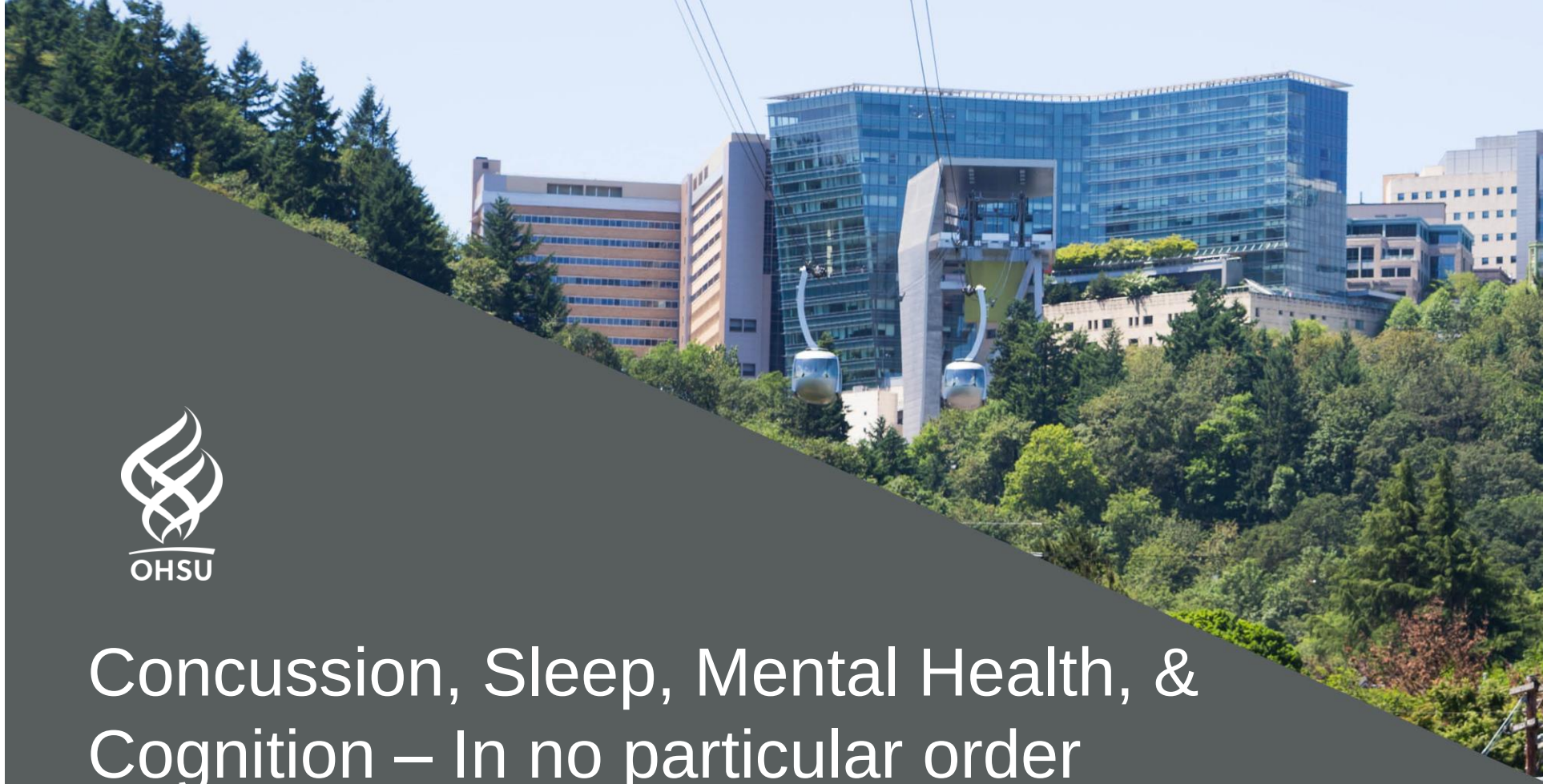

Concussion, Sleep, Mental Health, & Cognition – In no particular order

OHSU TBI Symposium – 2019

PRESENTED BY: Tyler Duffield, Ph.D.

Neuropsychology Application

- Distinguish injury from non-injury factors:
  - Neurologic vs.
  - Psychiatric vs.
  - Neurodevelopmental vs.
  - Psychosocial/Family factors

  - Or more often the case, a combination of these factors

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Epidemiology of Concussion

- CDC: approximately 1.7 million Americans sustain annual traumatic brain injury (TBI)
  - approximately 70% (i.e., 1.2 million) considered mild (mTBI)

- Several groups of authors have noted that the actual number of TBIs annually is likely much higher, as many go undiagnosed, unreported, and thus uncounted.

- Estimated total expenditures exceeding $21.5 billion per annum for mTBI alone

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Characterizing TBI

Table 1 Classification of traumatic brain injury

Mild ("concussion")	Moderate	Severe
Normal imaging	Normal or abnormal imaging	Abnormal imaging
Loss of consciousness (LOC): 0–30 min	LOC > 30 min < 24 h	LOC > 24 h
Alteration of consciousness (AOC): up to 24 h	AOC > 24 h	
Post-traumatic amnesia (PTA): 0–1 day	PTA > 1 and < 7 days	PTA > 7 days

NEUROSURGERY
THE REGISTER OF THE NEUROSURGICAL MEME

Article Contents

Concussion Guidelines Step 2: Evidence for Subtype Classification

Angela Lumba-Brown, MD ✉, Masaru Teramoto, PhD, MPH, PStat®, O Josh Bloom, MD, MPH, David Brody, MD, PhD, James Chesnutt, MD, James R Clugston, MD, MS, Michael Collins, PhD, Gerard Gioia, PhD, Anthony Kontos, PhD, Avtar Lal, PhD ... Show more

Neurosurgery, nyz332, https://doi.org/10.1093/neuros/nyz332
Published: 21 August 2019 **Article history** ▾

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- 5 subtypes:
  - Cognitive
  - Ocular-motor
  - Headache/migraine
  - Vestibular
  - Anxiety/mood

- Also considered sleep disturbance and cervical strain as associated conditions

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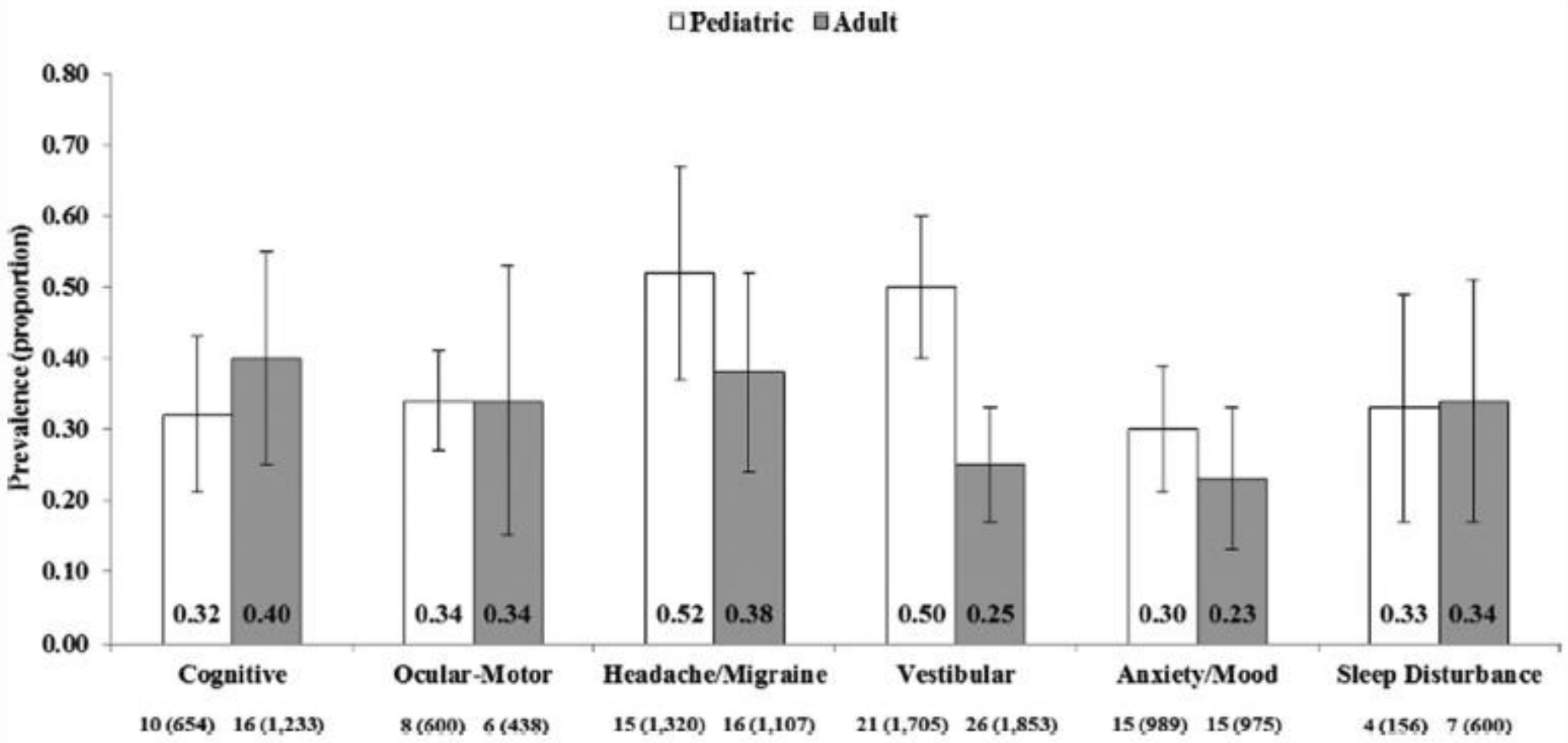

FIGURE 2. *Prevalence of concussion subtypes and sleep disturbance in concussion patients. Bars are 95% CI. Values below each subtypelassociated condition are study N (sample N).*

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Oregon Legislation

- Senate Bill 1547 (2018) takes effect in 7/2020
  - Allow a larger range of medical professions to make medical clearance decisions if they undergo an education module
  - Previously allowed:
    - Physicians, nurse practitioners, physician assistants and (neuro)psychologists
  - Now also allowed:
    - Chiropractors, naturopaths, physical therapists and occupational therapists
    - However, not athletic trainers!

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Research

Original Investigation

Point of Health Care Entry for Youth With Concussion Within a Large Pediatric Care Network

Kristy B. Arbogast, PhD; Allison E. Curry, PhD; Melissa R. Pfeiffer, MPH; Mark R. Zonfrillo, MD, MSCE; Juliet Haarbauer-Krupa, PhD; Matthew J. Breiding, PhD; Victor G. Coronado, MD, MPH; Christina L. Master, MD

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Why a Neuropsychologist in Primary Care?

- 82% (n = 6624) first visit within primary care
- 5% (n = 418) within specialty care (e.g., neurology)
- 12% (n = 947) within the ED
  - Age: Significantly higher rate of <4 y/o
  - Race/Ethnicity: 42% AA patients compared to 5% white patients
  - Payor:
    - 37% children insured by Medicaid
    - 24% self-pay
    - 7% private insurance

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Published in final edited form as:
J Pediatr. 2019 July ; 210: 13–19.e2. doi:10.1016/j.jpeds.2019.04.001.

Risk of Repeat Concussion Among Patients Diagnosed at a Pediatric Care Network

Allison E. Curry, PhD, MPH[1,2], Kristy B. Arbogast, PhD[1,2], Kristina B. Metzger, PhD, MPH[1], Ronni S. Kessler, MEd[1], Matthew J. Breiding, PhD[3], Juliet Haarbauer-Krupa, PhD[3], Lara DePadilla, PhD[3], Arlene Greenspan, DrPH[3], Christina L. Master, MD[1,4]

- 16% history of concussion at index concussion
  - 22% of those repeat within 2 years vs 15% w/o history of concussion

- 8.4% (n = 45) repeat concussion within 1 year

- 16.2% (n = 87) repeat concussion within 2 years
  - including 3.4% (n = 18) with 2 additional concussions

- Risk was 1.5 times higher ≥1 pre-existing co-occurring condition
  - Migraine/headache (28.6%)
  - Anxiety (25.0%)

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- Clinical course and symptom burden risk of repeat injury:
  - 2 times greater for one month vs. one week of symptoms
  - 2.5 times greater for ≥11 symptoms vs. 0–2 symptoms
  - Highly correlated, constructed multivariate models
    - Predicted risk increased
    - Presence of co-occurring condition non-significant

- The 2-year risk of a repeat concussion did not vary by:
  - Sex
  - Insurance payor
  - Mechanism of injury

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Concussion Severity/Grading & Return to Play (RTP)

- 14 guidelines identified by Collins et al. (1999)
- 3 emerged as the most widely used:
  - The Cantu Grading Scales
  - The Colorado Medical Society Guidelines (CMS)
  - The American Academy of Neurology guidelines (AAN)
- All use mild, moderate, severe ratings
- Generally based upon symptom duration, post-traumatic amnesia (PTA), and loss of consciousness (LOC)
- "An examination of the grading systems reveals little agreement in grading concussion severity."
  - Echemendia, Giza, and Kutcher (2015)

Defining Concussion…

Review

What is the definition of sports-related concussion: a systematic review

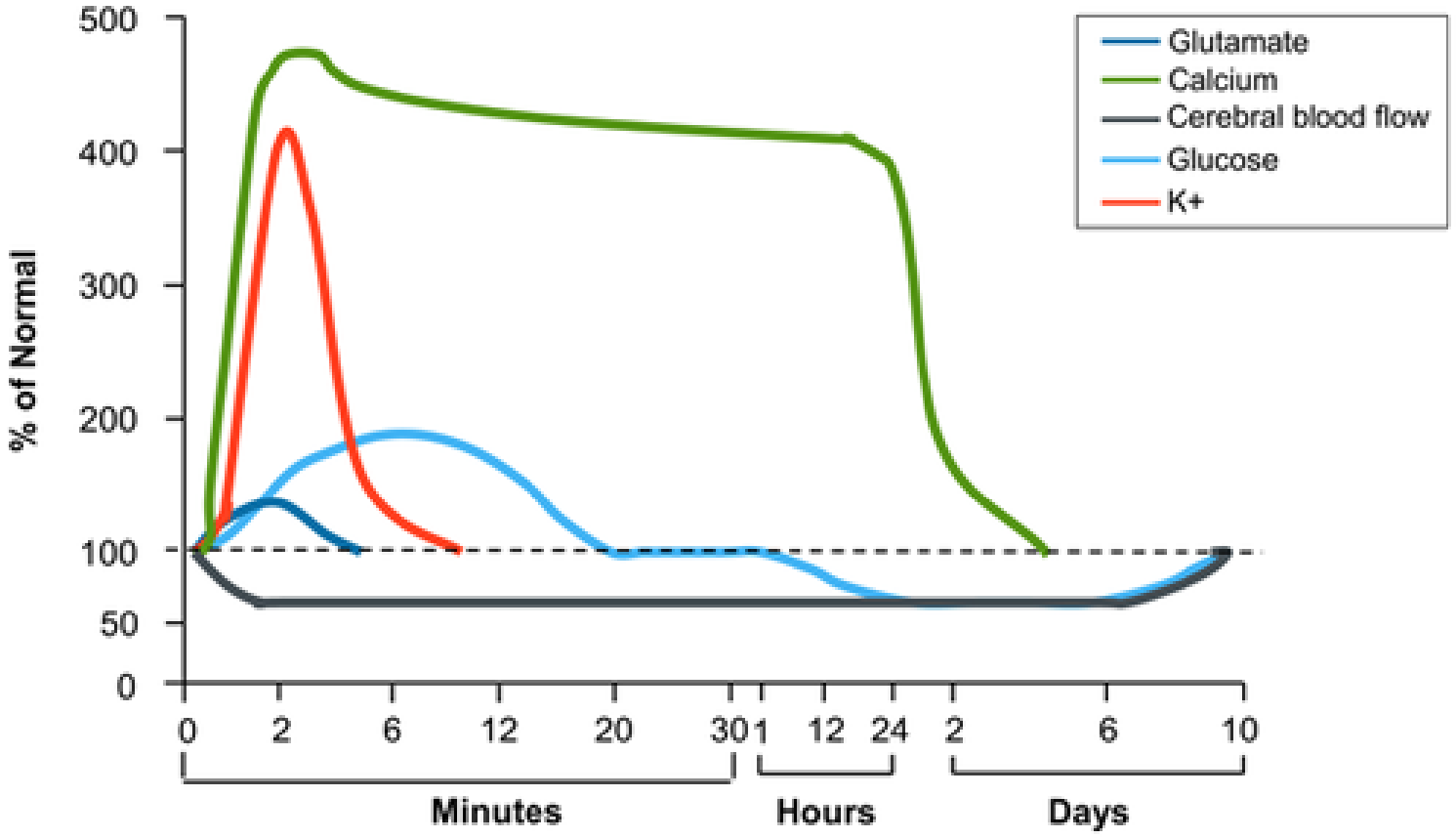
Paul McCrory,[1] Nina Feddermann-Demont,[2,3] Jiří Dvořák,[3,4] J David Cassidy,[5,6,7] Andrew McIntosh,[8,9] Pieter E Vos,[10] Ruben J Echemendia,[11,12] Willem Meeuwisse,[13] Alexander A Tarnutzer[2,3]

Defining Concussion…

- 1601 articles screened, 36 studies included
- 14 reported on criteria for SRC definitions
- 22 on biomechanical aspects of concussion
- 6 different operational definitions

- **Summary/Conclusions:** SRC is a TBI that is defined as a complex pathophysiological process affecting the brain, induced by biomechanical forces with several common features that help define its nature.

Neurometabolic Cascade Following Cerebral Concussion/mTBI



From Giza CC, et al.[10]

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Clin Sports Med. 2011 January ; 30(1): 19–vii. doi:10.1016/j.csm.2010.08.009.

Biomechanics of Concussion

David F. Meaney, PhD[a,*] and Douglas H. Smith, MD[b]

[a]Department of Bioengineering, University of Pennsylvania, 240 Skirkanich Hall, 210 South 33rd Street, Philadelphia, PA 19104-6392, USA

[b]Department of Neurosurgery, University of Pennsylvania, 105D Hayden Hall, 240 South 33rd Street, Philadelphia, PA 19104-6392, USA

- Direct or Impulsive forces
- Linear and rotational forces
- 70 – 100 g of force

- Hitting your head does <u>not</u> equate concussion
- Linear/sequential recovery process
- Physiologic recovery continues after resolution of clinical symptoms

Symptoms of concussion usually fall into four categories:

Thinking/ Remembering	Physical	Emotional/ Mood	Sleep
Difficulty thinking clearly	Headache Fuzzy or blurry vision	Irritability	Sleeping more than usual
Feeling slowed down	Nausea or vomiting (early on) Dizziness	Sadness	Sleep less than usual
Difficulty concentrating	Sensitivity to noise or light Balance problems	More emotional	Trouble falling asleep
Difficulty remembering new information	Feeling tired, having no energy	Nervousness or anxiety	

https://www.cdc.gov/traumaticbraininjury/symptoms.html

Non-specific Symptoms

- Symptoms of concussion have large overlap with:
  - Sickness (e.g., cold)
  - Poor sleep
  - Stress
  - Anxiety
  - Depression

General Symptom Resolution Trajectory

- Resolution of clinical symptoms from self-report and objective testing typically 1-2 weeks with age moderation

- Physiologic recovery as demonstrated by MRS, fMRI, qEEG, etc. is variable and outlasts clinical recovery, but latter recovery is 45 days to 3 months typically.
  - Kamins et al., 2017

- As a provider:
  - Linear/sequential recovery process, symptoms do not wax and wane
    - Consideration of premorbid/concomitant factors for prolonged recovery
    - Exception is symptom exacerbation with physical exertion in acute recovery period
  - Symptom report in acute recovery period is most reliable

Neuropsychology
2009, Vol. 23, No. 3, 283–296

0894-4105/09/$12.00 DOI:10.1037/a0015268

Neurocognitive Outcomes and Recovery After Pediatric TBI: Meta-Analytic Review of the Literature

Talin Babikian and Robert Asarnow
David Geffen School of Medicine at UCLA

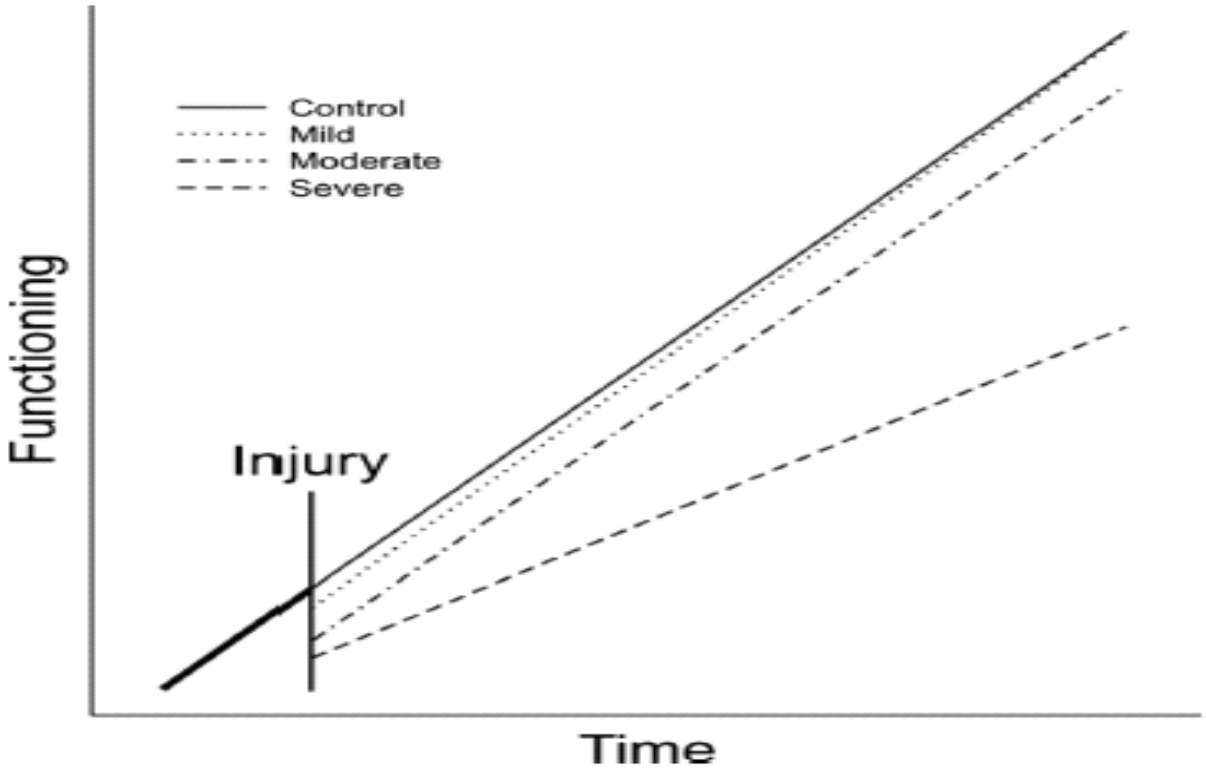

Figure 2. Summary diagram of trends in neurocognitive outcomes and recovery over time.

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Neuropsychology
2014, Vol. 28, No. 3, 321–336

0894-4105/14/$12.00 DOI: 10.1037/neu0000037

The Neuropsychological Outcomes of Concussion: A Systematic Review of Meta-Analyses on the Cognitive Sequelae of Mild Traumatic Brain Injury

Justin E. Karr, Corson N. Areshenkoff, and Mauricio A. Garcia-Barrera
University of Victoria

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- Single mTBI vs. multiple mTBI very small differences (d = .06)
  - Limited to trivial cumulative impact
- Executive functions most susceptible to multiple mTBI
  - White matter maturation occurs last in frontal lobes
- Yet to identify threshold (e.g., 5th concussion) that predicts longstanding neuropsychological impairment

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- The long term cumulative effects of concussion regarding cognition is a contentious research topic:
  - Some reviews find negligible impairments or inconclusive findings
    - Karr, Areshenkoff, & Garcia-Barrera, 2014;
    - Solomon, Ott, & Lovell, 2011;
    - Yumul & McKinlay, 2016
  - While others show long-term cognitive effects from repeated concussion primarily related to elite athlete status
    - Manley et al., 2017
    - Vos, Nieuwenhuijsen, & Sluiter, 2018

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Concussions vs. Repetitive Sub-Concussive Impacts

- High contact athletes (football) perform worse than low contact athletes (basketball, baseball, soccer, wrestling, volleyball, paddling, and cheerleading) on ImPACT testing.
  - Tsushima et al. (2016)

- High contact (lineman) youth football players perform worse than low contact (receivers and defensive backs) players on ImPACT testing.
  - Tsushima et al. (2017)

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Concussions vs. Repetitive Sub-Concussive Impacts

- Exposure to contact football before or after age 12
  - >2 times increased odds for problems with behavioral regulation (e.g., easily angered), apathy, and executive function (e.g., organizing/planning)
  - >3 times increased odds for depression
    - Alosco et al., 2017

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1-time NP Consultation as PCS Intervention

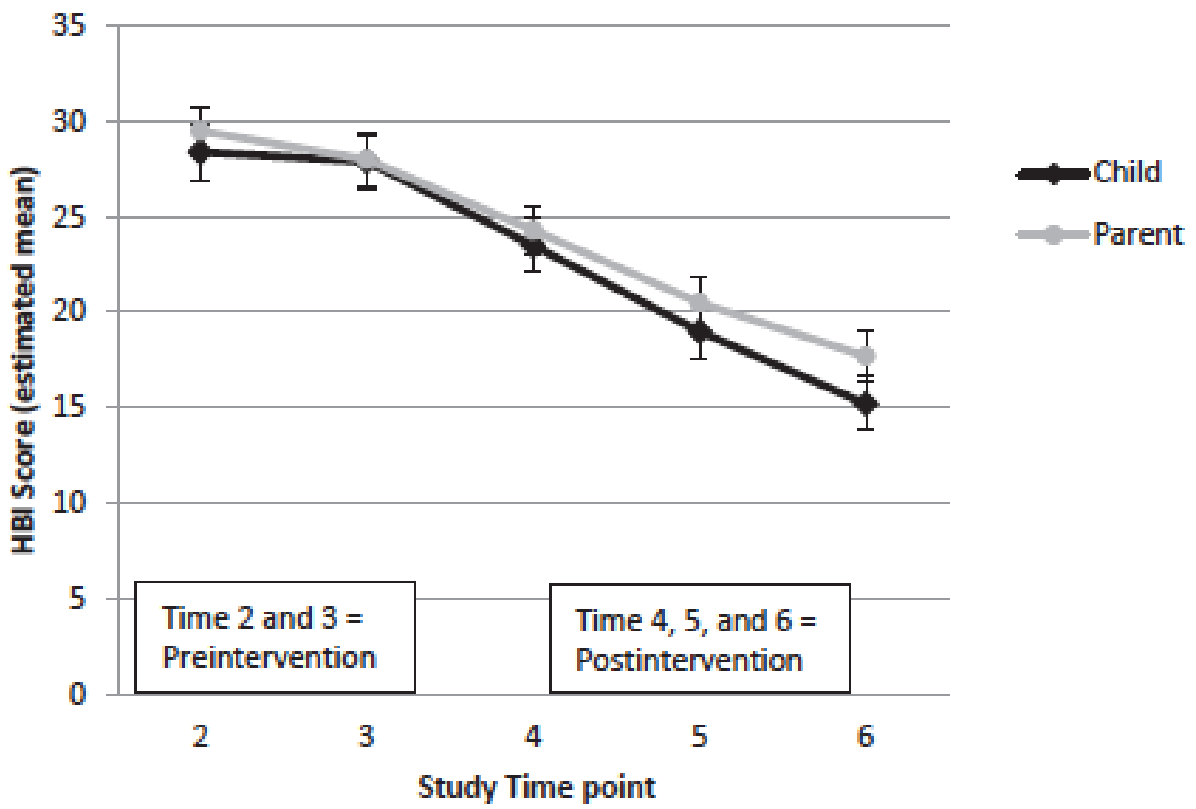

Figure 2. Child and parent estimated postconcussive symptom mean scores across time for the HBI.

Kirkwood et al., 2016

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Journal of Neurotrauma
© Mary Ann Liebert, Inc.
DOI: 10.1089/neu.2016.4765

The effect of concussion or mild traumatic brain injury on school grades, national exam scores and school attendance: A systematic review

Adrian Rozbacher A BSc[1], Erin Selci Bsc[3,6], Jeff LeiterPhD[2,5,7], Michael Ellis MD

Academic Outcomes in High-School Students after a Concussion: A Retrospective Population-Based Analysis

Kelly Russell[1,2,3□*], Michael G. Hutchison[4], Erin Selci[1,2], Jeff Leiter[3,5], Daniel Chateau[6], Michael J. Ellis[2,3,7]

Journal of the International Neuropsychological Society (2016), **22**, 1038–1049.

doi:10.1017/S1355617716000916

Applying an Evidence-Based Assessment Model to Identify Students at Risk for Perceived Academic Problems following Concussion

Danielle M. Ransom,[1] Alison R. Burns,[2,3] Eric A. Youngstrom,[4] Christopher G. Vaughan,[2,3] Maegan D. Sady,[2,3] AND Gerard A. Gioia[2,3]

[1]University of Miami Miller School of Medicine, Miami, Florida
[2]Children's National Health System, Washington, DC
[3]George Washington University School of Medicine, Washington, DC
[4]University of North Carolina, Chapel Hill, North Carolina

(Received March 14, 2016; Final Revision October 10, 2016; Accepted October 10, 2016)

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- Minimal impact on school grades, national exam scores, and graduation rates at a group level.
- PCS symptoms and self-reported executive dysfunction more predictive of poor school performance than cognitive testing.
- Concussion team at school still very important for reintegration into school following rest.
- How much does missed school matter?

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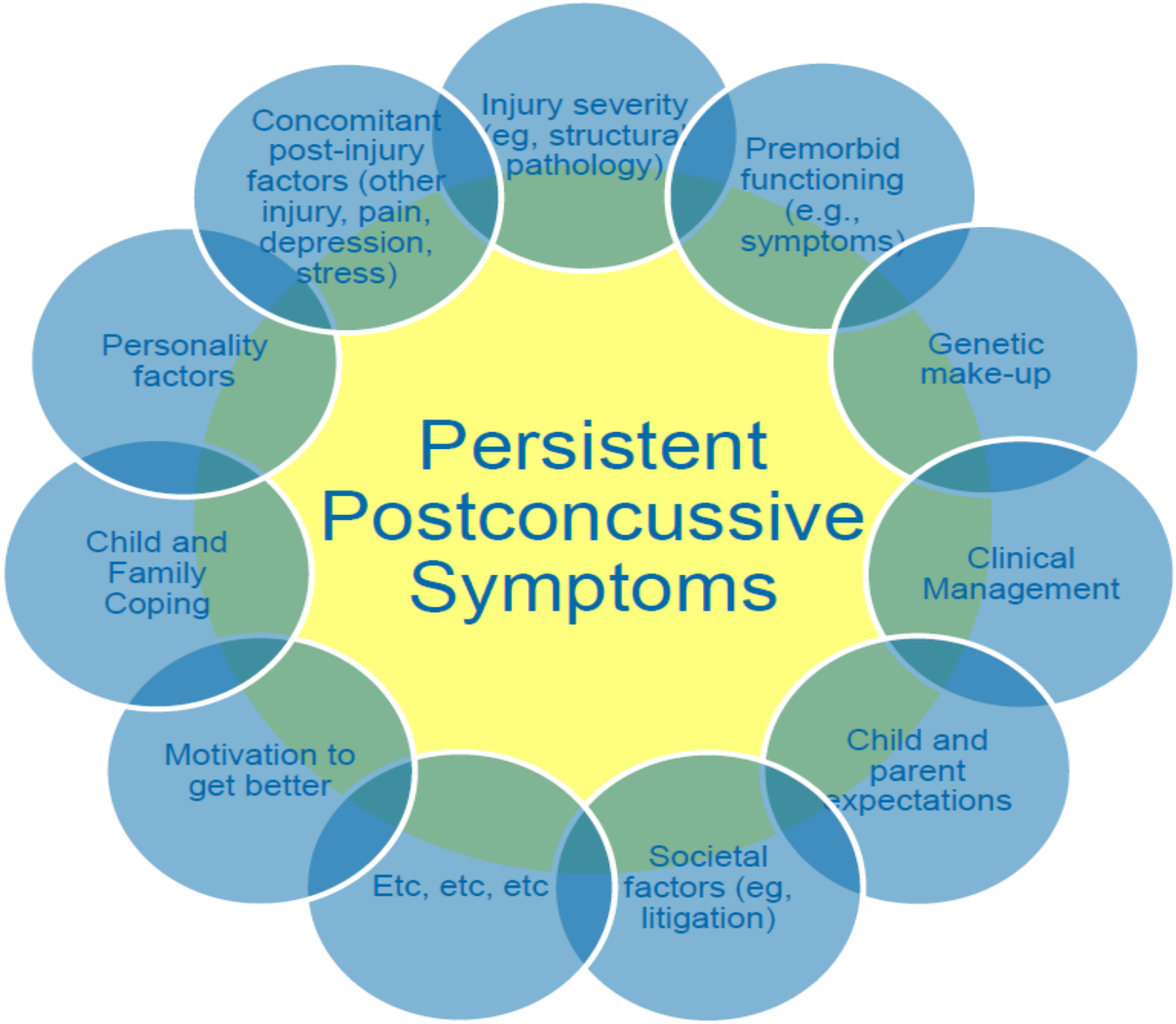

Adapted from Iverson et al. (2008)

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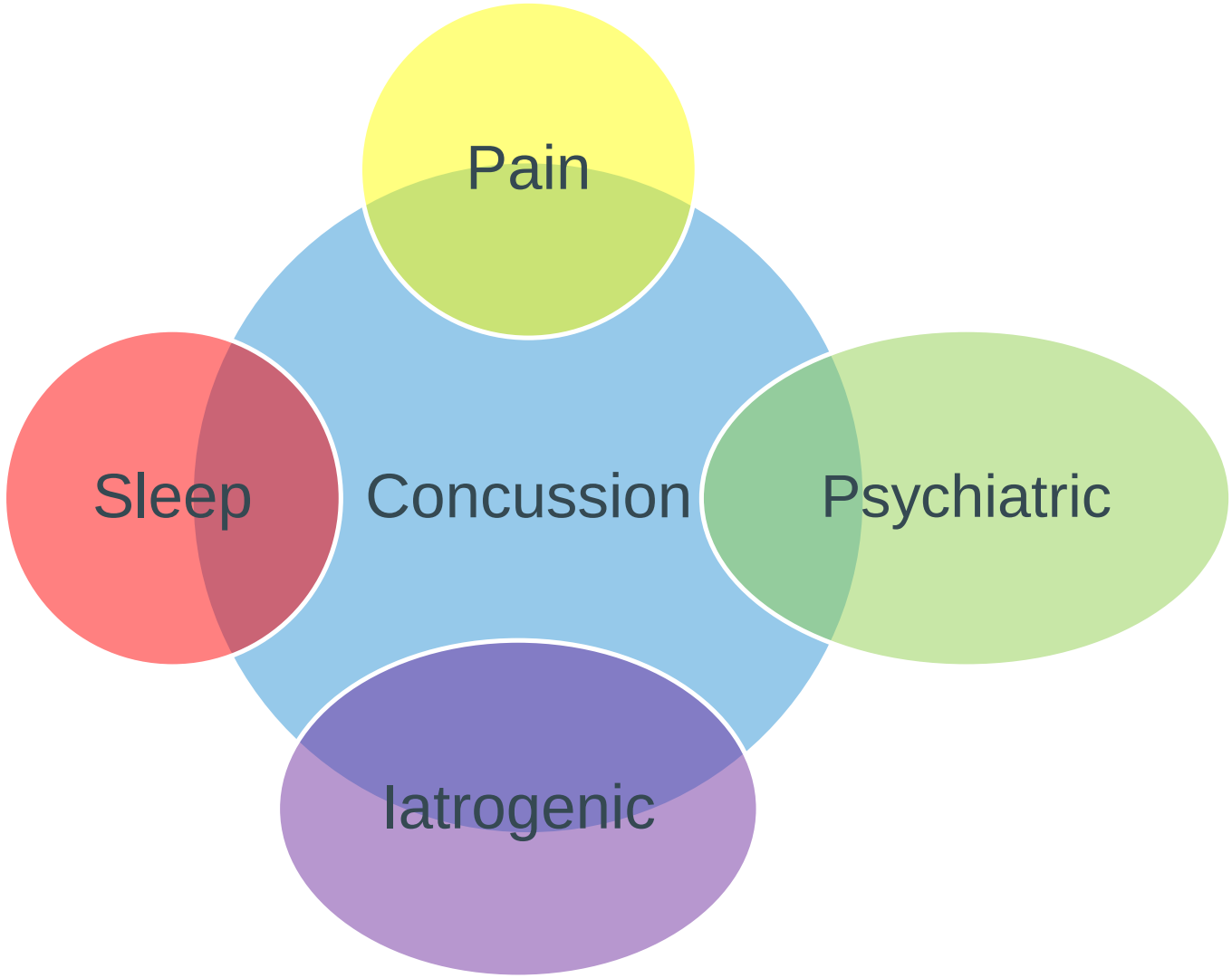

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Review

OPEN ACCESS

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 Solomon[7]

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Best Predictors of Outcome in Concussion

- **Age**: mixed findings
- **Sex**: mixed findings
- **Prior Concussions**: mixed findings
- **Migraine**: mixed findings
- **ADHD, LD, etc.:** minimal support
- **LOC**: minimal support
- **PTA**: minimal support
- **Headache (post-injury)**: worse outcomes
- **Total symptom report**: strong evidence of worse outcomes
- **Mental health history**: strong evidence of worse outcomes

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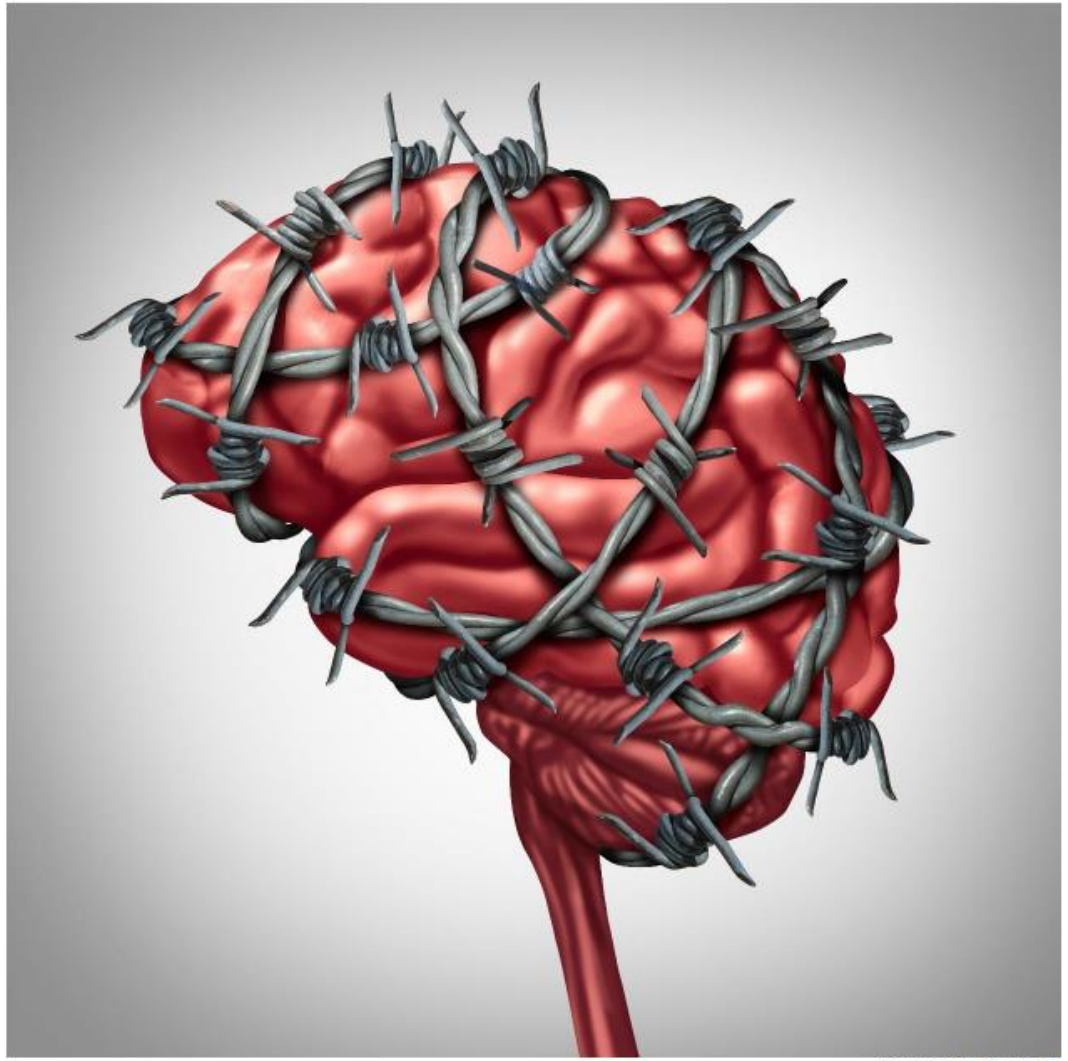
Cerebrum, December 2016

Finding the Hurt in Pain

By Irene Tracey, Ph.D.



Source: Shutterstock

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- Co-morbid problems like depression, anxiety, and sleeplessness are inherent in chronic pain.

- The brain responds to ‘painful’ or nociceptive events in a host of brain regions/ circuits in a flexibly accessible manner:
  - Sensory
  - Discriminatory
  - Emotional/affective
  - Cognitive/decision making
  - Brainstem modulatory
  - Motor

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- **People have higher ratings of pain when sad**
  - Higher activations in emotional regulatory circuitry (e.g., orbitofrontal cortex)

➔

    - higher pain processing activation (e.g. amygdala, insula, inferior frontal gyrus, anterior cingulate).

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- **People have higher ratings of pain when anxious**
  - hippocampus/entorhinal complex with interactions to the anterior insula and mid anterior cingulate

➔

  - higher pain processing activation (e.g. amygdala, insula, inferior frontal gyrus, anterior cingulate).

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Depression, anxiety, and threat act as a physiological amplifier for pain.

- **Descending Pain Modulatory System (DPMS)**
  - Inhibitory and facilitatory modulatory action largely based upon expectation
  - Healthy controls given intravenous painkiller during brain-imaging study while given painful stimuli throughout.
    - Hidden injection
    - Positive expectation
    - Negative expectation

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Original Investigation

Factors Associated With Concussion-like Symptom Reporting in High School Athletes

Grant L. Iverson, PhD; Noah D. Silverberg, PhD; Rebekah Mannix, MD, MPH; Bruce A. Maxwell, PhD; Joseph E. Atkins, PhD; Ross Zafonte, DO; Paul D. Berkner, DO

IMPORTANCE Every state in the United States has passed legislation for sport-related concussion, making this health issue important for physicians and other health care professionals. Safely returning athletes to sport after concussion relies on accurately determining when their symptoms resolve.

OBJECTIVE To evaluate baseline concussion-like symptom reporting in uninjured adolescent student athletes.

DESIGN, SETTING, AND PARTICIPANTS In this cross-sectional, observational study, we studied 31 958 high school athletes from Maine with no concussion in the past 6 months who completed a preseason baseline testing program between 2009 and 2013.

RESULTS Symptom reporting was more common in girls than boys. Most students with preexisting conditions reported one or more symptoms (60%-82% of boys and 73%-97% of girls). Nineteen percent of boys and 28% of girls reported having a symptom burden resembling an *International Classification of Diseases, 10th Revision* (*ICD-10*) diagnosis of postconcussional syndrome (PCS). Students with preexisting conditions were even more likely to endorse a symptom burden that resembled PCS (21%-47% for boys and 33%-72% for girls). Prior treatment of a psychiatric condition was the strongest independent predictor for symptom reporting in boys, followed by a history of migraines. For girls, the strongest independent predictors were prior treatment of a psychiatric condition or substance abuse and attention-deficit/hyperactivity disorder. The weakest independent predictor of symptoms for both sexes was history of prior concussions.

CONCLUSIONS AND RELEVANCE In the absence of a recent concussion, symptom reporting is related to sex and preexisting conditions. Consideration of sex and preexisting health conditions can help prevent misinterpretation of symptoms in student athletes who sustain a concussion.

JAMA Pediatr. doi:10.1001/jamapediatrics.2015.2374
Published online October 12, 2015.

Author Affiliations: Department of Physical Medicine and Rehabilitation, Harvard Medical School, Boston, Massachusetts (Iverson, Zafonte); Spaulding Rehabilitation Hospital, Boston, Massachusetts (Iverson); MassGeneral Hospital for Children Sports Concussion Program, Boston (Iverson, Zafonte); Red Sox Foundation and Massachusetts General Hospital Home Base Program Boston (Iverson, Zafonte); Division of Physical Medicine and Rehabilitation, University of British Columbia, and GF Strong Rehab Centre, Vancouver, British Columbia, Canada (Silverberg); Division of Emergency Medicine, Boston Children's Hospital, Boston, Massachusetts (Mannix); Department of Computer Science, Colby College, Waterville, Maine (Maxwell); Department of Psychology, Colby College, Waterville, Maine (Atkins); Health Services and Department of Biology, Colby College, Waterville, Maine (Berkner).

Corresponding Author: Grant L. Iverson, PhD, Center for Health and Rehabilitation, Department of Physical Medicine and Rehabilitation, Harvard Medical School, 79/96 13th St, Charlestown Navy Yard, Charlestown, MA 02129 (giverson@mgh.harvard.edu).

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The Database

- 32,855 student athletes from the state of Maine
- Age: 13-18
- No athlete reported sustaining a concussion in the past 6 months.

Iverson et al., 2015

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ICD-10 Criteria for Postconcussional Syndrome

- Must endorse symptoms in at least 3 domains
  - Physical
  - Emotional
  - Cognitive
  - Insomnia

  - Other domains not considered: Excessive worry over symptoms and intolerance for alcohol.

Iverson et al., 2015

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What percentage of boys and girls meet ICD-10 Criteria for a Mild Post-Concussional Syndrome During Baseline Preseason Testing?

- Boys = 19.7%
- Girls = 28.2%

Iverson et al., 2015

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What percentage of boys and girls meet ICD-10 Criteria for a Moderate-Severe Post-Concussional Syndrome During Baseline Preseason Testing?

- Boys = 4.4%
- Girls = 7.2%

Iverson et al., 2015

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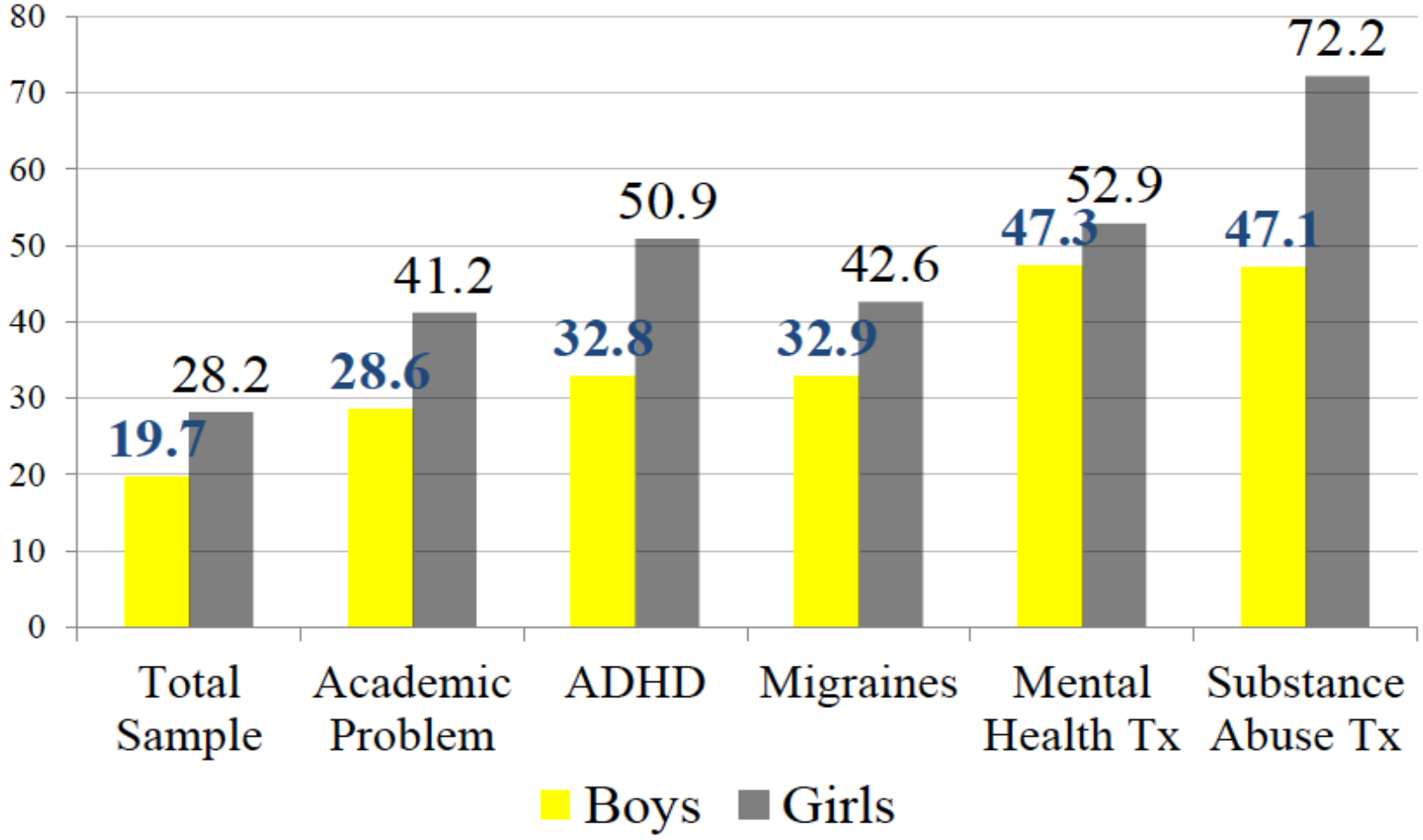
Percentages of Uninjured Athletes Meeting ICD-10 Criteria for a Mild Postconcussional Syndrome



Iverson et al., 2015

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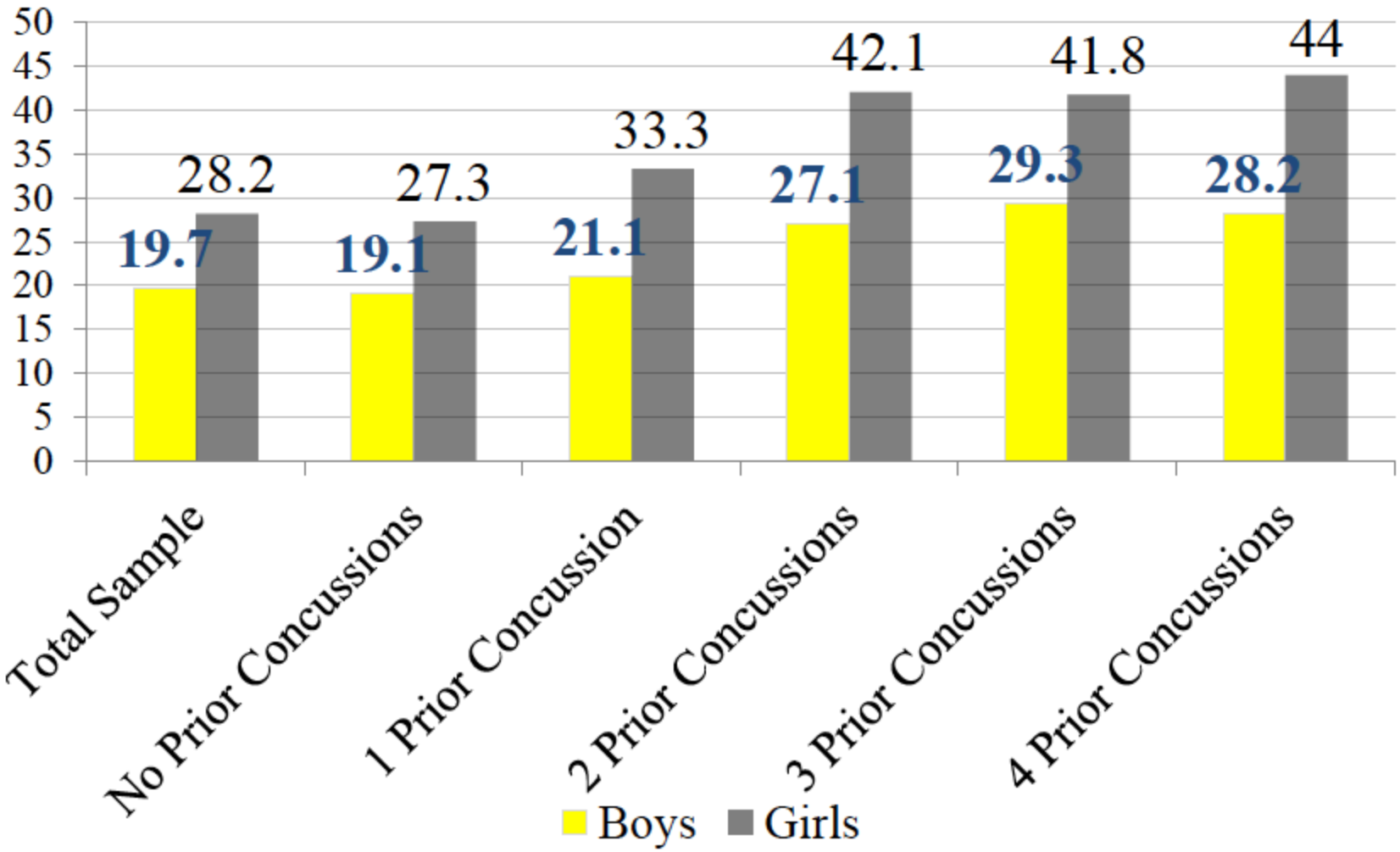
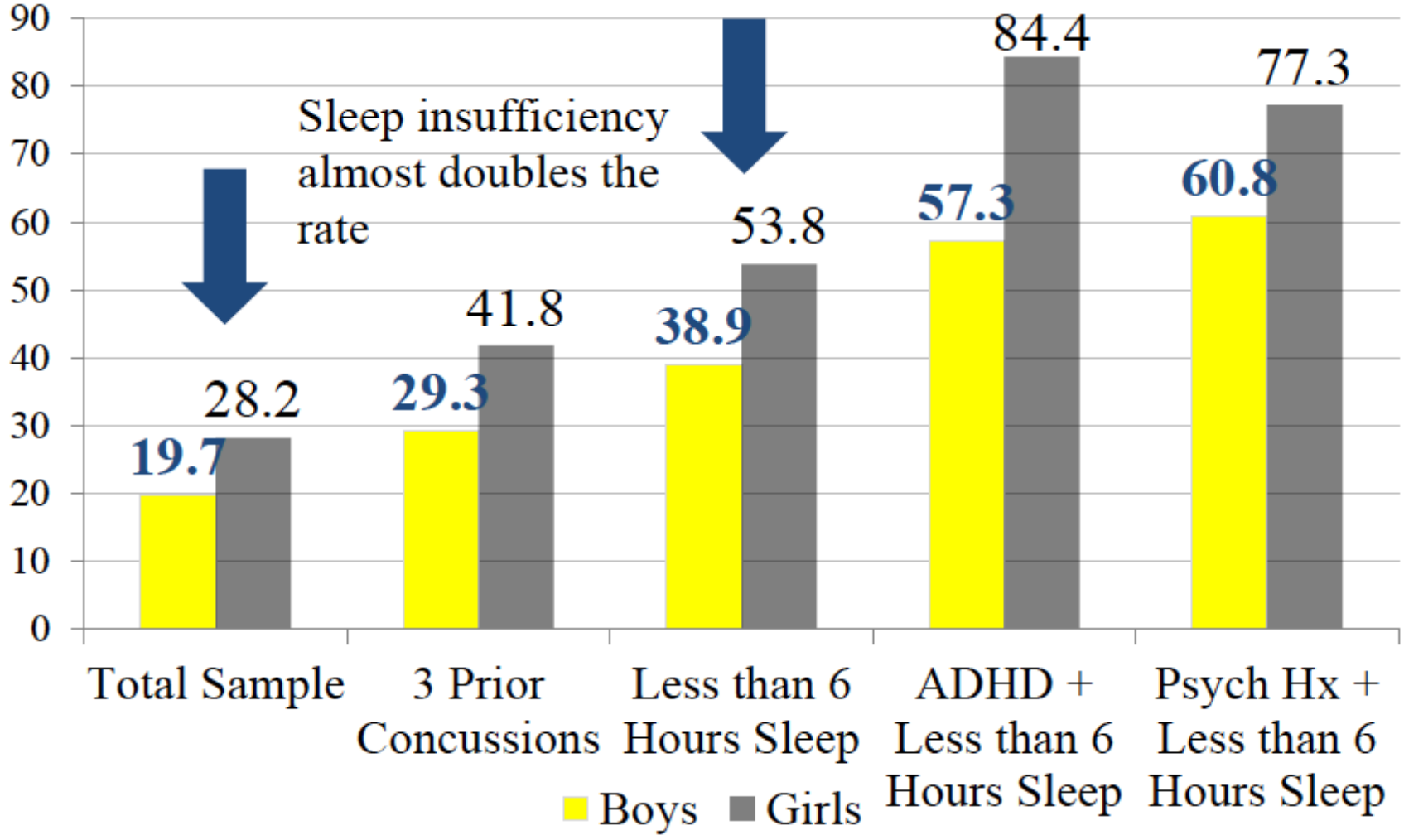
Percentages of Athletes Meeting ICD-10 Criteria for a Mild Postconcussional Syndrome



Iverson et al., 2015

Percentages of Athletes Meeting ICD-10 Criteria for a Mild Postconcussional Syndrome



Iverson et al., 2015

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Article

Prolonged Activity Restriction After Concussion: Are We Worsening Outcomes?

Marc DiFazio, MD[1], **Noah D. Silverberg, PhD**[2,3], **Michael W. Kirkwood, PhD**[4,5], **Raquel Bernier, MD**[1], **and Grant L. Iverson, PhD**[6,7,8,9]

Clinical Pediatrics
2016, Vol. 55(5) 443–451

DOI: 10.1177/0009922815589914

cpj.sagepub.com

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- The most methodologically rigorous studies to date have not demonstrated benefit of an initial period of 5 to 6 days of complete rest over an earlier return to activity.

- Authors could not find studies suggesting that thinking, reading, or studying cause neurometabolic demands, or changes in the brain that could be harmful.

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Harmful Effects?

- Nocebo effect
  - Remember the DPMS
  - Priming effects
- Activity Restriction Model of Depression
- Physical Deconditioning

- **Conclusion**: Gradual/graded return to normal life activities following 2-3 days in most cases.

- Similarly, a more recent systematic review concluded 24-48 hours of cognitive and physical rest is a appropriate for most patients.
  - Schneider et al., 2017

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Additional Psychological Factors Related to Recovery

- **Coping Style/Illness Perception**
  - Anderson & Fitzgerald, 2018

- **Good Old Days Bias**
  - The tendency to underestimate pre-injury problems and overestimate pre-injury health.
    - Brooks et al., 2014

- **Cogniphobia**
  - Avoidance of mental exertion out of a fear of developing or exacerbating a headache.
    - Silverberg, Iverson, & Panenka, 2017

- **Diagnosis Threat**
  - Form of stereotype threat - reduced cognitive/academic performance due to beliefs or reminders following a neurologic injury.
    - Fresson, Dardenne, & Meulemans 2018

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Risk Factors for Depression in College

- **College Students:**
  - transition into a post-secondary school
  - homesickness
  - academic pressures of meeting grade requirements
  - worries about financial security
    - Thurber & Walton, 2012

- **Collegiate Student-Athlete**
  - injury
  - involuntary career termination
  - performance expectations
  - possibly overtraining
    - Wolanin, Gross, & Hong, 2015

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Review

Traumatic Brain Injury, Sleep Disorders, and Psychiatric Disorders: An Underrecognized Relationship

Anne M. Morse [1,*] and David R. Garner [2]

[1] Janet Weis Children's Hospital, Department of Pediatric Neurology and Sleep Medicine, Geisinger Medical Center, MC 14-12, 100 N Academy Blvd, Danville, PA 17822, USA

[2] Department of Pediatrics, Geisinger Medical Center, Danville, PA 17822, USA; Drgarner@geisinger.edu

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Received: 28 December 2017; Accepted: 5 February 2018; Published: 15 February 2018

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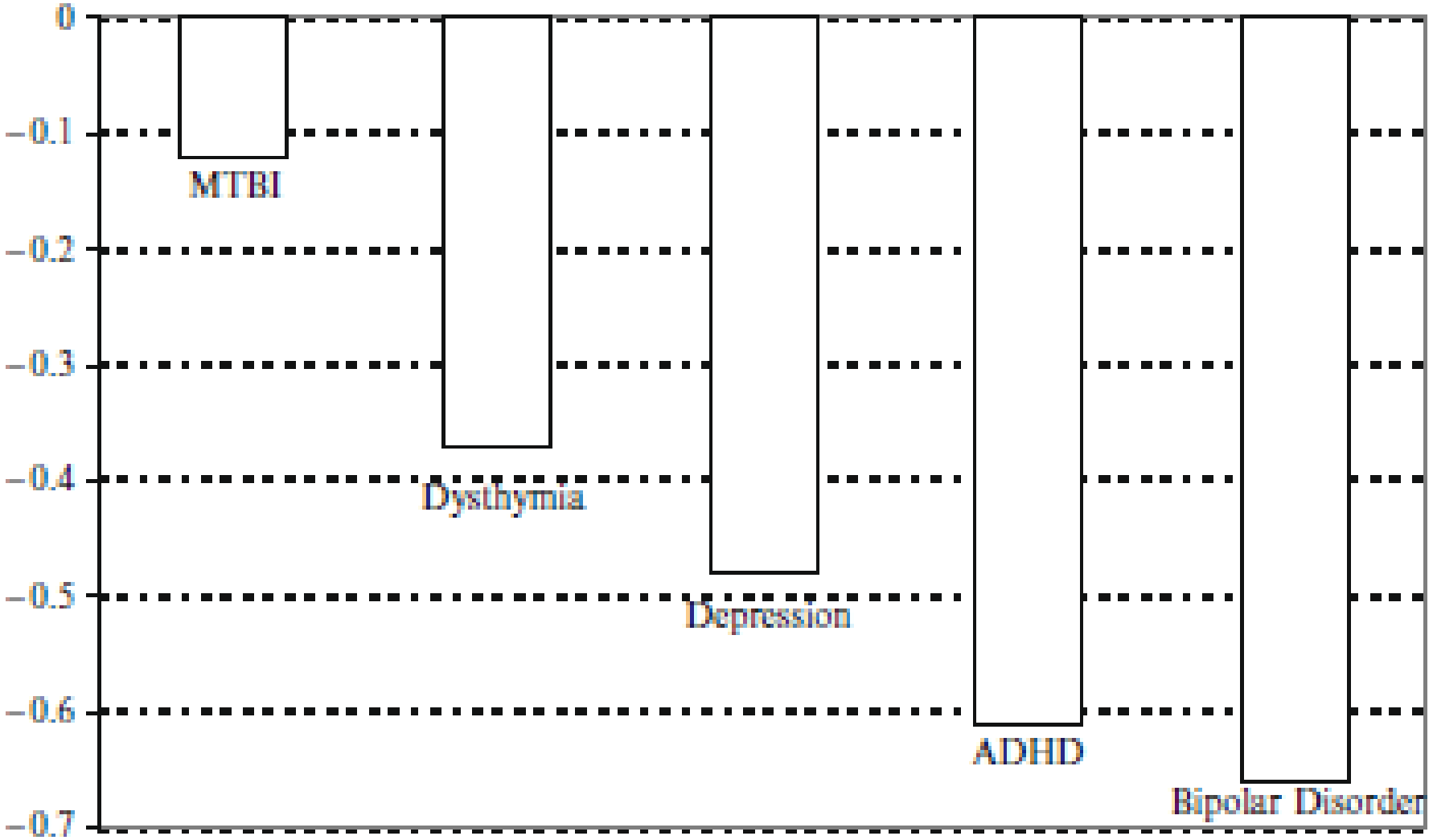

Fig. 22.3 Effects of MTBIs and various psychiatric conditions on neuropsychological functioning. MTBI (Binder et al. 1997), 11 studies, $n=314$ MTBI, $n=308$ controls; Dysthymia, Depression, and Bipolar Disorder (Christensen et al. 1997), 3 comparisons for dysthymia, 97 comparisons for depression, and 15 comparisons for bipolar disorder; ADHD (Frazier et al. 2004), based on Full Scale IQ, 123 studies

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Sleep and Mental Health – Blake et al., 2017

- 30-40% of US youth experience inadequate sleep
- 30% have a sleep disorder
  - Insomnia
  - Delayed Sleep Phase Disorder
- Pervasive in psychiatric disorders
  - Share highest % of connected symptoms within all symptoms of DSM-IV

- May precipitate and maintain psychiatric conditions

  - ↓ Sleep ➔ ↑ Anxiety & Depression

MORE THAN

  - ↑ Anxiety & Depression ➔ ↓ Sleep

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Sleep and General Health

- Sleep deprivation increases risk of:
  - Illness susceptibility (4x increase of cold less than 6 hours)
  - Orthopedic injuries
  - <8 hours 2x increase in concussion rates in youth
  - Lifestyle disease (e.g., diabetes, obesity, heart disease)
  - Dementias
    - 60% of Alzheimer's patients have sleep disorder that preceded diagnosis by several years
  - Mortality
    - Decades decrease in life expectancy with chronic sleep deprivation

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Sleep and TBI risk

- Sleep deprivation hinders:
  - Reaction time
  - Judgment
  - Balance
  - Coordination
  - Proprioception
  - General cognition (learning, memory, problem solving, etc.)

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College Athlete Sleep Estimates

- Athletic-academic schedules/demands (e.g., travel schedule), approximate to two full time jobs

- Collegiate athlete social and physical environments are not conducive to promoting healthy sleep

- American College Health Association survey data of 14,000 athletes (2015-2017) note 60% report insufficient sleep and daytime fatigue three or more days a week
    - Kroshus et al., 2019

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College Athlete Sleep Estimates

- Recent study of 628 collegiate athletes, Mah et al. (2018) found:
  - 42% experience poor sleep quality (PSQI ≥ 5)
  - 39% regularly obtain inadequate sleep (<7 hrs during week)
  - 51% report high levels of daytime sleepiness (ESS ≥ 10)
  - 1st and 2nd year athletes report highest daytime sleepiness
  - Sleep quality better during travel vs. home

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Sleep Disturbance Following Concussion

- 30-70% report sleep difficulties 1-3 weeks post-injury
  - Hypersomnia is common
- Following acute phase of recovery
  - 30% report insomnia
  - Approximately 40% can have circadian rhythm shift (delayed)
  - 40-70% report fatigue
  - 30% report sleep apnea
- The pattern and time frame of sleep disturbance may vary substantially among patients who have sustained a concussion.
  - Mosti, Spiers, & Kloss, 2016

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Sleep and Concussion

- Subjective sleep complaints are 3x more likely to develop concomitant headaches in the first 6 weeks following an MTBI.
  - Also more likely to have depressive symptoms and irritability.
    - Chaput et al., 2009

- Sleep disturbance in the acute TBI period was associated with increased symptoms of depression, anxiety and apathy (mild TBI group only) 12 months post-injury.
    - Rao et al., 2014

- In fact, sleep disturbance, even in the acute post-TBI period, predicted the development of anxiety and depression in the chronic period for all severities of TBI.
    - Morse & Garner, 2018

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REVIEW

Sleep-Wake Disturbances After Traumatic Brain Injury: Synthesis of Human and Animal Studies

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Human	Shared Findings	Animal
Neuropathology ↓Serum and salivary melatonin[66,123,124] ↓Serotonin in dorsal raphe[106] ↓Norepinephrine in locus coeruleus[106] ↑Metabolic glutamate in injured cortex[129] ↓Histaminergic neurons in hypothalamus[120] ↓MCH in hypothalamus[120]	↓Orexin in hypothalamus[6,118,120,155,165,168]	↓Acetylcholine in basal forebrain[168] ↓Synaptic glutamate in injured cortex[127,128,130] ↑Thalamic microglial activation[169] ↑Astrocytosis[169] ↑Pro-inflammatory cytokines[170] –Histaminergic neurons in hypothalamus[168] –MCH in hypothalamus[155]
Neurophysiology (EEG) ↓Number of K-complexes[99] ↑Sleep spindles during slow-wave sleep[99] –/↑NREM sleep time[52,96] ↑/↓Delta power[52,94-97,240]	↑Slow-waves during wakefulness[100]	↓Theta:Alpha ratio[100] –/↓NREM sleep time[161] ↑Delta power[160]
Sleep-Wake Phenotype ↓Sleep efficiency[94,95,239] ↑/↓Sleep latency[52,100,94,95,99] ↓REM sleep latency[239]	↑Sleep fragmentation[155,162,165,169,174] ↑Sleep time[52,155,160,162,165,167,168,170,172]	↑Number of sleep bouts[155,160] ↓Duration of wake bouts[160]
Treatment Options CBT for insomnia[187,188,220] Bright light therapy[222] Melatonin/Ramelteon[233] Modafinil/Armodafinil[229-232] Benzo/non-benzodiazepines[225] Aerobic exercise[223,224] Acupuncture[221]	*None*	Branched chain amino acids[165] gamma-Hydroxybutyric acid[162]

Figure 1—Summary table showing the findings from animal and human studies with regard to several levels of analysis: neuropathology, neurophysiology, sleep–wake phenotype, and treatment options. Findings that are shared between animal and human studies are depicted in the center "Shared Findings" column. An absence of any Shared Findings in the Treatment category suggests that there is opportunity to move potential treatments identified in animal studies into the human condition. Abbreviations: EEG, electroencephalography; NREM, nonrapid eye movement sleep; REM, rapid eye movement; MCH, melanin-concentrating hormone; CBT, cognitive–behavioral therapy.

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Consultation & Management Model

Brain Inj. 2015 ; 29(2): 195–206. doi:10.3109/02699052.2014.965210.

Multimodal Evaluation and Management of Children with Concussion: Using our heads and available evidence

Gerard A. Gioia, Ph.D
Division of Pediatric Neuropsychology, Children's National Health System, Departments of Pediatrics and Psychiatry & Behavioural Medicine, George Washington University School of Medicine

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Generally

- Set positive and realistic expectation!
  - Expectancy effect
  - Importance of early education – well validated intervention
  - Null effects for cognitive rehabilitation per 2 systematic reviews and empirical support for vision therapy is tenuous
- Resume normal activities as soon as reasonably possible, including light exercise!
- Reinforce progress!
  - Prolonged symptom pacing recommendations = iatrogenic

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JAMA | Original Investigation

Association Between Early Participation in Physical Activity Following Acute Concussion and Persistent Postconcussive Symptoms in Children and Adolescents

Anne M. Grool, MD, PhD; Mary Aglipay, MSc; Franco Momoli, PhD; William P. Meehan III, MD; Stephen B. Freedman, MDCM, MSc; Keith Owen Yeates, PhD; Jocelyn Gravel, MD; Isabelle Gagnon, PhD; Kathy Boutis, MD; Willem Meeuwisse, MD, PhD; Nick Barrowman, PhD; Andrée-Anne Ledoux, PhD; Martin H. Osmond, MDCM; Roger Zemek, MD; for the Pediatric Emergency Research Canada (PERC) Concussion Team

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- Prospective, multicenter cohort study (9 EDs)
  - 5-18 cohort (average was 12)
  - 2413 participants (40% female)

- Physical activity participation and PCS severity were rated using standardized questionnaires in the ED and at days 7 and 28 post-injury.

- Physical activity within 7 days of acute injury compared with no physical activity was associated with reduced risk of PCS at one month.

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JAMA Pediatrics | Original Investigation

Early Subthreshold Aerobic Exercise for Sport-Related Concussion A Randomized Clinical Trial

John J. Leddy, MD; Mohammad N. Haider, MD; Michael J. Ellis, MD; Rebekah Mannix, MD; Scott R. Darling, MD; Michael S. Freitas, MD; Heidi N. Suffoletto, MD; Jeff Leiter, PhD; Dean M. Cordingley, MSc; Barry Willer, PhD

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- N = 103
  - (aerobic exercise: n = 52; 24 female [46%]; stretching, n = 51; 24 female [47%])

- Exercise group seen a mean (SD) of 4.9 (2.2) days after SRC
- Stretching group seen a mean (SD) of 4.8 (2.4) days after SRC

- No differences in age, sex, previous concussions, time from injury, initial symptom severity score, or initial exercise treadmill test and physical examination results.

- Exercise recovered in a median of 13 (IQR = 10-18.5) days
- Stretching recovered in a median of 17 (IQR = 13-23) days
  - (P = .009 by Mann-Whitney test)

- Nonsignificant lower incidence of delayed recovery in the aerobic exercise group (2 participants [4%] in the aerobic group vs 7 [14%] in the placebo group; P = .08).

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What is CBT-I?

- Cognitive–behavioral sleep interventions are short-term, multicomponent, goal-oriented psychotherapeutic treatments. They aim to modify the patterns of thinking and behavior that may be underlying an individuals sleep disturbance, such as: poor sleep hygiene, irregular sleep–wake schedules, delayed bedtimes, pre-sleep hyperarousal, and maladaptive sleep-related cognitions.

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CBT-I Efficacy for Adults

- 87 RCTs, comparing 118 treatments (3724 patients) to non-treated controls (2579 patients) using at least one component of CBT-I

- **Overall, the interventions had significant effects on:**
  - Insomnia severity index (g = 0.98)
  - Sleep efficiency (g = 0.71)
  - Pittsburgh sleep quality index (g = 0.65)
  - Wake after sleep onset (g = 0.63)
  - Sleep onset latency (SOL; g = 0.57)
  - Number of awakenings (g = 0.29)
  - Sleep quality (g = 0.40)
  - Total sleep time (g = 0.16)
    - Van Straten et al., 2018

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Neuropsychology Service in Family Med/Sports Med

- **Evaluation**:
  - Half day and full day evaluations
    - Concussion/mTBI
    - Neurodevelopmental disabilities
    - General neurological conditions

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OHSU Concussion Program

- **Concussion Treatment Clinic**:
  - The concussion follow-up clinic: 3-6 sessions
  - Partnership of ATC, NP, Sports MD
    - ATC: treadmill test, sensory/motor intervention
    - NP: sleep protocol, behavioral activation, exposure

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	5/3/2017	5/9/2017	5/16/2017	6/6/2017
PHQ-15 (Somatization Symptoms)	17 (Severe)	13 (Moderate)	8 (Mild)	3 (No clinical concern)
GAD-7 (Anxiety Symptoms)	13 (Moderate)	10 (Moderate)	9 (Mild)	2 (No clinical concern)
PHQ-9 (Depressive Symptoms)	21 (Severe)	20 (Severe)	11 (Moderate)	2 (No clinical concern)
PSQI (Sleep Quality)	9 (>poor quality)	-	-	6 (>5 poor quality)

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	6/12/2017	6/19/2017	7/11/2017
PHQ-15 (Somatization Symptoms)	11(Moderate)	10 (Moderate)	7 (Mild)
GAD-7 (Anxiety Symptoms)	8 (Mild)	6 (Mild)	2 (No clinical concern)
PHQ-9 (Depressive Symptoms)	9 (Mild)	4 (No clinical concern)	2 (No clinical concern)
PSQI (Sleep Quality)	8 (>5 poor quality)	-	6 (>5 poor quality

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Screening Tools

- Insomnia
  - PSQI or ISI
- Daytime Sleepiness
  - ESS
  - ESS for Children and Adolescents
- Sleep Apnea
  - STOP-BANG
- Sleep Disturbance Scale for Children (6-15 y/o)
- Somatic complaints, Anxiety, Depression
  - PHQ-SADS
- PTSD
  - PCL-5

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Practical take homes

- Pre-injury mental health and sleep quality will predict outcomes
- High acute symptom burden (particularly headache), onset of sleep dysregulation and/or activity withdrawal will prolong recovery
  - Dr. Herring's perspective on disability
- Early exercise and sleep intervention will likely improve clinical outcome
- Returning to normal daily activities (physical, recreational, social) as soon as possible (2-3 days), often gradually/incrementally, will likely improve clinical outcome

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Practical take homes

- Linear/sequential recovery process, symptoms do not wax and wane
  - Consideration of premorbid/concomitant factors for prolonged recovery
  - Exception is symptom exacerbation with physical exertion in acute recovery period
- Symptom report in acute recovery period is most reliable
- Consider the person who sustained the concussion, not just persistent symptoms through the medical lens.
  - The more distal from injury, consider referring to a mental health therapist rather than a rehabilitation therapist.

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