

OPINION

Sports-related concussions — media, science and policy

Rebekah Mannix, William P. Meehan III and Alvaro Pascual-Leone

Abstract | Although growing awareness about the potential long-term deleterious effects of sport-related concussion has led to increased attention to the risks of collision sports, calls to ban these sports, such as American football, might be premature. Collision sports have a relatively high incidence of concussions, but participation in these sports also confers a host of benefits. In addition, the associated risks of participation, including concussion, have not been definitively shown to outweigh the benefits they provide, and the risk–benefit ratio might vary among individuals. The risks of concussion and repetitive concussions associated with collision sports are unknown in the general population and not well characterized even in elite athlete populations. In this article, we discuss current knowledge on sports-related concussion, its neurological consequences, and implications for regulation of the practice of collision sports.

Recent documentaries and dramatizations portray concussion as a common cause of long-term neurological disability and the direct cause of a chronic traumatic encephalopathy (CTE), a neurodegenerative tauopathy that is found in people with a history of exposure to severe or repeated head trauma. In children, adolescents and young adults, sport-related injuries are among the most common causes of concussion^{1,2}.

The increasing concern over the potential long-term sequelae of sport-related concussions has heightened scrutiny of the practice of collision sports, particularly American football, with some advocates even calling for its abolition^{3,4}. There is no debate that concussion and its potential neurological consequences warrant attention, and that the risks to athletes should be minimized. Nonetheless, calls to ban American football, or any other sport that might expose athletes to concussion, seem premature, given the gaps in knowledge about the potentially harmful consequences of concussion and the known benefits of participating in sport. Such calls potentially distract researchers from important epidemiological, clinical and mechanistic investigations into the

long-term effects of concussion. Research into long-term outcomes after concussion is still in its infancy, and is largely based on case series, with some support from preclinical models^{5–12}. The high incidence of concussions linked to collision sports is a legitimate public health concern, and demands both a sober assessment of existing data, and new research to enable evidence-based decisions on concussion management at the level of the individual and society. Here, we summarize what is currently known about long-term outcomes after sport-related concussion, highlight the knowledge gaps in concussion research, and discuss implications for the practice of youth and professional sports.

Long-term outcomes of concussion

The American Academy of Neurology (AAN) defines concussion as “a pathophysiological disturbance in neurologic function characterized by clinical symptoms induced by biomechanical forces” (REF. 13). The diagnosis and management of concussion are based primarily on self-report of subjective symptoms, such as headache, irritability and nervousness, many of which are highly prevalent in the general

population even in the absence of recent head trauma. The vast majority of patients who sustain a sport-related concussion recover quickly and completely within weeks¹⁴; however, a notable minority of patients — as many as 30% in some studies — experience persistent symptoms after concussion, sometimes referred to as ‘post-concussion syndrome’ (REFS 15,16). The cause and neurobiological correlates of these persistent symptoms are not known.

Effects of multiple concussions

The majority of experts agree that a single sport-related concussion is unlikely to result in long-term adverse outcomes¹⁴. By contrast, the potential effects of multiple concussions remain a source of controversy. Most published studies on long-term outcomes after multiple concussions are retrospective and based on self-reported concussion history by elite competitive individuals, such as collegiate and professional athletes (FIG. 1). For example, a seminal study by Guskiewicz *et al.* showed that former professional American football players who reported a history of multiple concussions were at increased risk of depression and memory problems¹⁷. In studies of collegiate American football players, multiple concussions were associated with reduced cognitive performance, prolonged recovery and increased risk of subsequent concussions^{18,19}. Several studies of soccer players have found that a history of multiple concussions is associated with increased symptomatology and impaired neuropsychological test performance months to years after injury^{20,21}. Many of these studies, however, were conducted on athletes who played sports before the current era of increased concussion awareness and without the benefit of modern tools for the assessment and monitoring of concussions. Furthermore, these athletes often returned to play within minutes of sustaining a concussion and, therefore, were presumably subjected to multiple repeated blows to the head before full recovery.

Current concussion management practices emphasize the need for recovery before return to activity. Players who have sustained a concussion might not

PERSPECTIVES

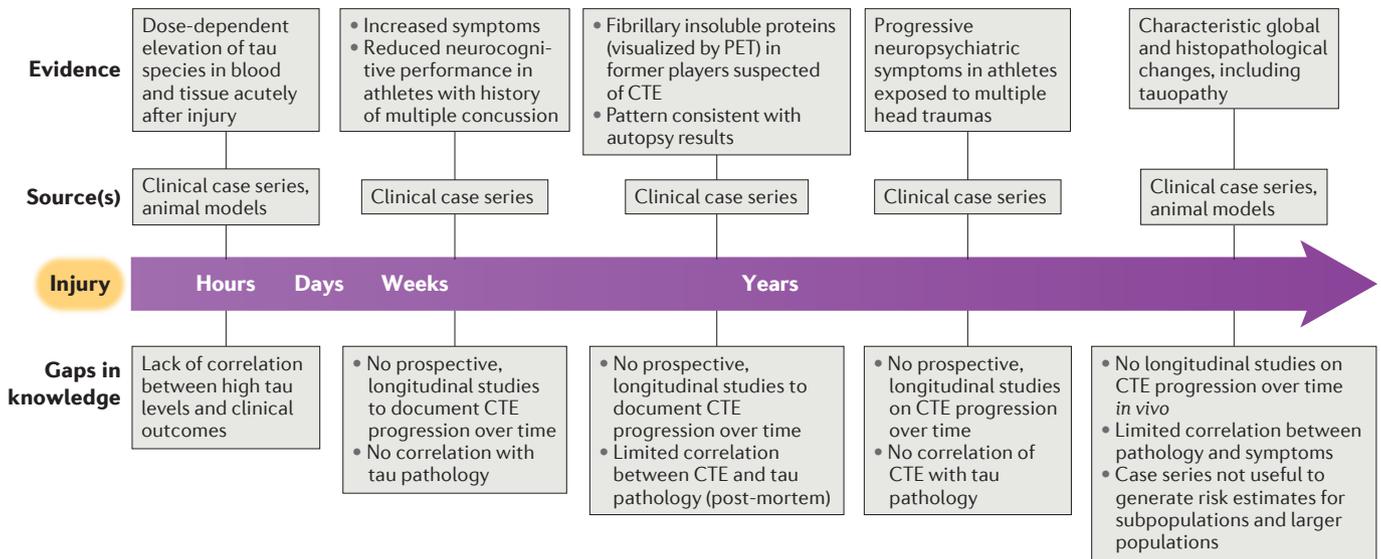


Figure 1 | From concussion to CTE — sequence of events and knowledge gaps. Data from clinical case series and animal models suggest that athletes who sustain concussions could develop a form of tauopathy, chronic traumatic encephalopathy (CTE), which leads to the deposition of fibrillary insoluble proteins and progressive deterioration of brain function. A definitive causal link between concussion and CTE has yet to be established, however.

be allowed to return to play until they are deemed by a medical professional to have recovered, and some players might even be prohibited from participating after a certain number of concussions. Whether such concussion management practices might mitigate the reported effects of multiple concussions is unknown, but it is possible that ongoing neurodegenerative changes occur in the absence of obvious clinical findings. Studies published in the past two decades suggest that imaging and electrophysiological biomarkers are altered in the brains of athletes who sustained prior concussions, even in the absence of overt signs or symptoms, and that these changes could be linked to cognitive decline^{22–27}. These findings, which point towards a link between concussion and long-term neurological consequences, are extremely important; however, the existing literature on the long-term effects of multiple concussions is not conclusive. A study of American and Australian rules football players published in the 1990s showed no long-term cognitive or behavioural effects of repetitive concussions²⁸. Moreover, studies published in the past decade did not detect lingering effects of multiple concussions on neurocognitive testing, although multiple prior concussions might be associated with increased reporting of baseline symptoms, even in the absence of recent injury^{29,30}.

The lack of consistent findings on long-term effects of multiple concussions could be attributed to a variety of factors, including the population studied (for

example, youth versus elite athletes), the time point studied (years versus decades after concussion exposure), the lifetime exposure to concussive and subconcussive injuries, the methods used to assess recovery, and other confounding factors such as cognitive reserve, age, sex, socioeconomic status, alcohol and/or drug use, health habits, and genetic predisposition, to name but a few. Moreover, assessment of cognitive and behavioural function at one time point, as opposed to serial assessments over time, is not adequate to document the progressive decline in functional outcomes that is characteristic of neurodegenerative disorders. Evaluation of the clinical significance of possible persistent brain changes after concussion will require properly powered, prospective, longitudinal studies.

Concussion and CTE

Retrospective case reports, predominantly from boxers and professional players of American football, have described neuropathological changes consistent with CTE in the brains of former athletes who manifested with mood disorders, headaches, cognitive difficulties, suicidal ideation, difficulties with speech, and aggressive behaviour^{3,6,11,31,32}. The vast majority of individuals in these studies had, presumably, experienced repetitive head trauma in the context of sport, although sometimes these injuries were reported as subconcussive injuries rather than concussions. The possibility that subconcussive injuries could

lead to CTE has raised the concern that a large number of athletes might be at risk of CTE in the absence of overt concussion history; in fact, some experts have argued that it is the chronic and repetitive nature of head trauma, irrespective of concussive symptoms, that is the most important driver of CTE³³. Indeed, several studies have suggested that white matter changes, neurocognitive impairment and diminished neurophysiological function can occur in the absence of clinical concussion^{34–36}. However, the populations in which CTE has been reported are likely to have extremely high exposure to repeated head trauma compared with the general population. In addition, the studies that link head trauma and CTE are limited by their retrospective nature: individual predisposing factors cannot be meaningfully addressed, and selection and recall biases limit generalizability.

Without prospective studies, accurate risk estimates are not possible; even in boxers and players of American football, which are, presumably, high-risk populations, the

Glossary

Post-concussion syndrome

Persistent symptoms after a head injury, including at least three of the following: headache, dizziness, fatigue, irritability, impaired memory and concentration, insomnia, and lowered tolerance for noise and light.

Lytic–bodig disease

Neurodegenerative disease with clinical symptoms of paralysis and dementia, and autopsy findings of neurofibrillary tangles

prevalence of CTE is unknown. Thus, the risk of CTE in the general population, who are exposed to injuries of lower intensity and shorter duration than those experienced by professional athletes, remains unclear.

Just as the prevalence of CTE, even in high-risk populations, is not known, the mechanistic link between head trauma and CTE has not been conclusively established. Animal models of traumatic brain injury, however, show that deposition of phosphorylated tau in a pattern consistent with the human characteristics of CTE is causally related to head trauma. Indeed, in one study, administration of an anti-*cis* phosphorylated tau antibody prevented the development and spread of tauopathy and brain atrophy, which are hallmarks of CTE⁹. Unfortunately, human studies to date have not addressed causality between head injury and CTE, and CTE pathology might not be unique to individuals with a history of repetitive head trauma or concussion. Indeed, a study published in 2016 suggests that CTE-like pathology can be found in the absence of a history of repeated trauma in patients with temporal lobe epilepsy³⁷. Medical and psychological conditions other than repetitive concussion can also lead to tauopathies and CTE-like symptoms. Moreover, *in vitro* studies showed that hypoxia and serum starvation can induce tau-mediated neurotoxicity⁹.

Further work might be needed to distinguish CTE pathology from the neuropathological findings in other neurodegenerative diseases, such as corticobasal degeneration, lytico–bodig disease and primary age-related tauopathy, which are also characterized by the presence of neurofibrillary tangles. Thus, we have yet to definitively establish whether CTE is distinct from other neurodegenerative diseases, and whether repetitive head traumas are sufficient to cause CTE. The use of symptomatic controls who have not been exposed to repetitive concussions might provide answers as to whether exposure to concussive and subconcussive injuries is necessary and sufficient to cause CTE.

Implications for sports practice

Assessing the risk of concussion

The available data warrant public health considerations for collision and contact sports, and should lead to careful assessment of sports rules by the appropriate governing bodies. Nonetheless, instigation of public health measures on a wide scale should be considered with caution. In high school and collegiate settings in the USA, American

football, wrestling, ice hockey, rugby, lacrosse, field hockey and soccer all have a relatively high incidence of concussion³⁸ (FIG. 2), and a more comprehensive assessment of the sequelae of concussion associated with these sports is necessary before suggesting the elimination of any of them. Worldwide, the cumulative incidence of concussion in sports such as boxing, martial arts, rugby, ice hockey, men's lacrosse and soccer is likely to account for substantially more injuries than American football alone^{38–40}. Thus, a selective ban on American football, though politically expedient, might not be an adequate public health measure to reduce exposure to multiple concussions in the context of sports. Furthermore, although the monitoring and reporting of injuries in the context of organized sports has improved in the past few decades, many concussion injuries are sustained in recreational settings, and public health efforts should also target injury prevention in these arenas.

Evaluating risks and benefits

When contemplating the implementation of public health measures aimed at reducing the potential exposure to concussive injuries,

counterbalancing factors — in particular the benefits of sports participation — should be thoughtfully considered. All athletic activities carry risks, including the risk of concussion, but they can also confer substantial benefits, including enhanced psychological well-being, higher educational and career success, improved cardiovascular outcomes, decreased obesity, and decreased risk of all-cause mortality^{41–49}. Such tangible social, psychological and physical benefits conferred by participation in organized sports could offset the risks of exposure to concussion or subconcussive injuries.

The restriction of available sports has the potential to deprive children of other important benefits linked to the practice of these activities. First, participation in sports, particularly team sports, provides the opportunity to work collaboratively, to learn group discipline, and to set and achieve goals — for example, winning a championship — that are not attainable with individual exercise regimens or recreational activities. The argument that non-collision sports or other recreational activities, such as music groups, might offer similar opportunities is valid in theory, although in practice many young people do not have

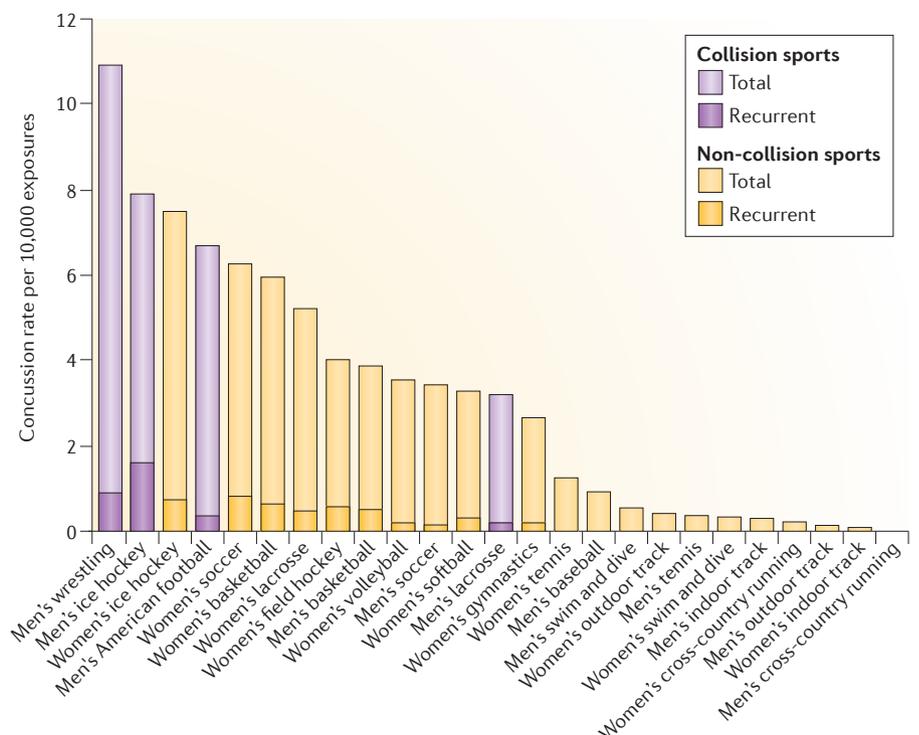


Figure 2 | **Rates of concussions linked to main collision sports in student athletes.** The rate of concussions (25 sports) and recurrent concussions (17 sports) per 10,000 exposures was measured by the National Collegiate Athletic Association Injury Surveillance Program from 2009–2010 to 2013–2014 in student athletes, during practice and competition. Adapted with permission from SAGE Publications Ltd © Zuckerman, S. L. et al. *Am. J. Sports. Med.* 43, 2654–2662 (2015).

the option to engage in such alternative activities. Second, complete risk elimination might actually impair children's ability to assess risk accurately later in life: physical activities that present a modest risk of injury might serve as an important training platform for young individuals to develop risk-assessment skills. Children and young adults often display increased risk-taking behaviour compared with older adults, especially in the context of ambiguous risk⁵⁰. Adolescents are particularly prone to physical risk-taking, including activities such as unsafe sexual behaviour, substance use, illegal behaviour, and risky driving⁵¹. The elimination of opportunities for physical risk-taking in the context of organized athletic activities could result in risk-taking in unsupervised activities that might, ultimately, be more deleterious to their health.

Decision-making

In the absence of definitive data, the decision to play collision sports, such as American football, should be taken at an individual level rather than being governed collectively through policies. Athletes, and in many cases their parents, must weigh the risks and benefits of taking part in a collision sport and decide for themselves whether or not to participate. For individual athletes, this risk–benefit ratio might change over time depending on individual circumstances, including concussion history. However, it is important for athletes to know that our current understanding of the risks and benefits linked to contact sports is limited. As clinicians and scientists, it is up to us to better characterize these risks and benefits, so as to offer evidence-based recommendations and guidelines to help governmental agencies define and implement appropriate public health measures, and athletes navigate their personal decision-making process.

Conclusions

Several important gaps in the existing literature need to be addressed in order to accurately assess the long-term risks associated with concussions. First, as mentioned above, the risk of neurological sequelae associated with multiple concussions and the possible dose-dependent effects of multiple concussions remain unknown in the general population (athletes and non-athletes). Second, the link between concussion, post-concussion syndrome, multiple concussions, and CTE remains unclear.

If CTE can occur in the absence of overt concussion symptoms, current management strategies focused on symptom monitoring, and burgeoning legislative requirements for concussion management, might not be adequate measures to protect athletes from the long-term neurodegenerative sequelae of head injury. Third, the causal relationship between head trauma, tauopathy and CTE is not clear: it is unknown whether a CTE-like syndrome can occur in the absence of head trauma exposure, and whether tauopathy, the primary pathology associated with CTE, causes the clinical manifestations of CTE. Identification of the causative agent of clinical outcomes after concussion will be essential if we are to develop treatments and prevention strategies.

To fill in the gaps in our understanding of the relationship between sports-related concussion and long-term neurological sequelae, prospective longitudinal studies are needed. Following young athletes throughout and after their sports careers would provide the much-needed rigorous assessment of the cumulative effect of concussions and subconcussive injuries, and the associated risks of long-term neuropsychological dysfunction. Prospective studies, including the [Football Players Health Study](#) and studies performed by the [National Collegiate Athletic Association CARE consortium](#), will be vital to evaluate the effects of collision sport exposure on athletes at an individual level, taking into account factors such as head trauma history, rather than assessing the outcome of concussion in isolation. Investigation of the clinical correlates of the pathological changes linked to CTE requires prospective studies with careful serial clinical evaluations, and comprehensive consideration of genetic and epigenetic individual differences and multisystemic interactions between exposure variables and individual risk factors.

Finally, some of the most pressing mechanistic questions, such as the effect of intervals between injuries on the development of CTE pathology, can best be answered by preclinical studies. In such investigations, dose–response studies can be undertaken in a precise manner, and the contribution of genetic and environmental factors can be studied over the course of several years, rather than over decades — the time required to complete prospective longitudinal studies. To be effective, all such studies must remain independent, shielded from the vicissitudes and potential influences of funding bodies or political forces.

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All authors researched data for article, discussed its content, and wrote and edited the article before submission.

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Football Players Health Study:
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