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Review

An overview of concussion in sport

Vini G. Khurana, Andrew H. Kaye *

Department of Neurosurgery, The Royal Melbourne Hospital, Grattan Street, Parkville, Victoria 3050, Australia
Department of Surgery, The University of Melbourne, Parkville, Victoria, Australia

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ABSTRACT

Concussion is a sudden-onset, transient alteration of consciousness due to a combination of functional and structural brain disturbances following a physical impact transmitted to the brain. It is a common, although likely underreported, condition encountered in a wide range of sports. In the Australian Football League, concussion is estimated to occur at a rate of approximately seven injuries per team per season. While many instances of concussion are clinically mild, there is emerging evidence that a player's full recovery from a concussive injury may be more delayed and the sequelae of repeated concussions more severe than previously thought. In this light, a more conservative and rigorous approach to managing players with concussive injuries may be warranted, with the guiding principle being the player's immediate and long-term welfare. The current paper reviews the sports concussion literature. The definition, epidemiology, aetiology, pathophysiology, structural pathology, clinical features, assessment and investigation, treatment principles, and short-term and potential long-term complications of concussion are discussed. Special considerations in paediatric sports concussion, and the return-to-play implications of immediate, evolving and repetitive brain injury are also considered, as are the emerging concept and possible implications of subconcussive injury.

1. Introduction

As evidenced by a spate of recent high-profile sports concussion injuries and lawsuits, concussion in sport is highly topical. While concussion is often trivialised in the media and sporting circles as a "knock" to the head, the 2010 publication of the forensic pathology findings in a series of deceased professional American athletes aged 50 years or younger who died following suicide or after multiple suicide attempts[1,2], raises concerns regarding the possibility of serious long-term sequelae of repeated concussions. Given the relatively high prevalence of concussion in sports, despite its likely underreporting, important questions arise including whether there are long-term sequelae such as early cognitive decline and psychiatric illness and, should the approach to sports-concussed athletes be more uniform and conservative? This review will present the pathophysiological basis of concussion and its possible long-term effects, in addition to its clinical manifestations and important management considerations.

2. General overview

2.1. Definition

While there is no universal agreement on the definition of "concussion[3]", it has been proposed that the term should *not* be used interchangeably with "mild traumatic brain injury" (TBI)[4–6] as the former can be a serious injury that, particularly with repetitive occurrences, may have longer-term neuropsychological sequelae. Further, as elaborated below, a clear distinction should be made between "concussion" and "post-concussion syndrome" (PCS).

Concussion refers to a sudden and transient alteration in consciousness induced by traumatic biomechanical forces transmitted directly or indirectly to the brain.[3,4,7] The word is derived from the Latin *concutere*, meaning "to shake violently". There may or may not be loss of consciousness, although a concussion typically *does* involve some period of transient amnesia.[3] While concussion does not cause a loss of autobiographical information (for example, one's name and date of birth), concussive amnesia tends to be antegrade (inability to retain new information).[3] However, some degree of retrograde amnesia (inability to recall moments prior to the impact or events hours or some days before the injury) often occurs initially but tends to resolve, usually within hours in most patients[8], while a period of the post-traumatic amnesia is often permanent. Although gross structural abnormalities on standard

* Corresponding author. Tel.: +61 3 9342 8218; fax: +61 3 9342 7273.
E-mail address: a.kaye@unimelb.edu.au (A.H. Kaye).

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CT scan and MRI are typically absent in concussion,[4,9,10] at a microscopic level there may be ultrastructural changes in the brain,[11] as elaborated below.

2.2. Epidemiology

Concussion is a common event, but in the sporting arena is known to be substantially underreported.[6,12,13] Reasons for its underreporting include players' lack of awareness of the symptoms or significance of concussion, their personal desire and outside pressure to continue playing, and the perception that reporting concussion could have adverse professional and financial consequences for the player and/or the team.[6,13,14] As expected, contact sports such as American and Australian football, rugby, soccer, boxing, wrestling, basketball, field hockey and lacrosse are all associated with a relatively high prevalence of concussion.[12,15]

In the Australian Football League, the overall rate of concussion is estimated to be 5–6 concussions per 1000 player hours, equivalent to an average of 6–7 concussive injuries per team per season.[16] In a recent study of 3207 Australian non-professional male rugby players, the incidence of concussion was even higher, at approximately 8 per 1000 player hours, with approximately 10% of all players in the study's cohort sustaining one or more concussions over 1–3 consecutive seasons.[17] In that study, it was reported that 7% of the cohort sustained a concussive injury within 10 hours of game-time, doubling to 14% within 20 hours (the average time participants spend on the field each season).[18] International studies of the rate of concussion among professional (2.9–9.1 per 1000 player hours), non-professional (0.6–5.0 per 1000 player hours), and school-level (1.03 per 1000 player hours) rugby players suggest that concussion is most common in professional rugby players.[15,17,19]

Based on data acquired in the late 1980s and early 1990s, the Centers for Disease Control and Prevention has estimated that in the United States (US), approximately 300,000 concussions or 20% of the then 1.5 million head injuries per year from sports are associated with loss of consciousness.[6,20,21] A more recent publication from the US suggested 1.6 – 3.8 million concussions per year in that country were related to sports.[22] The subgroup of US high-school footballers alone has a seasonal concussion rate of 15%,[13] however, rates among such sport participants may be as high as 30–45% as determined in studies in which players confidentially reported their symptoms after a blow to the head.[6,13,23,24]

2.3. Aetiology, including risk factors

As detailed in the Consensus Statement on Concussion in Sport,[4] concussion may be caused by a direct impact to the head, or by an impact to another part of the body with an impulsive force transmitted to the head. While falls and motor vehicle accidents are the most common causes in adults, contact sports and bicycle accidents account for the majority of concussions in children and adolescents.[3] A distinguishing feature of sports-related concussion compared with non-sports-related concussion, such as from motor vehicle or cycling accidents, is that it often results from lower-velocity impacts. As such, sports-related concussion is more often associated with disorientation or a relative impairment of conscious state rather than loss of consciousness.[1,6,25] Risk factors for sports concussion include organised sports as opposed to leisure physical activities, actual games rather than practice sessions, and the subgroup of high-school athletes compared with the college- or university-level subgroup.[3,6,12] With regard to high-school sports concussions, a contemporary study of 12 scholastic sports offered at 25 US high-schools found that football for males and soccer for females were the leading causes of sports concussion.[26] Further, high-school age females were noted to be at twice the risk of concussion compared with their male counterparts, and a 4.2-fold increase in concussion rate was observed by the authors over the 11 years of that study.[26] The increasing rate, particularly evident from 2005, was attributed by the authors to expanded access to athletic trainers across local high-schools from that year, thereby facilitating better recognition, reporting and treatment of concussion.

2.4. Pathophysiology

In their seminal 1943 study of head injuries sustained by motor-cyclists, Cairns and Holbourn[27] wrote that concussion is caused by a change in the rotational velocity of the head. The authors added that "in those patients who were wearing crash helmets, concussion, as measured by the duration of amnesia, was milder than in those who were not".[27] Their observations have remained true. From a biomechanical perspective, concussion is thought to be due to rotational or angular acceleration forces applied to the brain that cause neuronal shearing rather than the linear acceleration-deceleration forces that frequently produce focal macroscopic brain damage.[6,27–29] Brief loss of consciousness associated with concussion appears to be due to rotational forces centred on the midbrain and thalamus that cause the transient disruption of components of the reticular activating system.[3]

The ultrastructural basis of concussion involves the immediate stretching of axons and increased permeability and disruption of neuronal membranes, as part of diffuse axonal injury (DAI).[11,21,30] Biochemically (Fig. 1), there is an abrupt and indiscriminate release of neurotransmitters, particularly the excitatory neurotransmitter glutamate.[31] The ensuing abnormal ion fluxes lead to excessive accumulation of extracellular K+ and intracellular Ca2+. This results in a massive neuronal excitation and depolarisation, accompanied by a period of compensatory homeostatic ion pump-driven glucose catabolism in order to generate more of the cellular energy currency, adenosine triphosphate (ATP). This period of excitation and hyperglycolysis has been shown to last several minutes to a few hours in animal models.[30,32] The excitatory phase, which may be associated with seizure activity,[33] is followed by a wave of neuronal suppression referred to as *spreading depression.*[34] This may in part be due to decreased ATP production from failure of mitochondrial oxidative metabolism, possibly accounting for the pathophysiological basis of early loss of consciousness, amnesia or confusion seen in concussed individuals.[11,30] Persisting cognitive deficits following a concussive injury may also arise from dysfunctional neurotransmission in one or more of the glutamatergic, adrenergic and cholinergic systems.[30] Neuronal cell injury, including axonal swelling and disruption and even cell death through apoptotic pathways, can result from the abnormal elevation of intracellular calcium that is part of the neurometabolic cascade of concussion[11,30] (Fig. 1).

In animal models of concussion involving fluid-percussion injury, there is also an uncoupling of cerebral blood flow and cerebral glucose metabolism, with a substantial diminishment of the former by up to 50% of normal,[30,35] and an early increase of the latter. This supply-demand mismatch can cause a potentially damaging brain energy crisis that can increase neuronal vulnerability to a second injury with longer-lasting deficits.[30] In younger persons, a second impact syndrome (SIS) has been described that likely involves cerebrovascular autoregulatory mismatch.[12,36] Although rare, the syndrome is thought to occur during the incomplete resolution phase of an initial head injury sustained by a young person[12,36] where concussive symptoms (see below) precede impaired consciousness and death from malignant cerebral oedema within a few days of a "second" or subsequent head injury.[36] Such features were first described by Schneider in 1973, who reported the death of two young athletes following relatively minor subsequent head injuries.[37] The term SIS itself, however, was coined a decade later by Saunders and Harbaugh[38] who described a 19-year-old college football player who suffered a head injury with brief loss of

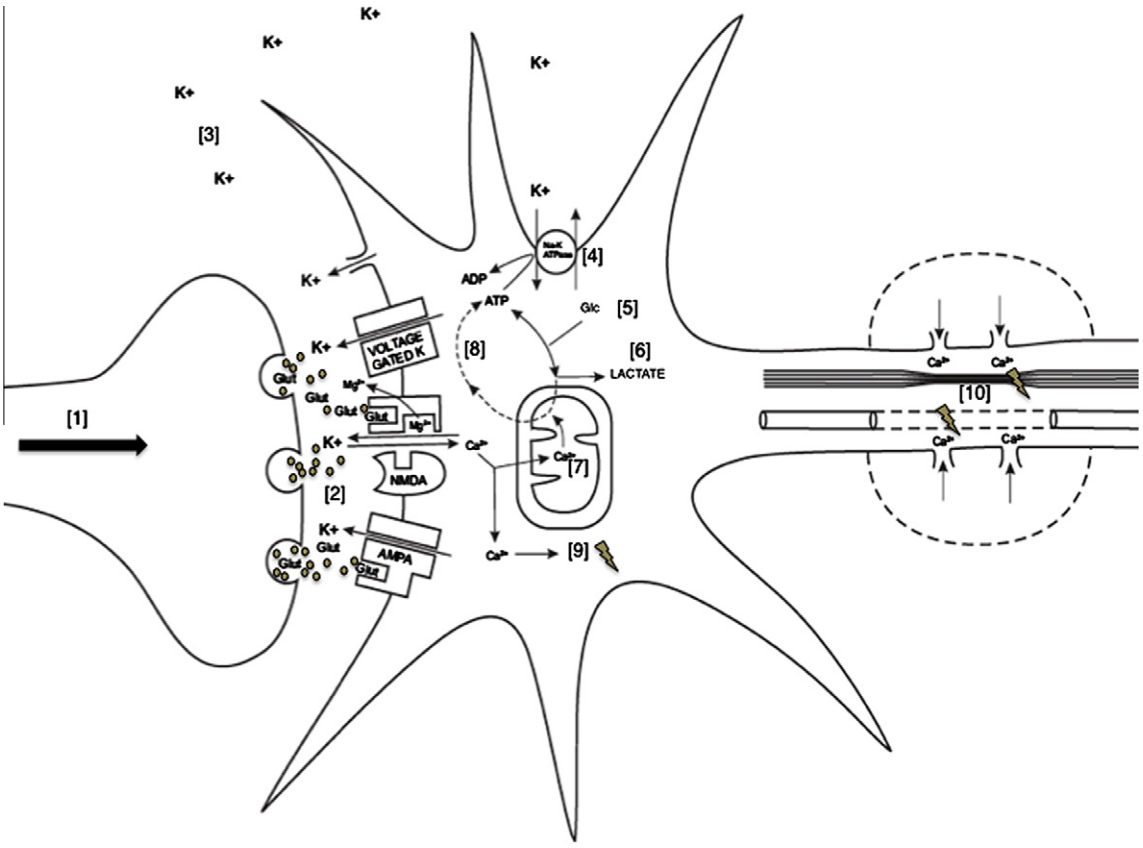

Fig. 1. Neurometabolic cascade of concussion: **1**. substantial neuronal depolarisation; **2**. excitatory neurotransmitter release; **3**. massive potassium (K^+) efflux; **4**. homeostatic cell membrane pumps in overdrive; **5**. glucose catabolism to generate more adenosine triphosphate (ATP); **6**. lactate accumulation; **7**. ongoing influx of calcium ions (Ca^{2+}) leading to mitochondrial dysfunction; **8**. ATP production starts to fail; **9**. Ca^{2+}-dependent enzymes such as calpain are activated and lead to apoptosis; **10**. metabolic and structural changes take place in axons, which swell and are disrupted (After Barkhoudarian et al.[11]).

consciousness, who then returned to play, reported a headache, and 4 days following the injury collapsed and died. Postmortem examination revealed extensive cerebral oedema (without any significant haematoma), the pathological hallmark of SIS.[36] It has been postulated that in younger head-injured patients, there is a predisposition towards failure of cerebrovascular autoregulation, with an inability of the dysfunctional cerebral arterial tree to respond to an abrupt elevation of blood pressure that can accompany a post-traumatic systemic catecholamine surge (“malignant storm”).[36] Under such circumstances, the substantially elevated arterial pressure is rapidly translated to raised intracranial pressure (ICP) by impaired autoregulatory vasoconstriction, resulting in cerebral blood volume expansion.[6,36] While SIS is rare, if a second impact is sustained before the symptoms of the first have resolved, it is postulated that vascular engorgement can occasionally occur with symptoms and signs of raised ICP and associated coma and death from malignant cerebral oedema and herniation.[12,36,39]

2.5. Structural pathology, including chronic traumatic encephalopathy

The degree of ultrastructural or microscopic pathology accompanying a TBI depends on its severity and whether or not the brain injury is an isolated event or multiple occurrence. At a cellular level, common to the spectrum of TBI is DAI which involves the physical disruption or demise of neuronal circuitry.[21,30] A typical sports concussive injury causes the previously mentioned ultrastructural changes[30], with an absence of findings on conventional neuroimaging studies, and it typically does not result in gross or macroscopic pathology such as contusion, subarachnoid haemorrhage, cerebral oedema, and haematoma.[4] Repetitive concussive injuries also do not typically lead to gross pathological findings, however, there is emerging evidence that they could set the stage for loss of neuronal protein homeostasis, or a proteopathy. Such proteopathy can manifest in a variety of syndromes ranging from chronic low-level neuropsychological impairment, to a Parkinsonian movement disorder, through to full-blown depression and dementia.[21]

In 2010, the neuropathology findings in a series of deceased professional American athletes was reported by Omalu et al.[2] The five athletes, four National Football League (USA) players and one World Wrestling Entertainment wrestler, had died following suicide or after multiple suicide attempts, and were aged between 36 years and 50 years at their time of death. Each had a history of repetitive concussions, manifested delayed but chronic symptoms and signs of cognitive and neuropsychiatric impairment (see below), and had common neuropathological findings. Together, these features are the hallmark of a syndrome referred to as chronic traumatic encephalopathy (CTE). The neuropathological findings were as follows: grossly normal appearing brain by unaided visual inspection; microscopic findings of mild neocortical neuronal loss; immunohistochemical findings of microtubule-associated protein (tau) positive neurofibrillary tangles and neuritic threads in the neocortex, basal ganglia and brainstem nuclei; there was a paucity or absence of beta-amyloid plaques.[2] This CTE series was recently updated[40] to include seven football players, two wrestlers, one boxer, and a high-school sports player. From other neuropathology studies of CTE in athletes, subtle macroscopic findings such as anterior cavum septum pellucidum, ventricular dilatation, and more widespread cerebral atrophy, and pallor of the substantia nigra have been described[41,42], as has the involvement of another protein in addition to tau, namely, TAR DNA-binding protein of 43 kD or TDP-43.[42,43]

2.6. CTE is a tauopathy

A recent review of the CTE literature suggests that CTE is a slowly progressive *tauopathy* with a clear aetiology: repetitive concussion.[41] Here, tauopathy refers to a neurodegenerative process characterised by prominent intracellular accumulation of abnormal filaments formed by the microtubule-associated protein, tau.[44] Human tau proteins, of which there are multiple isoforms owing to alternative exonal splicing, are predominantly expressed in central nervous system (CNS) axons where they bind to microtubules, are of low molecular weight, and are encoded by a single gene on chromosome 17q21. The key function of tau is the promotion of microtubular polymerisation and stabilisation, where tau's association with microtubules is highly regulated by protein kinases and phosphatases. As part of the perturbed signaling cascade of concussion (see above), deranged cellular homeostasis following brain injury can lead to cumulative, fibrillary tau pathology (tauopathy) marked by tau-rich neuropil threads and neurofibrillary tangles. Polymorphisms and rare mutations of the tau gene can increase the risk of developing sporadic and familial tauopathies, respectively, while CNS neurodegeneration can be accelerated in animal models in which wild-type mutant tau is overexpressed.[44–46] It is therefore likely that the accumulation of tau is not simply a byproduct of the loss of cellular homeostasis, but may actively contribute to clinical neurodegenerative pathology such as seen in tauopathies including Alzheimer's disease, Pick's disease, progressive supranuclear palsy, corticobasal degeneration, and possibly CTE.[41,43,44] Finally, at least 17% of individuals with a history of repetitive concussion, such as during boxing, develop a ''pugilistic'' subtype of CTE, also a tauopathy.[47] The precise incidence of CTE in the wider athletic and sporting community remains unknown, but has been reported to be 17%[41] among athletes who suffer repetitive concussions. This suggests there may be a substantial health risk particularly in competitive sports such as boxing, soccer, football, hockey and martial arts.[42]

2.7. Apolipoprotein E and neurodegeneration

Apolipoprotein E (ApoE) is a 299-amino acid protein encoded by the *ApoE* gene on chromosome 19.[48] This protein, found in lipoproteins, has been implicated in neurodegenerative processes and may be of relevance in predisposition to CTE.[11,48] ApoE binds to specific cell receptors in the liver and other tissues, and plays an essential role in the catabolism of triglyceride-rich lipoprotein constituents. In the CNS, ApoE is critical for lipid redistribution among neurons and glia, and for repairing injured neurons, maintaining synapses, and scavenging toxins.[49] Three common polymorphisms in the *ApoE* gene are denoted as *ApoE* -ε2, -ε3, and -ε4, each of the corresponding ApoE isoforms containing a single amino acid change.[48] The *ApoE*-ε4 allele, encoding ApoE-ε4 protein, is associated with the development of neurodegenerative disorders such as Alzheimer's disease, likely mediated by differential effects of ApoE on amyloid-β accumulation in the brain and its vasculature.[48] The metabolic cascade of brain injury is thought to promote ApoE synthesis in neurons, with the ApoE-ε4 protein being more susceptible to misconformation and therefore neuron-specific proteolysis. This, however, results in the production of bioactive toxic fragments that enter the cytosol, alter the cytoskeleton, disrupt mitochondrial function, and cause cell death.[49] Interestingly, transgenic mice expressing ApoE-ε4 show an age-dependent increase in tau phosphorylation that correlates with the level of ApoE-ε4 expression.[50] In a recent study of tissue obtained from autopsies of 14 professional athletes and three high-school football players who unexpectedly died, Omalu et al.[40] found that all seven CTE-positive professional athletes with known *ApoE* genotypes had at least one ε3 allele comprising five ε3/ε3 and two ε3/ε4. However, the study lacked a control group, and the authors stated that their preliminary observation required re-genotyping in larger cohorts of CTE-positive and negative athletes.[40]

2.8. Clinical features of concussion and post-concussion syndrome

In the sporting arena, the spectrum of concussion ranges from a player being dazed without a loss of consciousness, to an unconscious player who has had a seizure. Symptoms and signs from the time of the impact (*hyperacute*) to the hours-to-days (*acute*) or the first 4 weeks (*subacute*) thereafter are, for the purposes of this review, defined as part of a *concussion*. Persistence of concussive symptoms for more than four weeks and the development of additional symptoms are defined herein as part of a *post-concussion syndrome*. This syndrome, highly variable in its length, can last for a few, to several, months (*chronic*). As expected, a number of the symptoms and signs of concussion and PCS may overlap.[3,4,6] The symptoms and signs of concussion vary considerably, and are given in Box 1. The International Classification of Diseases, 10th revision, criteria for PCS[3,51] are given in Box 2.

Box 1 Symptoms and signs of concussion[4–6]

Symptoms

Somatic: Headache, nausea, vomiting, dizziness or ''wooziness'', vertigo, imbalance, changes in vision or hearing, tinnitus, photophobia, phonophobia, fatigue
Cognitive: Unclear or ''foggy'' thinking, difficulty concentrating or remembering, hallucinations
Emotional: Sadness

Signs

Depressed conscious state: Loss of consciousness, drowsiness
Cognitive state: Disorientation or confusion (e.g., inability to recall score, opponent, game rules or play assignments), appearance of being dazed, slowed reaction time, slowed verbal responses, poor neuropsychological test scores, antegrade or retrograde amnesia
Physical state: Seizure, impairment of balance, coordination, gait
Psychological state: Emotional lability, irritability

Box 2 The International Classification of Diseases (10th revision) criteria for post-concussion syndrome[3,51]

Development of symptoms in at least three of the following categories within four weeks of the concussive event:

1. Headache, dizziness, fatigue, noise intolerance
2. Irritability, depression, anxiety, emotional lability
3. Subjective concentration, memory or intellectual difficulties without neuropsychological evidence of marked impairment
4. Insomnia
5. Reduced tolerance to alcohol or stress
6. Preoccupation with aforementioned symptoms and fear of brain damage, with hypochondriacal concern and adoption of a sick role

The most common symptoms of concussion from a sporting related injury are headache (83%), dizziness (65%) and confusion (57%), while loss of consciousness is observed only in 10%.[1] The natural history of concussion among collegiate or university-level football and soccer players is such that 87–92% report no symptoms by 3 days and 95% report complete resolution within 7 days of the injury.[52] Although underreporting of symptoms may be a factor in this perceived natural history, it appears that for most concussed individuals, symptomatic recovery occurs within 2–10 days of the injury.[1] However, this is highly dependent on the severity of the concussive injury.

2.9. Assessment and investigation of concussion

The guiding principle in the assessment of a concussed player is that it should be timely, systematic and multifaceted. Management decisions, particularly regarding return-to-play (RTP), should be based on information obtained from the following types of evaluations.[1,6,7]

2.9.1. Initial on-field assessment

On-field assessment of a player suspected of having a concussion is carried out by the team's physician or, in the absence of a team physician, the athletics trainer or a suitably trained supervisor. It begins with medical evaluation using standard emergency management principles such as airway, breathing, circulation, and level of consciousness. It should be noted that the athlete may be unaware that he or she is concussed, may not have any overt signs of concussion, or may minimise or hide symptoms in order to return to the game.[6,25] Particular attention should be paid to the possibility of a concurrent cervical spine injury, and the cervical spine immediately immobilised if clinically indicated. The player should be moved out of the field-of-play to the sideline by stretcher for further medical assessment, including neurological examination of cranial nerves, and peripheral sensorimotor and cerebellar function. A standard and validated self-reported symptom inventory such the Post-Concussion Symptom Scale (PCSS),[20] which is a component of the Sport Concussion Assessment Tool (SCAT2) proforma (see Supplementary material), Graded Symptom Checklist,[12] or Head Injury Scale[20] should be used by the attending physician.[7,53] Symptom reporting should be used as a rough guide for functional recovery from an injury, but by no means as a definitive RTP tool.[1,54] Discrepancies between symptomatology and cognitive function are widely recognised,[55,56] as is the tendency towards symptom underreporting in the competitive sporting population[6] based on aforementioned reasons. Further, the numerous concussion grading systems, including Cantu's,[12,57] designed to grade concussions as mild, moderate or severe have been abandoned owing to their reliance upon the presence of loss of consciousness and a player's self-reported symptoms.[5,6] In their place, more comprehensive side-line assessment batteries, such as the SCAT2 (Supplementary material) or the Standardized Assessment of Concussion (a component of the SCAT 2 proforma; see Supplementary material) are recommended to assess basic cognitive function beyond the ability to self-report symptoms.[4,5,7,12] Questions regarding orientation to person, time, and place are regarded as unreliable tests of basic cognitive state compared with questions concerning the score, the opponent, specific game rules and play assignments[6] that contribute to the validated "Maddocks score", part of the SCAT2 proforma that also includes balance testing (Supplementary material). A player with a diagnosed concussion should not be allowed to return to play on the day of injury.[4–6] Rather, it has been recommended that a concussed player should be subject to one or more of the tests below and on more than one occasion post-injury.[4,12,20] It has also been recommended by some authors that the symptom inventory used at the time of injury be repeated at 2–3 hours, 24 hours, 48 hours and 72 hours after the injury.[12,58]

2.9.2. Postural stability testing

Postural instability in concussed athletes is a common observation based on both on-field and more sophisticated off-field testing.[1,54] This particular deficit, inadequately assessed by a simple Romberg test, is most apparent when athletes are subjected to vestibular system testing on foam or a mobile tilting surface, and generally resolves within 3-10 days post injury.[1,59] The Balance Error Scoring System (BESS; a component of the SCAT 2 proforma; see Supplementary material) was developed for postural testing on the sideline, that is, for immediate and quantifiable assessment in the absence of more sophisticated force-plate technology. BESS involves completion of a variety of specific stances on a firm surface and then on medium-density foam, with performance scored by adding an error point for each error committed over a total of six trials.[1] Errors during any part of the testing include stumbling or falling, opening eyes, lifting hands off the iliac crests, impermissible hip or foot posturing, or remaining out of a testing position for more than 5 seconds. More sophisticated testing, generally less practical in the immediate concussion assessment setting but carried out off-field, involves calculating sway measures via the administration of the Sensory Organisation Test on dedicated force-plate balance testing equipment such as the NeuroCom Smart Balance Master (Neurocom, Clackamas, OR, USA).[59] In a comparison of BESS and force-plate system testing in healthy young adults, a good intertester reliability of approximately 80–95% and significant correlations in five balance tests were reported.[60] Newer test paradigms may add cognitive tasks during balance testing, mimicking the demands of sport.

2.9.3. Neuropsychological testing

To date, much of the data derived from sports neuropsychology concussion research is based on studies involving male athletes, in particular American football players. Further, it was reported in a recent systematic literature review that almost one-third of published studies in this field involved pooling of data from both high school and collegiate levels, that is, did not take into consideration the age-dependent variability in neuropsychological scoring.[61] Despite these research biases, in practice, neuropsychological testing in sports concussion is a mandatory part of the assessment, focusing particularly on the player's attention, working memory and speed of information processing. Precisely who should conduct and interpret the neuropsychological assessment and the type of assessment in sports-related concussion remains unresolved. Over the last decade, there has been a move away from the traditional paper and pencil testing administered by clinicians towards computerised testing that can be administered by appropriately trained and supervised technicians.[62] The latter has been reported to be less labor-intensive, less time-consuming, more reliable and sensitive, and allows for the automation of result interpretation to occur, which is preferable to the idiosyncratic variability inherent to clinician-based test interpretation.[1,63] However, at the outset, it should be emphasised that the automation of result interpretation in computer-based assessments is optimal only when valid pre-injury "baseline" results have been acquired using the same assessment program.[63,64] Validity in this setting refers to pre-injury results acquired from a motivated subject, willing and able to interpret and follow the test's instructions appropriately.[63] Further, particularly in instances of moderate, severe or prolonged concussion and PCS, a comprehensive neuropsychological assessment of the player should best be carried out by a clinical psychologist.[62]

Significant augmentations in the sensitivity of diagnosing a concussion[65] and predicting the length of recovery[66] have been reported when computerised testing is used in conjunction with

post-concussion symptom scores compared with the use of post-concussion symptom scores alone. Two prominent computer-based neuropsychological assessments are the Immediate Post-concussion And Cognitive Testing (ImPACT) battery (www.impacttest.com; Pittsburgh, PA, USA), and the CogState Sport or "CogSport" test (www.cogstate.com; Melbourne, Vic., Australia). Other computer-based programs include HeadMinder Concussion Resolution Index (New York, NY, USA), and Automated Neuropsychological Assessment Metric (ANAM; OK, USA).

The ImPACT test involves six neurocognitive modules evaluating attention, verbal and visual memory and learning, numerical sequencing, processing speed and reaction time, and typically takes about 20 to 25 minutes to complete using a computer screen and mouse.[67] The CogSport test consists of eight tasks designed as card games which, in about the same overall timeframe, assess reaction time, matching, monitoring and learning tasks in a language-independent manner.[68] Using ImPACT, Fazio et al.[56] found that athletes who denied having any symptoms of concussion in the first few days following a concussive injury performed significantly worse across a number of ImPACT's neurocognitive composite scores compared to a matched control group. Further, Iverson et al.[69] reported that concussed athletes who reliably exhibited multiple composite deficits on ImPACT compared with their pre-injury baseline were 95% likely to require at least 10 days to recover to the point of being asymptomatic at rest and on exertion and regaining their baseline neurocognitive performance.

The use of computerised testing in sports concussion has been validated against post-concussion symptom scores[66,68] and batteries of paper-pencil measures[64,67,70] by several groups[1,64,66–68,70] with an overall sensitivity and specificity of between 80 and 90% in the independent diagnosis of concussion.[66] In a prospective study of 300 healthy young adults, including 240 non-concussed elite athletes, the creators of CogSport reported a high degree of reliability and reproducibility of their computerised test's results in measures of psychomotor function, decision making, working memory and learning compared with two conventional neuropsychological tests.[70] The reliability of CogSport was not as high in a case-control study by Chen et al.[68] examining the relationship between self-reported post-concussive symptom scores, neuropsychological performance utilising CogSport, and functional MRI (fMRI) findings. Despite certain limitations of their study design, Chen et al.[68] reported that in mildly concussed athletes (as defined by low self-reported post-concussive symptom scores, totaling 6–21 on their PCSS-revised), no significant abnormality was detected on the CogSport test battery but abnormal fMRI signal was found in prefrontal regions during verbal and non-verbal working memory tasks.[68] In moderately concussed athletes (as defined by higher self-reported post-concussive symptom scores totaling 22–84 on their PCSS-revised), inaccurate and slower performances were detected in some CogSport modules, as was abnormal fMRI signal in prefrontal regions during working memory tasks.[68] Schatz and Putz[64] carried out a cross-validation study of CogSport, ImPACT, and HeadMinder, as well as compared the results of these computerised tests with those of long-standing paper-based neuropsychological tests of processing speed in healthy, non-concussed young adult male and female volunteers.[64] The authors found all three computerised tests shared significant correlations with one-another in the domains of processing speed and reaction time but not memory. ImPACT was found to have shared the most consistent correlations with the other two computer-based tests and two paper-based tests, however, design limitations of the study precluded determination of the superiority of one computer-based test over others.[64] In a study of 100 neurologically intact, non-concussed volunteers, Allen and Gfeller[67] assessed the validity of ImPACT against a battery of traditional paper-pencil neuropsychological tests utilised by the National Football League. The authors found that ImPACT and traditional tests overlapped regarding constructs such as speed or cognitive efficiency and memory, but had notable differences in certain constructs such as in auditory and verbal working memory and inhibitory cognitive abilities.[67] Overall, correlational analyses in that study provided support for the ImPACT battery's validity in assessing memory and cognitive efficiency in a healthy volunteer cohort. Based on the aforementioned data, owing to differences between tests, and in the absence of any one superior computerised test, it is recommended that the same test be used on any given player from pre-injury (baseline) testing through to post-injury follow-up.

2.9.4. Electrophysiology

There is increasing interest in the use of focal electroencephalography (EEG) in sports concussion. Whereas neuropsychological tests assess overt verbal and motor responses, focal EEG in the form of event-related potential (ERP) recording assesses the physiological or electrical integrity of parts of the brain based on responses to a repetitive stimulus, typically an auditory or visual one. The technology is non-invasive, objective, relatively inexpensive, and can be deployed and used within 20 minutes.[1] ERP represent the averaged EEG signal recorded following the presentation of stimuli and consist of waves named according to their polarity and latency, and quantified by their amplitude.[71] Gaetz et al.[72] were one of the first groups to report a significant difference in the latency of visual ERP between non-concussed and concussed athletes. As reviewed elsewhere[71], numerous groups have now confirmed these and other findings in ERP sports concussion studies. Gosselin et al.[73] compared the results of auditory ERP testing versus conventional paper-pencil neuropsychological testing in three groups: symptomatic concussed athletes, asymptomatic concussed athletes, and non-concussed (control) athletes. They reported good correlation between ERP and conventional test results for all three groups, observed lower wave amplitudes and longer wave latencies in concussed athletes compared to controls, and found abnormal ERP in asymptomatic concussed athletes.[73] Long-term physiological effects of sports concussion, as measured by persistent ERP abnormalities, have also been reported by Broglio et al.[74] and De Beaumont et al.[75] In both studies, athletes were divided into two groups based on the presence or absence of a concussion history. However, the former study involved younger athletes with an average time from the latest concussion of approximately 3.5 years[74]; the latter study involved former athletes with a mean age of 61 years who sustained their last sport concussion decades earlier.[75] Of particular interest, the study by Beaumont et al.[75] found that, compared with the 21 age-matched former athletes with no history of concussion, the cohort of 19 former athletes with a remote history of concussion performed more poorly on neuropsychological tests of episodic memory and response inhibition and had significantly delayed and attenuated P3 and P300 wave components.[75] The aforementioned studies suggest that concussions sustained in early adulthood may lead to long-term brain dysfunction.[71,76]

McCrea et al.[76] have recently reported their experience with quantitative EEG (QEEG) in sports concussion. This tool represents a limited form of EEG assessing alpha, beta, delta, gamma and theta frequency bands mainly in the frontal region using approximately one-half of the number of electrodes as used in conventional EEG. In their case-control study, despite finding resolution of symptoms and neurocognitive dysfunction within the first week following the injury, QEEG abnormalities persisted at day 8 following injury but not at the next measure, which was at post-injury day 45.[76] Their findings support the hypothesis that electrophysiological abnormalities can persist beyond the time of symptomatic and neuropsychological impairment resolution in young adult sports concussion.

2.9.5. Biomedical imaging

As mentioned previously, traditional neuroimaging modalities such as CT and conventional MRI are typically unremarkable in concussion. Structural abnormalities such as contusions and extra-axial haematomas are generally absent in sports concussion injuries, but not always, and may need to be ruled out on an individual basis. Specific MRI sequences such as fluid-attenuated inversion recovery may show multiple areas of signal hyperintensity particularly at grey-white matter interfaces, the corpus callosum, and parts of the brainstem, in the most severe, but fortunately rare, cases of sports concussion associated with prolonged loss of consciousness. More recently, the possible use of magnetic resonance (MR) modalities such as fMRI, diffusion tensor imaging (DTI) or MR tractography, and MR spectroscopy (MRS) have emerged in the sports concussion literature. While still subject to research applications, and currently not widely accessible, one or more of these MR modalities may assist in optimising the assessment of concussed players and especially determining RTP decisions.

As reviewed elsewhere,[71] to date there are several fMRI studies that have been carried out in the setting of sports concussion. This particular MR modality measures regional brain activation and deactivation based on changes in cerebral blood flow or, specifically, blood oxygenation-level-dependent (BOLD) signal. BOLD signal differences between a cognitive task and a baseline control task have been compared in concussed (case) *versus* non-concussed (control) athletes. Six of the seven fMRI studies reviewed by Gosselin et al.[71] had a case-control design, although one assessed the same group of athletes pre-concussion and post-concussion.[77] Most studies utilised fMRI paradigms based on visual and/or verbal working memory tasks administered within 3 months of the concussion or between 3 months and 3 years of the concussion.[71] All studies found abnormal activation patterns in cases compared with control groups, with the authors of one study[68] correlating the fMRI abnormalities with time-to-clinical-recovery and RTP. One of the most recent studies utilising MR in sports-concussed individuals involved the combined use of fMRI and DTI.[78] DTI specifically assesses the direction of diffusion of water molecules in white matter tracts, with normal white matter tracts demonstrating a more organised directional diffusion referred to as anisotropy.[79] DTI calculates fractional anisotropy (FA), with a score of 1 representing anisotropic diffusion (expected to be associated with normal tracts or a "normal" FA score) and 0 representing isotropic diffusion (expected to be associated with disrupted tracts). That case-control study by Zhang et al.[78] failed to show any significant alteration of white matter integrity as evidenced by FA data but did show differences in regional brain functional activation between both groups. Other studies in non-athletes with mild TBI have shown inconsistent DTI results[79], suggesting that presently DTI is not a useful tool in the assessment of sports concussion.

MRS has been used to assess focal brain biochemistry in the context of sports concussion injury. MRS typically measures the following metabolites: N-acetyl aspartate (NAA), a marker of neuronal integrity; choline, a marker of membrane damage and turnover; creatine, a cellular energy marker for ATP resynthesis; lactate, an indirect marker for ischaemia and hypoxia; and myoinositol, a glial marker.[1,79] In sports concussion, Vagnozzi et al.[80] demonstrated that MRS could be used to identify metabolic disturbances, specifically, reduced NAA and reduced NAA:creatine ratios, in concussed athletes even following resolution of symptoms. A similar reduction in NAA was reported by Cimatti et al.[81] in the MRS profiles of concussed athletes. Finally, imaging studies assessing brain perfusion via single-photon emission computed tomography (SPECT) and metabolism via positron emission tomography (PET) in the setting of TBI have also been carried out, but as reviewed elsewhere,[1,79,82] at this time there is little information regarding the use of these technologies in concussed athletes.

2.10. Treatment principles

There are no specific medical therapies for concussion. The mainstay of treatment in the vast majority of concussion injuries is physical and cognitive rest[82] until the symptoms resolve, usually within 2–10 days. It should be noted that cognitive rest pertains to minimisation or avoidance of scholastic work, videogames, computing, and text messaging during the recovery period.[4,82] During the recovery period, general measures such as optimisation of hydration and the temporary use of mild analgesics such as paracetamol or ibuprofen for headache, and anti-nausea medications, may be of benefit, although narcotics should be avoided.[3] While there are no pharmacotherapies for concussion, the management of any sleep disturbance, anxiety or depression associated with PCS may, in part at least, be aided by the use of prescription medications under the guidance of a clinician experienced in concussion management.[4] Neurocognitive rehabilitation, used widely in severe TBI, is of inconclusive benefit in the setting of athletic concussion.[7] However, the education of players, parents and coaches regarding concussion, its associated risks, and principles of safe RTP is critical.[12]

2.11. Short-term complications

It is widely recognised that after a first concussion, a player is at increased risk of additional concussions, the peak incidence of repeat concussion being within the first 7–10 days of the original concussion.[6,83] The same-season repeat concussion rate among US high school- and college-level football players is approximately 10% (range 2.6–14.7%).[84] The key short-term complications of a sports concussion are related to a brain injury that may be evolving from the time of impact to the minutes or hours thereafter. Such injuries may include cerebral contusions and expanding intraaxial and extraaxial collections such as extradural, subdural and intracerebral haematomas, which may co-exist with injuries to the skull and cervical spine. The rare but documented occurrence of SIS in the paediatric population involves rapidly progressive diffuse cerebral oedema that can lead to death from brain herniation.[6,39] The risk of permanent disability or death as a result of acute cerebral injury in American football has been estimated to be 1 per 20,500 players per season.[84]

2.12. Long-term complications

TBI has been identified as a risk factor for chronic depression[85], and a potential risk factor for the occurrence or early expression of Alzheimer's disease and Parkinson's syndrome.[86,87] A survey-based study of over 2500 retired professional American football players found an 11.1% prevalence of clinical depression and, more notably, an increased incidence of depression with increasing number of concussions in a "dose-response" manner.[88] That is, compared with retired players with no history of concussion, retired players reporting one or two concussions were 1.5 times more likely to be diagnosed with depression, while those reporting three or more concussions were three times more likely to be diagnosed with depression.[88] These findings, however, may be subject to recall and participation biases inherent to the survey.

The occurrence of delayed neurocognitive decline following repeat sports concussions, most clearly demonstrated in boxers who have sustained multiple knockouts[3], is an emerging concern in the wider contact-sports community. While the term *dementia pugilistica* was coined to replace "punch drunk" as a description of the cognitive, behavioural and motor abnormalities described among a substantial proportion of professional boxers[42], the contemporary umbrella term "chronic traumatic encephalopathy" (CTE) is now used to cover the delayed biological effects of

repetitive concussions among professional athletes. The pathology of CTE in recent forensic series involving professional athletes has been described above. The features of CTE typically include a number of the following: progressive deterioration in social and cognitive functioning (including impaired memory, loss of executive function, breakdown in relationships); behavioural and psychiatric disturbance (including paranoia, rampant mood fluctuations, alcohol and drug abuse, major depression with suicidal ideation, suicide attempts or completed suicide); constitutional symptoms (including chronic headaches, generalised body aches and pain, and insomnia); and increasing religiosity.[2] The clinical onset of CTE appears to be insidious, with a mean age of onset of 42.8 years in a series of American athletes.[41] Its progression is gradual, often ending after several years in suicide or dementia.[41,42] The relationship between the development of neurocognitive and psychiatric sequelae from repetitive concussion and the precise number and timing of concussions, or the contribution of any adverse genetic predisposition such as carriage of the *ApoE-ε4* allele[6,48,49] among athletes, remains conjectural at this time. It should be noted that while concussions sustained in soccer may lead to delayed complications, recent attention has also been given to the possibility of long-term effects of repetitive subconcussive injury (see below) sustained during purposeful heading of the ball in soccer[3,6] and in American football.[89]

2.13. Special considerations in paediatric sports concussion

There is widespread agreement that in the young athlete, aged 18 years or less, concussion has special implications[4,12,20] and accounts for approximately 10% of all high-school athletic injuries.[90] Compared with adult athletes, the increased susceptibility of high-school age athletes to concussion[20,91–93] has been attributed to differences in physical features such as a thinner skull, weaker neck muscles, and a greater head-to-body ratio, as well as physiological features such as lower levels of myelination and underdeveloped autoregulatory responses.[12] In this age group, the risk of prolonged recovery is increased,[20,94] as is the risk of developing a potentially fatal complication of early repeat concussion, namely SIS,[20,57,95,96] described earlier and attributed to cerebral oedema from impaired cerebrovascular autoregulation. For these reasons, a more conservative approach to the management of concussed younger athletes is advised.[4,5,12] Further, underplaying the potential seriousness of concussion in this age group by parents, coaches, and peers should be strongly discouraged.[5,12]

Children, representing a growing and maturing cohort, may require more frequent updates of pre-participation baseline psychological and physical assessments compared with their older counterparts.[12] Any neuropsychological testing must be age-appropriate, and the co-presence of learning and/or attentional disorders must also be taken into consideration with both testing and recovery.[4] The SCAT2 proforma has been recommended to be used in athletes aged 10 years and above,[4] and its contained 22-symptom PCSS has been validated in athletes of high-school age and above.[5,20] However, data regarding the validation of sports concussion neuropsychological testing in children younger than 12 years is still lacking.[5] During recuperation from a sports concussion injury, young athletes and their parents should be reminded that "rest" includes both physical and cognitive rest, including minimisation or avoidance of text messaging, school work and reading, video games, computing, and loud music.[4,82] Regarding RTP in this age group, a recent study has suggested that neuropsychological impairment may be more prolonged,[5] up to 14 days post-concussion.[97] Therefore, a lengthening of the approximate 7-day graduated RTP protocol (Table 1) *following* the resolution of symptoms may be more appropriate for younger athletes,[4] for examples, to a minimum of 14 days following resolution of symptoms and normalisation of balance and neuropsychological tests.[12] Any concerns about ongoing impaired recovery, including the development or persistence of symptoms of PCS, should warrant early referral to a paediatrician or other clinical specialist. Finally, in the context of high percentages of young athletes returning to play prematurely[54], an understanding of and compliance with RTP guidelines also need to be reinforced and monitored by medical professionals, coaches and parents alike.

The parents and coaches of young athletes need to be well versed in recognising the symptoms and signs of concussion and PCS, and in understanding the seriousness of the condition, particularly with regards to re-injury. This is especially important as younger athletes may have less access to medical professionals and suitably trained athletics supervisors at their myriad of sporting venues.[20] In this context, in a survey as recent as 2007,[98] nearly one-half of youth coaches believed a concussion only occurred with loss of consciousness, and a quarter would allow the athlete to return to play despite ongoing symptoms of concussion.[20] As research emerges regarding the long-term effects of repeat concussive and subconcussive injuries, in the absence of consequential refinements to protective head gear that substantially reduce the effects of linear and rotational injury[27], the possibility of having a lower threshold to withdraw young players with multiple concussions or with PCS from contact sports altogether may become a reality.[5] The use of mouth guards in this age group is strongly recommended to protect against dental and orofacial injuries although at this time they are not regarded as protective against concussion.[4,17] In this age group, hard helmets are advised for activities such as skiing, snowboarding, cycling, all-terrain vehicle use, motocross, and horse-riding.[4,5] It has been recognised that hard helmets can be used as "weapons" by American footballers and may increase a tendency of a helmet-wearing player to engage in a more aggressive manner of play.[17] Addressing this particular issue may require a cultural shift and rule and penalty changes that may eventuate from better and wider concussion education, or if studies continue to show early neurodegenerative changes in the participants of these sports. The role of helmets in soccer, a sport that involves not only interplayer collisions but also the intentional "heading" of a relatively hard and high-velocity ball, remains to be determined. Their role may become defined by the findings of ongoing research into concussive and subconcussive injuries in this particular sport[5,99] (see below).

2.14. Return-to-play in the setting of immediate, evolving and repetitive injuries

In a concussed player, RTP recommendations based on reported symptom resolution alone are inadequate.[4–6,12,20] In the setting of a potentially serious brain injury that may be evolving during the acute assessment phase, a concussed player should be monitored closely and serially by suitably trained personnel in a medical examination room as mentioned previously.[4,5,12] A graduated RTP protocol (Table 1), as recommended in the Consensus Statement on Concussion in Sport,[4] should be followed over a period of one-week at the very minimum. A caveat, however, is the possibility that the concussed player has suffered previous concussions in which case further restrictions may need to be enforced[3,25] (see below).

The issue of repetitive concussion is an emerging area of concern, and underscores the need to obtain a detailed past concussion history from an injured player.[25,84] The concept arises of tailoring management recommendations, including RTP issues, according to the individual circumstances of a player.[4,100] It has been reported that the risk of recurrent concussive injury is greatest in the first 7–10 days of an acute concussive injury.[83,101] The reason for this may be a mechanical and/or physiological younger

Table 1
Graduated return-to-play protocol[4*]

Rehabilitation stage	Functional exercise at each stage of rehabilitation	Objective of each stage
1. No activity	Complete physical and cognitive rest	Recovery
2. Light aerobic exercise	Walking, swimming or stationary cycling keeping <70% maximum predicted heart rate. No resistance training	Increase heart rate intensity
3. Sport-specific	Skating drills in ice hockey, running drills in soccer. No head impact activities	Add movement
4. Non-contact training drills	Progression to more complex training drills; for example passing drills in football and ice hockey. May start progressive resistance training	Exercise, coordination and cognitive load
5. Full contact practice	Following medical clearance participate in normal training activities	Restore confidence and assess functional skills by coaching staff
6. Return to play	Normal game play	

[*] Each stage lasts for approximately 24 hours, and this graduated protocol should take approximately 1 week. However, if any neurological symptoms recur during any stage, the player should immediately rest for a minimum of 24 hours and, once asymptomatic, resume at the *preceding stage*, progressing through each subsequent stage every 24 hours, or as tolerated.[4] Any concerns should be discussed with the athlete's designated physician.

age-related susceptibility based on lower levels of myelination, a thinner skull and a greater head-to-body ratio in the young,[12] or an age-independent enhanced biochemical and/or genetic vulnerability of the brain to repeat injury in this early phase.[6,30,83] Therefore, in the setting of withdrawal from sports following a *first and typically self-limiting concussion*, it is plausible that a minimum duration of approximately 7 days be recommended *following* complete resolution of symptoms in adults.[4] A more conservative timeframe,[6] such as a minimum duration of 14 days, has been suggested for children and adolescents.[12] However, in the event of more than one concussion during the same playing season, or in the presence of a PCS, it is plausible that a player be subject to a prolonged absence from contact sport and only be allowed to RTP *after* normal pre-injury or "personal baseline" neuropsychological and balance scores are demonstrated.[3,12,20] These recommendations should also be followed if the severity of symptoms following a sporting head injury is greater than the severity of the impact, an event which may herald an athlete's progressive vulnerability to injury.[12] Given that the precise number of, and player age-threshold for, repeat concussive and subconcussive injuries (see below) that result in long-term neurocognitive and psychological sequelae are currently unknown, it is possible that the aforementioned recommendations may be found to be lenient in due course. The findings of advanced medical imaging and electrophysiological studies, in addition to genetic testing, may in the future weigh substantially on sports concussion RTP guidelines.

2.15. Subconcussive injuries: An emerging dilemma

A number of studies utilising accelerometers built into football helmets have determined that in American football, a very high number of subconcussive blows to the head occur.[102–105] In one season alone, some players each received over 1400 subconcussive head impacts during practice and game sessions, with the largest numbers occurring among linemen and linebackers.[102] Similar findings would be expected in boxers and soccer players, with the latter featuring "heading" as an essential skill.[6,106] Typical subconcussive impacts in American football and soccer players have not been significantly associated with discernible performance decline during games in which the impacts were recorded.[105,106] However, it is conceivable, although it is still speculative, that frequent subconcussive head impacts may cause cumulative ultrastructural and biochemical changes in the brain that, in turn, might lead to or accelerate CTE. The clinical and pathological sequelae of subconcussive injuries may become more apparent as the number of documented cases of CTE grows.

3. Conclusion

Concussion is a common, likely underrecognised and underreported condition that is potentially serious in the short-term. If sustained multiple times during an athlete's life, it may well have substantial adverse health consequences in the long-term, particularly in those athletes that have susceptible genotypes. In general a more conservative approach to managing players following concussion is recommended, as well as improved education of players, their families and trainers, and sporting officials. While there are validated computerised neuropsychological and balance tests that form part of a multifaceted approach to concussion assessment, in the foreseeable future, electrophysiological testing, advanced biomedical imaging and targeted genetic profiling may also have a role in management decisions.

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Appendix A. Supplementary material

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