Treatment of Recurrent Concussion

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The management of an athlete with recurrent concussions, whether persistently symptomatic or not, remains anecdotal. Currently, there are no evidence-based guidelines upon which a team physician can advise the athlete. All doctors involved in athlete care need to be aware of the potential for medicolegal problems if athletes are inappropriately returned to sport prematurely or, in the case of professional athletes, held out of sport or retired on the basis of nonscientific recommendations. This paper discusses such issues.

Introduction

The clinical management of repeated concussive injuries remains a complex and controversial area. For the most part, there are no evidence-based recommendations with which to guide the practitioner. When an athlete has not fully recovered and remains symptomatic, the decision is simple. The athlete needs to be prohibited from contact sport until full recovery ensues. Far more difficult is the situation when an injured athlete, either professional or otherwise, has suffered a number of concussive injuries, but has no residual neurologic or cognitive symptoms. Although the return-to-play decision should be straightforward, a number of anecdotal guidelines have been published, which serve to confuse rather than assist the team physician in his or her management of the athlete [1••]. Current approaches as outlined below are far too simplistic in their understanding of the clinical problem. At the end of the day, good clinical judgment and common sense must remain the mainstay of clinical management.

Background

It is often stated dogmatically that sustaining several concussions over a sporting career will necessarily result in permanent damage. In fact, the scientific evidence for such a statement is not compelling.

It is worth discussing the origins of this concept of a "three strike rule," namely, if an athlete has three concussions, he or she is ruled out of competition for a period of time, or retired from contact sport. This approach was originally attributed to Quigley in 1945, and subsequently discussed by Thorndike [2], who suggested that if any athlete suffered "three concussions, which involved loss of consciousness for any period of time, the athlete should be removed from contact sports for the remainder of the season." This approach has no scientific validity, yet continues to be the anecdotal rationale underpinning most of the current return-to-play guidelines.

Other commonly cited research deserves critical analysis. Apart from boxing-related head injuries, the most widely cited studies of the cumulative effects of concussion have evaluated patients with injuries sustained in motor vehicle accidents that were severe enough to warrant presentation to a hospital. Generally, concussive injuries suffered in sports such as football involve lesser degrees of acceleration-deceleration forces than experienced in motor vehicle accidents [3–6]. These sports-related injuries typically recover quickly, and usually do not require acute hospital admission.

Limitations of retrospective studies in concussion, such as the widely cited motor vehicle accident studies by Gronwall and Sampson [3], Gronwall [4], and Gronwall and Wrightson [5,6], include diagnostic uncertainty, relying on self-reported injury recall and medically unvalidated injury diagnosis. For example, some head injuries in the cited studies were assessed up to 8 years after their occurrence [3–6]. Although methodologic problems flaw these studies, they gave support to the contention proposed by Symonds that cumulative deficits may follow repeated concussive injury, such as evidenced by the punch drunk state of chronic traumatic encephalopathy seen in boxers [7,8]. Boxing, however, should not be considered as a model for cumulative head injury seen in other sports, because it presents unique risks to the athlete in terms of the frequency of repetitive head trauma [8–11]. Recently, specific genetic abnormalities involving the apolipoprotein E gene have been reported as the major risk factor for the development and progression of traumatic encephalopathy, and have been thought to influence the outcome of traumatic brain injury (TBI) [12••,13–15].

In another series of retrospective studies involving retired Scandinavian soccer players, cognitive deficits were noted. These findings were attributed to recurrent injury by repetitive heading of the ball in soccer [16–19]. In these studies, significant methodologic problems flaw the results. These problems include the lack of preinjury data,

selection bias, lack of observer blinding, and inadequate control subjects. Approximately 40% of the control group were found to be cognitively impaired. The authors conclude that the deficits noted in the former soccer players were explained by repetitive trauma, such as heading the ball. The pattern of deficits, however, is equally consistent with alcohol-related brain impairment, a confounding variable for which the study was not controlled. To date, there has been no replication of these findings by other independent groups [20••].

Experimental animal research also provides some supporting evidence against the concept that recurrent injuries necessarily cause permanent damage. In animal studies of experimental concussion, animals have been repeatedly concussed 20 to 35 times during the same day, and within a 2-hour period. Despite these unusually high numbers of injuries, no residual or cumulative effect was demonstrated [21]. This topic is more fully reviewed in a recent article [1••].

This issue becomes further confused when well-known athletes suffering from recurrent head trauma appear in the media. In some cases, the injuries suffered by such athletes are more severe than the typical sport-related concussive injuries, yet in the minds of the public no distinction is made. In such injuries, long-term symptoms are not wholly unexpected. In other cases, professional athletes suffer repeated concussions, yet are not banned from sport, as may be the advice to lesser athletes. Although professional athletes may be monitored more closely than other sporting participants, the variation in management between elite and recreational athletes is often seen as hypocritical.

In still other cases, the primary postconcussive symptom is headache. This symptom is nonspecific and can be the result of a variety of causes other than concussion. Occasionally an athlete said to have repeated concussions is in fact suffering from post-traumatic migraine on each occasion, and is misdiagnosed either by the treating practitioner or supposition of the media.

Much of the concern in relation to the management of repeated concussive injury relates to the absence of a consensus definition and severity grading of concussion, and to the lack of scientifically valid management guidelines. Until this central issue is resolved, it is unlikely that a clear answer to the problem of retirement due to chronic symptoms will ensue.

The Risk of Repeat Concussions in Sport

It has become a widely held belief that having sustained a concussive injury, one is then more prone to future concussive injury. The evidence for this contention is limited at best. In a widely quoted study by Gerberich *et al.* [22], which involved self-reported questionnaires relating the prior history of head injury in high school gridiron football players, an increased risk of subsequent concussions was reported in players with a past history of concussion. Significant methodologic problems flaw this study. Not least is the fact that the authors included cases of catastrophic brain injury. Furthermore, the reliability of a self-diagnosis of concussion is questionable, given that only 33% of athletes with loss of consciousness and 12% of athletes with other symptoms were medically assessed. The majority of the diagnoses of concussion were made by the coach, other teammates, or by the players themselves.

It would seem obvious that in any collision sport the risk of concussion is directly proportional to the amount of time playing the sport. In other words, the more games played, the greater chance of an injury occurring. Therefore, the likelihood of repeat injury may simply reflect the level of exposure to injury risk.

In addition, Gerberich *et al.* [22] acknowledge that the observed increased likelihood of concussion could also be explained by a player's style of play. The player's risk of injury may be increased by utilizing dangerous game strategies and illegal tackling techniques. Similar criticisms can also be levelled at another retrospective study, in which it was reported that once an initial concussion was sustained, the probability of incurring a second concussion greatly increased [23].

The underlying concern is that an athlete who suffers repeated concussions would then develop a gradual cognitive decline, similar to the so-called punch drunk syndrome, or chronic traumatic encephalopathy, seen in boxers [7,12••,24]. Based on published evidence, this fear is largely unfounded, and recent developments suggest that the risk of traumatic encephalopathy in this setting may be largely genetically based, rather than simply a manifestation of repeated concussive injury [13].

Does Repeat Concussion Result in Second Impact Syndrome?

Second impact syndrome (SIS) is frequently mentioned in the concussion literature, but surprisingly, has little scientific evidence for its existence [25•]. It is a term used to describe the potential catastrophic consequences resulting from a second concussive blow to the head before an individual has fully recovered from the symptoms of a previous concussion [26,27]. The second head injury is believed to result in loss of cerebrovascular autoregulation, which in turn leads to brain swelling, secondary to increased cerebral blood flow [28–30]. Mortality in this condition approaches 100%.

Although the scientific evidence for SIS is lacking, the repercussions of placing an athlete at risk of the potential consequences of a SIS is the basis of existing return-to-play guidelines that recommend removal of a concussed athlete from play. However, if SIS is not a real entity, such management recommendations may be inappropriate.

Published Guidelines for Return to Sport After Concussion

Published guidelines recommending termination of all contact sport following three concussions during the

Table 1. Return-to-sport guidelines

Severity grade	1st concussion	2nd concussion	3rd concussion
*Cantu system**			
Grade 1: No LOC, PTA < 30 min	RTP after 1 week if asymptomatic	RTP in 2 weeks if asymptomatic for at least 1 week	Terminate season; RTP next season if asymptomatic
Grade 2: LOC < 5 min, PTA > 30 min	RTP after 1 week if asymptomatic for at least 1 week	Minimum of 1 month off sport; RTP if asymptomatic for at least 1 week; consider terminating season	Terminate season; RTP next season if asymptomatic
Grade 3: LOC > 5 min, PTA > 24 hr	Minimum of 1 month off sport; RTP if asymptomatic for at least 1 week	Terminate season. RTP next season if asymptomatic	
Colorado guidelines†			
Grade 1: No LOC, confusion, no amnesia	RTP after 20 min if asymptomatic	RTP if asymptomatic for at least 1 week	Terminate season; RTP next season if asymptomatic
Grade 2: No LOC, confusion, amnesia	RTP after a minimum of 1 week with no symptoms	RTP after a minimum of 1 month with no symptoms for at least 1 week	Terminate season; RTP next season if asymptomatic
Grade 3: LOC	RTP after a minimum of 2 weeks with no symptoms	Terminate season; RTP next season if asymptomatic	Terminate season; RTP next season if asymptomatic

**Adapted from* Cantu [33].
†*Adapted from* Kelly *et al.* [34].
LOC—loss of consciousness; PTA—post-traumatic amnesia; RTP—return to play.

course of an athletic season need to be considered carefully. In the absence of documented objective evidence of brain injury, there is no scientific support for this generalization. Athletes excluded from competition on such a basis may consider a medicolegal appeal that would be impossible to defend in a court of law.

There are several anecdotal guidelines available in the literature. As mentioned above, these are not supported by published scientific evidence, and should be considered management options at best. The issue of validity of the scales themselves has been recently reviewed [31•].

The main guidelines for return to sport after repeated concussive injury are those published by Cantu [32,33], and Kelly *et al.* [34], of the Colorado Medical Society. The recent American Academy of Neurology guidelines are derivative of the latter approach [35].

It can be seen that there are many superficial similarities between the two scale systems. Although the criteria for injury severity differ, the mandatory requirement is that two grade-3 injuries or three injuries of any grade result in termination of the athlete's season. Given that a Cantu grade 2 is equivalent to a Colorado grade 3, it can be seen that the scales give differing recommendations for the same injury.

Is There a Genetic Susceptibility to Brain Injury in Sports?

Recent research in boxers has suggested that chronic traumatic encephalopathy may be associated with a particular genetic predisposition. The apolipoprotein E ε-4 gene (*ApoE*), a susceptibility gene for late onset familial and sporadic Alzheimer's disease, may be associated with an increased risk of chronic traumatic encephalopathy in boxers [12••,13,36,37]. In a nonboxing population, an *ApoE* polymorphism was significantly associated with death and adverse outcomes following acute TBI, as seen in a neurosurgical unit [14]. In a recent prospective study, *ApoE* genotypes were tested for their ability to predict days of unconsciousness and functional outcome after 6 months [38]. There was a strong association between the *ApoE* allele and poor clinical outcome.

Furthermore, *ApoE*-deficient (knockout) mice have been shown to have memory deficits, neurochemical changes, and diminished recovery from closed head injury when compared with controls [39]. It is suggested that ApoE plays an important role in both neuronal repair [40] and antioxidant activity [39], resulting in ApoE knockout mice exhibiting an impaired ability to recover from closed head injury. Although only in the early stages of our understanding of these issues, the interaction between genetic and environmental factors may be critical in the development of the postconcussive phenomena or concussive sequelae.

Conclusions

How should the sports clinician manage an athlete with recurrent injury? With an athlete who remains persistently symptomatic following a concussion, the consensus of

experts in the field would suggest withholding the athlete from play until full recovery occurs. There is no strong published evidence for this approach, and the fear is that the symptoms may be prolonged, or premature return to play may put the athlete at risk of further injury.

In the setting of repeated uncomplicated concussive injury with full recovery following each episode, the situation is somewhat confused. Although published guidelines exist, they do not have any scientific validity, and should be seen only as anecdotal suggestions for the clinician, rather than proven fact. Whether three concussions is a reasonable limit to warrant termination of a season or career cannot be supported on the available scientific evidence, and a clinician thus advising an athlete may have to justify his anecdotal approach in a court of law.

The recent developments suggesting that some athletes may have a genetic risk of poor outcomes following TBI indicates that the number of impacts in a season is far too simplistic an approach [41].

It is my practice in professional sport to routinely perform neuropsychologic testing on all athletes preseason, and following concussive injury. More importantly, no athlete returns to sport until he is symptom-free and has returned to his neuropsychologic baseline performance. In the 16-year period since such management strategies have become routine in elite Australian football (where the incidence of concussion in this sport is 16 times that of American football), no athlete has been retired because of chronic neurologic or cognitive symptoms.

The central issue relates to the nature of the injury. Although there is no doubt that severe concussion with persistent symptoms does occur, the typical concussive injury heals quickly and the player returns to sport without difficulty. In this setting, scientific evidence that sustaining a number of concussions over the course of a season or over a career, causing chronic neurologic dysfunction, is nonexistent. Clinicians should be aware of the neuromythology surrounding this issue, and manage their patients on evidence-based guidelines, or if they are lacking the *vade mecum* of good common sense.

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