# Revisiting the modifiers: how should the evaluation and management of acute concussions differ in specific groups?

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#### **ABSTRACT**

**Background** One of the key difficulties while managing concussion in sport is that there are few prognostic factors to reliably predict clinical outcome. The aims of the current paper are to review the evidence for concussion modifiers and to consider how the evaluation and management of concussion may differ in specific groups.

**Methods** A qualitative review of the literature on concussion was conducted with a focus on prognostic factors and specific groups including children, female athletes and elite versus non-elite players. PubMed, MEDLINE and SportsDiscus databases were reviewed. **Results** The literature demonstrates that number and severity of symptoms and previous concussions are associated with prolonged recovery and/or increased risk of complications. Brief loss of consciousness (LOC) and/ or impact seizures do not reliably predict outcomes following a concussion, although a cautious approach should be adopted in an athlete with prolonged LOC or impact seizures (ie, >1 min). Children generally take longer to recover from concussions and assessment batteries have yet to be validated in the younger age group. Currently, there are insufficient data on the influence of genetics and gender on outcomes following a concussion.

**Conclusions** Several modifiers are associated with prolonged recovery or increased risk of complications following a concussion and have important implications for management. Children with concussion should be managed conservatively, with an emphasis on return to learn as well as return to sport. In cases of concussions managed with limited resources (eg, non-elite players), a conservative approach should also be taken. There should be an emphasis on concussion education in all sports and at all levels, particularly in junior and community-based competitions.

# INTRODUCTION

Concussion in sport reflects a disturbance of brain function and is characterised by a set of clinical features that typically come on rapidly and resolve spontaneously over a sequential course. 1-3 While the time course of recovery is variable, evidence suggests that the majority of concussed athletes recover clinically within 10 days of injury. 1-3 Concussion, however, is not a benign injury. A small percentage of athletes suffer complications such as persistent symptoms and in rare instances of concussion in children and adolescents, malignant cerebral oedema may result. 1-3 Furthermore, there is growing concern regarding an association

between repeated head trauma and long-term risk of depression and/or dementia.<sup>4–7</sup>

One of the key difficulties for the clinician is the absence of prognostic factors to help predict outcomes following a concussion. <sup>1–3</sup> At the Third International Conference on Concussion in Sport, a number of clinical features or 'modifiers' were identified as being associated with an increased risk of prolonged recovery or complications following a concussion (table 1). <sup>3</sup> Other factors, such as female gender and genetics were considered; however, it was decided that there was insufficient evidence for their inclusion as modifiers. <sup>3</sup>

The objectives of the current report are to review the evidence for concussion modifiers, and to consider how the evaluation and management of concussion may differ in specific groups (particularly children and adolescents, male vs female athletes and elite vs non-elite athletes).

#### **METHODS**

Searches of MEDLINE (ISI Web of Science, PubMed) and SportDiscus databases were undertaken using keywords 'concussion', 'mild traumatic brain injury', 'head injury', 'sport' or 'athlete/ athletic'.

These were combined with the following key words to identify the literature for specific modifiers as well as key aspects of investigation and management: 'clinical features', 'symptoms', 'post-concussion syndrome', 'balance', 'postural control', 'cognition', 'cognitive deficit', 'persistent', 'neuropsychological', 'neurocognitive', 'prognostic factors', 'recurrence', 'cumulative effect', 'injury severity', 'genetic', 'child', 'children', 'pediatric', 'elite', 'non-elite', 'professional', 'recreational' and 'epidemiology'.

The search was limited to English language and focused on original papers published in the past 10 years. Articles on moderate to severe traumatic brain injury (TBI) were excluded. Reference lists from retrieved articles were searched for additional articles, and the authors' own collections of articles were included in the search strategy.

#### RESULTS

## **Clinical features**

**Symptoms** 

There is consistent evidence of a relationship between the number and severity of symptoms reported following a concussion and the overall severity of injury. Studies have used different populations (including Australian football players, <sup>9</sup> 10 professional American football players <sup>11</sup> and US

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Factor	Modifier
Symptoms	Number
	Duration (>10 days)
	Severity
Signs	Prolonged loss of consciousness (>1 min), amnesia
Sequelae	Concussive convulsions
Temporal	Frequency—repeated concussions over time Timing—injuries close together in time
	'Recency'—recent concussion or traumatic brain injury
Threshold	Repeated concussions occurring with progressively less impact or slower recovery after each successive concussion
Age	Child and adolescent (<18 years old)
Comorbidities and premorbidities	Migraine, depression or other mental health disorders, attention deficit hyperactivity disorder, learning disabilities, sleep disorders
Medication	Psychoactive drugs, anticoagulants
Behaviour	Dangerous style of play
Sport	High-risk activity, contact and collision sport, high sporting level

high school and collegiate athletes<sup>12–14</sup>), different measures of injury severity (including return to play on the day of injury<sup>9</sup> and time to clinical recovery<sup>10</sup> <sup>12</sup> <sup>13</sup>) or stratified populations based on time-course of clinical recovery and compared their initial presentation.<sup>11</sup> <sup>14</sup> The consistent finding is that the higher the number and severity of symptoms at the time of injury, the higher the severity of concussion. In addition, athletes reporting four or more symptoms appear to be more likely to have a prolonged recovery.

Other clinical features that have been associated with prolonged recovery include amnesia,  $^{11}$   $^{15-17}$  prolonged headache,  $^{10}$   $^{16-18}$  fatigue or fogginess,  $^{10}$   $^{11}$   $^{17}$   $^{19}$  self-reported cognitive or memory problems  $^{11}$   $^{13}$   $^{20}$  and dizziness at the time of injury.  $^{21}$ 

Overall, research suggests that the nature, burden and duration of symptoms should be retained as concussion modifiers.

#### Loss of consciousness

Traditionally, LOC was a clinical marker for higher injury severity in TBI.<sup>22</sup> Prospective cohort studies on concussion in sport, however, have consistently demonstrated that brief LOC does not reflect injury severity or predict time to clinical recovery.<sup>10 15 21 23</sup> One study however demonstrated that concussed players with prolonged LOC (>1 min) were more likely to miss 7 or more days of sport.<sup>11</sup> No other studies have been published on prolonged LOC.

The literature does not support the inclusion of brief LOC as a concussion modifier. Caution should be used in cases of concussion with prolonged LOC; however, further research is still required.

#### Impact seizures

In a large-scale retrospective series in Australian football, impact seizures were demonstrated to be benign with no adverse clinical, cognitive or neuroimaging outcomes observed either at the time of injury or long-term follow-up.<sup>24</sup> No new studies have been published on outcome following impact seizures since that time.

The literature does not support the inclusion of impact seizures as a concussion modifier. In athletes with prolonged seizures (ie, >1 min); however, other causes (eg, structural head injury or underlying seizure disorders) should be considered.

## Biomechanics of injury

There has been increasing use of helmet and/or mouthguard-based accelerometer systems to measure the direction and force of head impacts. The studies have not shown any association between number of head impacts and risk of concussion, <sup>25</sup> nor has there been an association demonstrated between the magnitude of the impacts and probability or severity of concussion. <sup>26</sup>

Currently, there is little evidence to support the use of telemetry systems in routine clinical practice beyond their role as a research tool.

## **Concussion history**

Concussion history and malignant cerebral oedema

Malignant cerebral oedema following head injury is a rare but well-recognised condition.<sup>27</sup> It is more common in children than in adults and typically has a poor outcome.<sup>27</sup> Although the condition (previously called 'second impact syndrome') has been linked to recurrent head trauma, the scientific evidence to support this concept is limited.<sup>28</sup>

Concussion history and risk of acute concussion

A number of studies have consistently demonstrated that a previous concussion is a risk factor for future concussion. <sup>29–33</sup>

While it has been proposed that a previous head trauma reduces the threshold for future concussions, there is little evidence to support this concept. In one study, the majority of repeat concussions were observed within 10 days of an initial injury, suggesting a possible 'window of vulnerability' for further concussion. This finding has not been replicated in other prospective cohort studies, with no obvious pattern demonstrated in the incidence or timing of repeat concussions. Furthermore, in a head impact telemetry study of 95 high school football players, neither the volume nor the intensity of subconcussive head impacts was found to influence the threshold for concussion. Style of play may be an important confounding variable, where by tackling technique and illegal tackles may be important risk factors for head injury.

Concussion history and timing of recovery following a concussion A number of prospective studies have assessed the relationship between concussion history and delayed recovery (summarised in table 2).

Paper	Subject characteristics	Concussion reporting	Outcome measures	Findings/results
Guskiewicz <i>et al</i> <sup>31</sup>	US College football athletes followed over 3 seasons (196 concussions were reported in 184 players, 12 repeat concussions)	Prospective and retrospective	Graded symptom checklist, health questionnaire	Slowed recovery was associated with a history of previous concussions (30% of athletes reporting 3 or more previous concussions had symptoms lasting >1 week, compared with 14.6% of those reporting 1 previous concussion)
Slobounov et al <sup>103</sup>	Male and female collegiate rugby players (38 players with no history of concussion, 9 with a repeat injury)	Prospective	Symptoms, NP testing, computerised balance measures (using a virtual reality system)	All athletes were clinically asymptomatic at day 10 and allowed to return to competition. Balance deficits were present for at least 30 days after injury. Rate of recovery of balance function was significantly slower after a second injury
Echlin <i>et al</i> <sup>34</sup>	Male fourth tier ice hockey players followed over 1 season (17 concussions, 5 of which suffered repeat concussion)	Prospective and retrospective	SCAT2 and computerised NP test battery	Minimal difference in return to play times between those who reported no previous concussions (8 players, mean 11.5 ±7.6 days to return to play) and 1 or 2 previous concussions (6 players 10.7±2.94 days). Two players who reported 3 or more previous concussions had delayed recovery
Benson et al <sup>17</sup>	Professional ice hockey players followed over 7 seasons (559 concussions)	Prospective	Symptom checklist and time loss from sport postinjury	On average, time loss (in days) increased 2.25× (95% CI 1.41 to 3.62) for every subsequent concussion
Castile et al <sup>12</sup>	US high school students (data on 2417 concussions obtained from an injury surveillance database entered by certified athletic trainers)	Prospective	Symptoms and time to return to play	Symptoms took 1 week to 1 month to resolve in 20.9% of recurrent concussions compared with 13.8% of new concussions (p=0.012). Similarly, symptoms in 6.5% of recurrent concussion took >1 month to resolve, compared to 0.6% of new concussions (p<0.001) A greater proportion of athletes sustaining a recurrent concussion returned to play in >3 weeks (7.5%) or were medically disqualified (16.2%) than athletes sustaining a new concussion (3.8% and 2.9%)

In general, athletes with a previous history of concussion are more likely to present with a longer duration of symptoms and are withdrawn from competition for longer following their injury. There is limited evidence to suggest that the timing or 'recency' of injury makes any difference to timeframe of recovery following a concussion. There is also limited evidence to suggest longer timeframes of recovery for each subsequent concussion. The subsequent concussion.

NP, neuropsychological; SCAT2, Sport Concussion Assessment Tool 2.

# Concussion history and long-term deficits

Many of the early studies on long-term deficits following a concussion were cross-sectional in design and used performance on cognitive testing to estimate impairment. Major limitations included a reliance on retrospective recall of concussion history, which is known to be inaccurate and unreliable,<sup>37–38</sup> and failure to account for important variables that can impact cognitive performance, such as age, education, alcohol use and other socioeconomic factors.<sup>39</sup> Not surprisingly, the results of these studies were conflicting regarding the effect of repetitive head injury on brain function, with some studies demonstrating impaired cognitive performance in athletes reporting a history of two or more concussive injuries,<sup>40</sup> and others failing to demonstrate any significant effects of self-reported concussion history on cognitive performance.<sup>41</sup>

Higher-quality studies using prospective designs and/or medically verified concussions have been published in recent years. These are summarised in table 3.

The relationship between repeated head trauma and long-term deficits remains unclear. More sophisticated investigations such as EEG, functional MRI (fMRI) and balance assessments demonstrate persistent changes in some individuals after concussion. At present, the clinical significance of these changes remains unclear. Nevertheless, in the clinical setting it is prudent to adopt a conservative approach in the management of

athletes involved in sports with a high risk of recurrent head trauma or those who present with recurrent concussions.

#### Genetics

Preliminary studies suggest an association between Apolipoprotein epsilon (APOE) genotype and the chronic effects of concussion on brain function. Jordan et al<sup>42</sup> demonstrated greater neurological impairment secondary to boxing among high-exposure athletes (≥12 bouts) who possessed the APOE4 allele compared to high exposure athletes without the allele and low-exposure boxers regardless of genotype. Similarly, Kutner et al<sup>43</sup> demonstrated that professional American football players with at least one copy of the APOE4 allele scored lower on tests of attention and information processing speed and accuracy. In a neuropathological study of athletes with Chronic Traumatic Encephalopathy (CTE), an increased frequency of the APOE4 allele was noted among 10 cases of pathologically confirmed CTE.<sup>6</sup> Recently, a large case series did not find a definite relationship between APOE genotype and lesser grades of CTE; however, a higher incidence of APOE4 genotype was noted in higher grades.44

While there may be a relationship between APOE genotype and chronic changes following concussion, the role of APOE in acute concussion is less clear. A prospective cohort study of collegiate athletes failed to demonstrate an association between APOE genotype and risk of concussion. Conversely, other studies have demonstrated an association between APOE promoter genotypes and history of self-reported concussion. In one study carriers of all three rare (or minor) alleles were 10 times more likely to report a previous concussion.

A large multicentre prospective cohort study of 3218 collegiate or high school athletes failed to demonstrate an association between acute concussion risk and APOE and APOE promoter polymorphisms.<sup>48</sup> However, in a subset of 131 concussed

Prospective cohort 9 Concussions, 6 healthy controls  Prospective cohort 9 Concussions (sessed at day 3 15, 22)  Prospective cohort 9 Concussions (sessed at day 3 15, 22)  Prospective cohort 1 Collegate students with profotograd of the concussions (sessed at day 3 0 days postniym), 30 healthy controls  To concussions (some day 10 postniym)  Prospective cohort 1 Collegate students with midd 181 (injunits stratamed in 181 controls of the concussions (scanned at 5 days and formal controls of concussions (scanned day 10 postniymy)  Prospective cohort 1 Collegate students with midd 181 (but date at a concussions (scanned day 10 postniymy)  Prospective cohort 2 Concussions (scanned day 10 postniymy)  Prospective cohort 3 (all parties)  Cross-sectional 48 Concussions (scanned day 10 postniymy)  Prospective cohort 3 (all parties)  Cross-sectional 48 Concussions (scanned day 10 postniymy)  Prospective cohort 3 (all parties)  Cross-sectional 48 Concussions (scanned day 10 postniymy)  Cross-sectional 48 Concussions (scanned day 10 postniymy)  Cross-sectional 19 Individuals with midd 181 (but data properties)  Cross-sectional 19 Individuals with midd 181 (but data properties)  Prospective cohort 3 (all parties)  Cross-sectional 48 Concussions (scanned day 10 postniymy)  Recent concussion, crowered 64 (all postniymy)  Cross-sectional 19 Individuals with midd 181 (but data properties)  From the postniymy of the concussions (scanned day 10 postniymy)  Recent concussion, crowered 64 (all parties)  Cross-sectional 19 Individuals with midd 181 (but data properties)  From the postniymy of the concussions (scanned day 10 postniymy)  From the postniym of the concussions (scanned day 10 postniymy)  From the postniym of the concussions (scanned day 10 postniymy)  From the concussions (scanned	Paper	Study type	Subject characteristics	Inclusion criteria	Outcome measures	Findings/results
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Prospective   40 Concussions (essessed at day 3, 15, 22)   Recent concussion of multicenter)   and 30 days postalyjuny), 30 healthy controls of olores sectional   10 Collegate students with prolonged prospective color   10 Collegate students with mid 18 (injunée sustained horse-sectional college athletes and motor while technical shift technical shift technical shift technical shift technical shift technical lobe), and character symptoms, and a fall, 10 healthy controls and motor while a fall patients. Coss-sectional college athletes and motor while a fall patients accidentely, 23 controls (scanned at fine 0 and 17 controls).    Prospective color   College athletes   Prospective color   College athletes   Prospective color   College athletes   Prospective color   College athletes   Prospective color   Prospective	Chen <i>et al</i> <sup>104</sup>		9 Concussions, 6 healthy controls	Persistent symptoms following concussion	Symptom reporting and fMRI (working memory task)	Significantly reduced task-related BOLD changes in the prefrontal cortex in athletes with prolonged symptoms following concussion. Activation patterns improved as symptoms improved
To Collegiate students with polonged and prosting prosting to conserved during spot 1 injured in a family consequence of the prostate of the	Vagnozzi et al <sup>105</sup>	Prospective (multicentre) cohort	40 Concussions (assessed at day 3, 15, 22 and 30 days postinjury), 30 healthy controls	Recent concussion Age 16–35	Symptom reporting and MRS Used single voxel (ROI: right frontal lobe), and chemical shift techniques to analyse data	Self-reported symptoms recovered within 3–15 days Significant differences between concussed and control groups were observed in metabolite ratios at day 3 postinjury. Metabolite changes gradually recovered to control levels within 30 days of injury
Prospective cohort   14 Patients with mild TBI (injuries sustained in recreational activity, work and motor whicle recreated   19 Prospective cohort   College athletes   10 concussions (scanned at 16 days and 6 months post injury)   10 controls (scanned at 10 months post injury)   10 controls (scanned at 10 months post injury)   10 controls (scanned day 10 postinjury)   17 controls   17 controls   18 months   18 months   19 controls   19 contro	Cubon et al <sup>106</sup>	Cross-sectional	10 Collegiate students with prolonged symptoms (9 injured during sport 1 injured in a fall), 10 healthy controls, 5 moderate-to-severe TBI patients	Persistent symptoms 1 month postinjury	DTI (MD and FA analysed using tract-based spatial statistics)	Significant increase in MD in concussed compared to controls. Similar results were observed in the moderate but not severe TBI patients when compared to controls
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Cross-sectional College athletes  To concussions (scanned day 10 postinjury) To concussions To concussions To concussions To concussions To concussion assessed To concussion adults (n=30) To concussions To concussions To concussion assessed To concussion adults (n=30) To concussions To concussion adults (n=30) To concussions To concussion assessed To concussion adult (n=30) To concussion assessed To concussion adult (n=30) To concussion assessed To concussion adult (n=30) To concussion assessed To concussion adult (n=34) To concussion adult (n=30) To concussion adult (n=34) To concussion adult (n=3	Henry et al <sup>108</sup>	Prospective cohort	College athletes 10 concussions (scanned at 5 days and 6 months post injury) 10 controls (scanned at time 0 and 18 months)	Recent concussion	Symptom reporting and MRS (ROI: prefrontal and primary motor cortex)	Neurometabolic differences between concussed and control were observed in the acute phase (lower N-acetylaspartate: creatine levels in the prefrontal cortex and lower glutamate :creatine levels in the motor cortex) as well as the delayed phase (increase in the myoinositol levels in the motor cortex)
geon Gross-sectional 48 Concussions 49 Additional concussions 59 Additional concussions 50 Additional concussion	Slobounov et al <sup>109</sup>	Gross-sectional	College athletes 17 concussions (scanned day 10 postinjury) 17 controls	Recent concussion, clinically recovered	Symptom checklist, NP testing, rsFMRI	All athletes had recovered clinically within 10 days rsFMRI revealed disrupted functional network both at rest and in response to a graded physical test (reduced interhemispheric connectivity in the primary visual cortex, hippocampus and dorsolateral prefrontal cortex)
Cross-sectional Collegiate athletes 14 Concussions 15 Controls 9 Additional concussions Cross-sectional 19 Individuals with mild TBI (No data provided on the mechanism of mild TBI)—11 earlier, GCS 13—15 on persistent symptoms, 8 clinically recovered), 9 admission, normal MRI measure MT healthy controls ed head impact (subconcussive blows) and prolonged deficits Prospective cohort 9 High school athletes, 6 controls between 26 and 399 subconcussive blows	Baillargeon et al <sup>110</sup>	Cross-sectional	48 Concussions 48 Controls (9–12 years (n=32), 13–16 years (n=34), adults (n=30))	Concussion assessed >6 months postinjury	Postconcussion symptom scale, NP tests, EEG (visual 3-stimulus oddball paradigm)	Concussed athletes had lower P3b amplitudes than the control athletes Adolescent athletes showed persistent deficits in working memory
Cross-sectional 19 Individuals with mild TBI (No data Injury sustained 5 years Used navigated transcranial magnetic provided on the mechanism of mild TBI)—11 earlier, GCS 13–15 on stimulation and electromyography to persistent symptoms, 8 clinically recovered), 9 admission, normal MRI measure MT healthy controls head impact (subconcussive blows) and prolonged deficits  Prospective cohort 9 High school athletes, 6 controls between 26 and 399 subconcussive blows	Johnson et al <sup>111</sup>	Gross-sectional	Collegiate athletes 14 Concussions 15 Controls 9 Additional concussions	Recent concussion, recovered clinically	rsFMRI (measured the default mode network)	Significant default mode network connectivity differences were observed between concussed and control groups Regression analysis revealed a significant reduction in magnitude of connection between various structures in the brain as a function of the number of concussions
ed head impact (subconcussive blows) and prolonged deficits 1 Concussion, others suffered DTI at baseline and postseason Prospective cohort 9 High school athletes, 6 controls between 26 and 399 subconcussive blows	Tallus et al <sup>112</sup>	Cross-sectional	19 Individuals with mild TBI (No data provided on the mechanism of mild TBI)—11 persistent symptoms, 8 clinically recovered), 9 healthy controls	Injury sustained 5 years earlier, GCS 13–15 on admission, normal MRI	Used navigated transcranial magnetic stimulation and electromyography to measure MT	MT was higher in some (but not all) mild TBI subjects than in controls. Changes were observed even in subjects who had recovered their symptoms Authors suggested that subtle prolonged changes may exist in some patients following mTBI and that in a proportion of these patients the changes may be 'compensated'
	B. Repeated h Bazarian e <i>t al<sup>113</sup></i>	lead impact (subconcu. Prospective cohort	ssive blows) and prolonged deficits 9 High school athletes, 6 controls	1 Concussion, others suffered between 26 and 399 subconcussive blows	DTI at baseline and postseason	Percentage of voxels with significant prepost FA or MD changes was highest for the concussion subject, intermediary for those with subconcussive head blows and lowest for controls

Paper	Study type	Subject characteristics	Inclusion criteria	Outcome measures	Findings/results
Breedlove et al <sup>114</sup>	Prospective cohort (2 seasons)	Prospective cohort 24 Male high school football players followed (2 seasons) in season 1, 28 players followed in season 2 (including 14 from previous season)	All players monitored, concussions diagnosed by clinician	Helmet telemetry system, computerised NP testing, fMRI	Divided groups into concussed, not concussed and not concussed but demonstrable cognitive or functional deficit. Found 'substantial' portion of the cohort without concussion demonstrated neurophysiological changes on fMRIThere was also a relationship between number of head impacts and changes on NP testing
Gysland et al <sup>115</sup>	Prospective cohort	Prospective cohort 46 Male collegiate football players	No concussions in the 3 months before baseline testing	Computerised NP test battery, SAC, SOT, BESS and graded symptom checklist, self-reported concussion history and Head impact telemetry	Changes in symptoms, balance function or NP function were independent of prior concussion history and total, number magnitude and location of impacts over 1 season
Neselius et al <sup>116</sup>	Prospective cohort	Prospective cohort 30 Boxers and 25 non-boxing controls	High-level amateur boxers (national or international level) with a minimum of 45 bouts	CSF samples collected by lumbar puncture (1–6 days after a bout and after at least 14 days of rest)	Increase in biomarkers for acute brain injury in the boxing group (NFL, GFAB, T-Tau and SB-100) compared to controls. NFL and T-Tau concentrations remained elevated even after a period of rest
BESS, balan EEG, electro rsFMRI, resti	ce error scoring system; B encephalogram; GCS, Gla ing state fMRI; SAC, Stand	BESS, balance error scoring system; BOLD, blood oxygenation level-dependent; CSF, cerebrospinal fluid; DTI, Diffusion tensor imaging; ERP, event-related brain potential; FA, fractional aniss EEG, electroencephalogram; GCS, Glasgow Coma Score; GFAB, glial fibrillary acidic protein; MD, mean diffusivity; MRS, MR spectroscopy; MT, motor threshold; NFL, neurofilament light prors-rs-MRN, resting state fMRI; SAC, Standardised assessment of concussion; SOT, Sensory organisation test (computerised test of balance function); 1-Tau, total Tau, TBI, traumatic brain injury.	rospinal fluid; DTI, Diffusion tensor in n; MD, mean diffusivity; MRS, MR st panisation test (computerised test of	maging; ERP, event-related brain potential; FA, fra pectroscopy; MT, motor threshold; NEL, neurofilam balance function); T-Tau, total Tau.TBI, traumatic I	BESS, balance error scoring system; BOLD, blood oxygenation level-dependent; CSF, cerebrospinal fluid; DTI, Diffusion tensor imaging; ERP, event-related brain potential; FA, fractional anisotropy; fMRI, functional magnetic resonance imaging: EEG, electroencephalogram; GCS, Glasgow Coma Score; GFAB, glial fibrillary acidic protein; MD, mean diffusivity, MRS, MR spectroscopy; MT, motor threshold; NRI, neuroilament light protein; NP, neuropsychological; ROI, regions of interest; rsFMRI, resting state fMRI; SAC, Standardised assessment of concussion; SOT, Sensory organisation test (computerised test of balance function); T-Tau, total Tau, total Tau. TBI, traumatic brain injury.

athletes, an association between neuropsychological testing and genetic polymorphisms was identified. 48

Overall, more research is required to determine the genetic risks of concussion and the role of specific genes in neurocognitive recovery in both acute and chronic TBI.

#### Age

It has been suggested that the impact force required to produce a concussion is greater in children than adults. The poorly developed cervical musculature, in combination with the increased head to neck ratio in children, results in greater injury to the child's brain for the same impact force. <sup>49</sup> <sup>50</sup> Recovery from concussion in children generally takes longer than that in adults. This is evident in time taken for symptom resolution, as well as neurocognitive recovery. <sup>51–54</sup>

# Management considerations in children

Children differ from adults in a number of ways, including: (1) physiological and cognitive development, (2) impact forces and protective abilities, (3) physical and cognitive recovery, (4) effects on school and learning and (5) potential for long-term sequelae (including malignant cerebral oedema). Furthermore, concussion in children typically occurs in a community rather than in an elite setting, where resources and expertise may be limited.

#### Assessment tools in children and adolescents

There are limited data on clinical assessment tools in children and adolescents with concussion.

Many symptom scales have been developed for use in adults, but few have been developed specifically for children. <sup>55</sup> <sup>56</sup> Some symptom scales have been used in children to assist with the diagnosis of concussion, <sup>57</sup> while others have been tested as markers of persistence of symptoms, <sup>58–62</sup> or to monitor stages of recovery. <sup>63</sup>

The Balance Error Scoring System has limited data in young children. No validity studies have been published and reliability studies in children aged between 9 and 14 years demonstrate a significant learning effect with repeated exposure, and variability in results between the different leg stances. 64 65

The Standardised Assessment of Concussion (SAC), <sup>64–66</sup> Acute Concussion Evaluation <sup>67</sup> and Sport Concussion Assessment Tool 2 (SCAT2) <sup>68 69</sup> have all been used, but none has been specifically developed for the assessment of young children at the sideline, nor have they been adequately evaluated for use in children.

#### Return to learn

Return to school should be a priority for children and adolescents following a concussion. Return to learn should precede return to play.

There are no clear guidelines for return to school for youths who have sustained a concussion, although this is an area of increasing interest. A temporary absence from school after a concussion may be necessary to allow symptoms to abate.<sup>70 71</sup> Once symptoms have decreased and the child is able to complete more cognitive tasks without exacerbation of symptoms, a gradual return to school is advocated.<sup>70-73</sup> Specific accommodations, or modifications, to a patient's academic schedule may be required (eg, attending for only half-days or for only certain classes). Accommodations should be individualised, depending on the symptoms or difficulties that the youth is experiencing (eg, frequent breaks in class and extra time for assignments for those having trouble concentrating).<sup>72 73</sup> As with many aspects

of medicine, transitioning students recovering from a concussion back to school is best achieved with a team approach.  $^{72}$   $^{73}$ 

#### Return to play

It is recommended that return to play protocols be cautious and individualised in paediatric athletes, <sup>3</sup> <sup>70</sup> <sup>71</sup> <sup>74</sup> as younger athletes take longer to recover and have more significant neurocognitive effects following a concussion. <sup>52</sup> <sup>53</sup> <sup>75</sup>

#### Gender differences

Data suggest that in sports that use the same rules, the reported incidence of concussion is greater in females than their male counterparts. <sup>76–80</sup> In studies of high school and college sports, women had significantly higher concussion rates than men in soccer and basketball, <sup>76–79</sup> whereas concussion risks between genders were not significant in lacrosse, softball/baseball or gymnastics. <sup>79</sup> In addition, there appear to be differences in how women experience concussive symptoms as well as how long symptoms persist compared with men. <sup>79–84</sup>

It is unclear why these gender differences occur. They may be owing to reporting and selection bias, with women and/or healthcare providers more likely to report injury. In addition, female athletes have been shown to have decreased head–neck segment mass compared with male athletes so and this may contribute to greater angular acceleration of the head after concussive impact as a mechanism for more severe injury. Oestrogen and differential cerebral blood flow may also play a role in influencing concussion severity and outcome. The data thus far are inconclusive, and further study is needed to understand if gender is a risk factor for concussion. In addition, other differences may exist in how females experience and respond to concussion, in the deficits that are seen with comprehensive neurobehavioral assessments, and in the return-to-play progression. States and selection bias, with women and/or head-neck segment to report the second segment to the second segment to report the second segment to return to the second segment to return to the second segment to return to-play progression. States are seen with comprehensive neurobehavioral assessments, and in the return-to-play progression.

Whether there are differences in the chronic responses to concussive injury in women compared with men is unclear. One study found slower reaction times, more symptoms, and lower neurocognitive scores among female athletes compared with male athletes. <sup>81</sup> In another study involving 260 youth, high school and collegiate athletes, chronic impairments were more frequently reported in adult females but not in female minors. <sup>90</sup> In a study of high school and collegiate athletes, women with a history of 2–3 concussions performed better in the ImPACT test battery than males with ≥2 concussions, with specific differences observed in visual memory, motor-processing speed and reaction time. <sup>89</sup> These limited studies are inconclusive, and make it clear that additional research is needed.

## Elite versus non-elite

In distinguishing elite versus non-elite athletes' management, it is more important to consider the level of care provided to the athlete. In general, elite athletes have greater resources available to them, such as trained medical providers and the availability of neuropsychological and postural stability testing that allow for a more multifaceted approach to management. In the absence of resources to assess recovery following a concussion, the same basic concussion management principles should apply, but a more conservative approach be adopted, no matter what the level of the athlete.

#### Reducing the risk of concussion

Suggestions that tackling in youth collision sport be outlawed<sup>92</sup> are likely to be effective in decreasing concussion incidence but will alter the fabric of collision sports too significantly to allow

for widespread acceptance. More pragmatic law changes to collision sports may significantly influence injury incidence at both elite and non-elite levels. Examples include strict enforcement of below-shoulder height tackling and forbidding tip or spear tackles in rugby union, <sup>93</sup> head-to-head and head-to-body contacts in American Football <sup>94–96</sup> and body checking in youth ice hockey. <sup>97</sup>

Concussion awareness among sportspersons and medical professionals

Evidence across a number of sports including rugby union, <sup>98</sup> ice hockey <sup>99</sup> and soccer <sup>100</sup> indicates that athletes' understanding of concussion is poor. Moreover, non-elite athletes may present to emergency rooms and family practitioners who may not be as well informed as sports physicians and neurologists regarding the most appropriate assessment tools and management strategies for concussion. <sup>91</sup> In addition, the SCAT2 has been described as being incomplete for the serial office assessment of concussed athletes and better tools, which could be made available to a wider range of practitioners, have been proposed. <sup>101</sup>

An emphasis on efficient dissemination and implementation of concussion consensus protocols, within and beyond the elite circle of sports care, would help address the issue of accessibility to appropriate care for all.

#### **SUMMARY AND CONCLUSIONS**

In adults, the majority of concussions resolve clinically within 10 days of injury. The current study reviewed the literature regarding clinical factors associated with prolonged recovery or poor outcome.

### Concussion modifiers—an update

The current literature supports the role of a number of clinical factors as concussion modifiers. These include number and severity of symptoms, previous concussions and younger age. It is important to note that, while an association has been demonstrated between the modifiers and risk of poor outcome following concussion, in many cases (eg, recurrent head trauma) a causal link has not been clearly established. Nevertheless, presence of any of these modifiers should alert the clinician to the potential for prolonged recovery and/or long-term complications.

Brief LOC and/or impact seizures cannot be relied upon to predict the outcome following a concussion. In athletes with prolonged LOC or impact seizures (ie, >1 min), a cautious approach to management should be followed and structural head injury or underlying seizure disorders should be considered.

Currently, there are insufficient data on the role of genetics and gender on the outcome following concussion.

#### Age

Children generally take longer to recover from concussions and therefore should be managed more conservatively.

The development of the child's brain and the associated physical growth, especially between the ages 5 and 15 years, <sup>102</sup> necessitate a specialised approach to concussion management. Assessment tools need to be developed and validated for the paediatric group. Such tools need to allow for cognitive and physical development. Symptom scales must include language that is understood by young children. The addition of parent or teacher reports of symptoms can be integrated into recovery and return-to-play decision-making. Cognitive tests must be developmentally appropriate, and demonstrate validated changes to

concussion and recovery. Physical tasks such as balance testing, must be reliably performed by normal children to demonstrate impaired response in concussion, which can be corrected with recovery.

Finally, unlike the adult concussion protocols that assume a primary endpoint of return to play, the child protocol must assume a primary endpoint of return to school. Management of symptoms that impact on the child's ability to learn in school requires a cooperative approach between the child, parents, teachers and medical staff.

# Elite versus non-elite

In all athletes with concussion there should be an evidencebased 'gold-standard' of care as determined by international consensus. In cases with limited resources, a more conservative approach is warranted. Overall, there should be an emphasis on education at all levels of competition, particularly in junior and community-based competitions, where personnel with expertise in concussion and resources for assessment and evaluation of concussion may be limited.

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