OPEN

Concussion in Ice Hockey: Current Gaps and Future Directions in an Objective Diagnosis

Aynsley M. Smith, RN, PhD, Michael J. Stuart, MD,† William O. Roberts, MD, MS,‡ David W. Dodick, MD,§ Jonathan T. Finnoff, DO,¶ Janelle K. Jorgensen, BA,|| and David A. Krause, PT, DSc***

Objective: This review provides an update on sport-related concussion (SRC) in ice hockey and makes a case for changes in clinical concussion evaluation. Standard practice should require that concussions be objectively diagnosed and provide quantitative measures of the concussion injury that will serve as a platform for future evidence-based treatment.

Methods: The literature was surveyed to address several concussion-related topics: research in ice hockey-related head trauma, current subjective diagnosis, promising components of an objective diagnosis, and current and potential treatments.

Main Results: Sport-related head trauma has marked physiologic, pathologic, and psychological consequences for athletes. Although animal models have been used to simulate head trauma for pharmacologic testing, the current diagnosis and subsequent treatment in athletes still rely on an athlete's motivation to report or deny symptoms. Bias-free, objective diagnostic measures are needed to guide quantification of concussion severity and assessment of treatment effects. Most of the knowledge and management guidelines of concussion in ice hockey are generalizable to other contact sports.

Conclusions: There is a need for an objective diagnosis of SRC that will quantify severity, establish a prognosis, and provide effective evidence-based treatment. Potential methods to improve concussion diagnosis by health care providers include a standardized concussion survey, the King–Devick test, a quantified electroencephalogram, and blood analysis for brain cell-specific biomarkers.

Key Words: King–Devick test, biomarkers, QEEG, ice hockey, concussion

(*Clin J Sport Med* 2017;0:1–7)

Submitted for publication May 31, 2016; accepted October 9, 2016.

From the *Department of Orthopedic Surgery and Physical Medicine and Rehabilitation, Sports Medicine Center, Mayo Clinic, Rochester, Minnesota; †Department of Orthopedic Surgery, Mayo Clinic Sports Medicine Center, Mayo Clinic, Rochester, Minnesota; ‡Department of Family Medicine and Community Health, University of Minnesota-Twin Cities, Minneapolis, Minnesota; §Department of Neurology, Mayo Clinic, Scottsdale, Arizona; ¶Department of Physical Medicine and Rehabilitation, Mayo Clinic Sports Medicine Center, Minneapolis, Minnesota; ||Sports Medicine Center, Mayo Clinic, Rochester, Minnesota; and **Department of Physical Medicine and Rehabilitation, Mayo Clinic, Rochester, Minnesota.

The authors report no conflicts of interest.

Corresponding Author: Aynsley M. Smith, RN, PhD, Desk LC, Sports Medicine Center, Mayo Clinic, 200 First St SW, Rochester, MN 55905 (smith.aynsley@mayo.edu).

INTRODUCTION

In the past decade, there has been growing public awareness and concern regarding the risk and consequences of concussion in contact sports.[1] However, there has not been a corresponding increase in the ability to objectively diagnose and effectively treat concussion. At the 2010 Ice Hockey Summit I: Action on Concussion, prioritized action items included improved recognition, diagnosis, and return-to-play protocols in addition to rule changes and rule enforcement aimed at reducing head contact. The main priorities of the 2013 Ice Hockey Summit II: Action on Concussion were elimination of all hits to the head and fighting. Data presented at Summit II showed that the "uppercut" (knock out) punch has much greater forces than other on-ice hockey-related infractions.[2] Unfortunately, targeting the head, fighting in games, and locker room boxing are all dangerous exposures that continue in hockey. The fighting-related data combined with lawsuits filed by players against the National Hockey League (NHL) may eventually lead to the elimination of fighting in ice hockey. Body checking,[3–5] particularly when accompanied by "checking from behind," boarding, and head hits are also dangerous, but can be addressed by rule changes[6,7] as has occurred in PeeWee hockey in both Canada and the United States and high school hockey in the United States.

BACKGROUND

The potential link between head trauma and long-term neurologic deficits has increased public health concerns regarding sport-related concussion (SRC).[8–11] High-impact head trauma occurs in all contact sports, such as hockey, football, and soccer, but strategies to reduce incidental and eliminate intentional head impact are essential for player safety.[12–15] Hockey is played at high speeds on hard, slippery ice, surrounded by boards and Plexiglas. Consequently, SRC frequently results from body checks, accidental collisions and deliberate infractions.[3–5,16–26] In hockey, the incidence of concussion and other injuries increases as players physically mature, because of increased size, speed, and their competitive aggression.[12,14,27,28]

Video reconstruction is a bioengineering procedure that contributes to our understanding of head trauma and impact on the brain. Video reconstruction uses 2 orthogonally positioned cameras to capture head impact events and to calculate both impact speed and head accelerations.[29–31] This process has established the relationship between the magnitude of head acceleration and the severity of head injury.[30] Video reconstruction output is used in finite element models (FEM). The FEM output provides acceleration magnitude, strain rates, and brain tissue orientation at the time of injury.[29,31–37] These impact characteristics can be used in the translational laboratory and animal research to evaluate responses to simulated head impacts and potential therapies.

Wearable accelerometers and instrumented helmets have also been developed to measure and track head impacts and their relation to SRC. The Head Impact Telemetry System (HITS) has been used extensively to record impacts.[1,2,22,26,38–41] The magnitude, frequency of head hits, and linear and rotational accelerations have been studied in both male and female hockey players, at youth, high school, Junior A and college age levels of participation.[1,2,17,22,26,38,40–45]

A study of Bantam players (ages 13–14 years) recorded 2753 impact events over 10 g with an average linear acceleration of 15.8 g (SD 13.8). Five players experienced >180 impacts each, with some exceeding 98 g.[39] In another study of high school, Junior A, and collegiate (men's and women's) teams, over 100 000 head impacts were measured with player-to-player contact accounting for 50% of the impacts. Sport-related concussion was diagnosed most often on days with higher frequency and magnitude of recorded head impacts.[43] Head impact exposure, which includes parameters of frequency, magnitude, and head impact location,[2] was correlated with both concussion signs and symptoms and abnormalities on functional magnetic resonance imaging and diffusion tension imaging.[46–48]

High linear and rotational accelerations have been simulated in the laboratory using an HITS hockey helmet and a Hybrid III head–neck complex to study impact characteristic correlations during 3 common infractions: static cross-checking, dynamic cross-checking, and slashing to the head–neck complex.[49] Mean linear accelerations ranged 26.5 g from a crosscheck to 138 g from a slash, and mean rotational accelerations ranged from 2260 rads/s^2 during a dynamic cross check, to 14 100 rads/s^2 during a slash.[49]

A 2-season study of Junior A players (N = 28) wearing HITS[17,29,45] helmets at home games looked at HITS accelerations, SRC diagnosed in season (6 in 2011–2012 and 4 in 2012–2013), individual exposure time, penalties, and video data. These players reported between 0 and 6 concussions each before enrolling in the study. During the 2011 to 2012 season, 5201 impacts over 10 g were recorded and 2780 in 2012 to 2013. The number of impacts ranged between 103 and 186 per player per season and between 6.8 and 7.06 per player per game per season. There were 47 fights in the 2011 to 2012 season and 34 in the 2012 to 2013 season, based on the penalties recorded for fighting.

Highest single linear and rotational accelerations per player were graphed separately on 80% probability of the concussion scale of Zhang,[50] and diagnosed concussions were marked with an X (Figure 1).[51] All but one of the concussed players recorded linear and rotational accelerations above an 80% probability of concussion. However, 10 players with accelerations over the 80% probability line were not diagnosed with a concussion; was this due to impact measurement error? To answer this question, drop testing was performed with a Hybrid III Head Form fitted with an HITS hockey helmet. Results showed a strong correlation between accelerations recorded from the Hybrid III and the HITS helmet, except for drops onto the ridged vertex of the helmet. Assured by the strong correlations that the head impacts were being accurately recorded, the accuracy of the concussion diagnostic methods, including the Sport Concussion Assessment Tool 3 (SCAT3), were questioned.[52–54] Other potential explanations for head hits above the 80% concussion probability levels without a diagnosis of concussion include the lack of player motivation to report head trauma, acquired resiliency to head hits, and fear of reporting consequences such as missed playing time or loss of a scholarship opportunity.

Despite technological advances that allow a quantitative evaluation of head impact that measure accelerations during games showing the magnitude and frequency of head impact events in hockey, our ability to diagnose concussion at rinkside or point of care has not advanced beyond the currently available subjective clinical assessment tools.[1,2]

Subjective Concussion Diagnosis Process

The currently available "objective" diagnostic tools, such as the SCAT3, are subject to players underreporting or exaggeration of symptoms. The absence of an objective, readily available and affordable quantitative measure of brain function impairs our ability to accurately assess SRC. Likewise, the inability to clinically measure the initial magnitude of neuronal injury and objectively monitor brain recovery over time weakens informed decision making for treatment, prognosis, and return to sport.[1,2] The lack of objective measures for diagnosis of concussion and serial quantitative measures of recovery compromise the identification and assessment of prospective therapies. Currently, no Food and Drug Administration (FDA)-approved therapy is available for acute concussion, and treatment options are limited to rest, time, and nonpharmacologic rehabilitation strategies.

The SCAT3 has been recommended as an aid to the diagnosis of concussion.[54] This test battery queries concussion history, 22 symptoms, orientation, memory, delayed recall, and balance testing. All of the SCAT3 responses are vulnerable to manipulation during baseline and postconcussion testing, if players are motivated to avoid a concussion diagnosis. Players who "cheat" the test often remain on the field of play and are subject to the risk of subsequent head trauma. Recognition, scholarships, professional contracts, or starting positions are motivation to deny symptoms. A recent review of the psychology of athletes with concussion highlights limitations of diagnosing concussions due to the subjectivity of the evaluation.[55]

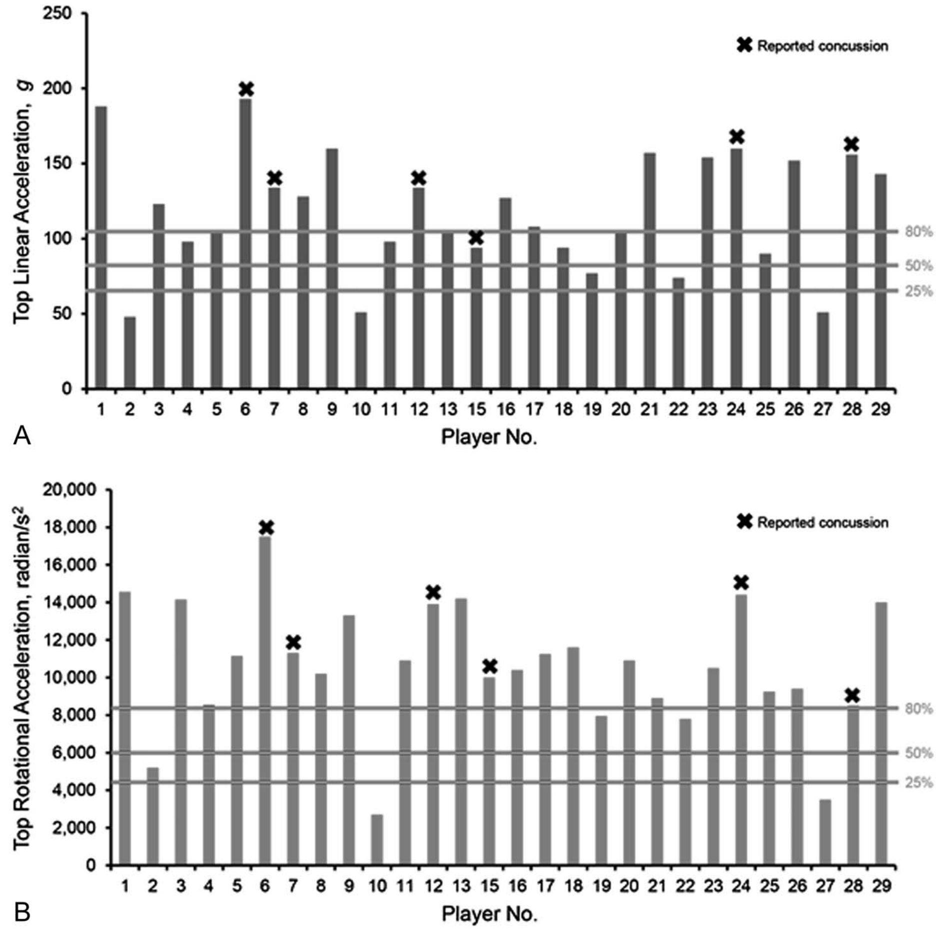

FIGURE 1. The highest recorded single linear (A) and rotational (B) accelerations per player across 1 season of data collection. Horizontal thresholds indicate the probability of the concussion scale of Zhang. X's represent clinically diagnosed concussions using the SCAT3. All except 1 concussion are above the 80% probability of concussion line.

Gaps in Current Concussion in the Hockey Literature

Clinicians are challenged by the absence of reliable objective measures to diagnose, quantify severity, and inform the management of concussion. The clinical evaluation of concussion resembles chest pain management in the 1950s. Electrocardiograms were challenging to interpret and provided only a semiquantitative measure of cardiac injury, serum biomarker assessments did not exist, and the sole treatment was rest for several weeks with comfort care, often including morphine and oxygen. A few decades later, clinicians can expediently and accurately evaluate and treat chest pain, track myocardial injury recovery, and return patients to "normal" life in a matter of days. Although the SCAT3 provides a structured assessment of the athlete's after head trauma event, more objective diagnostic protocols are emerging, which will provide much needed objectivity to the concussion evaluation.

Components of an Objective Diagnosis of Concussions

Our hockey concussion research team is investigating objective diagnostic measures that use a repeated measure design, so the players serve as their own control. The team selected 4 time points to use for measuring: (1) preseason baseline, (2) after head trauma, (3) before return to sport, and (4) after season testing.

Mayo Clinic Ice Hockey Concussion Survey

This demographic survey queries an athlete's concussion history and hockey profile (years in hockey, player position, and on-ice playing style) before segueing into the objective diagnostic measures using the King–Devick test, the quantified electroencephalogram (QEEG), and neurobiomarker measurements.

King–Devick Test

The King–Devick (KD) test, a time-based measure of saccades and other eye movements, detects concussion with high levels of sensitivity (86%) and specificity (90%) at rinkside or point of care.[56] A preseason baseline is performed with players wearing practice/competition eyewear. Examiners record the time it takes to complete each of 3 trials and the number of errors per trial.[56] Recently, 141 youth hockey players underwent KD testing before season, after season, and immediately after suspected concussion.[57] Testing was also performed in a subgroup of nonconcussed athletes immediately before and after games to determine the impact of fatigue on KD scores. Twenty athletes sustained a concussion, and all 20 had immediate postconcussion KD testing times, which deviated more than 5 seconds from baseline (average 7.3 s) and all but 2 had worse postseason scores (46.4 seconds vs 52.4 seconds, $P < 0.05$). In contrast, 51 nonconcussed players assessed before and after a game revealed no significant time change as a result of fatigue. This study indicated that the KD test accurately identified real-time, symptomatic concussion in youth athletes. Players will benefit from having provided preseason and postseason KD testing, as sports medicine providers will have a real-time objective evaluation at point of care to support the diagnosis of concussion.

Quantified Electroencephalogram

During a QEEG evaluation, event-related potentials (ERPs) reveal ongoing, covert neurologic processing deficits not fully assessed by behavioral measures. Event-related potentials are sensitive measures of neurofunctional deficits, which are not influenced by either player motivation or by the practice effects of repeated testing, a limitation of KD testing. A QEEG was used to assess concussed athletes between 2010 and 2012 in a repeated measure design (baseline, immediately after injury, 45 days after concussion, and before return to play). Although most SRC symptoms and cognitive dysfunction resolved within the first week after injury, QEEG results showed that postconcussion neurofunctional recovery, as measured on the QEEG, lags behind clinical recovery.[58–60]

Authors used the NeuroCatch (NC; NeuroTech Lab, Surrey, BC, Canada), a QEEG device, which identifies changes in waveform amplitude and latency, after head trauma compared with baseline. The NC requires 1 to 2 minutes to set up and 5 minutes to record the brain waveforms The NC allows comparison of the preseason baseline with a postinjury recording, which may aid in making a concussion diagnosis and guide the return-to-play decision.

Neurobiomarkers

To date, the neurobiomarker measurements of neuron-specific enolase, S100B, and Tau have yielded equivocal results for diagnosis and severity of head trauma in several studies.[61–65] Two novel neurobiomarker tools recently used in hockey studies are metabolomics[66–68] and αII-spectrin N-terminal fragment (SNTF).[69,70] These biomarkers show promise of improved accuracy for diagnosis of SRC after head trauma in hockey. The metabolomics involves analyzing blood plasma to detect metabolite "footprints" indicative of head trauma. Metabolomic profiles have distinguished mild cognitive impairment from Alzheimer disease,[67,68] and similar profiles have differentiated concussed adolescent male hockey players from nonconcussed players.[66]

The SNTF measurements detected axonal trauma after head injury in Swedish professional hockey players.[69] Although undetectable at baseline, SNTF rises after head trauma and is used in a repeated measure design to provide a clinical profile of readiness for return to play as SNTF levels return to undetectable levels.

In future research, the goal is for these and other objective diagnostic tests to confirm concussion diagnosis, quantify severity, and contribute to the study of potential concussion treatment. Although virtually no evidence-based treatment for acute SRC is now available, evolving information on an objective diagnosis of concussion will result in a framework capable of assessing treatment efficacy. Objective and accurate concussion diagnoses in hockey players and other contact sport athletes are essential to allow for controlled, randomized trials to evaluate effects.

Treatment with Promising Medication

Treatment with medications requires understanding of the postconcussion neurometabolic cascade. This cascade is characterized by increases in intracellular glutamate and calcium, coincident with potassium exiting the intracellular space into the extracellular fluid, a chemical process that impedes phosphorylation of ATP necessary for brain energy function. Consequently, the postconcussion acute cellular energy demand exceeds the intracellular energy supply.[71,72] As such, effective treatment of concussion at point of care will likely require the ability of agents that expediently cross the blood–brain barrier and promptly reduce the neurometabolic energy crisis.

To date, evidence supporting pharmacologic concussion treatment is symptom driven and equivocal in patients with postconcussion syndrome.[73] Symptom categories reviewed were (1) somatic complaints, (2) sleep disturbance, (3) emotional difficulties, and (4) cognitive difficulties. Although administration of most medications is symptom driven, some agents show promise in circumventing the cell energy crisis that produces concussion symptom constellations.

In a military study performed in Iraq, a clinician administered either N-acetyl cysteine (NAC) or a placebo to combat soldiers after blast-related traumatic brain injury at point of care. N-acetyl cysteine has a 40-year history of clinical use in acetaminophen overdose without discernable side effects. Study participants were randomized into either NAC treatment (N = 41) or placebo group (N = 40), with the NAC group showing significant symptom improvement. N-acetyl cysteine has also shown neuroprotective benefits and use in treating neurological disorders; however, it does not easily cross the blood–brain barrier, which limits brain cell bioavailability.[74–76] An amide derivative of NAC, NAC amide, has been synthesized that crosses the blood–brain barrier efficiently resulting in increased brain cell bioavailability. Animal model studies of N-acetylcysteine amide (NACA) show significant benefit in rodent traumatic brain injury (TBI), spinal cord injury, and focal penetrating brain injury models with no side effects. A review of NACA studies concluded that NACA may soon be available as a treatment for SRC.[77] There are also some animal data supporting potential neuroprotective benefits from the use of common fish oils, such as docosahexaenoic acid,[78,79] but additional research is needed to prove efficacy. It is hoped that the reported neuroprotective benefits from these promising treatments will show the ability to prevent and alleviate post-SRC symptoms in athletes to a level that will attain FDA approval.

Promising Treatment Without Medication

Recent nonpharmacologic treatment has challenged the use of complete physical and cognitive rest with prolonged activity restrictions in concussed athletes. Although relative rest is useful in the acute concussion period, exercise at a subsymptom threshold using the Balke treadmill protocol has proven benefits in postconcussion syndrome.[80–85] In addition to exercise, other interventions are often necessary including oculomotor, cervical spine, and vestibular rehabilitation.[86,87] Additional interventions to decrease the risk of postconcussion musculoskeletal injuries may also be necessary with some athletes.[88]

DISCUSSION

Considerable effort has been invested in developing a comprehensive version of the SCAT3 that includes a concussion history, extensive symptom assessment, severity rating, orientation awareness, memory and delayed recall, and a preliminary vestibular assessment; however, collectively, these evaluations remain subjective. As illustrated by investigative reports,[89] many committed athletes escape concussion detection based on their motivation to remain in the game. At all levels of participation, pressure on clinical providers from coaching staff, general managers, and players can also impede the accuracy of the concussion diagnoses. As objective diagnostic tools become available, the diagnosis will be less vulnerable to subjective overlay of overly aggressive athletes and assertive coaches.

Practical Guidelines for Clinicians

Medical personnel evaluating athletes who sustain significant head impact should be aware that most currently used diagnostic tests are imprecise, require athlete cooperation, and are vulnerable to player and evaluator bias. The SCAT3, despite being well studied and widely used, consists of a series of subjective questions, or tests requiring player cooperation, and thus, is susceptible to player deception. Although psychometrics ensure validity, they do not necessarily ensure objectivity. Clinicians should use tests with the greatest objectivity, availability, and affordability.

This review provides sports medicine team physicians and athletic trainers with action(s) that can be integrated into their concussion assessment. The diagnostics discussed in this article are most helpful at this time when a baseline comparison test is available. Important information for clinicians to know before objectively diagnosing a hockey-related concussion includes risk factors such as: (1) a history of previous concussions, (2) head contact exposures along with the frequency to known accelerations at over 80% probability, and (3) the on-ice position of forward in ice hockey.

CONCLUSIONS

To advance the science of concussion, objective measures to diagnose concussion and document the resolution of brain-related changes must be developed. Variations from baseline in 3 objective measures—the KD test, the QEEG, and neurobiomarkers—may confirm concussion and measure of severity of the brain injury. These potential objective measures will enable promising therapeutic options to be studied for efficacy in concussion management. Using objective diagnostic methods is a critical step to reduce the frequency and consequences of undiagnosed concussion and inappropriate return to play.

ACKNOWLEDGMENTS

The authors thank Douglas Fraser, MD, PhD (University of Western Ontario), Robert Siman, PhD (University of Pennsylvania), and Ryan D'Arcy, PhD, and his team (Sujoy Ghosh Hajra, Careesa Liu, Shaun Fickling, Gabriela Pawlowski at Simon Fraser University) for their contributions to an objective diagnosis of concussion. The authors also thank Chad Eickhoff, ATR, ATC, Kristen Greek, ATR, ATC, Eric Crowley, ATR, ATC, and Andrew Thoreson, MS, for contributing their input and insights into this project as it has evolved; and Pam Otterbein for her editorial assistance, Pat Erwin for her reference librarian skills, and the USA Hockey Foundation for partial funding support.

REFERENCES

1. Smith AM, Stuart MJ, Greenwald RM, et al. Proceedings from the ice hockey summit on concussion: a call to action. *Clin J Sport Med.* 2011; 21:281–287.
2. Smith AM, Stuart MJ, Dodick DW, et al. Ice Hockey Summit II: zero tolerance for head hits and fighting. *Curr Sports Med Rep.* 2015;14:135–144.
3. Lacny S, Marshall DA, Currie G, et al. Reality check: the cost–effectiveness of removing body checking from youth ice hockey. *Br J Sports Med.* 2014;48:1299–1305.
4. Emery CA, Kang J, Shrier I, et al. Risk of injury associated with body checking among youth ice hockey players. *JAMA.* 2010;303:2265–2272.
5. Emery CA, Kang J, Schneider KJ, et al. Risk of injury and concussion associated with team performance and penalty minutes in competitive youth ice hockey. *Br J Sports Med.* 2011;45:1289–1293.
6. Smith AM, Jorgenson M, Sorenson MC, et al. Hockey Educational Program (HEP): a statewide measure of fair play, skill development, and coaching excellence. *J ASTM Int.* 2009;6:1–14.
7. Smith AM, Gaz DV, Larson D, et al. Does fair play reduce concussions? A prospective, comparative analysis of competitive youth hockey tournaments. *BMJ Open Sport Exerc Med.* 2016;2:e000074.
8. Tartaglia MC, Hazrati LN, Davis KD, et al. Chronic traumatic encephalopathy and other neurodegenerative proteinopathies. *Front Hum Neurosci.* 2014;8:30.
9. McKee AC, Cantu RC, Nowinski CJ, et al. Chronic traumatic encephalopathy in athletes: progressive tauopathy after repetitive head injury. *J Neuropathol Exp Neurol.* 2009;68:709–735.
10. Lin AP, Ramadan S, Box H, et al. Neurochemical changes in athletes with chronic traumatic encephalopathy. Chicago, IL: Radiological Society of North America; 2010.
11. Kelly DF, Chaloner C, Evans D, et al. Prevalence of pituitary hormone dysfunction, metabolic syndrome, and impaired quality of life in retired professional football players: a prospective study. *J Neurotrauma.* 2014; 31:1161–1171.
12. Marar M, McIlvain NM, Fields SK, et al. Epidemiology of concussions among United States high school athletes in 20 sports. *Am J Sports Med.* 2012;40:747–755.
13. Lau BH, Benson BW. Ice hockey. *Epidemiol Inj Olympic Sports.* 2010; XVI:411–446.
14. Benson BW, Meeuwisse WH. Ice hockey injuries. *Med Sport Sci.* 2005; 49:86–119.
15. Benson BW, McIntosh AS, Maddocks D, et al. What are the most effective risk-reduction strategies in sport concussion? *Br J Sports Med.* 2013; 47:321–326.
16. Reid SR, Losek JD. Factors associated with significant injuries in youth ice hockey players. *Pediatr Emerg Care.* 1999;15:310–313.
17. Mihalik JP, Greenwald RM, Blackburn JT, et al. Effect of infraction type on head impact severity in youth ice hockey. *Med Sci Sports Exerc.* 2010;42:1431–1438.

18. McKay C, Meeuwisse W, Emery C. Informing body checking policy in youth ice hockey in Canada: a discussion meeting with researchers and community stakeholders. *Can J Public Health.* 2014;105:445–449.
19. Klein J. *With Focus on Youth Safety, a Sport Considers Changes*. New York City, NY: New York Times; 2010:D6.
20. Klein J. *Hockey Urged to Ban All Blows to Head by Concussions Panel*. New York, NY: New York Times; 2010:B19.
21. Emery CA, Hagel B, Decloe M, et al. Risk factors for injury and severe injury in youth ice hockey: a systematic review of the literature. *Inj Prev.* 2010;16:113–118.
22. Duhaime AC, Beckwith JG, Maerlender AC, et al. Spectrum of acute clinical characteristics of diagnosed concussions in college athletes wearing instrumented helmets. *J Neurosurg.* 2012;117:1092.
23. Decloe MD, Meeuwisse WH, Hagel BE, et al. Injury rates, types, mechanisms and risk factors in female youth ice hockey. *Br J Sports Med.* 2013;48:51–56.
24. Covassin T, Elbin RJ, Sarmiento K. Educating coaches about concussion in sports: evaluation of the CDC's "Heads Up: concussion in youth sports" initiative. *J Sch Health.* 2012;82:233–238.
25. Brust JD, Leonard BJ, Pheley A, et al. Children's ice hockey injuries. *Am J Dis Child.* 1992;146:741–747.
26. Brainard LL, Beckwith JG, Chu JJ, et al. Gender differences in head impacts sustained by collegiate ice hockey players. *Med Sci Sports Exerc.* 2012;44:297–304.
27. Langlois JA, Rutland-Brown W, Wald MM. The epidemiology and impact of traumatic brain injury: a brief overview. *J Head Trauma Rehabil.* 2006; 21:375–378.
28. Benson BW, Meeuwisse WH, Rizos J, et al. A prospective study of concussions among National Hockey League players during regular season games: the NHL-NHLPA Concussion Program. *CMAJ.* 2011;183:905–911.
29. Benson BW, Meeuwisse WH, Rizos J, et al. The relationship between head impact characteristics and brain trauma. *J Neurol Neurophysiol.* 2013;5:181.
30. Oeur A, Karton C, Post A, et al. A comparison of head dynamic response and brain tissue stress and strain using reconstructions of concussion, concussion with persistent post-concussive symptoms, and subdural hematoma. *J Neurosurg.* 2014;123:415–422.
31. Post A, Hoshizaki TB, Gilchrist M, et al. Analysis of the influence of independent variables used for reconstruction of a traumatic brain injury event. *J Sport Eng Tech.* 2012;226:290–298.
32. Fijalkowski RJ, Yoganandan N, Zhang J, et al. A finite element model of region-specific response for mild diffuse brain injury. *SAE Tech Paper.* 2009;53:193–213.
33. Franklyn M, Fildes B, Zhang L, et al. Analysis of finite element models for head injury investigation: reconstruction of four real-world impacts. *SAE Tech Paper.* 2005;49:1–32.
34. Horgan T, Gilchrist MD. The creation of three-dimensional finite element models for simulating head impact biomechanics. *Int J Crashworthiness.* 2003;8:353–366.
35. Kendall M, Post A, Zanetti K, et al. Comparison of dynamic versus static head impact reconstruction methodology by means of dynamic impact response and brain deformation metrics. International IRCOBI Conference on the Biomechanics of Impact, Gothenburg, Sweden; 2013.
36. Kleiven S. Evaluation of head injury criteria using a finite element model validated against experiments on localized brain motion, intracerebral acceleration, and intracranial pressure. *Int J Crashworthiness.* 2006;11:65–79.
37. Post A, Oeur A, Walsh E, et al. A centric/non-centric impact protocol and finite element model methodology for the evaluation of American football helmets to evaluate risk of concussion. *Comput Methods Biomech Biomed Engin.* 2014;17:1785–1800.
38. McAllister TW, Flashman LA, Maerlender A, et al. Cognitive effects of one season of head impacts in a cohort of collegiate contact sport athletes. *Neurology*. 2012;78:1777–1784.
39. McPherson M, Montelpare W, Keightley M, et al. An analysis of head impact profiles and Safe hockey behaviors in youth hockey players. *J ASTM Int.* 2009;6:1–7.
40. Wilcox BJ, Beckwith JG, Greenwald RM, et al. Head impact exposure in male and female collegiate ice hockey players. *J Biomech.* 2014;47:109–114.
41. Beckwith JG, Burmeister E. Head-impact mechanisms in men's and women's collegiate ice hockey. *J Athletic Train.* 2014;49:514–520.
42. Beckwith JG, Greenwald RM, Chu JJ, et al. Timing of concussion diagnosis is related to head impact exposure prior to injury. *Med Sci Sports Exerc.* 2013;45:747–754.
43. Beckwith JG, Greenwald RM, Chu JJ, et al. Head impact exposure sustained by football players on days of diagnosed concussion. *Med Sci Sports Exerc.* 2013;45:737–746.
44. McAllister TW, Ford JC, Flashman LA, et al. Effect of head impacts on diffusivity measures in a cohort of collegiate contact sport athletes. *Neurology*. 2014;82:63–69.
45. Mihalik JP, Blackburn JT, Greenwald RM, et al. Collision type and player anticipation affect head impact severity among youth ice hockey players. *Pediatrics.* 2010;125:e1394–e1401.
46. Helmer KG, Pasternak O, Fredman E, et al. Hockey Concussion Education Project, Part 1. Susceptibility-weighted imaging study in male and female ice hockey players over a single season. *J Neurosurg.* 2014;120:864–872.
47. Pasternak O, Koerte IK, Bouix S, et al. Hockey Concussion Education Project, Part 2. Microstructural white matter alterations in acutely concussed ice hockey players: a longitudinal free-water MRI study. *J Neurosurg.* 2014;120:873–881.
48. Sasaki T, Pasternak O, Mayinger M, et al. Hockey Concussion Education Project, Part 3. White matter microstructure in ice hockey players with a history of concussion: a diffusion tensor imaging study. *J Neurosurg.* 2014;120:882–890.
49. Coulson N, Foreman S, Hoshizaki T. Translational and rotational accelerations generated during reconstructed ice hockey impacts on a Hybrid III head form. Fifth International Symposium on Safety in Ice Hockey 2009, Denver, CO: ASTM International.
50. Zhang L. A proposed injury threshold for mild traumatic brain injury. *J Biomechanical Eng.* 2004;126:226–236.
51. Jorgensen JT, Thoreson AR, Stuart MB, et al, Interpreting instrumented ice hockey helmet oblique impact data for Junior A players. *J Sports Eng Technol.* In review for publication.
52. Aubry M, Cantu R, Dvorak J, et al. Summary and agreement statement of the 1st International Symposium on Concussion in Sport, Vienna 2001. *Clin J Sport Med.* 2002;12:6–11.
53. McCrory P, Meeuwisse W, Johnston K, et al. Consensus statement on concussion in sport: the 3rd International Conference on Concussion in Sport held in Zurich, November 2008. *Br J Sports Med.* 2009;43 (suppl 1):i76–90.
54. McCrory P, Meeuwisse WH, Aubry M, et al. Consensus statement on concussion in sport: the 4th International Conference on Concussion in Sport held in Zurich, November 2012. *Br J Sports Med.* 2013;47: 250–258.
55. Wiese-Bjornstal DM, White AC, Russell HC, et al. Psychology of sport concussions. *Kinesiology Review.* 2015;4(2):169–189.
56. Galetta KM, Liu M, Leong DF, et al. The King-Devick test of rapid number naming for concussion detection: meta-analysis and systematic review of the literature. *Concussion.* 2015;15:1–15.
57. Dhawan P, Starling A, Tapsell L, et al. King-Devick test identifies symptomatic concussion in real-time and asymptomatic concussion over time. (S11.003). *Neurology.* 2015;8:131–139.
58. Barr WB, Prichep LS, Chabot R, et al. Measuring brain electrical activity to track recovery from sports related concussion. *Brain Inj.* 2012;26:58–66.
59. Ellemberg D, Henry LC, Macciocchi SN, et al. Advances in sport concussion assessment: from behavioral to brain imaging. *J Neurotrauma.* 2009;26:2365–2382.
60. Kutcher JS, McCrory P, Davis G, et al. What evidence exists for new strategies or technologies in the diagnosis of sports concussion and assessment of recovery? *Br J Sports Med.* 2013;47:299–303.
61. Delacourte A, Buée L. Tau pathology: a marker of neurodegenerative disorders. *Curr Opin Neurol.* 2000;13:371–376.
62. Goldstein LE, Fisher AM, Tagge CA, et al. Chronic traumatic encephalopathy in blast-exposed military veterans and a blast neurotrauma mouse model. *Sci Transl Med.* 2012;4:134ra60.
63. Goldstein LE, McKee AC, Stanton PK. Considerations for animal models of blast-related traumatic brain injury and chronic traumatic encephalopathy. *Alzheimer's Res Ther.* 2014;6:64.
64. Stern RA, Daneshvar DH, Baugh CM, et al. Clinical presentation of chronic traumatic encephalopathy. *Neurology.* 2013;81:1122–1129.
65. Terrell TR, Bostick RM, Abramson R, et al. APOE, APOE promoter, and Tau genotypes and risk for concussion in college athletes. *Clin J Sport Med.* 2008;18:10–17.
66. Fraser D, Daley M. Metabolomics profiling of concussion: a novel diagnostic method. Traumatic Brain Injury Conference 2015, Washington, D.C.

67. Trushina E, Dutta T, Persson XM, et al. Identification of altered metabolic pathways in plasma and CSF in mild cognitive impairment and Alzheimer's disease using metabolomics. *PLoS One.* 2013;8:e36344.
68. Trushina E, Nemutlu E, Zhang S, et al. Defects in mitochondrial dynamics and metabolomic signatures of evolving energetic stress in mouse models of familial Alzheimer's disease. *PLos One.* 2012;7:e32737.
69. Shahim P, Tegner Y, Wilson DH, et al. Blood biomarkers for brain injury in concussed professional ice hockey players (S11.005). *Neurology.* 2014;82 (suppl 10):S11.005.
70. Siman R, Shahim P, Tegner Y, et al. Serum SNTF increases in concussed professional ice hockey players and relates to the severity of postconcussion symptoms. *J Neurotrauma.* 2015;32:1294–1300.
71. Giza CC, Hovda DA. The neurometabolic cascade of concussion. *J Athl Train.* 2001;36:228–235.
72. Giza CC, Hovda DA. The new neurometabolic cascade of concussion. *Neurosurgery.* 2014;75:S24–S33.
73. Petraglia AL, Maroon JC, Bailes JE. From the field of play to the field of combat: a review of the pharmacological management of concussion. *Neurosurgery.* 2012;70:1520–1533.
74. Eakin K, Baratz-Goldstein R, Pick CG, et al. Efficacy of N-acetyl cysteine in traumatic brain injury. *PLoS One.* 2014;9:e90617.
75. Hoffer ME, Balaban C, Slade MD, et al. Amelioration of acute Sequelae of blast induced mild traumatic brain injury by N-acetyl cysteine: a double-blind, placebo controlled study. *PLoS One.* 2013;8:e54163.
76. Shahripour RB. N-acetylcycsteine (NAC) in neurological disorders: mechanisms of action and therapeutic opportunities. *Brain Behav.* 2014;4:108–122.
77. Semple BD. Early preservation of mitochondrial bioenergetics supports both structural and functional recovery after neurotrauma. *Exp Neurol.* 2014;261:291–297.
78. Bailes JE, Mills JD. Docosahexaenoic acid reduces traumatic axonal injury in a rodent head injury model. *J Neurotrauma.* 2010;27:1617–1624.
79. Mills JD, Hadley K, Bailes JE. Dietary supplementation with the omega-3 fatty acid docosahexaenoic acid in traumatic brain injury. *Neurosurgery.* 2011;68:474–481.
80. Baker JG, Freitas MS, Leddy JJ, et al. Return to full functioning after graded exercise assessment and progressive exercise treatment of post-concussion syndrome. *Rehabil Res Pract.* 2012;2012:705309.
81. Darling SR, Leddy JJ, Baker JG, et al. Evaluation of the Zurich guidelines and exercise testing for return to play in adolescents following concussion. *Clin J Sport Med.* 2014;24:128–133.
82. Leddy JJ, Kozlowski K, Donnelly JP, et al. A preliminary study of subsymptom threshold exercise training for refractory post-concussion syndrome. *Clin J Sport Med.* 2010;20:21–27.
83. Leddy JJ, Kozlowski K, Fung M, et al. Regulatory and autoregulatory physiological dysfunction as a primary characteristic of post concussion syndrome: implications for treatment. *NeuroRehabilitation.* 2007;22: 199–205.
84. Leddy JJ, Sandhu H, Sodhi V, et al. Rehabilitation of concussion and post-concussion syndrome. *Sports Health.* 2012;4:147–154.
85. Leddy JJ, Willer B. Use of graded exercise testing in concussion and return-to-activity management. *Curr Sports Med Rep.* 2013;12: 370–376.
86. Schneider KJ, Iverson GL, Emery CA, et al. The effects of rest and treatment following sport-related concussion: a systematic review of the literature. *Br J Sports Med.* 2013;47:304–307.
87. Schneider KJ, Meeuwisse WH, Kang J, et al. Preseason reports of neck pain, dizziness, and headache as risk factors for concussion in male youth ice hockey players. *Clin J Sport Med.* 2013;23:267–272.
88. Brooks MA, Peterson K, Biese K, et al. Concussion increases odds of sustaining a lower extremity musculoskeletal injury after return to play among collegiate athletes. *Am J Sports Med.* 2016;44:742–747.
89. Carroll L, Rosner D. *The Concussion Crisis: Anatomy of a Silent Epidemic*. New York, NY: Simon & Schuster; 2012.