

## At-Risk Populations in Sports-Related Concussion

Jeffrey S. Kutcher<sup>1</sup> and James T. Eckner<sup>2</sup>

<sup>1</sup>Department of Neurology, University of Michigan, Ann Arbor, MI; <sup>2</sup>Department of Physical Medicine & Rehabilitation, University of Michigan, Ann Arbor, MI

KUTCHER, J.S. and J.T. ECKNER. At-risk populations in sports-related concussion. *Curr. Sports Med. Rep.*, Vol. 9, No. 1, pp. 16–20, 2010. Concussion is a physiological injury to the extremely complex and dynamic human brain. Individual variability adds to the challenge of concussion management, and sports medicine practitioners recently have begun to realize the need for an individualized approach. Adequately assessing an athlete with concussion requires consideration of many risk factors, including age, gender, and certain comorbid conditions. Understanding how these factors may affect concussion risk and outcome is becoming an essential aspect of management. This article reviews what is known or assumed about how some of these risk factors affect concussion. We conclude by providing several key concepts that we feel are important to keep in mind when managing an athlete with concussion.

### INTRODUCTION

The human brain possesses a complexity of function far beyond that of any other organ or body part. When injured, it is this complexity that creates tremendous clinical challenges for the sports medicine practitioner. Recognizing concussion and differentiating it from other diagnoses can be a daunting task, but one of critical clinical importance. Once diagnosed, the natural history of any one concussion can be hard to predict, and knowing when it is safe for an athlete to return to competition is fraught with unknowns. In an attempt to simplify management and improve clinical outcomes, many efforts have focused on classifying concussion in a clinically relevant way (2,6). In practice, however, no classification schema has proven to be clinically useful, and there is a growing sense that each concussion should be managed individually (20).

Athletic trainers and sports medicine physicians understand from experience that not all athletes have the same threshold for concussion. Some may be prone to the injury, while others seem to be relatively immune. What sets these athletes apart? Experience tells us that if different athletes receive the same type and magnitude of mechanical force applied to their brains, some will be concussed while others will not. What accounts for the difference? While a specific pathophysiologic answer eludes us, it is safe to conclude that

individual differences between athletes account for the disparate outcomes we see in real life. The sports medicine provider can elucidate these differences by considering such factors as the athlete's past concussion experience, concurrent diagnoses, physiologic state, and family history. As we continue to adopt a more individual approach to concussion management, it is essential that we place the most proximal or ongoing injury in this larger clinical context.

A large part of concussion management is the estimation of risk. Return-to-play decisions are made with the risks of possible symptom exacerbation, subsequent concussion, or catastrophic injury in mind. Every athlete, whether previously concussed or not, walks on to the field of play with some inherent risk of being concussed. One begins the estimation of an athlete's concussion risk by considering his or her sport and position. By understanding that this risk ultimately is defined by far more than just these two parameters, however, we become better advocates for our patients and are able to provide a higher standard of clinical care. While we are just beginning to understand how factors such as age, gender, and comorbid conditions play a role in the natural history of concussion, keeping these factors in mind becomes key to more accurately stratifying risk. The goal of this article is to aid this process by providing the reader with the evidence, or in some cases the current thinking, regarding particular "populations at risk" for sports-related concussion.

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Address for correspondence: Jeffrey S. Kutcher, M.D., Department of Neurology, University of Michigan, A. Alfred Taubman Health Care Center, 1500 East Medical Center Drive, Floor 1 Reception: C, Ann Arbor, MI 48109 (E-mail: jkutcher@med.umich.edu).

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### METHODS

PubMed searches were performed for the years 2008–2009 combining the keyword "concussion" with the following keywords: gender, female, pediatric, mood disorder, depression, learning disability, migraine headache, genetics, family history, and apolipoprotein E (ApoE). When necessary,

historical searches were performed to provide adequate background; however, emphasis remained on studies published within the past year.

## FEMALE ATHLETES

The potential effect of gender on concussion incidence recently has been summarized in the literature (10). The author collected and critically reviewed injury surveillance studies that provided data on concussion incidence by gender. In total, 10 prospective surveillance studies were identified, including data from 3 sports that were felt to be adequately similar between genders (soccer, basketball, and ice hockey) to allow for comparison. For each sport, the pooled data demonstrated a higher incidence for women than men, with the trends in soccer and basketball reaching statistical significance. Since these studies included U.S. high school and collegiate athletes and international-level soccer players, it is unclear how these findings might apply to younger athletes.

There are some data to suggest that gender also may play a role in concussion outcome. In a cohort study published in 2009, Colvin *et al.* concluded that female soccer players performed worse than males on postconcussive neurocognitive testing. Women in the study also were shown to report more postconcussive symptoms (8). Body mass index was found to be similar between males and females and did not appear to be a confounding factor. This study supports the earlier work of Broshek *et al.* who found a larger prolongation in postconcussion reaction time and greater symptom severity in female high school and college athletes (5). In this study, participating in a sport that required the use of a helmet did not affect outcome. Also in 2009, Preiss-Farzanegan *et al.* published the results of a prospective nested cohort study investigating the effect of gender on developing prolonged symptoms. They found that women were at higher risk of experiencing postconcussive symptoms 3 months after injury (24). In the pediatric population, one recent study of children (mean age, 14.1 yr) showed that concussed girls had a significantly higher mean symptom score at the time of their initial presentation than boys (4).

Gender is emerging as an important consideration in concussion management. Although the data available are limited, there are enough to suggest that female gender increases the risk of being concussed and may portend worse outcomes. The explanation of this trend is up for debate and may include biomechanical, hormonal, and cultural factors. We know of several ongoing research protocols aimed at expanding this growing body of knowledge that may clarify further our understanding. In the meantime, we feel that it is prudent to consider the possible unique characteristics of the female population and to incorporate them in all concussion management paradigms.

## CHILDREN

There are many reasons why the pediatric population warrants special consideration. Biologically, the developing brain has a unique set of physiologic variables that are chang-

ing continuously as children grow. It is unclear how the ongoing brain development that occurs throughout childhood affects a child's susceptibility to concussion. Nonetheless, there is a sense that one should be more careful when making return-to-play decisions in children because of the uncertainty of dealing with a developing brain, the moving target of the patient's baseline cognitive function, and the potential unreliability of pediatric patients in reporting subjective symptoms (17). For these reasons, when dealing with a pediatric patient, the sports medicine practitioner should seek to include the input of parents, teachers, and coaches, as appropriate, to provide additional clarity as to the history.

It also is important to consider the appropriate age range that typical concussion management strategies can be applied to. The Zurich consensus statement uses 10 yr of age as the lower cut-off point of this range, noting that children below this age need a different, age-specific symptom inventory (20). We also advocate that when specialist referral is needed, clinical personnel specifically trained in caring for this age group are consulted for further evaluation. The pediatric group also is unique simply because of the fact that they are minors, not legally responsible for their own safety. In this way, they already are a population at risk because their safety ultimately depends on the actions of the adults charged with their protection.

## MOOD DISORDERS

Anxiety and depression are well recognized to occur after traumatic brain injury. Although there is active disagreement as to the degree of causative effect, there are enough data to suggest that patients with more mild brain injuries (Glasgow Coma Scale = 13–15) have a higher risk of developing postconcussive symptoms including fatigue, depression, and anxiety (18,25). Others have reported that subjective cognitive complaints from patients 6 months after a "mild to moderate" traumatic brain injury were linked closely with comorbid depression (7). Recently, the importance of mood disorders and posttraumatic stress disorder (PTSD) in the setting of mild traumatic brain injury in U.S. military personnel has been highlighted (13), demonstrating that PTSD and depression account for the majority of a wide range of predicted health outcomes.

To our knowledge, no study has been published that directly addresses the question of whether patients with a preexisting mood disorder such as depression or generalized anxiety are at a higher baseline risk of being concussed. This concept is intriguing given the possible common substrate of neuronal dysfunction in both mood disorders and concussion. As well, many of the symptoms of common mood disorders overlap to a large degree with those of concussion. The sports medicine practitioner, being ever more vigilant for concussive symptoms, is then faced with a difficult diagnostic dilemma. It also is possible that the degree of signs and symptoms seen in concussion seem more severe in athletes with mood disorders, given their baseline symptom levels. This underscores the value of knowing athletes well, considering all aspects of their health status, and individualizing their concussion management.

## LEARNING DISORDERS

Patients with learning disorders present a particularly difficult challenge to the sports medicine practitioner's concussion management paradigm. Some of the common effects of concussion, such as decreased attention level and difficulty with memory and learning, also can be caused by an underlying learning disorder or attention deficit hyperactivity disorder (ADHD). When using neuropsychological assessment as one part of a concussion protocol, great care should be given to establish each athlete's baseline function. This is a good opportunity to screen athletes for learning disorders both through interpretation of computerized neuropsychological test results as well as the taking of a careful medical and social history. Any suspicion of a learning disability or attention disorder warrants a more formal evaluation from a neurologist and/or neuropsychologist specifically trained in this area (20). As was the case with mood disorders, we are unaware of any published research that was designed to address the question of learning disorders as a risk factor for concussion. Having symptoms in common with concussion, it is clinically relevant to consider the possibility that one of these concurrent diagnoses exists and may be responsible for some of the presenting symptoms. Return-to-play decisions, as well as continue-to-play decisions, always should be made with close consideration of the athlete's accurate estimate of baseline cognitive function. Learning disabilities and attention disorders add another complex layer to this already complex management problem.

## MIGRAINE HEADACHE

While the relationship between migraine headache and concussion has been discussed in the literature and is garnering increased attention in clinical practice, there is little epidemiological data to help us understand how these two diagnoses may be related. In 2006, Gordon *et al.* performed an exploratory analysis of the Canadian Community Health Survey, identifying 270 patients between the ages of 12 and 24 yr reporting a history of sport-related concussion. Their multivariate analysis showed concussion to be associated with "being younger, male, and having migraine diagnosed by a health professional" (11). Given its nature, this population-based, cross-sectional study does not provide any information regarding causality, but it does give us cause to consider the relationship more carefully. In 2005, McCrory *et al.* used the standardized International Headache Society criteria for migraine headache to compare the prevalence of migraine in elite Australian soccer players to that of age- and sex-matched community controls, finding a statistically significant increase in the athlete population (21). Again, no causal relationship can be inferred. More recently, Lau and colleagues conducted a case-control study to identify patterns of symptom presentations and neuropsychological test results that might predict recovery in concussed U.S. high school football players (16). They found a preinjury migraine headache diagnosis in 14% of concussed athletes. Further, those athletes reporting migraine-type symptoms

at presentation were more likely to have a longer time to clinical recovery.

There are many ways that migraine headache and concussion could be related. Early thoughts on this relationship were that migraine headache could occur as the result of sports-related head trauma. In 1972, Mathews defined the term "footballer's migraine" to describe the migraine-type headaches experienced by soccer players after heading the ball (19). It is possible that migraine headache is a risk factor for concussion. It also is possible that concussion leads to the development of migraine headaches, or even that migraine headaches are being misdiagnosed as concussions. It is the experience of the authors that people who have migraines seem to be at an increased risk of sustaining a concussion, and they have more severe and prolonged concussion courses after injury. Understanding the exact nature of this relationship will prove to be difficult given the similarities in the clinical presentations of the two diagnoses and the possibility that they may even share a common pathophysiologic pathway (23).

## APOLIPOPROTEIN E

ApoE is a fat-binding protein that is essential for a multitude of biological functions. Three isoforms of the protein have been described, epsilon 2, 3, and 4. The epsilon 4 isoform (ApoE-E4) has been shown to be a risk factor for developing Alzheimer's disease (14). Recent efforts have focused on the possible roles of ApoE-E4 and the ApoE promoter gene in concussion risk (15,27). Kristman and colleagues performed a prospective cohort study of athletes from the University of Toronto and found no association between the presence of ApoE-E4 and the incidence of concussion (15). Terrell *et al.* reported a similar finding from their multi-center, cross-sectional study, but did find a nearly threefold increase in concussion risk associated with the presence of the subtype of the G-219T TT subtype of the ApoE promoter gene (27). The exact role of the ApoE promoter gene in concussion pathophysiology is unclear, but these early data suggest that further research is warranted. At this time, however, large-scale screening is impractical and not recommended.

## FAMILY HISTORY

Three of the potential risk factors for concussion that were mentioned previously have described some familial or genetic relationship. Migraine headache, mood disorders, and the particular ApoE genotypes each run in families to varying degrees. While the science behind the understanding of these entities as risk factors for concussion continues to move forward, and until we have a better understating of these relationships, it may be clinically useful to further consider the one common aspect between them: family history. Can a family history of sports-related concussion be of value in estimating concussion risk? The heterogeneity of concussive mechanisms and experiences as well as the varying sports experiences of family members make this a

difficult question to answer. The real clinical value of knowing an athlete's family history of concussion is reliant on the detail of the history. It is of little value to know that the father of an athlete "had a concussion or two in high school." In contrast, if one is told that the father had a history of multiple concussions with decreasing force requirements, escalating symptoms, changing personality, retirement from contact sports, and prolonged cognitive and mood effects, it is easier to see the clinical relevance. If further questioning reveals siblings or other relatives with similar histories, suddenly the risk profile of the athlete in question begins to change. Although we are aware of no published studies examining the relationship between a family history of concussion and concussion risk, we feel that it is an essential part of a complete approach to concussion management.

## FATIGUE

Concussion is widely considered to be a physiologic injury (20). Although the exact pathophysiology of concussion has not been described, most clinicians and scientists specializing in the field agree that concussion symptoms are the result of neuronal dysfunction that is linked closely with an "energy crisis" resulting from biomechanical forces applied to the brain. In this construct, it is easy to propose that an athlete's physiologic state plays a role in determining his or her risk of being concussed. In other words, if concussion is an injury of energy mismatch, it follows that it is more likely to occur in the setting of an energy-demand physiologic state. With this in mind, we feel that athletes are more likely to be concussed after significant physical exertion, especially in the setting of inadequate hydration or caloric intake. In 2008, Stevens and colleagues presented data from the National Hockey League (NHL) that supported this hypothesis (26). Using data on 787 players from the 2001–2002 NHL season, they concluded that in-game fatigue played a role in concussion risk.

A second, more speculative, role for physical fatigue in increasing concussion risk is based on the observation that physical exertion to the point of fatigue can lead to slowed reaction time (22). An athlete with slowed reaction time will, naturally, have a more difficult time avoiding contact and may be at a higher risk of concussion as a result. It also is important to note that physical exertion alone has been shown to produce concussive symptoms (1). We consider physical fatigue to be a risk factor both for developing concussive symptoms in the absence of a concussive injury as well as for sustaining a true concussion.

## THE ATHLETE STILL RECOVERING FROM CONCUSSION

It is important to keep in mind that there likely is a significantly increased risk of sustaining a concussion when an athlete is still recovering from a previous concussive injury. While we did not find any published epidemiologic data that describes this relationship directly, it is the personal experience of the authors that patients presenting to clinic

for a concussion evaluation often describe two distinct impacts that occurred during the game in question. Having only mild symptoms from the first hit, they continue to play without notifying a coach, athletic trainer, physician, or parent of their symptoms. A second impact, often of less or even minimal force, then produces signs and symptoms that are severe enough to be observed directly. In extreme cases, it is likely that this same scenario produces the "second impact syndrome" (3).

There is some published evidence that a recent concussion predisposes an athlete to a second injury. Without knowing which athletes were still experiencing the symptoms of an initial concussion, Guskiewicz *et al.* showed that high school football players who suffered a concussion were three times more likely to sustain a second concussion during the same season, as compared with their nonconcussed teammates (12). In another report, Delaney and colleagues showed that athletes who experienced concussion with a loss of consciousness were six times more likely to sustain another concussion than those who had been concussed but never lost consciousness (9).

## CONCLUSION

The current clinical practice of sports-related concussion management is dominated by the concept of resting an athlete until he or she is asymptomatic. The sports medicine practitioner then uses whatever objective data are available to best document a return to the athlete's functional baseline and challenges them with graded exercise and a progressive return to physical activity. After that, what then? Once we determine that a concussion has run its course, can we assume that each athlete returns to play with the same risk of a subsequent concussion? When we conduct preparticipation physical examinations and baseline cognitive and balance testing on a new group of athletes, can we assume that each athlete carries the same risk of being concussed when practice starts? In both cases, our practical experience tells us that the answer is "no." Each individual possesses his or her own risk of concussion that is determined by a host of intrinsic and extrinsic factors. By considering these factors and how they may affect concussion risk, we are better able to manage our athletes in the short term, as well as keeping an eye on their long-term health.

We consider the stratification of concussion risk to be an essential aspect of concussion management. The following recommendations are based mainly on our own clinical experience as well as the opinions expressed by other concussion experts. In some cases, as noted below, our recommendations also are supported by published data. We keep the following concepts in mind when making return-to-play decisions or giving advice on continued participation in contact sports:

- Data suggest that female athletes may have a higher incidence of concussion and experience more severe concussive symptoms.
- We believe that children should be managed more conservatively, and young children under the age of 10 yr need age-specific care.

• In our experience, the presence of preexisting mood or learning disorders can confound preinjury baseline testing as well as concussion diagnosis and management.

• Migraine headache and concussion have similar presentations, creating a diagnostic challenge. Athletes who have migraines also may be at a higher risk of being concussed, as is suggested by the data from the Canadian Community Health Survey.

• While the genetics of concussion remain a mystery, and the role of factors such as the ApoE promoter gene are being investigated, we feel that a complete family history can be clinically useful.

• There are some data to suggest that concussion risk may increase as an athlete fatigues or if he or she continues to participate in the sport after sustaining an initial mild head injury.

This approach represents a focus of concussion management that is patient-based, rather than injury-based. No concussion should be managed in isolation, as a point-in-time event. Instead, every concussion should be considered in terms of the individual athlete's complex and dynamic risk profile.

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