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Review Article

Sports Related Concussion: A Review

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Abstract

With an ever increasing participation in sports ranging from recreational to professional, there has been a substantial rise in the incidence and identification of sports related concussion (SRC). Therefore, assessment and management strategies are vital to aid in the recovery and safe return of players to their chosen sport. The following review article will detail the current strategies and consensus in the identification, assessment and management of SRC.

Keywords: Sports; Related; Concussion

Introduction

Concussion and mild traumatic brain injury (mTBI) have gained increased attention and exposure in medical, athletic and research communities in recent years. Focus has also grown in the public domain with increased media coverage and legislation passed [1,2]. There has been a greater incidence rate of concussion in the last 10 years which has prompted an influx of research studies in the scientifiditerature [3]. However, research has yet to yield an objective diagnosis for concussion, with a strong reliance on subjectivity relating to the mechanism of injury (MOI) and ensuing sequelae of post-concussive symptoms [4,5]. Symptom reportingis also used as an indicator of concussion recovery and in the management of returnto play (RTP) [6]. However, the time frame for physiological recovery can outlast clinical recovery, which may predispose athletes to further injury [1,4,5,7].

Definition of a concussion

The terms concussion and mTBI are often used interchangeably in both clinical and research settings. The latter is associated with the non-athlete populationand is defined by a Glasgow Coma Scale score of 13-15 with limited post-traumatic amnesia and the absence of abnormal neuroimaging, this permits differentiation frommoderate to severe forms of TBI [8,9]. Although the MOI may differ between sports-related concussion (SRC) and mTBI, the underlying pathophysiology is consistent [10,11]. To provide a more robust definition amongst medical professionals and researchers the development of consensus statements on concussion were established. The most recent conference by the Concussion inSport Group (CISG) was held in Berlin in 2016, where a definition of SRC was defined by the following characteristics

- SRC may be caused either by a direct blow to the head, neck, face orelsewhere in the body with an impulsive force transmitted to the head.
- SRC typically results in the rapid onset of short-lived impairment of neurological function that resolves spontaneously. However, in some cases,signs and symptoms evolve over several minutes to hours.
- SRC may result in neuropathological changes, but the acute clinical signs andsymptoms largely reflect a functional disturbance rather than a structural injury and, as such, no abnormality is seen on standard structural neuroimaging studies
- SRC results in a range of clinical signs and symptoms that may or may notinvolve loss of consciousness. The resolution of the clinical and cognitive features typically follows a sequential course. However, in some cases, symptoms may be prolonged [4].

A similar definition is provided by the American Medical Society for Sports Medicine by defining concussion as a traumatically induced transient disturbance ofbrain function involving a complex pathophysiological process [1]. This alteration in brain function may or may not present with loss of consciousness along with post-traumatic amnesia [12].

Symptom presentation

After sustaining a concussion symptom resolution normally occurs within 7 to10 days,however, in approximately 30% of the population symptoms can persist andare subsequently defined as persistent post-concussion symptoms (PPCS) [13,14]. Symptom presentation is heterogeneous and can affect different clinical domains.

Some of the signs and symptoms typically encountered after sustaining a concussion can include physical (headache, fatigue, dizziness, gait disturbance), physiological (exercise intolerance), ocular (sensitivity to light, blurred vision, eye strain), cognitive (executive functioning, memory, concentration problems), affective (depression, anxiety, emotional lability) and sleep disturbance (hypersomnia, insomnia) [1,15].

Currently there is no objective gold standard criteria for concussion diagnosis.

A diagnosis is usually performed from a multimodal approach through clinical evaluation involving the MOI and administration of a battery of tests including subjective symptom reporting, neurocognitive testing and physical assessment suchas balance and exertion testing [16]. Symptoms are commonly reported using a standardised scale such as the Post-Concussion Symptom Scale (PCSS), which consists of a 22-item inventory scale ranging from 0 (none) to 6 (severe) and detailssymptom presentation in the aforementioned clinical domains. However, a limitationof this measure is a focus on the total number of symptoms and not on symptom specificity. For example, after sustaining a concussion, increased levels of dizzinessalone is associated with a protraction in recovery time by six-fold [16]. Other factorssuch as genetics, age, sex, premorbid illness and a prior history of concussion can elongate recovery also, with children and adolescents, specifically females, experiencing the highest rate of symptoms and protracted recovery [17,18].

Epidemiology

The prevalence rates of SRC have been estimated at 1.6 to 3.8 million annually in the United States, however, this number may be higher than estimated due to unreported and undiagnosed cases [19,20]. Increased awareness, knowledgetranslation and new legislation has facilitated recognition of concussion and contributed to a lower threshold of diagnosis [2].

According to the Centre for Disease Control and Prevention, an estimated 75% of 2.5 million emergency department visits are due to mTBI [21]. Willer and colleagues [22] reported head injury rates of 3.98 per 100 for children aged 6-16 in Canadian schools in Ontario. Young children presented with more head injuries thanolder children, with the predominant MOI sustained from falls. Findings from an evaluation of the Canadian National Population Health Survey found a rate of concussion of 110 per 100,000 (23). An increased rate of concussion was reported for younger individuals with 200/100,000 for 0-14 years, 160/100,00 for 15-34 years and 50/100,000 for 35 years or older. SRC was the most common MOI with an incidence rate of over 54% and over 85% of concussions in the 15-34-year-old groupwere sustained from playing sports. Sex-related incidences were higher in males (140/100,000) compared to females (80/100,00). However, in a review by Koerte andcolleagues [12], studies indicate that females have a more prolonged recovery trajectory and worse outcomes compared to males. This may be caused by differences such as decreased neck girth and strength as well as physiological and hormonal variations [4].

Differences in incidence rates vary between sports with men's American football consistently rated highest (36.1%), followed by men's ice hockey (13.4%) and women's soccer (8.1%) [3,24]. Marshall and colleagues [25] reported increasedincidence rates for American football compared to six other U.S high school and collegiate sports. Similar findings were reported in a systematic review where 19 of the 33 prospective studies consisted of concussions sustained from American football, with an 87.3% incidence rate of adolescent and young male athletes [16]. In high school, concussion accounts for 9-13% of all reported injurieswith the top 3 sports being rugby, ice hockey and American football (4.18, 1.20 and 0.53 athlete-exposure (AE) per 1000) (26,27). AE is an athlete's participation methodequating to 1 athlete participating in 1 practice or game.

Men's wrestling (10.92/1000 AE) and women's ice hockey (7.50/1000 AE) were reported to surpass the incidence rate of collegiate football (6.71/1000 AE) in adescriptive epidemiological study conducted on National Collegiate Athletic Association (NCAA) sports from 2009-2010 to 2013-2014 [28]. In this study approximately 53% of all concussions sustained by NCAA athletes occurred during competition and concussion alone represented 6% of all collegiate athletic injuries [28,29]. In another NCAA study [30], it was reported that athletes who sustained a concussion were three times more likely to sustain a second concussionin the same season compared to athletes who did not have a concussion history.

Furthermore, 91.7% of the repeated concussions occurred within 10 days of the first injury. However, a recent update conducted by the NCAA-Department of Defense Concussion Assessment, Research and Education (CARE) Consortium from 2014 to 2017 reported a 41% reduction in the rate of same season repeat concussions [31]. Findings also indicated a significant increase of 10 additional days before athletes returned to play compared to the previous study. This signifies improvements in the clinical management of concussion over the past 15 years in respect to the risk of repetitive injury following the critical period of cerebral vulnerability. It is therefore of utmost importance to understand the physiological impairments at play during this critical period and the management strategies that are currently employedfor RTP.

Pathophysiology

Concussion represents a functional disturbance of the brain that involves microscopic neural damage, therefore conventional neuroimaging techniques such as Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) are unableto clearly delineate structural neural anomalies [10,32,33]. However, novel imaging techniques such as Diffusion Tensor Imaging (DTI) have found axonal damage in brain regions such as the corpus callosum which is a key region for inter-hemispheric integration of sensory, motor and cognitive information [34]. Following an injury to the brain, there are alterations in the cellular environment with Giza and Hovda [33] coining the phrase 'the neurometabolic cascade of concussion'. Functional alterations to cellular or physiological function can include ionic shifts, neurometabolic changes such as an increase in glucose metabolism (hyperglycolysis) and impaired function in neurotransmission. The neurometabolic cascade initiates an ionic flux and depolarization with the release ofthe excitatory neurotransmitter glutamate [35]. Ionic fluctuations occur when potassium exits and calcium enters the cells, resulting in changes in cellular physiology such as vasoconstriction, alterations in cerebral blood flow (CBF)and an increase in cerebral glucose metabolism. Consequently, the sodium-potassium pump attempts to maintain homeostatic cell membrane permeability which requires increased amounts of adenosine triphosphate (ATP) andresults in a metabolic energy crisis [33,36].

After the initial period of hyperglycolysis, impairments in metabolism can lastup to 10 days, corresponding to the typical timeline of symptom resolution [4,5,10]. During this vulnerable period, there is a decrease in the brains ability to adequatelyrespond to a second concussive blow and an increased susceptibility to reinjury [10,33]. Much of the mitochondrial dysfunction following a concussion is related to prolonged cellular exposure to high levels of calcium [36]. This disruption in mitochondrial activity inhibits the production of ATP and can lead to cellular necrosisand death via apoptosis [37]. Animal models have predominantly provided information regarding the neurophysiological response to concussion and therefore the severity of the injury can be greater when extrapolated to a human population.

Ellis and colleagues [14] have suggested that concussion pathophysiology may becaused by impairments in specific neurological sub-systems such as the cervicogenic and vestibulo-ocular systems or at a more global cellular level in the form of autonomic dysfunction.

Autonomic dysfunction

The Autonomic Nervous System (ANS) is composed of two complementary systems called the Sympathetic Nervous System (SNS) or the "fight or flight system"and the Parasympathetic Nervous System (PNS) or the "rest and digest system" [38]. The ANS is responsible for many homeostatic functions including the regulationof cardiac and smooth muscle contractility to brain tissue via the baroreflex [39]. Theability to maintain constant perfusion in cerebral tissue in response to fluctuations in perfusion pressure, such as when exercising, is known as dynamic cerebral autoregulation (CA). A review of the literature relating to autonomic dysfunction or dysautonomia in mTBI concluded that impairments in CA regulation are seen in boththe acute and subacute stage post-injury [40]. Dysautonomia increases sympathetic neural activation which

contributes to neuroinflammation, oxidative stress and CBF impairments [40]. This can manifest clinically with symptom presentation such as headaches, anxiety, cognitive impairments and exercise intolerance [41]. Uncouplingof the ANS is measured through various techniques such as heart rate variability (HRV), pupillary dynamics, eye pressure, arterial pulse wave and graded exercise testing [40,41].

Clausen and colleagues [42] evaluated dysautonomia by measuring CBF velocity with transcranial doppler ultrasonography during a graded exercises test ona treadmill in 9 female athletes experiencing PPCS. Findings indicated statistically significant decreased arterial carbon dioxide (CO2) sensitivity in the concussed group (1.35 Å} 2.11 L/min/mmHg CO2) in comparison to the control group (2.88 Å} 0.60 L/min/mmHg CO2). This altered CO2 sensitivity blunted the ventilation response during exercise, which in turn increased arterial CO2 and CBF velocity in the concussed group correlating with increased symptom presentation of headacheand dizziness and thus limited exercise tolerance. These findings indicate impairedCBF velocity may be due to decreased CO2 sensitivity and alterations in CA after aconcussion. CBF is an important indicator of neuronal function, with impairments potentially leading to alterations in functional integrity in the brain [40].

HRV is also used as an indirect measure of ANS function and reflects the totalvariation of consecutive HRs or more specifically the standard deviation of consecutive 10 heartbeats of the R-R intervals (39,41). Increased HRV is associated with adaptation to physiological requirements and is considered a putative marker for effective ANS modulation [41]. Gall., *et al*. [43] found HRV to be decreased 5 days post-concussion when performing low to- moderate intensity exercise on a cycle ergometer. In contrast, no difference in HRV was found at rest in the concussed group compared to controls. Reduced HRV has been associated with exercise intolerance and decreased prefrontal cortical activity [40]. This may haveimplications for the presentation of exercise intolerance and cognitive complaints after sustaining a concussion.

Management of concussion

An initial period of 24 to 48hours of physical and cognitive rest is advocated postconcussion [44]. During this vulnerable period, the brain is undergoing an "energy crisis" and prematurely returning to activities can have deleterious effects onrecovery such as reducing neuroplasticity and predisposing the athlete to a risk of re-injury or the more fatal second impact syndrome [6,33,44]. However, after this initial period, strict rest or "cocoon therapy" is associated with slower recovery rates and increased levels of stress, anxiety, depression, irritability and physical deconditioning [1,45]. Establishing an exact period of rest post concussion remains elusive due to undefined prognostic factors and the heterogeneous nature of concussion. It is therefore recommended that a multifaceted management approachinvolving symptom monitoring, neurocognitive assessment, and physical and exertion testing be implemented [4,8,16,44].

Return to play

Returning to activities or play after concussion involves a graduated approachto ensure an individual's safety and to mitigate the risk of re-injury. Exercise is a formof physical activity usually performed recreationally that involves a plan, structure and repetition leading to the objective of maintaining or improving physical fitness [46]. In contrast, sporting activities encompass a set of rules or goals to train and excel in specific athletic skills competitively. Examples include individual sports suchas skiing or team sports such as football. For the latter, the CISG recommends a stepwise graduated RTP protocol which is guided by clinical evaluation and symptom reporting [6]. The RTP protocol involves: 1) no physical/sporting activity, 2)light aerobic exercise, 3) sport-specific activities, 4) non-contact training drills, 5) full-contact practice and eventually RTP [4]. Twenty-four hours is recommended between each stage, approximating one week before unrestricted RTP is allowed. Symptoms are reported at each stage of the protocol and progression is dictated bysymptom resolution along with objective measurements of neurocognitive and balance function [4,6].

However, the protocol is currently not validated for progression sequence or time spent at each stage and is guided by individual subjective reporting to assess recovery [1]. Although self report symptom scales and checklists such as the PCSS are shown to have good validity, they are limited by the presentation of exercise-induced symptoms that are not due to concussion [8,47,48]. In fact, in non-concussed populations, there can be a prevalence of symptom provocation that presents as concussive symptoms after completing moderate-intensity exercise [49].This has prompted recent consensus guidelines by the CISG to evaluate symptomology 15 minutes after exercising [4]. However, there is limited evidence

to support this time specification for symptom reporting [50]. The psychometric properties of self-reported symptom scales are further challenged by athletes inaccurately reporting symptoms in order to RTP and inter-day variability affective states rather than a direct relationship to the neurological insult of a concussion [20,51].

Neurocognitive assessment

Impairments in cognitive function such as speed of information processing, visual and verbal memory and executive functioning are some of the common symptoms encountered postconcussion [16]. Frontal lobe dysfunction relating to thedorsolateral prefrontal cortex (DLPC) and the default mode network (DMN) have been implicated in neuroimaging studies [52-54]. Neurocognitive testing is considered the cornerstone of concussion diagnosis and management [16,55].

Assessment of cognitive function is typically administered by the neuropsychologistand consists of a battery of tests such as questionnaires and computerised neurocognitive tests (CNTs) that assess different cognitive domains.

However, the test-retest reliability of CNTs in determining a diagnosis hasbeen challenged, with a meta-analysis reporting both false-positive and false-negative results [56]. The former has been estimated to occur in 40% to 80% of tests in a systematic review conducted on the most commonly administered CNT,the Immediate Post Concussion Assessment and Cognitive Test (ImPACT) [55]. In another study, CNT results found one or more subtests below average in 48% of asymptomatic athletes (n = 117) who were following RTP guidelines [57]. However, these results had no relationship with successfully completing the RTP protocol.

Confounding factors such as age, education, sleep habits, drug intake, motivation, language, practice effects and length of time between testing can play a significant role in test results [16,56]. Due to the poor reliability of CNTs, inaccurate decisions may lead to either an unnecessary protraction of recovery time or a premature RTP.This can have serious consequences for the physical and psychological wellbeing ofthe individual or of more concern, a risk of re-injury [1].

Exercise assessment

Exercise tolerance is defined as the ability to complete exercise to one's predicted age and ability without developing concussive symptoms or as the heartrate threshold (HRt) at symptom exacerbation [58-60]. It has emerged as both a determinant for recovery and as an intervention in the management of concussion [1,6,44,61]. As mentioned previously, factors such as ANS dysfunction and CBF impairment have been implicated in concussion for the presentation of exercise intolerance [39,42]. However, specific neurological sub-systems such as the cervicogenic and vestibulo-ocular motor system may also present with exercise intolerance due to symptom presentation such as dizziness, headaches and pain [62].

The Buffalo Concussion Treadmill and Bike Tests (BCTT and BCBT) are graded exertion tests based on exercise tolerance [62,63]. Symptoms, HR, andrating of perceived exertion (RPE) are monitored throughout the tests providingobjective measurements of physiological function in response to exercise.

Participants with ANS dysfunction will typically experience increased symptom presentation during the tests and be forced to stop prematurely. Physiological dysfunction would then be implied as a domain of concussive impairment. Studies exploring the use of the BCTT and BCBT have primarily focused on their prognostic utility for concussion recovery. Findings from such studies include an association of protracted recovery with a HRt of < 135 beats per minute (bpm) at symptom exacerbation (60). A lower HRt on initial assessment has also been associated with an increase in recovery time [60]. Another study evaluated the difference between resting HR and HRt using the BCTT and found that a value of ≤50 bpm is 73% sensitive and 78% specific for predicting a protracted recovery [64]. In a retrospective study, Darling and colleagues [57] reported a safe and successful RTPfor 117 concussed athletes aged between 13 to 19 years with the implementation ofthe CISG consensus statement guidelines and the BCTT. The BCTT has also been shown to be safe to administer within 1 week of injury, demonstrating no negative effects on concussion recovery [60].

Conclusion

Despite the clinical and prognostic utility of exercise tolerance, limitations such as fitness level, emotional status, attitude, motivation, time of day and sleep quality can confound results [64]. Furthermore, the aforementioned studies predominantly consisted of cohorts of adolescent athletes and thus results cannot

beextrapolated to the general population. Although exercise testing can differentiate physiological impairment from cervicogenic or vestibular/ocular motor impairments, there is limited research identifying functional brain activity in response to exercise in a concussed cohort [17]. Also, recovery was defined as being asymptomatic or returning to a "normal level of symptoms" in these studies which does not imply that impairments in brain function are not still present. One would expect there to be a more pronounced response in the concussed versus non-concussed brain after exercising especially in the acute stage as neurometabolic adaption has not yet beenachieved. Also, if a concussion is representative of impairments relating to distinctivedomains or systems, it could be hypothesised that exercise would induce a greater physiological demand on brain function in a cohort of exercise intolerant concussed participants who present with PPCS.

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