
<td>Balance Problems or Dizziness</td>
<td>75 (76.5)</td>
</tr>
<tr>
<td>Sensitivity to Light or Noise</td>
<td>48 (49.0)</td>
</tr>
<tr>
<td>Numbness or Tingling</td>
<td>28 (28.6)</td>
</tr>
<tr>
<td>Headaches</td>
<td>92 (93.9)</td>
</tr>
<tr>
<td>Vision Problems</td>
<td>42 (42.9)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>81 (82.7)</td>
</tr>
<tr>
<td><strong>Cognitive Symptoms</strong></td>
<td></td>
</tr>
<tr>
<td>Feeling Mentally Foggy or Slowed Down</td>
<td>59 (60.2)</td>
</tr>
<tr>
<td>Difficulty Remembering or Concentrating</td>
<td>49 (50.0)</td>
</tr>
<tr>
<td>Dazed, Stunned or Confused</td>
<td>59 (60.2)</td>
</tr>
<tr>
<td><strong>Emotional Symptoms</strong></td>
<td></td>
</tr>
<tr>
<td>Irritability</td>
<td>31 (31.6)</td>
</tr>
<tr>
<td>Sadness</td>
<td>34 (34.7)</td>
</tr>
<tr>
<td>More Emotional</td>
<td>39 (39.8)</td>
</tr>
<tr>
<td>Nervousness</td>
<td>31 (31.6)</td>
</tr>
<tr>
<td><strong>Sleep Symptoms</strong></td>
<td></td>
</tr>
<tr>
<td>Drowsiness</td>
<td>75 (76.5)</td>
</tr>
<tr>
<td>Trouble Falling Asleep</td>
<td>12 (12.2)</td>
</tr>
<tr>
<td>Sleeping More Than Usual</td>
<td>18 (18.4)</td>
</tr>
<tr>
<td>Sleeping Less Than Usual</td>
<td>9 (9.2)</td>
</tr>
<tr>
<td>Loss of consciousness</td>
<td>15 (15.3)</td>
</tr>
<tr>
<td>Seizure</td>
<td>0 (0.0)</td>
</tr>
</tbody>
</table>
Results

High incidence of PCS:
- 65% symptomatic at 1-week
- 56% symptomatic at 2-week
- 48% symptomatic at 1-month
  - 26 had a total symptom score of 3 or more at 1 month
- 46% symptomatic at 3-month
Risk factor: sex

Percentage of symptom scores >= 3 at 1 month

<table>
<thead>
<tr>
<th></th>
<th>Female</th>
<th>Male</th>
</tr>
</thead>
<tbody>
<tr>
<td>17 / 34</td>
<td>9 / 43</td>
<td></td>
</tr>
</tbody>
</table>

Odds ratio 0.27, 95% CI 0.09 – 0.79, p = 0.01
Risk factor: Any psychiatric history

Percentage of symptom scores $\geq 3$ at 1 month

- No psychiatric history: 21 / 69
- Psychiatric history: 5 / 8

Odds ratio 3.7, 95% CI 0.66 – 26.3, $p = 0.11$
Risk factor: Longest previous symptom duration

Percentage of symptom scores $\geq 3$ at 1 month

Odds ratio 2.7, 95% CI 0.68 – 11.3, $p = 0.11$
Risk factor: Age

Symptom score $\geq 3$ at 1 month

Symptom score $< 3$ at 1 month

Age (years)
MDs are poor predictors

Maximum duration prediction correct 39% (95% CI: 28%, 50%)
Relative Frequency of Parental Anxiety

Baseline 2 Weeks 1 Month 3 Months

0.0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8

Time Point

Relative Frequency

Baseline 2 Weeks 1 Month 3 Months

20-29 30-39 40-49 50+

CHEO
Baseline parental anxiety [STAI-S mean=37.0 (SD=10.4)] NOT predictive of children’s PCS

[Spearman’s rho=0.04, p=0.75]
Parental anxiety remained significantly higher in parents whose children had PCS as compared to those whose children’s symptoms resolved before 1 month.

STAI-S median=30.0(IQR: 21.8, 44.3) vs. 21(IQR: 20, 25) P<0.001 [Mann-Whitney]
Summary

• Baseline parental anxiety levels are not predictive of PCS presence.

• Parents of children with PCS remain significantly more anxious than parents whose children’s symptoms have resolved.

• Future trials must determine which components available at initial presentation best predict the time until full symptom resolution.

• Clear guidelines are needed to help guide parental management of children at high risk of suffering from persistent post-concussive symptoms at the time of injury.
Subsequent Progress

• CIHR Meeting grant
  – Experts across Canada and US
  – 2-day March 2012 meeting

• Application to CIHR for multicentre study
Planned Future Research

• Multicentre, Canada-wide prospective study
  – 1792 patients to develop a Clinical Prediction Rule
  – 800 additional patients to validate rule
  – 10 pediatric ED academic centres (PERC network)

• Knowledge-translation using TREKKK and PERC
  – Pairs academic hospitals with 30 community EDs

• Interventional trial
  – Pharmacotherapy, Behavioral interventions
“Now this is not the end. It is not even the beginning of the end, but it is, perhaps, the end of the beginning.”