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REVIEW

# Concussion and long-term cognitive impairment among professional or elite sport-persons: a systematic review

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## ABSTRACT

**Introduction** Understanding whether concussion in sport is associated with worsening cognitive function in later life will likely have immediate repercussion on sports concussion prevention and management policy and sporting rules and regulations. This systematic review aims to summarise the evidence on the association between concussion sustained by professional/elite athletes and long-term cognitive impairment.

**Methods** Embase, PubMed and Web of Science were used to search for eligible studies. Studies including professional/elite athletes from any sport were considered. Three comparison groups were considered: internal comparison (concussed vs non-concussed athletes within the same sample); between-sport comparison (contact sport athletes vs non-contact sports ones); external comparison (athletes vs samples of the general population or population norms).

**Results** 14 studies were included (rugby, American football, ice hockey players, boxers and marital art fighters). The general quality of the evidence was poor. The overall evidence, weighted for type of comparison and study quality, points towards an association between sustaining a sport-related concussion and poorer cognitive function later in life in rugby, American football and boxing, although it is unclear to what extent this is clinically relevant. Data on ice hockey and martial arts were too sparse to allow conclusions to be drawn.

**Conclusion** High-quality, appropriately designed and powered epidemiological studies are urgently needed to assess the association between sustaining a sport-related concussion and cognitive impairment later in life. Particular emphasis should be put on the clinical translational value of findings.

## INTRODUCTION

Since Martland, in 1928,[1] first described the clinical syndrome of 'dementia puglistica' in boxers presenting with confusion, slowed movement and parkinsonian symptoms following repeated blows to the head, our understanding of the association between concussion and dementia in boxers has advanced considerably.[2] Neuropathological features of dementia pugilistica, identified by Corsellis *et al* in 1973,[3] showed a consistent pattern of neuropathological changes in the post-mortem examination of the brains of retired boxers. Since then, further investigations into the mechanisms that may underlie these changes, in both boxing and other contact sports have been conducted.[4]

More recently, research has suggested an association between traumatic brain injury and neurodegenerative conditions.[5–9] Specifically, chronic traumatic encephalopathy (CTE) encompasses a clinical spectrum of motor, psychological and cognitive symptoms and is a progressive neurodegenerative condition thought to be caused by single or repetitive concussion-related trauma.[4 10] The clinical features of CTE show some resemblance to the progressive cognitive decline and neuropsychiatric presentation associated with Alzheimer disease,[11] including an insidious onset with amnestic mild cognitive impairment, and similar hallmark pathological features.[11 12] However, CTE has been described as a separate condition,[13] although the pathology is potentially overlapping with that of Alzheimer diseases in up to 25% of the cases.[14]

The theoretical and operational definitions of sport-related concussion are a matter of ongoing debate, although they are all consistent in suggesting that it should be regarded as a mild traumatic brain injury. The latest 2016 Berlin Consensus Statement on Concussion in Sport concluded that 'concussion is a traumatic brain injury which (1) might be caused by a direct or indirect blow to the head; (2) typically results in the rapid onset of short-lived impairment of neurological function that resolves spontaneously; (3) may result in neuropathological changes but the acute clinical signs and symptoms largely reflect a functional disturbance rather than a structural injury and, as such, no abnormality is seen on standard structural neuroimaging studies and (4) might or might not involve loss of consciousness'.[15] According to this definition, it has been shown that numerous athletes have been exposed to head injury events resulting in concussion during playing careers[16]; however, it is reasonable to assume that many more have been exposed to repetitive subconcussive head impact events (eg, when heading a football), the majority of which were below the threshold for a clinical diagnosis of concussion, depending on the nature of the often short-lived neurological symptoms and their interpretation—particularly a few decades ago, when there was less awareness about sport-related concussion.

While there is now a stronger understanding of the potential mechanisms involved in the processes underlying concussion, the epidemiological evidence and the strength of this evidence, to support the long-term effects on cognition remains unclear.[17] A recent systematic review aimed at assessing the long-term neurological sequelae of sport-related concussion concluded that there might be an association with repeated concussion and later cognitive impairment.[18] However, this review included also varsity and amateur athletes, and did not provide an in-depth analysis of the limitation of study design and potential for bias and confounding of the included papers. Understanding whether concussion in sport is significantly associated with worsening of cognitive function in later life is of great importance. Uncovering this possible association would likely have immediate repercussions on current concussion prevention and management policy, sports rules and regulations, and possibly on the listing of cognitive impairment as an occupational diseases for former professional sportspersons.

This systematic review aims to assess and summarise the evidence on the association between concussion sustained by professional/elite athletes and long-term cognitive function as assessed on neurocognitive testing or by clinical diagnosis. Given the recent changes of definitions of concussion, this is considered in broader term, but results are described by the adopted definition and its consistency with the latest consensus.[15]

## METHODS

A review protocol was written up and agreed on by two of the co-authors (KM and VG), before the review started. It is available on request.

### Search strategy and terms

Three databases, Embase, PubMed and Web of Science, were used to search for eligible studies. The key search terms 'sport (football, rugby, boxing, wrestling, ice hockey), athlete, concussion, traumatic brain injury, Alzheimer disease, dementia, MCI' were included in the database search. Prior to conducting each search, search terms were tested for suitability to maximise the focus of results relative to the search criteria outlined. Where appropriate, MeSH and Emtree indexing terms were utilised to broaden the coverage of the search. Full details of each search including the Population, Intervention, Control, and Outcome (PICO) criteria are included in online supplementary table 1. The search was conducted in February 2017 and updated in September 2018.

### Selection criteria and eligibility

One reviewer screened the titles and abstracts of the output of the search to identify potentially eligible studies. Full texts for potentially eligible papers were obtained where possible, and independently assessed for eligibility by two reviewers. All included papers were additionally reviewed for references to other potentially relevant papers. To schematise the steps used for the selection of studies, a flowchart diagram was developed based on the PRISMA recommendations.[19]

#### Inclusion criteria

- Original, peer-reviewed articles
- Articles written in English
- Study designs: all designs were evaluated, including case–control studies, cohort studies, cross-sectional studies and case-series
- PICO criteria:
  - Population–studies including professional or elite athletes, from any sport, with at least one season of competitive participation
  - Exposure (intervention)–history of at least one sport-related concussion. Any definition of concussion was considered in this review, however, the Berlin consensus definition[15] (or analogous) was considered as the gold standard. Definition of concussion was extracted and noted, both clinically assessed or self-reported concussions were included. Repeated subconcussive head impacts were also considered for inclusion but results described separately for concussion and repeated sub-concussive head impacts. Exposure to blow to the head resulting in concussion or repeated subconcussive head impact approximated by length of career of participating in sport or other suitable proxy measures, were included.
  - Comparison group–three comparison groups were considered: (1) **internal comparisons**, when concussed athletes were compared with non-concussed athletes within the same sample; (2) **between sport comparisons**, when contact sport athletes were compared with non-contact sports athletes; (3) **external comparisons**, when athletes were compared with samples of the general population or population norms.
  - Outcome–long-term cognitive function as assessed by neurocognitive tests or clinical evidence of mild cognitive impairment or Alzheimer disease or dementia assessed as clinical diagnosis (including self-reported doctor-diagnosed), and/or additionally supported by cognitive testing. The methods used to assess cognitive impairment were recorded.

#### Exclusion criteria

- Single-case reports
- Research conducted on varsity athletes or high school sport participants
- Review articles and conference abstracts (but references were cross-checked to include any paper which might have been missed)
- Exposure to concussion in a setting different from professional or elite-level sport
- Acute rather than long-term effects of cognition investigated
- Neuropathological studies

When two or more papers reported results of a (partially) overlapping sample, the largest study was included. The PICO criteria, used to guide the inclusion and exclusion criteria, and to create the search criteria, are detailed in online supplementary table 1.

### Data collection

Each search was run individually and each result transferred to a separate file using a referencing programme (Endnote). Results from all three searches were then combined and any duplicates removed. An outline of this process is shown in figure 1.

A spreadsheet for data extraction was created. Articles to be included in the review, were assessed and data extracted. Data including author, publication date, study design, participants and recruitment method were extracted in addition to any potential confounders for each study and source of funding. Outcome ascertainment and exposure assessment methods were extracted, with definitions, as applicable. Overall findings for each study plus any relevant subgroup analysis were also recorded.

Appraisal of study quality was conducted using the Newcastle–Ottawa scale.[20] An adapted version of the scale was used for cross-sectional studies. This assessment tool aims to formulate a

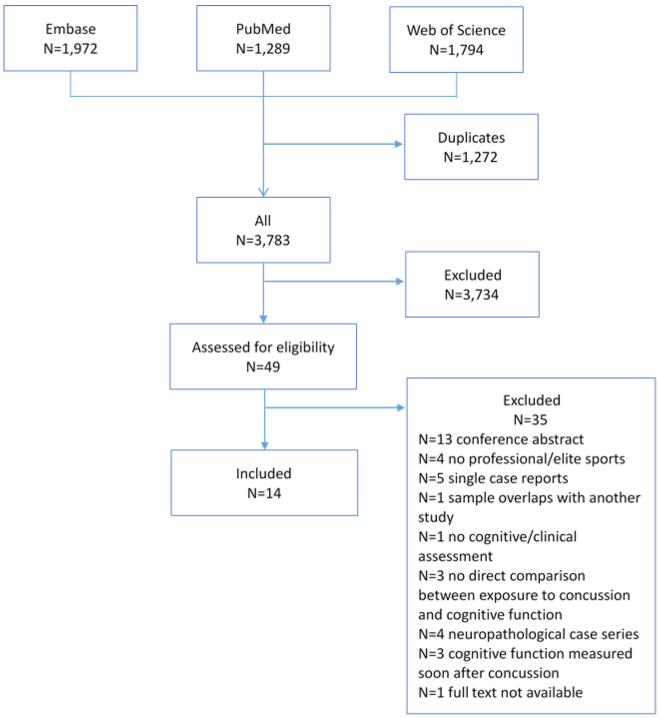


**Figure 1** Flow chart of search process. Adapted from Moher *et al*[19].

quality score for non-randomised studies included in a systematic review[20 21] (online supplementary table 2).

## RESULTS

### Study selection

Overall, 14 studies met the inclusion/exclusion criteria and were therefore included in the review[22–35] (online supplementary table 3). A total of 35 studies were excluded because used a partially overlapping sample, did not include professional or elite-level athletes, were single case-reports, were based on neuropathological/brain bank series, were missing essential information on details of the cognitive assessment, there was no direct or suitably indirect comparison between concussion and cognition, cognitive assessment was measured immediately after concussion or because the full text was not available (figure 1).

### Study characteristics and design

The data extracted are shown in tables 1–4 and in online supplementary table 3. All studies, but one, had a cross-sectional design, with varying degree of representativeness of the source population, some with an external comparison group. Bang *et al* reported a case-series of five boxers.[25] Nine studies compared different degrees of concussion within the same group of sportsmen (internal comparison)[23 26–33]; three studies also used as a comparison group another athlete population less exposed to concussion (between-sports comparison),[24 27 31] with the remaining using only non-athlete controls (external comparison).[22 25 34 35]

Three studies included rugby players,[27 31 32] eight included American footballers,[22–24 29 30 33–35] with two including ice hockey players,[24 28] and two studies included boxers,[25 26] one of which compared boxers with martial arts fighters[26] (online supplementary table 3).

Four studies did not disclose their source of funding[23 26 29 31]; one study was funded by a sport federation,[27] seven by academic/governmental institutions[22 24 25 28 30 33 34] and one by a corporation for cognitive testing tools.[35]

### Quality of evidence

The quality of the evidence was assessed against the most appropriate analysis assessing the effects of concussion, namely the internal comparison. Overall only two studies scored six or more on the Newcastle–Ottawa Scale.[22 26] Three studies had what appeared to be representative samples[27 29 32] and only one study contained an a priori sample size calculation.[26] None of the studies contained a description of the non-respondents. Four studies did not contain descriptions of exposure to concussion[24 25 27 35]; and only half of the studies had an appropriate method of analysis for the internal comparison.[22 26–29 32 33] One study included both ice hockey players and American footballers making comparisons between each of these sport groups particularly difficult.[24]

### Exposure assessment

Concussion was self-reported in all studies, unless it was estimated indirectly by the number of bouts fought,[25 26] or assumed to be high given the playing/fighting history.[22 24 35] These proxy measures probably reflect more a cumulative exposure to repeated subconcussive head impacts rather than concussion per se. Where concussion was self-reported, eight articles included a definition or explanation of how concussion was defined within the study[23 28–34]; however, only in six of them[28 29 31–34] was this aligned with the latest Berlin consensus definition.[15] In two studies, the definition was more compatible with repeated subconcussive head impact.[23 30] Notably, definition of concussion was not provided in two studies which performed an internal comparison[26 27] and approximated by length of career[35] and number of matches fought (bouts)[25] in other two. The prevalence of concussion was reported here only for those studies whose sampling frame was considered to be appropriate[27 29 32] (online supplementary table 2, online supplementary table 3).

### Outcome ascertainment

Eight cross-sectional studies reported the prevalence of cognitive impairment, dementia or Alzheimer disease among professional/elite athletes; however, only data coming from the three studies with appropriate sampling were considered here[27 29 32] (see online supplementary table 4). All studies measured the outcome with various screening instruments used for neurocognitive function, five attempted defining a threshold of cognitive impairment using specified cut-offs, that is, the Montreal Cognitive Assessment (MOCA),[32 36] the Modified Telephone Interview for Cognitive Status (TICS-m),[27 37] multiple cognitive domain scores,[24 38] the AD8[35 39] and the Mild Cognitive Impairment Screen.[23 40] One study used research doctor diagnoses of fixed cognitive deficit, mild cognitive impairment and dementia,[30] another the self-reported doctor diagnosis of mild cognitive impairment and Alzheimer disease together with spouse reported memory problems[29] (online supplementary table 3). Only five studies attempted a more comprehensive assessment of the cognitive function through a wider battery of tests[22 24 26 31 32] (online supplementary table 4).

### Cognitive function in former elite/professional rugby players

Three studies investigated the cognitive function of retired elite/professional rugby players in a total of 239 players and 138 in the comparison group from a study conducted in France,[27] 103 players and 263 in the comparison group from another

**Table 1** Concussion assessment and outcome measurements among rugby players in the included studies

| Ref. | Study design | Method of assessing concussion and its definition | Measurement of outcome(s) | Prevalence of outcome | Internal comparison | Between-sport comparison | External comparison |
|---|---|---|---|---|---|---|---|
| McMillan TM et al, 2017[32] | Cross-sectional with external comparison group ('population' controls) | ▶ Self-reported<br>▶ Definition of concussion: a blow or injury to your head where you may or may not have lost consciousness and then had symptoms such as dizziness, blurred vision, nausea, vomiting, headache, poor concentration. It might be that symptoms were not noticeable straight away but you may have noticed them later or have had 'gaps' in your memory for the game that were unusual or you might have remembered little at all about the game<br>**Prevalence of concussion among retired international rugby players: 92%**<br>**Mean (SD) number of concussions: 13.9 (18.9)** | ▶ **Neurocognitive tests**<br>▶ **Cognitive function assessed by MoCA[36]**<br>▶ Anxiety and depression<br>▶ Quality of life<br>▶ Allostatic load<br>▶ Alcohol use | **Prevalence of cognitive impairment defined as MOCA<26: 9/52** (17%) | ▶ No differences in terms of cognition, among players, according to the number of concussions (no repeat concussion, 0–1; moderate, 2–9 and high 10+) | | ▶ Players performed worse on a test of verbal learning and of fine motor coordination of the dominant hand<br>▶ Prevalence of cognitive decline 17% among former players and 3% among controls (p=0.087) |
| Hume *et al*, 2017[31] | Cross-sectional with between sports (community rugby players and non-contact sportspeople) and external comparison group (US norms) | ▶ Self-reported by online questionnaire<br>▶ Definition of concussion: 'Concussion was defined as being a blow to the head followed by a variety of symptoms (loss of consciousness, headache, dizziness, loss of balance, blurred vision, 'seeing stars', feeling in a fog or slowed down, memory problems, poor concentration, nausea or throwing up)"<br>**Elite rugby players: Prevalence of concussion: 85%**<br>**Mean concussions: 3.5±2.0**<br>**Community rugby players: Prevalence of concussion: 77%**<br>**Mean concussions: 2.9±2.2** | ▶ **Neurocognitive tests** | | ▶ Former players (including elite rugby, community rugby and non-contact sports) who recalled one or more concussions had worse scores on cognitive flexibility, executive functioning, and complex attention than players who did not recall experiencing a concussion | ▶ The elite-rugby group performed worse on tests of complex attention, processing speed, executive functioning, and cognitive flexibility than the non-contact sport group, and worse than the community-rugby group on complex attention | ▶ Compared with US norms, all three former player groups performed worse on verbal memory and reaction time; rugby groups performed worse on complex attention, processing speed, cognitive flexibility and executive functioning<br>▶ Elite rugby group performed better in relation to motor speed than US norms |
| Decq *et al*. 2016[27] | Cross-sectional with a between sports comparison group (high-level retired sportspeople) | ▶ Self-reported by questionnaire.<br>▶ Definition of concussion not provided<br>**Prevalence of concussion among rugby players: 77%**<br>**Mean concussions: 3.1 (SD 5.0)**<br>**Median concussions: 2 (IQR 1–3)**<br>**Mean concussions with loss of consciousness: 1.5 (2.7)**<br>**Mean concussions with loss of memory: 0.9 (SD 1.3)** | ▶ **Cognitive function assessed by TICSm[37]**<br>▶ Depressive disorders (PHQ-9 score)<br>▶ Fluency disorders (Isaacs Set Test)<br>▶ Headache severity (HIT-6 score) | **Prevalence of cognitive impairment defined as TICS-m ≤30: 57%** | ▶ No association between concussion and cognitive function among rugby players and other athletes together | ▶ Mild cognitive disorder (TICS ≤30) prevalence: 57% among rugby players and 40% among other sports (univariate p=0.005)<br>▶ Mean TICS score 30. (SD 3.5) among rugby players and 31.3 (3.6) among other sports (univariate p=0.007) | |

PHQ-9 Patient Health Questionnaire; Hit-6, Headache Impact Test; IQR, inter quartile range; IQR, Inter-quartile range
; MoCA, Montreal Cognitive Assessment; SD
, Standard deviation
; TICSm, Modified Telephone Interview for Cognitive Status.

**Table 2** Concussion assessment and outcome measurements among ice hockey players in the included studies

| Ref. | Study design | Method of assessing concussion and its definition | Measurement of outcome (s) | Prevalence of outcome | Internal comparison | Between sport comparison | External comparisons |
|---|---|---|---|---|---|---|---|
| Esopenko C *et al* 2018[28] | Cross-sectional study with external comparison group ('community' controls) | ► Self-reported concussion history (only concussions reported from ≥15 years of age were included in the analyses)<br>► Concussion was defined as a blow to the head followed by clinical symptoms, including altered consciousness, confusion, dizziness, headache, fogginess, memory problems and sensitivity to light or sound<br>**Mean (SD) concussion among hockey players: 4.8 (2.7)**<br>**Median (IQR) number of concussion among hockey players: 5.0 (3.0)** | ► **Neurocognitive tests**<br>► Psychiatric disorders<br>► Neurological examination | N/A (principle component analysis used) | ► Executive/intellectual functioning from the neuropsychological battery was significantly associated with the number of concussions after accounting for variance due to age | | ► Former players performed worse on the executive/intellectual function, relative to comparison participants |
| Baker JG, *et al* 2018[24] | Cross-sectional study with between sports comparison group (non-contact master athletes) | ► Information on concussion not collected because deemed to be too inaccurate | ► **Neurocognitive tests**<br>► **Cognitive impairment as defined by Jak and coll.[38]**<br>► Depression<br>► Vascular risk factors | **Prevalence of cognitive impairment as defined by Jak and coll.[38] among contact sport athletes: 38%** | | ► The contact sport athletes scored significantly lower on this measure of estimated IQ, but did not significantly differ from non-contact sport athletes on most of the primary scores in the five domains (executive function, attention, memory, language, perceptual motor skills). They only performed worse in letter fluency and immediate recall<br>► Eight contact sport athletes (38%) versus three non-contact controls (14%) met the criteria for MCI | |

MCI, mild cognitive impairment.

**Table 3** Concussion assessment and outcome measurements among American football players (US and Canadian) in the included studies

| Ref. | Study design | Method of assessing concussion and its definition | Measurement of outcome(s) | Prevalence of outcome | Internal comparison | Between sport comparison | External comparison |
|---|---|---|---|---|---|---|---|
| Baker JG, *et al* 2018[24] | Cross-sectional study with between sports comparison group (non-contact master athletes) | ▶ Information on concussion not collected because deemed to be too inaccurate | ▶ **Neurocognitive tests**<br>▶ **Mild cognitive impairment as defined by Jak and coll.**[38]<br>▶ Depression<br>▶ Vascular risk factors | **Prevalence of cognitive impairment as defined by Jak and coll.[38] among contact sport athletes: 38%** | | ▶ The contact sport athletes scored significantly lower on this measure of estimated IQ, but did not significantly differ from non-contact sport athletes on most of the primary scores in the five domains (executive function, attention, memory, language, perceptual motor skills). They only performed worse in letter fluency and immediate recall<br>▶ Eight contact sport athletes (38%) versus three non-contact controls (14%) met the criteria for cognitive impairment | |
| Misiquitta K *et al*, 2018[33] | Cross-sectional study with two external comparison groups ('population' controls and controls from the Cambridge Centre for Ageing and Neuroscience) | ▶ Self-reported<br>▶ Concussion defined according to the Zurich consensus statement[62]<br>**Median number of concussion among former CFL players (IQR): 4 (3–8.5)** | ▶ **Neurocognitive tests**<br>▶ **Neuroimaging**<br>▶ Personality Assessment Inventory | | | | ▶ No difference in neurocognitive tests between former footballers and study controls |
| Alosco *et al*, 2017[22] | Cross-sectional study with external comparison group | Concussion not measured | ▶ **Neurocognitive tests**<br>▶ Neuroimaging<br>▶ Olfactory function<br>▶ Depression<br>▶ Behaviour and mood | | | | ▶ **NFL players exhibited significantly worse Performance across most of the cognitive and behavioural/mood measures (attention, executive function, psychomotor speed, visual and verbal episodic memory, language, motor and visuospatial functions)** |
| Multani *et al*. 2016[34] | Cross-sectional with external comparison group | ▶ Self-report<br>Definition: 'injuries caused by a blow to the head or body that resulted in concussion symptoms, including at least one of the following: headache, nausea, vomiting, dizziness/balance problems, fatigue, trouble sleeping, drowsiness, sensitivity to light or noise, blurred vision, difficulty remembering, and trouble concentrating'[61]<br>**Prevalence of concussion impossible to calculate due to study design (concussion is an inclusion criterion)** | ▶ **Neurocognitive tests**<br>▶ Neuroimaging | | | | ▶ **No difference in Visuospatial learning and memory, or premorbid intellectual functioning between former players and healthy controls** |

Continued

**Table 3** Continued

| Ref. | Study design | Method of assessing concussion and its definition | Measurement of outcome(s) | Prevalence of outcome | Internal comparison | Between sport comparison | External comparison |
|---|---|---|---|---|---|---|---|
| Hart *et al*. 2013[30] | Cross-sectional with external comparison group | ▶ Concussion history was obtained retrospectively from participants and informants<br>Definition of the 1997 American Academy of Neurology practice parameter guidelines for grading concussion: 'trauma-induced alteration in mental status that may or may not involve loss of consciousness. Confusion and amnesia are the hallmarks of concussion'[63]<br>**Prevalence of concussion: 94%**<br>**Mean concussions: 4 (range 1–13)** | ▶ **Neurocognitive tests**<br>▶ Neuroimaging<br>▶ Depression | **Research doctor diagnosis:**<br>▶ **Prevalence of fixed cognitive deficit: 4/34 to 12%**<br>▶ **Prevalence of cognitive impairment: 8/34 to 24%**<br>▶ **Prevalence of dementia: 6/34 to 6%** | ▶ **No difference between neuropsychological measures and concussion or the number of years played in the NFL** | | |
| Randolph *et al*., 2013[35] | Cross-sectional with two external comparison groups (one of patients diagnosed with MCI) and population norms | **Exposure to concussion not assessed** | ▶ **Neurocognitive tests** | **Prevalence of cognitive impairment as defined by AD8** (39): **35%** | ▶ **Among players with cognitive impairment (score 2+on AD8), length of career was not associated with cognitive test performance** (**r=0.016**) | | |
| Amen *et al*. 2011[23] | Cross-sectional with external comparison group | ▶ Self-reported at interview<br>▶ Definition: Centre for Diseases Control and Prevention (CDC) definition of concussions: 'conditions of temporarily altered mental status as a result of head trauma' that may or may not involve a loss of consciousness[64]<br>**Prevalence of episodes of 'loss of consciousness': 63%** | ▶ **Neurocognitive tests**<br>▶ Overall general and mental health (DSM-IV)<br>▶ Cognitive Impairment as defined by the Mild Cognitive Impairment Screen[40] | **Prevalence of cognitive impairment as defined by the Mild Cognitive Impairment Screen**[40] **: 19% (increasing with increasing age**) | | | ▶ **Players scored in the bottom half of the percentile placements on all cognitive measures except spatial processing and reaction-time, which were both in the top half of the percentile placements compared with population norms** |
| Guskiewicz *et al* 2005[29] | Cross-sectional with external comparison group | ▶ Self-reported by questionnaire<br>▶ Definition: 'injury resulting from a blow to the head that caused an alteration in mental status and one or more of the following symptoms: headache, nausea, vomiting, dizziness/balance problems, fatigue, trouble sleeping, drowsiness, sensitivity to light or noise, blurred vision, difficulty remembering, and difficulty concentrating'<br>**Prevalence of concussion: 61%** | ▶ Mental Component Score (MCS) of SF-36<br>▶ Self- or spouse-reported MCI defined according to the American Academy of Neurology Practice Parameter | **Prevalence of self-reported doctor diagnosed AD: 1.3%**<br>**AD age-adjusted prevalence ratio 1.37 (95% CI 0.98 to 1.56) in former footballers compared with the general population**<br>**Prevalence of self-reported doctor-diagnosed MCI:3%**<br>**Prevalence of spouse reported cognitive impairment: 12%** | ▶ Retired players with a history of concussion, especially recurrent concussion, scored lower (worse) on the MCS than those without a history of recurrent concussion (p<0.001).<br>▶ Recurrent concussion significantly associated with MCI diagnosis in athlete population (p=0.002), self-report memory impairment (p=0.001), and spouse/relative reported memory impairment (p=0.04)<br>▶ Dose–response relationship between number of concussion and memory impairment | | ▶ MCS scores on the SF-36 were similar between the NFL retirees and population-based normative values for all age groups |

AD, Alzheimer disease; CFL, Canadian Football League; DSM-IV, Diagnostic and Statistical Manual of Mental disorders – IV revision; MCI, Mild Cognitive impairment; NFL, National Football League; SF-36, Short form Health survey; SPECT, single-photon emission CT.

Table 4 Concussion assessment and outcome measurements among boxers and martial art fighters in the included studies

| Ref. | Study design | Method of assessing concussion and its definition | Measurement of outcome(s) | Prevalence of outcome | Internal comparison | Between sports comparison | External comparison |
|---|---|---|---|---|---|---|---|
| Bang *et al* 2016[25] | Case series with external comparison group | ► Concussion approximated by number of matches fought (bouts) and number of KO<br>**Participants had a mean number of bout of 30 (range 23–37) and a mean number of KO of 1.4 (range 0–4)** | ► **Neurocognitive tests**<br>► Neuroimaging<br>► Neurological tests<br>► Personality tests<br>► Mood | | – | | ► **Boxers performed significantly worse in the delayed recall of visuospatial memory**<br>► **Boxers performed significantly worse in the assembly task of the Purdue Pegboard test (p=0.028) but not in the other tasks** |
| Bernick *et al* 2015[42] | Cross-sectional study (baseline of a cohort study). with external comparison group | ► Fight Exposure Score (FES) function of cumulative fights and intensity of exposure[26]<br>**Mean (range) KO sustained by professional boxers: 0.9 (0–13)**<br>**Mean (range) KO sustained by professional Martial Art Fighters: 0.6 (0–6)** | ► **Neurocognitive tests**<br>► Neuroimaging | | ► **Reduced processing speed in those exposed to more fights (p0.041), worse in boxers than MMA**<br>► **Reduced processing speed in those with a higher FES with (p=0.023) with the effect increasing at high levels of FES (however, the effect was lost when restricting to participants within an impaired range** | | |

KO, knock-out; MMA, Mixed Martial Arts.

conducted in New Zealand,[31] and 52 retired players and 46 in the comparison group from one in Scotland.[32] While the study conducted in France was limited to middle-aged former players with a narrow age range (49–55 years),[27] the age ranges of the sample of former players in New Zealand and Scotland were much wider (29–72 years in New Zealand; mean age 53.5 (SD 13.0) in Scotland); being younger in New Zealand (mean age 41.3 years (SD 7.5))[31 32] (table 1).

Interpretation of the evidence is hampered by the potential for selection bias. One study was based on participants volunteering to take part,[31] one study recruited only 15% of the eligible participants,[32] and in another study 46% of former players were invited to participate (corresponding to only 22% of those initially contacted).[27]

Concussion was self-reported in all studies, and its definition was aligned with the Berlin consensus in two of them.[31 32] The prevalence of concussion among former rugby players was estimated to range from 77%[27] to 92%.[32] The mean number of concussions (SD) per player ranged from 3.1 (5.0)[27] to 13.9 (18.9).[32]

More than half of the players evaluated in one study (57%) aged 49–55 years were defined as cognitively impaired,[37] compared with 40% among the non-contact sport players.[27] In another, between 2% and 17% of former players with a mean age of 53.5 (SD 13.0) were considered cognitively impaired[32] (table 1).

## Internal comparison

The association between cognitive function and concussion among former rugby players is difficult to assess. The only study reporting this is based on only 52 retired rugby players, divided into no repeated concussion (0 to 1 concussion), moderate[2–9] and high repeated concussions (10+), and no association with cognitive function was shown[32]; this included processing speed, executive function, memory and learning, sustained attention and visual perception. Two of the studies only reported an internal association between concussion and cognitive function among rugby players and other athletes combined. In one of the studies, former elite-rugby players, community-rugby players and non-contact sport players reporting one or more concussions had worse scores on cognitive flexibility, executive function and complex attention than players not reporting concussions[31] (table 1). In another study, concussion was not associated with cognitive function among retired rugby players and high-level sport athletes together in adjusted models[27] (table 1).

### Between-sports comparison

In one study, the elite-rugby group performed worse on tests of complex attention, processing speed, executive functioning and cognitive flexibility than the non-contact sport group; and worse than the community-rugby group on complex attention.[31] Additionally, they performed worse than the US norms on verbal memory, reaction time, processing speed, cognitive flexibility and executive functioning.[31] In another study, overall cognitive function showed median scores lower in retired rugby players than in other sport athletes (p=0.007), and a higher prevalence of mild cognitive disorders among retired rugby players compared with other sport athletes (p=0.005)[27] (table 1).

### External comparison

General cognitive function was not different between 52 retired Scottish rugby players and 46 in the comparison group. Only one former player was considered cognitively impaired; however, using a less conservative cut-off nine former players (17%) and one comparison group member (3%) were defined as impaired (p=0.087).[32] When considering single tests, former players exhibited a poorer performance on a test of verbal learning (RAVLT-immediate recall) and on a test of fine motor coordination in the dominant hand (Grooved Pegboard Test), compared with the comparison group.[32]

One of the studies compared the cognitive performance of former elite rugby players and other athletes with US norms. Former rugby players performed worse on processing speed, cognitive flexibility and executive functioning. All athletes (including community rugby players, and cricket and field hockey players) performed worse on verbal memory and reaction time, compared with US norms[31] (table 1).

## Cognitive function in former professional/elite ice hockey players

Two small studies investigated the association between concussion and cognitive function among former ice hockey players[24 28] including a total of 33 and 21 former players with a mean age of ~55 years[24 28] (table 2).

Interpretation of results is mainly hampered by the extremely limited sample size in both studies, and by the potential for selection bias: one study recruited former players who volunteered to participate,[24] in the other, it is not clear how the sample was chosen.[28]

In the only study where information on concussion was collected, its definition was aligned with the Berlin consensus.[28] The other study deliberately discontinued the collection of data about concussion because the authors deemed the data to be unreliable.[24]

### Internal comparison

Among 33 former ice hockey players, executive/intellectual functioning from the neuropsychological battery was negatively associated with the number of concussions after accounting for age[28] (table 2).

### Between sports comparison

A total of 21 contact sport athletes (including American football and ice hockey players combined) scored lower in measures of estimated IQ, but did not differ from non-contact sport athletes on most of the primary scores in the five cognitive domains (executive function, attention, memory, language and perceptual motor skills). However, former players selectively performed worse in letter fluency and immediate recall.[24] This analysis is largely underpowered to detect even moderately large differences (table 2).

### External comparison

When considering 33 former ice hockey players and 18 members of a comparison group, former players performed worse on executive/intellectual function compared with the comparison group[28] (table 2).

## Cognitive function in former professional/elite American football players

Eight cross-sectional studies investigated the association between cognitive function and concussion among American football players,[23 24 29 30 33–35 41] with samples varying from 758[29] to 18 former players,[34] with a wide age range (table 3).

Interpretation and generalisability of results is potentially hampered by selection bias. One of the two larger studies selected participants on the basis of their cognitive function, and reported information on a follow-up questionnaire with a response rate of 57% sent out to an initial sample of former players previously recruited with a response rate of 68%.[35] The other larger study involved former players likely from the same source (but assessing a different outcome measure), but did not report a response rate, nor gave information on recruitment.[29] Of two smaller studies, one recruited participants through CTE and Alzheimer disease social media,[41] the other at former player association meetings and word of mouth.[23] One of those studies explicitly recruited participants with 'self-reported complaints of cognitive, behavioural and mood symptoms for at least 6 months before study entry', making the differences in cognitive performance when compared with non-concussed and non-symptomatic controls, difficult to interpret.[41] Recruitment in smaller studies was not clear,[24 33 34] apart from one which recruited at former player association meetings, by word of mouth and on a volunteering basis.[30]

Concussion was self-reported in five studies, with a definition aligned with the Berlin consensus in three of them[29 33 34]; in the remaining two studies the definition of concussion was potentially overlapping with repeated subconcussive head impacts.[23 30] The prevalence of concussion among former professional American footballers was estimated to be 61% among 758 former players[29]; this raised to 63%–94% relaxing the definition criteria to include also repeated subconcussive head impacts[23 30] (table 3).

The prevalence of poor cognitive function was estimated to be 3% among 758 former players with a mean age of 53.8 years (SD 13.4) who self-reported symptoms compatible to MCI; however, this raised to 12% when it was spouse-reported[29] (table 3).

### Internal comparison

The largest, good quality cross-sectional study compared the self-reported or spouse-reported diagnosis of dementia or cognitive impairment among 758 retired professional American footballers. The study performed performing an internal comparison among concussed and non-concussed, and then compared the prevalence with estimates from the general population.[29] The internal comparison found that recurrent concussion was associated with a self-reported doctor-diagnosed cognitive impairment (p=0.002), self-reported memory impairment (p=0.001) and spouse-reported memory impairment (p=0.04) (p values refer to chi-square tests).[29] A dose–response relationship between number of concussions and cognitive impairment was also found (p<0.001). Retired players sustaining three or more concussion during their career, have a fivefold prevalence of being diagnosed with MCI and a threefold prevalence of being diagnosed with memory impairment, compared with players with no reported concussion.[29] Significantly lower scores on the Mental Component Score of the short form health survey (SF-36) were found between concussed (especially recurrently concussed) players and the age-adjusted population norms (p=0.001).[29]

The other large study screened 513 former American footballers for cognitive function, conducted an analysis of cognitive test results among the 41 found to be cognitively impaired: among them, length of career was not associated with poorer performance.[35]

The only other study reporting an internal comparison was small. Among 34 retired players, no significant correlation between neuropsychological measures and concussion/repeated subconcussive head impact or length of career was found (data not shown)[30] (table 3).

### Between-sports comparison

The only study conducting a comparison with another sport group, compared a total of 21 retired American football and ice hockey players with 21 non-contact sport master athletes, both with age ranges of 36 to 72 years and similar mean age.[24] Overall, the contact sport athletes scored significantly lower on scores of IQ, letter fluency and immediate memory recall, but did not differ significantly from non-contact athletes in executive function, attention, memory, language and perceptual motor skills (table 3).

### External comparison

The self-reported prevalence of physician-diagnosed Alzheimer diseased among American footballers was estimated to be 1.3%, resulting in an estimated age-adjusted prevalence ratio of 1.37 (95% C.I. 0.98 to 1.56) when compared with the general population.[29]

Five studies conducted an external comparison between former American footballers and samples more or less representative of the general population. In the largest study, involving a sample of 758 retired American footballers, the Mental Component Scale of the SF-36 was similar between the recruited sample and the age-adjusted population-based normative values (although scores were significantly lower when restricted to those concussed).[29] In an analysis of 128 former players and 28 age-matched volunteers, former players performed worse in the majority of tests assessing attention, executive function, psychomotor speed, visual and verbal episodic memory, language, motor and visuospatial functions, although the significance level did not take into account multiple comparisons.[22] An analysis of 100 retired American footballers compared with a standardised sample of 810 subjects for the MicroCog test revealed that all players scored in the bottom half of the percentile placements in all measures except spatial processing and reaction-time (both in the top half).[23]

Smaller studies reported no significant differences in neurocognitive tests between former players and the comparison group[33,34] (table 3).

## Cognitive function in former boxers and other fighting sports

Two papers assessed the cognitive function of former boxers: a case series of five professional retired boxers from Korea aged 42–49 years,[25] and a cross-sectional study with an external comparison group including 93 former boxers and 131 martial art fighters from the US with an age range of 18–44 years[26] (table 4).

Interpretation of results is hampered by the potential for selection bias, as both studies lack information on sampling or response rate[25,26] (see online supplementary table 2). Concussion per se was not recorded in either of the studies. The larger study on boxers and martial art fighters used a Fight Exposure Score (FES)[42] to assess the cumulative exposure to concussion as a function of number of professional/elite fights and intensity of exposure.[26] Exposure to concussion was also measured with number of knock-outs (KOs) sustained.[26]

### Internal comparison

Processing speed among boxers and martial art fighters aged 18–44 years was associated with both number of professional fights (p=0.041), and the FES (p=0.023) with an estimated 0.19% and 2.1% reduction in processing speed per fight and unit of FES score increase, respectively.[26] The proportion of participants impaired in each of the cognitive categories (verbal memory, psychomotor, processing and reaction speed) was calculated for scores below 1.5 the SD of age- and education-matched samples. The proportion of participants with verbal memory and psychomotor speed impairment increased with increasing categories of FES (p=0.036 and p=0.046, respectively).[26] Increasing exposure to concussion (measured either as number of fights or years in professional fighting, or FES) was associated with a decrease in brain structure volumes, particularly of thalamus and caudate[26] (table 4).

### Between sport comparison

Boxers were shown to have significantly lower scores for processing speed compared with martial art fighters (data not shown)[26] (table 4).

### External comparison

No significant differences in verbal memory were detected between boxers, fighters and controls after adjustment for age, education and ethnicity.[26] However, both boxers and martial art fighters showed worse scores of processing speed than the external comparison group, after adjusting for education (data not shown).[26]

In the smaller case series, no significant difference in cognitive function was detected among the five boxers and the four comparison people. However, boxers performed worse on the delayed recall of visuospatial memory compared with the external comparison group[25] (table 4).

## DISCUSSION

Evidence on the long-term cognitive consequences of concussion experienced in professional/elite sports is accumulating, and overall it suggests the presence of an effect. However, many points to be clarified and dissected remain.

Importantly, the magnitude of the effect is not clear. Studies comparing the prevalence of cognitive impairment and/or dementia among former professional/elite players with different instruments,[23,24,27,29,30,32,35] with other athletes[24,27] or other comparison groups,[29,32] almost invariably[29] find a difference, with contact sports athletes more affected than the comparison group.[24 27 32] However, these differences are very unlikely to be exclusively due to concussion, they could be confounded by any other characteristics of the athletes included (eg, use of licit/illicit drugs, alcohol intake, lifestyle and psychosocial risk factors, etc). Moreover, one would expect to see among the former athletes a healthy cohort effect with decreased prevalence of cardiovascular disease and cancer risk factors,[43 44] although to what extent this is consistent across generations and across sport disciplines, is to date unclear.[45] On the other hand, studies investigating cognitive functions with neuropsychological batteries, in most cases find subtle, although statistically significant, differences which are not easy to interpret in terms of clinical significance.[28 29 31 33 42] Small differences on a single test might not reflect a true impairment in that area of functioning of the individual, or may not be noticeable; poor performance on a set of tests does not directly equate to functional disability.[46] Cognitive test measurements would be more meaningful if they were conducted assessing intra-individual differences (ie, pre-exposure and post-exposure to sport-related concussion(s)), but this would require prospective cohort studies with long follow-up periods which are much more difficult to deliver, and are considerably more expensive and more time consuming than the studies included in this review.

Interestingly, the current evidence summarised in this review is derived by the integration of evidence coming from different comparisons, implying different study designs, but also different inherent risks of bias and errors. It is therefore important to derive and interpret the appropriate conclusion from each comparison under analysis. The internal comparisons, by comparing two groups of people sharing broadly the same characteristics in terms of lifestyle and socioeconomic status, are best positioned to assess the effect of concussion on the outcome, minimising unmeasured and residual confounds. The between-sport comparisons, although aimed at assessing the effect of concussion when comparing contact sports athletes with non-contact sport ones, are also affected by any other systematic difference between sports. For example, dietary supplement and medication use have been shown to be very different among sporting disciplines.[47] Finally, evidence from the external comparison groups provide grounds for assessing the overall effect of sport participation, including all pros and cons, and it is expected to be associated with better health due to a selection effect, and also partially to the physical activity, and general healthy habits that athletes display in comparison with any non-athlete group (healthy cohort effect), as previously found.[43 44] Nonetheless, this selection effect might be heterogeneous across sports,[45] and it might be mitigated by the emergence of some lifestyle choices after retirement, as demonstrated for increased body mass index.[48] However, overall, an inverse associations between participating in sports and general health (specifically for cardiovascular diseases and cancer outcomes) is expected, including the overall risk of dementia when athletes are compared with the general population.

Importantly, the current results refer to professional/elite players only; and it is not clear to what extent this evidence is extendable to varsity or younger pre-professional athletes who might be exposed to an overall lower level of concussion, but might be as or more vulnerable to its consequences.[49] Unfortunately, the current data do not allow any strong conclusions about potential concussion/cognitive function differences between contact sports. Many sports involve concussion or repetitive low-level head trauma, but it has been argued that each sport should be viewed differently depending on the unique technical and physiological profile that a player is exposed to over the course of a career.[50 51] The ongoing HEalth and Ageing Data IN the Game of football (HEADING) study[52] will add important information about external and internal comparison of the association between low-impact repetitive head injury and cognitive function among British-based footballers. Recently, Scottish footballers have been shown to be at increased risk of mortality from neurodegenerative diseases, and above all dementia, compared with the general population.[53]

## Rugby

The available evidence indicated an association between sustaining rugby-related concussions and having a worse cognitive function later in life, although to what extent this might be clinically significant, is not entirely clear. None of the reviewed studies produced strong evidence for an effect. The association between concussion and cognitive function (internal comparison) was not detected among Scottish players, although the study was underpowered to detect less than very large effects,[32] and was small, possibly not very relevant clinically, and at least partially due to multiple comparison in the New Zealand study.[31] The association was null among French players, although the prevalence of mild cognitive disorders was significantly higher among rugby players compared with other athletes.[27] This apparent inconsistency might reflect the fact that concussion was not accurately assessed in the study, or might hint to some other systematic differences between these two groups of athletes responsible for the association. The currently ongoing BRAIN study[54] has used a timeline-assisted interview to increase accuracy of exposure assessment, and it is appropriately powered to detect a difference of 7% in the Preclinical Alzheimer Cognitive Composite score.[54 55]

Nonetheless, the fact that the prevalence of cognitive impairment was estimated to be 17% among rugby players and 3% among the comparison group (external comparison),[32] strongly points towards the presence of an effect, as one would expect former players to be generally healthier compared with the general population, with reduced incidence of non-communicable diseases (healthy cohort effect), as previously observed.[43 44] However, this external comparison does not allow estimation of the relative impact of concussion or other factors potentially increasing the risk of cognitive impairment among rugby players.

Rugby union only became a professional sport in 1995, and since then the game's dynamics and training has changed substantially increasing the speed of the game, the number of contact events, and the potential for more severe impacts. As a consequence, between-sports comparisons including elite players who played about 30 years ago might underestimate the burden of ill health due to the overall exposure to concussion and other impacts that would apply to current players. On the other hand, the attention to concussion management has increased substantially in the last few years,[56] leading to measurable health outcomes in other sports.[57]

## Ice hockey

The evidence available for the association between concussion and cognitive impairment among ice hockey players is too sparse to allow any meaningful summary. The only study investigating the association among ice hockey players[28] provided very limited evidence for an effect of concussions on cognitive health.

## American football

Despite the greatest number of research papers identified investigating the association between concussion and long-term cognitive function among American Footballers, the quality of reporting does not always allow a thorough assessment of the evidence. Nonetheless, overall the evidence points to an association between increasing number of concussions and poorer cognitive function among American footballers. The strongest evidence comes from the largest, well reported study, which suggested that having sustained a concussion during playing career was associated with worse cognitive function performance with a dose–response effect.[29] The same result was not replicated when duration of career was used as a proxy measure for exposure to concussion, possibly due to misclassification error.[35] Importantly, some of the evidence, although not all,[34] also indicates a possible poorer cognitive function of former players with respect to an external comparison group (external comparison),[23 41] which is consistent with a lack of healthy cohort effect when American footballers were compared with population-based normative values.[29]

Interestingly, a linguistic analysis of interviews of active American football players suggested that exposure to the high-impact sport was associated with an overall decline in language complexity scores over time, suggesting that language complexity decline might be a very early sign to be monitored to predict potential CTE onset.[58]

## Boxing

The evidence on boxing and other fight-based sport relies only on a single research study and a very limited case series.[25 42] Nonetheless, results are indicative of an association between sustaining KOs or number of fights with poorer cognitive function which is more pronounced for boxers compared with martial art fighters.[42]

## Limitations

The evidence collated in this systematic review does not allow a quantitative summary from a meta-analysis to be derived from the association between sustaining a concussion, or participating in a contact sport, and risk of long-term cognitive function impairment. However, in some studies, the evidence could be indicative of an effect that should be explored in more depth. The main methodological critical points encountered when summarising the available evidence were poor reporting of study methods, evidence coming from non-conventional study designs, and limited adjustment for potential confounders. Embracing more consistently the STROBE[59] and STROBE-ME[60] recommendations when reporting epidemiological and molecular epidemiological studies, respectively, would dramatically increase the ability to assess the available evidence and draw meaningful conclusions from existing studies. Most studies reviewed here have opted for a cross-sectional design (with a selection of a more or less representative sample of the sport population) and had an external comparison group, selected with varying methodology. However, in many cases, the comparison group has been chosen explicitly selecting individuals who never sustained a concussion. This increases the potential for differences among the two groups resulting likely in residual and unmeasured confounding. As a consequence, evidence from these studies should be interpreted with caution. Recently, the FIELD study (Football's InfluencE on Lifelong health and Dementia risk) provided strong evidence for an increased mortality from Alzheimer disease and other neurodegenerative diseases among Scottish footballers when compared with the general population.[53] Evidence for external comparison should be limited to cross-sectional studies with unbiased sample selection. Moreover, cross-sectional studies suffer from recall bias in relation to exposures, and this is particularly important in this setting as the outcome measure is cognitive function, in which early manifestation of impairment is memory problems. In this context, the accuracy of the retrospective assessment of concussion is crucial, and no study validated the tool used for exposure assessment. This is also an additional reason why it is important to contrast the evidence from internal comparisons and between sport comparison, where concussion is assumed to be higher in contact sports compared with non-contact ones. Prospective studies assessing the long-term cognitive and neurological health of current players, thus measuring exposure at the time when it occurs, would be ideally placed to overcome these problems. Moreover, cognitive decline—measured as the difference in measures of cognitive function over time—would be a better way of measuring the outcome, when using measures of cognitive function such as cognitive tests. This would allow for the most refined adjustment for individual variability in terms of intelligence and cognitive function. In addition, a large part of the evidence comes from cognitive function measured using screening instruments such as (TICS-m),[27 37] brief tests of general cognition (MoCA),[32 36] or self-report measures (AD-8)[35 39] with very few reporting a comprehensive neuropsychological battery assessment aimed at assessing multiple domains of cognitive functioning thoroughly.[24 31 32 42 49]

The definition of concussion and the method for its assessment varied greatly across studies, hampering the synthesis of the evidence. While the definition of concussion used in the studies which reported it was aligned with the latest Berlin consensus,[15 61–64] there were some differences: some did not explicitly state that loss of consciousness was not required for the definition, and others did not mention that symptoms could appear after a time delay. In addition, studies which approximated the cumulative exposure to concussion with length of career,[35] or bouts fought[25] failed to provide a measure enabling comparison a consistent definition of exposure is essential for comparing and synthesising evidence coming from future studies. Of particular interest would be to study the age at first concussion/repeated subconcussive head impact, and the concussion density (ie, number of concussion over a specific period of time) in relation to clinical outcomes. Some evidence suggest that the earlier the impact, the more severe the consequences in terms of cognition.[49] Moreover, this needs to be clearly differentiated from repeated subconcussive head impacts which do not necessary comply with concussion definition. Better clinical and histopathological definitions of CTE expected from future studies, such as the UNITE (Understanding Neurologic Injury and Traumatic Encephalopathy) study[65] and the DETECT (Diagnosing and Evaluating Traumatic Encephalopathy using Clinical Tests) Study, will also be essential for conducting appropriate epidemiological studies.

Another caveat preventing the drawing of strong conclusions from the existing evidence is the overall poor adjustment for potential confounders which potentially play a major role, even in internal comparisons. A minimum set of confounders represented by age, sex (when not stratified) and a proxy measure for socioeconomic status and/or education must be considered in all cases when assessing associations with cognitive function. Ideally, also a number of cardiovascular/metabolic risk factors such as hypertension, anthropometry and diabetes should also be taken into consideration, given their strong association with the increased risk of dementia.[66–68] Previous attempts to summarise the available evidence have not consistently taken these methodological characteristic into account, focussing more on the synthesis of results.[18]

Publication bias must be taken into consideration when coming to conclusions from this systematic review. As with many systematic reviews, it could be shaped by the fact that only published results in peer-reviewed journals were considered, and could therefore be excluding research with important and differing results and findings, that could potentially affect deductions made. In addition to this, only publications written in English were included in the review. Unfortunately, the lack of a unique measure of association prevented an analysis using funnel plots or significance tests for publication bias.

In conclusion, high-quality, appropriately designed and powered epidemiological studies are urgently needed to assess the long-term association between sustaining a sport-related concussion (or repetitive subconcussive head impacts) and cognitive impairment later in life.

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*Supplementary Table 1: Search criteria used for the systematic review according to the PICO definition*

| | **Embase** | **PubMed** | **Web of Science** |
|---|---|---|---|
| **Key terms** | **P** Professional sports-persons (football, rugby, boxing, wrestling, hockey), at least one season of competitive play | | |
| | **I** Concussion (transient loss of normal brain functioning following a blow to the head) sustained during sporting participation, at least one documented | | |
| | **C** Lay population or other suitable comparison groups (i.e. non-concussed athletes in case-control studies) | | |
| | **O** Diagnosis of Alzheimer’s dementia or mild cognitive impairment, assessed through formal clinical diagnosis, cognitive testing or neuroimaging showing structural brain changes | | |
| **Database search** | ('athlete' OR ‘sport’ OR ‘football’ OR ‘rugby’ OR ‘boxing’ OR ‘wrestling’ OR ‘hockey’) | ("sports" OR "sport" OR ("athletes" OR "athletes") OR (“football”) OR (“rugby”) OR (“boxing”) OR (“wrestling”) OR (“hockey”) | (athlete OR sport OR football OR rugby OR boxing OR wrestling OR hockey) |
| | ('concussion' OR 'head injury' OR 'brain injury') | ("brain concussion" OR "concussion" OR "traumatic brain injuries") | (concussion OR brain injury OR head injury) |
| | ('dementia' OR 'Alzheimer disease' OR 'mild cognitive impairment' OR ‘neurocognitive test’ OR ‘cognitive test’ OR ‘magnetic resonance imaging’) | ("alzheimer disease" OR "dementia" OR cognitive dysfunction" OR "mild cognitive impairment" OR “neurocognitive test” OR “cognitive test” OR “MRI”) | (dementia OR Alzheimer's disease OR mild cognitive impairment OR neurocognitive test OR cognitive test OR magnetic resonance imaging) |
| **Full search** | 'sport'/exp OR 'sport' OR 'athlete'/exp OR 'athlete' OR 'football'/exp OR 'football' OR 'rugby'/exp OR 'rugby' OR 'boxing'/exp OR 'boxing' OR 'wrestling'/exp OR 'wrestling' OR 'hockey'/exp OR 'hockey' AND ('concussion'/exp OR 'concussion' OR 'brain injury'/exp OR 'brain injury' OR 'traumatic brain injury'/exp OR 'traumatic brain injury' OR 'head injury'/exp OR 'head injury') AND ('alzheimer disease'/exp OR 'alzheimer disease' OR 'dementia'/exp OR 'dementia' OR 'mild cognitive impairment'/exp OR 'mild cognitive impairment' OR (neurocognitive AND ('test'/exp OR test)) OR 'cognitive test'/exp OR 'cognitive test' OR 'nuclear magnetic resonance imaging'/exp OR 'nuclear magnetic resonance imaging') | (((((((("sports--"[MeSH Terms] OR "sports"[All Fields] OR "sport"[All Fields]) OR ("athletes"[MeSH Terms] OR "athletes"[All Fields] OR "athlete"[All Fields])) OR ("football"[MeSH Terms] OR "football"[All Fields])) OR ("football"[MeSH Terms] OR "football"[All Fields] OR "rugby"[All Fields])) OR ("boxing"[MeSH Terms] OR "boxing"[All Fields])) OR ("wrestling"[MeSH Terms] OR "wrestling"[All Fields])) OR ("hockey"[MeSH Terms] OR "hockey"[All Fields])) AND (("brain concussion"[MeSH Terms] OR ("brain"[All Fields] AND "concussion"[All Fields]) OR "brain concussion"[All Fields] OR "concussion"[All Fields]) OR ("brain injuries, traumatic"[MeSH Terms] OR ("brain"[All Fields] AND "injuries"[All Fields] AND "traumatic"[All Fields]) OR "traumatic brain injuries"[All Fields] OR ("traumatic"[All Fields] AND "brain"[All Fields] AND "injury"[All Fields]) OR "traumatic brain injury"[All Fields]))) AND (((("alzheimer disease"[MeSH Terms] OR ("alzheimer"[All Fields] AND "disease"[All Fields]) OR "alzheimer disease"[All Fields] OR ("alzheimer's"[All Fields] AND "disease"[All Fields]) OR "alzheimer's disease"[All Fields]) OR ("dementia"[MeSH Terms] OR "dementia"[All Fields])) OR ("cognitive dysfunction"[MeSH Terms] OR | (athlete OR sport OR football OR rugby OR boxing OR wrestling OR hockey) AND (concussion OR brain injury OR head injury) AND (dementia OR Alzheimer's disease OR mild cognitive impairment OR neurocognitive test OR cognitive test OR magnetic resonance imaging) |

| | | | |
|---|---|---|---|
| | | ("cognitive"[All Fields] AND "dysfunction"[All Fields]) OR "cognitive dysfunction"[All Fields] OR ("mild"[All Fields] AND "cognitive"[All Fields] AND "impairment"[All Fields]) OR "mild cognitive impairment"[All Fields])) OR ((((neurocognitive[All Fields] AND tests[All Fields]) OR "cognitive"[All Fields]) AND "test"[All Fields]) OR ("magnetic resonance imaging"[MeSH Terms] OR ("magnetic"[All Fields] AND "resonance"[All Fields] AND "imaging"[All Fields]) OR "mri"[All Fields]))) | |

*Supplementary Table 2: Results of the Newcastle-Ottawa Scare stars assigned to each paper, by domain*

| | **Representativeness** * | **Sample size** * | **Non-respondents** * | **Exposure assessment** ** | **Comparability** ** | **Outcome assessment** ** | **Statistical test** * | **Total (Out of10)** |
|---|---|---|---|---|---|---|---|---|
| McMillan et al, 2017 (32) | Sampling frame identified (*) | Not justified | No description of non-respondents | Description of concussion (*) | No adjustment for confounding with rugby cohort | Self-reported (*) | Examined number of concussions within rugby players (*) | 4 |
| Hume et al, 2017 (31) | Self-selected cohort | Not justified | No description of non-responders | Definition of concussion (*) | No adjustment for confounding within rugby cohort | Self reported (*) | No test of concussion in elite cohort | 2 |
| Decq et al, 2016 (27) | Sampling frame identified (*) | Not justified | No description of non-responders | No description of concussion data | No attempt to examine effect of concussion | Self-reported using scale (*) | Examined number of concussions within rugby players (*) | 3 |
| Esopenko et al, 2018* (28) | No clear sampling frame identified | Not justified | No description of non-respondents | Description of concussion (*) | Adjusted for age in analysis of alumni group (*) | Self-reported (*) | Examined concussion within ice-hockey players (*) | 4 |
| Baker et al, 2018 (24) | No clear sampling frame identified | Not justified | No description of non-respondents | No mention of concussion data | No attempt to examine effect of concussion | Self-reported (*) | No test of concussion in ice hockey players | 1 |
| Misquitta et al, 2018 (33) | No clear sampling frame identified | Not justified | No description of non-respondents | Zurich guidelines on concussions used (*) | Regression model adjusted for age (*) | Imaging data – not clear if done in absence of knowledge of exposure (*) | Appropriate regression analysis (*) | 4 |

| | **Representativeness** * | **Sample size** * | **Non-respondents** * | **Exposure assessment** ** | **Comparability** ** | **Outcome assessment** ** | **Statistical test** * | **Total (Out of10)** |
|---|---|---|---|---|---|---|---|---|
| | | | | (Career used as a proxy for repeated concussions) | | | | |
| Alosco et al 2017 (22) | No description of sampling strategy | Not justified | No description of non-responders | Cumulative head impact index (**) | Mixed effect models adjusted for age and BMI (**) | Neuropsychological test battery and self-reports (*) | Appropriate statistical modelling (*) | 6 |
| Multani et al, 2016 (34) | No description of sampling strategy | Not justified | No description of non-responders | Description of concussion (*) | No reported analyses within football players | Neuro-psychological testing (*) | Test not appropriately applied to examine concussion | 2 |
| Hart et al, 2013 (30) | Probably not representative | Not justified | No description of non-responders | Concussion using 1997 AAN guidelines (**) | Main analysis within NFL players (*) | Neuro-psychological testing (*) | No test of concussion within players | 4 |
| Randolph et al, 2013 (35) | Selected as having MCI | Not justified | No description of non-responders | No mention of concussion data | Analysis of NFL players by cumulative years of professional play (*) | Modified telephone interview of cognitive status (*) | Cumulative years of play (surrogate for cumulative concussions) | 3 |
| Amen et al, 2011 (23) | Probably not representative | Not justified | No description of non-responders | Self-reported concussion (*) | Not obvious that controlled analysis performed | Neuro-psychological tests (*) | Analysis of concusison within cohort (*) | 3 |

| | **Representativeness** * | **Sample size** * | **Non-respondents** * | **Exposure assessment** ** | **Comparability** ** | **Outcome assessment** ** | **Statistical test** * | **Total (Out of10)** |
|---|---|---|---|---|---|---|---|---|
| Guskiewicz et al, 2005 (29) | Questionnaire sent to all retired players (69% response rate) (*) | Not justified | No description of non-responders | Self-rerported concussion (*) | Analysis stratified by age (*) | MCI questionnaire (*) | Chi-squared test for trend (*) | 5 |
| Bang et al, 2016 (25) | Small case series | Not justified | No description of non-responders | No concussion data collected | Not sufficient simple size | Purdue pegboard test (*) | To small a simple to be meaningful | 1 |
| Bernick et al, 2015 (26) | Not clear how representative | Comparison of sample with population (*) | No specific mention of results of the comparison | Knockouts and technical knockouts (forms of concussion) (*) | Multivariable modelling (*) | Computerised battery of test (*) | Appropriate analysis including Cis (*) | 6 |

* One “control” excluded due to a history of concussion with extended post-concussion symptoms. Another was diagnosed with Parkinson’s shortly after testing and so was excluded.

*Supplementary Table 3: Characteristics of included studies*

| Ref. | Study design | Sport and duration of career | Sportspeople population and recruitment | Comparison group | Variables adjusted for in the analysis | Funding | NOS score |
|---|---|---|---|---|---|---|---|
| **Rugby** | | | | | | | |
| McMillan TM et al, 2017 (32) | Cross-sectional with external comparison group ("population" controls) | Retired international rugby players (Scottish Rugby Union)<br><br>Average number of international matches played: 24 (SD 24; IQR 5-40) | – 52 retired rugby international players<br>– Mean age (SD); 53.5 (13.0)<br>– Recruited through Scottish Rugby Union<br>– Response rate: 52/~350 former players, 71 of whom volunteered and were eligible (15%) | – 46 population controls<br>– Mean age (SD): 55.1 (9.0)<br>– Recruited as friends and family members of the ruby players, members of community groups, or teachers | Age, Scottish Index of Multiple Deprivation, education | Sackler Foundation, Chief Scientist Office, NHS Research Scotland Career Researcher Fellowship | 4 |
| Hume et al, 2017 (31) | Cross-sectional with between sports (community rugby players and non-contract sportspeople) and external comparison group (US norms) | Elite New Zealand rugby players<br><br>Mean career duration in years 23.0 (SD 8.1) | – 103 former elite rugby players (national or international)<br>– Age range: 29-72, mean age 41.3 (SD 7.5)<br>– Self-selected cohort from the larger Rugby Health project (N=485)<br>– Response rate (including elite rugby N=103, community rugby N=198, non-contact sport retiree N=65): 75% but impossible inferring on the original response rate | **BETWEEN SPORTS COMPARISON**<br>– 198 community rugby players<br>– Age range: 29-72, mean age 44.9 (SD 8.4)<br><br>– 65 non-contact-sport retirees (cricket and field hockey players)<br>– Age range: 29-72, mean age 42.1 (SD 7.7)<br><br>– Both groups self-selected cohort from the larger Rugby Health project<br><br>**EXTERNAL COMPARISON**<br>– US norms | None ("No significant correlations were observed between former players' demographic characteristics (e.g. age, education level, ethnicity, alcohol use) or sport played/level with the neuropsychological variables, therefore these factors were not used as covariates in analyses") | Not disclosed | 2 |
| Decq et al. 2016 (27) | Cross-sectional with a between sports comparison group (high level retired sportspeople) | Retired rugby players who have reached the first division championship level in France between 1985 and 1990<br><br>Minimum 10 years | – 239 retired rugby players<br>– Age range: 49-55 years<br>– Identified from French first division championship game sheets<br>– 1,491 players identified, 1,047 contacted, 524 invited to participate, and 239 included. Response rate: 46% or 23% depending on selection criteria used | – 138 control from high levels sports with 'low risk' of recurrent concussion<br>– Age range: 49-55 years<br>– Identified through sporting federations<br>– Out of 637 sportsmen, 455 were invited to participate and 138 were included. Response rate 30%, or 22% depending on selection criteria used | Not clear which variables collected were adjusted for in the analysis (smoking and education?) | Fédération Française de Rugby and the Ligue Nationale de Rugby | 3 |
| **Ice Hockey** | | | | | | | |
| Esopenko C et al,2018 (28) | Cross-sectional study with external comparison group ("community" controls) | National Hockey League and other professional and minor professional leagues<br><br>No information given on length of career | – 33 former professional hockey players<br>– Mean age (SD): 54.3 (10.4)<br>– Recruited through NHL Alumni Association by email, media presentations, participation in local hockey tournaments and word of mouth<br>– Response rate not given | – 18 age-matched comparison group of healthy males recruited from the community with no history of concussion<br>– Mean age (SD): 53.5 (10.2)<br>– Recruited from the "community"<br>– Response rate not given | N/A (Principle component analysis used) | Canadian Institute of Health Research Catalyst, Ontario Neurotrauma Foundation | 4 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **American Football (US and Canadian)** | | | | | | | |
| Baker JG, et al 2018 (24) | Cross-sectional study with between sports comparison group (non-contact master athletes) | National Football League (NFL) and National Hockey League (NHL) players<br><br>Minimum 2 season play (85) | – 21 retired players<br>– Age:36 to 72 years<br>– Mean age: 56.7 years<br>– Recruitment through the alumni association with not clear procedures but based on volunteering (the authors reported that alumni too sick to participate and those with a public role were underrepresented) (85) | – 21 non-contact sport master athletes<br>– Age: 36- 72 years<br>– Mean age: 55.4 years<br>– No history of concussion<br>– Recruitment and response rate not clear | Age education and ethnicity normative scores used | Not stated | 1 |
| Misiquitta K et al, 2018 (33) | Cross-sectional study with two external comparison groups ("population" controls and controls from the Cambridge Centre for Aging and Neuroscience) | Former Canadian football players<br><br>Played at least a season with Canadian Football League Median (IQR) years in CFL: 9 (5-11) | – 53 former Canadian football players<br>– Mean age: 55 ± 13 years<br>– Recruitment unclear<br>– Response rate not reported | FIRST COMPARISON GROUP<br>– 25 age- and education-matched controls<br>– Mean age: 51 ± 10 years<br>– Recruited from the general population<br><br>SECOND COMPARISON GROUP<br>– 321 age-matched male controls from the Cambridge Centre for Aging and Neuroscience (CAMCAN)<br>– Mean age: 58 ± 16 years | None | Physicians' Services Incorporated Foundation and the Toronto General and Western Hospital Foundation | 4 |
| Alosco et al, 2017 (22) | Cross-sectional study with external comparison group | NFL players<br><br>Minimum 2 years of active playing time in the NFL<br><br>12 or more total years of participation in tackle football | – 124 retired NFL players<br>– Age range: 40-69 years<br>– Median years in CFL (IQR): 9 (5-11)<br>– With self-reported complains of cognitive, behavioural and mood symptoms for at least 6 months<br>– Sample of participants recruited in DETECT though e-mails, NFL Alumni Association, Boston University Alzheimer's Disease and CTE Center social media<br>– Response rate not reported | – 28 age-matched controls<br>– Aged 40-69<br>– No history of participating in contact sport nor of concussion<br>– Recruited through social media and word of mouth | Age and education | National Institute of Health (NIH) | 6 |
| Multani et al. 2016 (34) | Cross-sectional with external comparison group | Canadian Football players with history of multiple concussions<br><br>Duration of career 7.8±4 years | – 18 retired Canadian Football players selected on the basis of history of multiple concussion<br>– Mean age: 49.6±12 years<br>– Playing history: 7.8±4 years<br>– Recruitment unknown | – 17 age- and education- matched controls, no reported concussion history<br>– Mean age: 46.7±10 years<br>– Recruitment not stated | None | PSI Foundation and the Canadian Sports Concussion Project, Krembil Neuroscience Centre, Toronto Western Hospital | 2 |
| Hart et al. 2013 (30) | Cross-sectional with external comparison group | American Football players<br><br>2-15 years | – 34 retired NFL players<br>– Age range: 41-79 years<br>– Mean age 61.8 years (95% CI, 57.8-65.7)<br>– Recruited from meeting of the NFL Players Association local chapter (North Texas), word of mouth and advertising. Sample made of volunteers who asked to participate | – 26 healthy controls with no history of concussion<br>– Age range: 41-79<br>– Mean age: 60.1 (95% C.I. 54.6-64.1)<br>– Recruited from normal aging studies at the Centre for Brain Health at the University of Texas at Dallas<br>– 26 out of the original (31%) 85 screened included | | Brain-Health Institute for Athletes at the Center for Brain-Health (University of Texas Dallas) and National Institute on Aging | 4 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Randolph et al., 2013 (35) | Cross-sectional with two external comparison groups (one of patients diagnosed with MCI) and population norms | American Football NFL players<br><br>Lenght of career not stated<br><br>Among those cognitively impaired, mean (SD) career: 7.5 (3.4) years | – 513 retired NFL players<br>– Mean age 64.2 years (SD 5.5)<br>– Initial sample of NFL players affiliated with the NFL Player's Association invited (N=3729) with 68% response rate<br>– New data collection on 908 of them aged 50+ (response rate 57%) | – 81 patients diagnosed with MCI by a neuropsychologist according to the core clinical criteria of the revised NIA-AA guidelines (88)<br>– 41 cognitively normal subjects was extracted from the RBANS standardization database to match the NFL sample on the basis of age, education, and gender | None (the healthy control sample was matched on demographic variables) | Martek Biosciences Corporation | 3 |
| Amen et al. 2011 (23) | Cross-sectional with external comparison group | American Football<br><br>In active NFL roster for a minimum of 3 years | – 100 Active and retired NFL players<br>– Age range: 25-82 years<br>– Mean age: 52.3 (SD 12.4)<br>– Recruited from retired NFL Players Association meetings and word of mouth. | – 20 healthy controls, no documented concussion history for SPECT<br>– Standardized sample (N=810), chosen to be representative to the U.S. population of adults between the ages of 18 and 89 with regard to education, gender, and ethnicity for the MicroCog test | None | Not disclosed | 3 |
| Guskiewicz et al. 2005 (29) | Cross-sectional with external comparison group | American football players<br><br>Mean duration of overall career of 15.1 years (SD 4.3)<br><br>Mean duration of professional career 6.6 years (SD 3.6) | – 758 retired footballers aged 50+ years<br>– Mean age: 53.8 years (SD 13.4)<br>– Members of National Football League Retired Player's Association, US<br>– Minimum 2 seasons as professional footballers<br>– Recruitment procedures not clear, response rate not given | – External comparison: age-adjusted prevalence ratios using estimates from the general population<br>– Internal comparison: concussed vs. not concussed | Not clear which variables collected were adjusted for in the analysis | Not disclosed | 5 |
| **Boxing and Martial Arts** | | | | | | | |
| Bang et al. 2016 (25) | Case-series with external comparison group | Boxing<br><br>At least 10 years | – 5 professional retired boxers<br>– Age range: 42-49 years<br>– Career duration of 8-19 years<br><br>– Recruitment criteria not stated | – 4 age matched controls with no history of concussion<br>– Age range: 46-53 years<br><br>– Recruitment criteria not stated | None | Ministry of Health & Welfare, Republic of Korea and Ministry of Science, ICT and Future Planning, Republic of Korea | 1 |
| Bernick et al. 2015 (26) | Cross-sectional study (baseline of a cohort study). with external comparison group | Fighters (both martial arts fighters and boxers)<br><br>Licensed to fight professionally in one of the combat sports | – 224 fighters (93 boxers, 131 MMA)<br>– Age range: 18-44 years<br>– Career duration: 0 – 24 years (mean: 4 years)<br>– Professional fights range: 0-101 (mean:10)<br><br>– Recruited from the Professional Fighters Brain Health Study | – 22 age and education matched controls<br>– No history concussion, or participation in high risk sport | Results adjusted for intracranial volume, age, race and education | Not disclosed | 6 |

*Supplementary Table 4: Detailed data on neurocognitive assessment extracted from the included papers*

| Reference | Type of neurocognitive test | Domain | Results |
|---|---|---|---|
| McMillan et al. 2018 (32) | Montreal Cognitive Assessment (MOCA) | General cognitive function | Mean 27.4 for retired international rugby players (RIRP) vs 28.0 for comparison group (p=0.806) |
| | Symbol Digit Test | Processing speed | - 50.9 mean for Scottish International rugby players (RIRP) vs 53.0 for comparison group (p=0.490) |
| | Trail Making Test B | Executive Function | - 56.1 mean for RIRP vs 51.9 for comparison group (p=0.434) |
| | Rey Auditory Verbal Learning Test (RAVLT) | Memory & Learning | - Immediate recall 50.2 for RIRP vs 56.1 for comparison group (p=0.022)<br>- Delated recall 10.5 for RIRP vs 11.6 for comparison group (p=0.165) |
| | Sustained Attention to Response Task (SART) | Sustained Attention | - Sustained attention in response task (SART) commission errors 10.3 for RIRP vs 10.0 for comparison group (p=0.860)<br>- SART reaction time 336 for RIRP vs 313 for comparison group (p=0.618) |
| | Judgement Line Orientation Task | Visual perception | - Mean of 28.2 for RIRP vs 28.1 for comparison group (p=0.442) |
| | Lafayette Grooved Pegboard | Fine hand coordination | - Dominant hand 74.9 mean for RIRP vs 68.7 for comparison group (p=0.038)<br>- Non-dominant hand 85.4 mean for RIRP vs 80.1 for comparison group (p=0.126) |
| Hume et al., 2017 (31) | CNS-Vital Signs (VS) Test battery | Composite memory | - The community-rugby group performed worse than the US norms on composite memory (-0.31, -0.48 to -0.14) |
| | | Psychomotor speed | - No significant difference between the groups |
| | | Reaction time | - All three former-player groups performed worse than the US norms on reaction time (elite rugby: -0.50, -0.69 to -0.30; community rugby: -0.61, -0.78 to -0.45; non-contact sport:-0.73, -0.98 to -0.48) |
| | | Complex attention | - Elite-rugby group performed worse on tests of complex attention (effect size -0.67, 95 % confidence interval [CI] -1.07 to -0.26) than the non-contact-sport group and the community-rugby group (-0.38, -0.71 to -0.05)<br>- Community-rugby group and the non-contact- sport group performed slightly better than the US norms on complex attention (community rugby: 0.22, 0.08–0.35; non-contact sport: 0.40, 0.20–0.60) |
| | | Cognitive flexibility | - The elite-rugby group performed worse on tests of cognitive flexibility (-0.37, -0.74 to 0.00) than the non-contact-sport group<br>- The community-rugby group performed worse than the non-contact group on cognitive flexibility (-0.39, -0.69 to -0.08)<br>- Rugby groups performed worse on cognitive flexibility (elite rugby: -0.26, -0.47 to -0.05; community rugby: -0.27, -0.41 to -0.13) than the US norms |

| | | | |
|---|---|---|---|
| | | Processing speed | - Rugby groups performed worse on processing speed (elite rugby: -0.51, -0.75 to -0.26; community rugby: -0.32, -0.48 to -0.17), than the non-contact-sport group |
| | | Executive functioning | - The elite-rugby group performed worse on tests of executive functioning (-0.41, -0.80 to -0.02) than the non-contact-sport group<br>- The community-rugby group performed worse than the non-contact group on executive functioning (-0.51, -0.89 to -0.12)<br>- Rugby groups performed worse on executive functioning (elite rugby: -0.24, -0.45 to -0.03; community rugby: -0.23, -0.37 to -0.10) than the US norms |
| | | Verbal memory | - All three former-player groups performed worse than the US norms on verbal memory (elite rugby: -0.36, -0.60 to -0.12; community rugby: -0.54, -0.72 to -0.36; non-contact sport: -0.39, -0.69 to -0.08 |
| | | Visual memory | - No significant difference between the groups |
| | | Simple attention | - No significant difference between the groups |
| | | Motor speed | - The elite-rugby group performed slightly better than the US norms in relation to motor speed (0.38, 0.19–0.57) |
| Decq et al., 2016 (27) | F-TICS-m MCI score | Mild cognitive disorders (TICS-m score ≤30 was considered to be compatible with mild cognitive disorder) | - Median (IQR) TICS-m score in former rugby player 30 (28-32), in other sports 31 (29-34) (p=0.07)<br>- Mean (SD) TICS-m score in former rugby player, 30.2 (3.5) in other sports 31.3 (3.6)<br>- Mild cognitive disorder (TICS-m≤30) 57% of former rugby player and 40% of other sports (p=.005)<br>- TICS-m score did not vary across the number of reported concussions<br>- In multivariate analysis, number of concussions were not associated with TICS-m score (only education, smoking, and perceived health were positively associated with good cognitive function, playing rugby and age were negatively associated with good cognitive function) |
| Esopenko et al. 2017 (28) | Rey-Osterrieth Complex Figure Test (RCFT); Wechsler Abbreviated Scale of Intelligence (WASI); Brief Visual Memory Test Revised (BVMT-R); Wechsler Abbreviated Scale of Intelligence (WASI) Matrix reasoning; Symbol Digit Modalities Test (SDMT); Judgement of Line Orientation (JLO); Rey Auditory Verbal Learning Test (RAVLT); Brief Visual | Intellectual functioning, speeded attention, memory, visuospatial processing and executive functioning | - Lower performance on the executive/intellectual function, t(49)=5.53, p<0.001, in alumni athletes vs comparison group<br>- Group effect was evident on the WCST, t(43.41)=6.08, p<0.001; and WASI vocabulary, t(49)=4.43, p<0.001 and similarities, t(49)=2.17, p=0.035, but not matrix reasoning t(49)=1.95, p=0.057.<br>- No significant differences for the other factors (visuospatial, t(49)=1.18, p=0.25; verbal memory, t(49)=1.16, p=0.25; speeded attention, t(49)=0.16, p=0.87).<br>- No significant effects or interactions involving Group detected on the computerised cognitive test battery. |

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| | Memory Test-Revised (BVMT-R); Self-Ordered Pointing Task (SOPT); Paced Auditory Serial Addition Task (PASAT); Phonemic Word List Generation (FAS); Paced Auditory Serial Addition Task (PASAT); Trail Making Test (TMT) (Version B and A); Wisconsin Card Sorting Task; and computerized cognitive tests including Switching Stroop/Colour Word Remapping | | |
| Baker et al. 2018 (24) | Wisconsin Card Sorting Test (WCST) & Delis-Kaplan Executive Function System (D-KEFS) | Executive function | - D-KEFS Colour-Word Interference Inhibition: 57.67 mean score for contact sport athletes and 57.19 in non-contact sport athletes, t-test 0.23 (p=0.82)<br>- WCST Total Errors: mean of 49.43 for contact sport and 52.45 in non-contact sport athletes, t-test -1.17 (p=0.25) |
| | WASI-III Digit Span | Attention | - 54.9 mean score for contact sport athletes and 57.33 in non-contact sport athletes, t-test -0.73 (p=0.47) |
| | Neuropsychological Assessment Battery (NAB) (list learning and story learning test) | Memory (immediate and delayed recall) | - List B Immediate Recall: 50.9 in contact sport athletes and 57.24 in non-contact sport athletes, t-test -0.62 (p=0.05)<br>- List A Short Delay: 53.48 in contact sport and 57.33 in non-contact sport athletes, t-test -1.29(p=0.2) |
| | Controlled Oral Word Association Test (COWAT) & NAB Naming test | Language | - Letter Fluency (FAS Total score) mean of 52.95 in contact sport athletes and 47.43 in non-contact sport athletes, T-test score 1.96 (p=0.06)<br>- NAB Naming score 49.33 in contact sport athletes and 53.33 in non-contact sport athletes, T-test -2.12 (p= |
| | WASI-III Digit Symbol Subtest and Trail Making Part B | Perceptual motor skills (visuospatial) | - WASI-III Digit Symbol: 55 mean score for contact sport athletes and 53.38, t-test 0.57 (p=0.57)<br>- Trail B: 48.52 mean for contact sport and 53.38 in non-contact sport athletes, t-test -0.89 (p=0.38) |
| Misquitta et al. 2018 (33) | Rey Auditory Verbal Learning Test (RAVLT) | Verbal learning and memory | - RAVLT short delay mean for retired Canadian Football League players (Ex-CFL) 8.8 vs 9.2 for controls (p=0.497)<br>- RAVLT long delay mean for Ex-CFL 8.1 vs 8.9 for controls (p=0.298) |
| | Rey Visual Design Learning Test (RVDLT) | Visual learning and memory | - RVDLT long delay mean for Ex-CFL and controls was 9.2 (p=0.977) |

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| Alosco et al. 2017 (22) | Trail Making Test (TMT) Parts A and B; Wechsler Adult Intelligence Scale-Revised (WAIS-R) Digit Span and Digit Symbol Tests; Wisconsin Card Sorting Test; Controlled Oral Word Association Test (COWAT); Delis-Kaplan Executive Function System Colour-Word Interference Test (DKEFS); Boston Qualitative Scoring System for the Rey-Osterrieth Complex Figure (ROCF); Neuropsychological Assessment Battery (NAB) Story Learning Test, List Learning Test, Map Reading Test, and Naming Test; and Animal Fluency. | Attention, executive function, psychomotor speed, visual and verbal episodic memory, language, motor, and visuospatial functions | - More impaired factor scores for NFL players vs control group in the psychomotor speed/executive function, t-test 2.61 (p=0.012) but not for the verbal (p=0.209) or visual (p=0.102) memory domains.<br>- NFL players performed worse across most of the cognitive measures compared to the comparison group<br>- Trails A Time: T-score, 54.18 (10.37) mean score for comparison group vs 49.01 (11.72) mean for NFL group, p=0.030<br>- Digit Symbol: scaled score, 11.71 (2.05) mean score for comparison group vs 10.15 (2.03) mean for NFL group, p=0.003<br>- Trails B Time: T-scores, 52.75 (15.38) mean score for comparison group vs 43.77 (15.86) mean for NFL group, p=0.005<br>- DKEFS Inhibition/Switching completion time: scaled score, 12.00 (2.68) mean score for comparison group vs 10.60 (2.92) mean for NFL group, p=0.078<br>- COWAT: T-score, 52.21 (9.80) mean score for comparison group vs 48.96 (11.38) mean for NFL group, p=0.197<br>- ROCF Immediate Copy, Presence & Accuracy: T-score, 53.39 (7.69) mean score for comparison group vs 47.91 (9.93) mean for NFL group, p=0.021<br>- ROCF Delayed Presence & Accuracy: T-score, 55.00 (7.88) mean score for comparison group vs 48.43 (11.01) mean for NFL group, p=0.006<br>- NAB Phrase Unit (1 & 2) Immediate Recall: T-score, 43.00 (10.82) mean score for comparison group vs 39.19 (8.45) mean for NFL group, p=0.045<br>- NAB Phrase Unit Delayed Recall: T-score, 46.79 (10.12) mean score for comparison group vs 41.75 (7.77) mean for NFL group, p=0.006<br>- NAB List A Short Delay: T-score, 51.96 (11.99) mean score for comparison group vs 44.55 (13.03) mean for NFL group, p=0.014<br>- NAB List A Long Delay: T-score, 49.75 (12.88) mean score for comparison group vs 41.55 (13.77) mean for NFL group, p=0.010 |
| Multani et al., 2016 (34) | Rey Visual Design Learning Test (RVDLT) | Visuospatial learning and memory | - RVDLT total learning score: 41.39 $\pm$ 13.1 in retired players, and 35.59 $\pm$ 8.7 in comparison group (p=0.303)<br>- RVDLT long delay total score: 10.11 $\pm$ 3.3 in retired players, and 9.76 $\pm$ 2.1 in comparison group (p=0.443) |
| | Wechsler Test of Adult Reading (WTAR) | Pre-morbid intellectual functioning, verbal memory | - WTAR standard score: 113.87 $\pm$ 6.6 in retired players, and 11.94 $\pm$ 8.2 in comparison group (p=0.781) |
| Hart et al., 2013 (30) | Trail Making Test Parts A and B & Digit Span Subtest from the Wechsler Adult Intelligence Scale | Attention and cognitive flexibility | - Trail Making Test Part A score: 49.0 (45.8-52.1) for comparison group, 50.2 (44.2-56.2) for unimpaired NFL players, 52.0 (47.8-56.2) for cognitive impaired NFL players (p=0.58)*<br>- Trail Making Test Part B score: 54.1 (50.6-57.5) for comparison group, 51.9 (44.9-58.9) for unimpaired NFL players, 46.8 (40.5-53.1) for cognitive impaired NFL players (p=0.12)* |

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| | | | - WAIS-IV Digit span SS: 11.0 (10.0-12.0) for comparison group, 9.3 (7.2-11.5) for unimpaired NFL players, 10.3 (8.4-12.2) for cognitive impaired NFL players (p=0.35)* |
| Randolph et al., 2013 (35) | Wechsler Adult Intelligence Test-III (WAIS-3) and the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) | Verbal memory, processing speed, visuospatial ability, language, attention | - RBANS Total Scale score mean for the NFL sample was significantly lower than the comparison group, F= 10.4; p= 0.002. |
| Amen et al. 2011 (23) | MicroCog Assessment of Cognitive Functioning | Attention/mental control, memory, reasoning, spatial processing and reaction time | - Players scored in the bottom half of the percentile placements on all measures except spatial processing and reaction-time, which were both in the top half of the percentile placements. |
| | Conners' Continuous Performance Test II (CCTP II) | Response inhibition and attention (validated screening tool that assigns a clinical probability of having attention-deficit hyperactivity disorder (ADHD)) | - 84% of the players had a 50% greater chance of having ADHD based on CCPT II |
| Bang et al. 2016 (25) | Mini-Mental State Examination (MMSE) | Visuospatial skills, language, concentration, working memory, memory recall, and orientation | - Mean (SD) MMSE in former boxers 28.6 (1.5) in comparison group 30.0 (0.0) (p=0.212) |
| | Hopkins Verbal Learning Test (HVLT) : verbal memory | Verbal episodic memory | - Mean (SD) Immediate recall in boxers 15.2 (3.0) in comparison group 19.5 (4.4) (p=0.127)<br>- Mean (SD) delayed recall in boxers 4.8 (1.9) in comparison group 6.8 (3.1) (p=0.282)<br>- Mean (SD) recognition in boxers 20.8 (0.8) in comparison group 21.0 (1.9) (p=0.832) |
| | Rey-Osterrieth Complex Figure test: visuospatial memory | Visuospatial memory | - Mean (SD) Immediate recall in boxers 15.3 (3.4) in comparison group 18.4 (4.7) (p=0.291)<br>- Mean (SD) delayed recall in boxers 14.7 (3.3) in comparison group 20.6 (4.0) (p=0.045)<br>- Mean (SD) recognition in boxers 20.2 (1.8) in comparison group 20.3 (2.1) (p=0.97) |
| Bernick et al. 2015 (26) | CNS Vital Signs (including verbal memory, symbol digit coding, Stroop and a finger tapping test) | Verbal memory | - No difference detected |
| | | Processing speed | - There was a significant relationship between the number of professional fights and speed of processing (p=0.041), with an estimated 0.19% reduction in processing speed per fight<br>- There was a significant relationship between the Fight Exposure score (FES) and speed of processing (p=0.023), with an estimated 2.1% reduction in processing speed scores for each increase in FES<br>- Processing speed was related to fighter type (adjusting for years of education) with both fighter groups scoring worse than controls, but boxers being overall slower than MMA fighters |
| | | Psychomotor speed | - Not clear |
| | | Reaction time | - Not clear |