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History of Sport-Related Concussion and Long-Term Clinical Cognitive Health Outcomes in Retired Athletes: A Systematic Review

Joice Cunningham, BSc*; Steven P. Broglio, PhD, ATC, FNATA†; Megan O'Grady, BSc*; Fiona Wilson, PhD, MSc*

*Trinity Centre for Health Sciences, St James Hospital, Trinity College Dublin, Ireland; †University of Michigan, Ann Arbor

Background: Sport-related concussions (SRCs) are known to have short-term effects on cognitive processes, which can result in diverse clinical presentations. The long-term effects of SRC and repeated exposure to head impacts that do not result in SRC on specific cognitive health outcomes remain unclear.

Objectives: To synthesize and appraise the evidence base regarding cognitive health in living retired athletes with a history of head-impact exposure or SRC.

Data Sources: A systematic search of the EMBASE, PsycINFO, MEDLINE/PubMed, CINAHL, Cochrane Central Register of Controlled Trials, and Web of Science databases was conducted from inception to April 2018 using common key words and medical subject headings related to 3 components: (1) the participant (eg, retired athlete), (2) the primary outcome measure (eg, cognitive test used), and (3) the secondary outcome measure (eg, history of sport concussion).

Study Selection: Cross-sectional studies of living retired male or female athletes in which at least 1 cognitive test was used as an outcome measure were included. Two reviewers independently screened studies.

Data Extraction: Data extraction was performed using Strengthening the Reporting of Observational Studies in Epidemiology guidelines. Methodologic quality was assessed independently by 2 reviewers using the Downs and Black tool.

Data Synthesis: The search yielded 46 cross-sectional observational studies that were included in a qualitative synthesis. Most included studies (80%, n = 37) were published in the 5 years before our review. A large proportion of these studies (n = 20) included retired American National Football League players. The other research investigated professional, university, high school, and amateur retired athletes participating in sports such as American and Australian football, boxing, field and ice hockey, rugby, and soccer. The total sample consisted of 13 975 participants: 7387 collision-sport athletes, 662 contact-sport athletes, 3346 noncontact-sport athletes, and 2580 participants classified as controls. Compared with control participants or normative data, retired athletes displayed worse performance in 17 of 31 studies (55%) of memory, 6 of 11 studies (55%) of executive function, and 4 of 6 studies (67%) of psychomotor function and increased subjective concerns about cognitive function in 11 of 14 studies (79%). The authors of 13 of 46 investigations (28%) reported a frequency-response relationship, with poorer cognitive outcomes in athletes who had greater levels of exposure to head impacts or concussions. However, these results must be interpreted in light of the lack of methodologic rigor and moderate quality assessment of the included studies.

Conclusions: Evidence of poorer cognitive health among retired athletes with a history of concussion and head-impact exposure is evolving. Our results suggest that a history of SRC may more greatly affect the cognitive domains of memory, executive function, and psychomotor function. Retired athletes appeared to have increased self-reported cognitive difficulties, but the paucity of high-quality, prospective studies limited the conclusions that could be drawn regarding a cause-and-effect relationship between concussion and long-term health outcomes. Future researchers should consider a range of cognitive health outcomes, as well as premorbid ability, in diverse samples of athletes with or without a history of concussion or head-impact exposure to delineate the long-term effects of sport participation on cognitive functioning.

Key Words: mild traumatic brain injury, neurocognitive function, brain health

Key Points

- The literature in this area has been largely dominated by investigations of retired American National Football League players, who are a unique cohort.
- Evidence of decreased cognitive function in retired athletes was mixed. The greatest decreases were in memory, psychomotor function, executive function, and self-reported cognitive function.
- Certain key cognitive domains, such as language, visuospatial processing, psychomotor function, perceptual abilities, and reaction time, have been underassessed.
- A frequency-response relationship (ie, poorer cognitive outcomes in those with greater levels of exposure to head impacts or concussions) was demonstrated in only 13 of 46 studies.

The need to understand the relationship between a history of concussions or head-impact exposure and the development of later-life cognitive impairment is increasing. The current dialogue on this topic has largely stemmed from postmortem investigations of athletes, particularly retired American National Football League

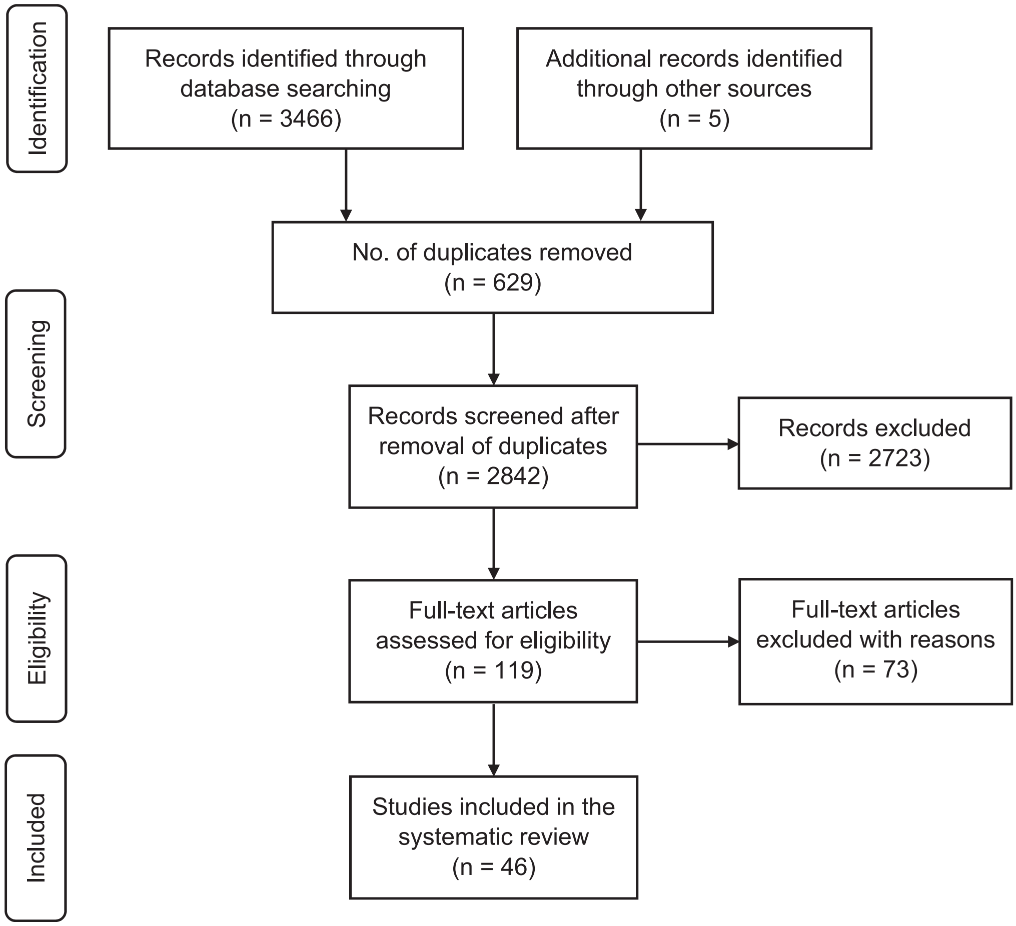


Figure 1. Preferred reporting items for systematic reviews; flow diagram of study-selection process.

(NFL) players, with a history of substantial head-impact exposure throughout their careers. In the last decade, a dramatic shift in both public and scientific perceptions about the long-term consequences of concussion has been evident. An injury that was once viewed as a short-lived impairment of neurologic function and often trivialized is now implicated in a number of long-term neurologic sequelae.[1–5] Research in non–sport-related traumatic brain injury (TBI) has supported a link between TBI and increased risks of cognitive impairment and dementias, such as Alzheimer disease in older adults,[6] with data indicating that moderate and severe TBIs increased the risk of dementia between 2- and 4-fold.[7] However, the long-term consequences of concussion, which is on the mild end of the TBI spectrum,[8] remain poorly understood. Whereas a full recovery of cognitive functioning is generally the norm,[9–11] the clinical pathway to recovery and return to sport is much more prolonged and less clear for a minority of athletes.[8] Therefore, the purpose of our review was to investigate the literature on the long-term cognitive health status of retired athletes.

METHODS

This review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (PRISMA; www.prisma-statement.org) and was recorded in PROSPERO, a registry of systematic reviews. The flow diagram is presented in Figure 1. Registration is available at https://www.crd.york.ac.uk/prospero/ (registration number: CRD42016050750).

Eligibility Criteria

Studies were included if the authors evaluated retired male or female athletes who participated in organized sport at the amateur to professional level. At least 1 form of cognitive testing must have been used as an outcome measure. Studies were excluded if the investigators explored only athletes still actively involved in sport or did not report data on retired athletes as a subgroup or if they were case studies with 5 or fewer participants. Neurocognitive testing must have been conducted with and the results obtained from the participant (ie, rather than from friends or family). The primary outcomes of interest were a variety of cognitive domains: attention, memory, executive function, intelligence, processing speed, visuospatial abilities, and psychomotor speed. The secondary outcome variable of interest was a history of sport-related concussion (SRC).

Search Strategy

We searched the electronic databases EMBASE, PsycINFO, MEDLINE/PubMed, CINAHL, Cochrane Central Register of Controlled Trials, and Web of Science from their inception to April 2018 using the relevant database search engines. Common key words and medical subject headings were related to 3 components: (1) the participant (eg, retired athlete), (2) the primary outcome measure (eg, cognitive test used), and (3) the secondary outcome (eg, history of sport concussion). No search restrictions for date or language were imposed. The search strategy for each database and corresponding number of hits per database are presented in Appendix 1.

The electronic database searching was supplemented by searching the abstracts of the "International Conference on Concussion in Sports" consensus meetings (2001–2018) and conducting a gray-literature search and a hand search of the reference lists of the included studies. Two reviewers (J.C. and F.W.) independently screened the titles and abstracts to identify studies that potentially met the eligibility criteria. Full texts of these reports were retrieved and independently assessed for eligibility by the same 2 reviewers. Any disagreements on study inclusion were resolved through discussion and consultation with a third reviewer (S.P.B.) to reach a consensus. A total of 46 studies were included in this review.

Data Extraction and Analysis

A data-extraction template was used as a checklist of items that should be included in reports of cross-sectional studies based on the Strengthening the Reporting of Observational Studies in Epidemiology guidelines.[12] One reviewer (J.C.) recorded the study's aim, participant characteristics, details of concussion history, outcome measures used, and relevant outcome data (group means and standard deviations; Table 1).

Methodologic Assessment

Two reviewers (J.C. and F.W.) independently evaluated the methodologic quality of the studies using an adapted Downs and Black checklist.[59] Disagreements between the reviewers were resolved through discussion to achieve consensus. If agreement could not be reached, a third reviewer (S.P.B.) arbitrated. The checklist was modified to a maximum of 17 applicable questions that addressed the following methodologic components: reporting, external validity, internal validity (bias and confounding), and power. Seventeen items were rated on a 2-point scale (*yes* = 1 and *no/unable to determine* = 0), and 1 item was rated on a 3-point scale (*yes* = 2, *partial* = 1, and *no* = 0). The maximum achievable score was 18, with higher scores indicating better methodologic quality. Results were categorized according to the adapted Downs and Black checklist[59] from Hartling et al[60] and Hignett[61] and were interpreted as follows: *strong quality* ($\geq$14) represented the top 75%, *moderate quality* (scored 9–13) represented 50% to 74%, *limited quality* (5–8) represented 25% to 49%, and *poor quality* (<5) represented less than 25%.

RESULTS

Literature Search

After duplicates were removed, this review yielded a total of 2842 records. We screened the titles and abstracts of these records and identified 119 studies that potentially met the inclusion criteria and, hence, were subject to full review. Of these, 46 cross-sectional studies published between 1984 and 2018 met the criteria and were included in a quantitative synthesis. Given the heterogeneity of the study design and outcome measures, a meta-analysis could not be conducted for all studies. Where possible, we performed a meta-analysis depending on the homogeneity of the included studies.

Methodologic Assessment

Detailed information on the quality appraisal of the 46 studies is presented in the Supplemental Table (available online at http://dx.doi.org/10.4085/1062-6050-297-18.S1). A total of 11 (24%) studies had a methodologic quality score of poor or limited. The overall mean methodologic quality score was 10.3 $\pm$ 2.9 (out of a maximum of 18), which is considered moderate. A breakdown of the quality appraisal can be seen in Figure 2.

Study Characteristics

The key study characteristics and findings of the 46 cross-sectional studies are summarized and presented in Table 1. The sample consisted of 13 975 participants: 7387 collision-sport athletes, 662 contact-sport athletes, 3346 noncontact-sport athletes, and 2580 participants classified as controls. Collision sports were boxing, football, ice hockey, and rugby. All contact-sport athletes were soccer players. Sports classified as noncontact were archery, athletics, badminton, ballroom dancing, canoeing, cricket, fencing, field hockey, gliding, golfing, horseback riding, paragliding, pelota, rock climbing, running, sailing, skiing, squash, swimming, table tennis, track and field, triathlon, and weightlifting. Only 3 (7%) of the 46 studies included female participants.[35,54,56] Participants varied in age, medical history, socioeconomic background, concussion exposure, number of concussions reported, and types of sports played. A large proportion of these studies (n = 20) included retired NFL players.* In 7 studies, retired rugby players were investigated.[13,15,17,22,31,33,54] Participants in the remaining studies included boxers (n = 3)[29,57,58] and soccer athletes (n = 4),[26,32,38,56] whereas other authors examined a combination of former professional and amateur athletes, including university and high school football and hockey athletes (n = 12).† Of the 46 studies, 33 included a control group,‡ and 13 did not.§

Types of Outcome Measures Used

Results from a wide variety of cognitive tests were reported. The tests and their corresponding cognitive domains are presented in Table 2. Objective neuropsychological tests alone were used in 31 studies‖ to assess different aspects of cognition. Six studies[15,32,35,46,52,55] used subjective (self-reported) cognitive tests alone. The re-

References 14, 19, 21, 23, 24, 27, 28, 30, 34, 36, 37, 39, 41, 43, 44, 47, 49–51, 55.

†*References 16, 18, 20, 25, 35, 40, 42, 45, 46, 48, 52, 53.*

‡*References 13–17, 21–23, 25–27, 29, 31, 33–40, 42–45, 48–50, 52–54, 56, 57.*

§*References 18–20, 24, 28, 30, 32, 41, 46, 47, 51, 55, 58.*

‖*References 13, 14, 18, 19, 21, 24, 26–31, 33, 36–45, 48–51, 53, 56–58.*

Table 1. **Summary of Extracted Data of 46 Studies, Including Main Characteristics, Concussion Reports, Types of Cognitive Measures Used, and Primary Results[a]** **Continued on Next Page**

Study or Subgroup	Objective(s)	Participants	No. of Concussions (Mean ± SD[b])	Cognitive Measures	Primary Findings
Pearce et al[13] (2018)	Investigate long-term neurophysiologic and cognitive effects of repeated concussion injuries in former professional rugby players	25 former professional rugby athletes (mean age = 48.4 y [95% CI = 45.8, 51.0 y]) 25 controls (mean age = 48.8 y [95% CI = 45.9, 51.7 y])	Rugby athletes: Mean (CI) = 8.5 (4.7, 11.3) Controls: NA	CANTAB–IED, CANTAB–PAL, CANTAB–RTI, CANTAB–SWM, CANTAB–VRT, O'Connor Finger Dexterity test[c]	Performance on cognitive testing showed that the performance across all tests was different between groups (CANTAB–IED: $P < .01$, d = 1.04; CANTAB–PAL: $P < .01$, d = 1.06; CANTAB–SWM: $P = .02$, d = 0.77).
Clark et al[14] (2018)	Investigate the relationship between exposure to concussive/subconcussive head impacts, white-matter integrity, and functional task-related neural activity in former US football athletes	61 players (age = 58.5 ± 3.66 y): 31 collegiate players, 30 professional players	Overall = 61 (3.87 ± 5.85)	MMSE, RBANS, WAIS	No group differences were observed across the concussion history–career duration stratifications for any neuropsychological test (all $P > .05$).
Lewis et al[15] (2017)	Assess measures of corticomotor excitability and inhibition in retired rugby players	23 elite rugby players (age = 43 ± 7 y) 28 community-level rugby (age = 45 ± 8 y) 22 retired controls (age = 44 ± 9 y)	Elite rugby players: 0 concussions (n = 0; 0%), 1–2 concussions (n = 3; 13%), ≥3 concussions (n = 20; 87%) Community-level rugby: 0 concussions (n = 1; 4%), 1–2 concussions (n = 3; 11%), ≥3 concussions (n = 23; 85%) Controls: 0 concussions (n = 16; 75%), 1–2 concussions (n = 5; 21%), ≥3 concussions (n = 1; 4%)	RPQ: predominantly early (RPQ–3) and late (RPQ–13) symptoms of brain injury	No between-groups differences in RPQ
Esopenko et al[16] (2017)	Characterize retired professional ice hockey players' cognitive and psychosocial functioning in relation to concussion exposure and apolipoprotein E 4 status	33 retired professional ice hockey players (age = 54.3 ± 10.4 y) 18 controls (age = 53.5 ± 10.2 y)	Retired professional ice hockey players: 4.8 ± 2.7 Controls: 0.6 ± 0.8	BVMT–R, Cambridge Brain Sciences, Cogstate,[d] CFQ, DQ, FAS, JLO, PASAT, RAVLT, ROCFT, SDMT, SOPT, TMT–A and –B, WASI, WCST	Reliable group differences in cognitive performance were observed on 1 test of executive (WCST) and 3 tests of intellectual function (WASI vocabulary, similarities, and matrix reasoning).
Gardner et al[17] (2017)	Examine brain neurometabolite concentrations in retired rugby league players with a history of self-reported concussions	16 retired rugby players (age = 38.3 ± 4.6 y) 16 controls (age = 37.9 ± 4.9 y)	Retired players Concussions: average = 33.44 (median = 20; IQR = 7–20; range = 3–100) Concussions with loss of consciousness sustained during career; average = 5.9 (median = 3.5; IQR = 3.5–6; range, 0–30)	ACS–TOPF, COWAT, GPT, RAVLT, RCFT, RPQ, TMT–A and –B, WAIS–IV	No between-groups differences for measures of depression, anxiety, or cognitive functioning
Deshpande et al[18] (2017)	Estimate the association of playing high school football with cognitive impairment and depression at age 65 years	3904 retired high school players (age = 64.4 ± 0.8 y)	Not specified	DWR, LF	Composite cognition scores did not differ between football players and all controls, including nonsport controls and non–collision-sport controls (−0.04; 97.5% CI = −0.14, 0.05; $P = .37$).
Kuhn et al[19] (2017)	Investigate relationships among neuroimaging, neuropsychological testing, and symptoms in a cohort of retired NFL players	45 NFL players (age = 46.7 ± 9.1 y)	Concussions = 6.9 ± 6.2 "Dings" = 13.0 ± 7.9	BVMT–R, COWAT, CVLT-II, ImPACT, TMT–A and –B, TOMM, WAIS–III, WTAR	Correlations that were minimal and not different were present among the neuroimaging, neurocognitive, and symptom scores examined in this cohort of NFL retirees.

Table 1. Continued From Previous Page

Study or Subgroup	Objective(s)	Participants	No. of Concussions (Mean ± SD[b])	Cognitive Measures	Primary Findings
Montenigro et al[20] (2017)	Develop a metric to quantify cumulative repeated head-impact exposure from football and to examine the association between repeated head-impact and long-term clinical outcomes	93 former high school and collegiate football players (age = 47.3 ± 13.9 y)	Concussion history median ± IQR = 20 ± 3	BRIEF–A, BTACT	Mean scores on the BTACT indicated that the entire sample was, on average, cognitively normal.
Strain et al[21] (2017)	Assess the relationship of white-matter integrity and performance on the BNT in a group of retired professional football players and a control group	25 retired NFL players (age = 59.4 ± 11.8 y) 22 controls (age = 61.1 ± 12.2 y)	Not specified	BNT	The mean BNT *T* score of the retired athletes was lower than that of the control group (*P* = .005).
McMillan et al[22] (2017)	Investigate symptoms and a range of cognitive and health outcomes in retired rugby players with a history of repeated concussion	52 retired international rugby players (age = 53.5 ± 13.0 y) 29 controls (age = 55.1 ± 9.0 y)	Retired international rugby players = 13.9 ± 18.9 Controls = 0.3 ± 0.5	GPT, JLO, MOCA, RAVLT, RPQ, SDMT, SART, SF–36, TMT–B	Retired international rugby players performed poorer than controls on a test of verbal learning (*P* = .02). No differences on all other cognitive tests were found (*P* > .05).
Alosco et al[23] (2017)	Examine olfactory function between former NFL players and controls Investigate the association between the B–SIT and behavioral/mood and neuropsychological tests in the former NFL players	95/96 former NFL players (age = 55.29 ± 7.88 y; 1 player was excluded due to poor effort on testing) 28 controls (age = 57.14 ± 6.94 y)	Former NFL players Concussions: median = 50 Concussions resulting in loss of consciousness = 4.63 ± 16.45	BRI, BRIEF–A, B–SIT, COWAT, D-KEFS, NAB–LL, ROCFT, TMT–A and –B, WAIS–R, WCST, Map Reading Test, Naming Test, Animal Fluency	In the former NFL players, lower olfactory test scores were correlated with worse neuropsychological and neuropsychiatric functioning.
Solomon et al[24] (2016)	Investigate an association between years of exposure to pre–high school football (< 12 y) and neuroradiologic, neurologic, and neuropsychological outcomes in later life	45 retired NFL players (age = 46.7 ± 9.1 y)	6.9 ± 3.2	BVMT–R, COWAT, CVLT–II, ImPACT, MMSE, TMT–A and –B, TOMM, WAIS–III, WTAR	Neurocognitive test scores did not demonstrate a relationship with years of exposure to pre–high school football.
Multani et al[25] (2016)	Evaluate the effect of repetitive concussions in retired professional football players on white-matter tracts, self-reported symptoms, and neuropsychological assessment	18 retired professional football players (age = 49.6 ± 12 y) 17 healthy male controls (age = 46.7 ± 10 y)	Retired professional male football players = 5.4 ± 4 Healthy male controls = 0	Cognitive self-report questionnaire, RVDLT, WTAR	Retired players reported more neuropsychiatric and cognitive symptoms than healthy controls and worsening of these symptoms since their last concussion.
Koerte et al[26] (2016)	Evaluate cortical thickness in former professional soccer players using high-resolution structural magnetic resonance imaging	15 former soccer players (age = 49.3 ± 5.1 y) 15 controls (age = 49.6 ± 6.4 y)	Not specified	TMT–A and –B, ROCFT	All soccer players and controls tested within normal range for age for all cognitive tests.
Gardner et al[27] (2016)	Characterize magnetic resonance imaging features of the septum pellucidum between retired NFL players with a history of repeated concussive/subconcussive head traumas and controls	17 retired NFL players (age = 54.6 ± 15.8 y) 17 controls (age = 54.7 ± 15.8 y)	Not specified	MMSE	No difference in MMSE score (27.1 ± 1.7 versus 25.9 ± 3.3; *P* = .3)
Wright et al[28] (2016)	Determine whether concussion history and cognitive reserve could be used to create an index to predict cognitive outcomes in retired American football players	40 retired NFL players (age = 46.38 ± 10.75 y)	3.93 ± 3.95	AMNART, CVLT–II, FAS, ROCFT, SDMT, TMT–A and –B,	Retired NFL players displayed deficits in attention and processing speed, verbal memory, nonverbal memory, and executive ability.
Wilde et al[29] (2016)	Evaluate the effects of boxing on brain structure and cognition	10 boxers (8 retired, 2 active; age = 45.7 ± 9.71 y) 9 controls (age = 43.44 ± 9.11 y)	Not specified	SRTT, VSRT	Word-list recall was impaired in the boxers (*P* = .006), and implicit memory was preserved (*P* < .04).

Table 1. Continued From Previous Page

Study or Subgroup	Objective(s)	Participants	No. of Concussions (Mean ± SD[b])	Cognitive Measures	Primary Findings
Amen et al[30] (2016)	Determine whether low perfusion in specific brain regions on neuroimaging can accurately separate professional football players from healthy controls	161 retired NFL players (age = 52 ± 14.2 y) 124 for SPECT control group (age = 44 ± 16.6 y)	Not specified	CPT–II, MicroCog, or WebNeuro	Neuropsychological assessments showed 92% of players had decreased general cognitive proficiency, 86% had decreased information processing speed, 83% had memory loss, 83% had attentional deficits, and 85% had executive-function impairment.
Hume et al[31] (2017)	Investigate cognitive function in former professional rugby players and assess the association between concussion history and cognitive function	103 retired elite rugby players (age = 41.3 ± 7.5 y) 198 retired community rugby players (age = 44.9 ± 8.4 y) 65 retired noncontact sport players (age = 42.1 ± 7.7 y)	Elite rugby players = 3.5 ± 2.0 Community rugby players = 2.9 ± 2.2 Noncontact-sport players = 0.4 ± 0.8	CNS Vital Signs	The elite rugby players performed worse than the noncontact-sport players on tests of complex attention, processing speed, executive functioning, and cognitive flexibility.
Vann Jones et al[32] (2014)	Investigate the hypothesis that chronic low-level head trauma due to heading is associated with persistent cognitive decline	92 former professional players (age = 67.45 ± 6.96 y)	Not specified	TYM	Compared with the only large United Kingdom-based MCI prevalence study of men, the authors demonstrated no difference between MCI among the sample of ex-professional footballers and a large sample of men in Wales.
Decq et al[33] (2016)	Assess the prevalence of major depressive disorder, mild cognitive disorders, and headache in retired rugby players and explore the link between scores and the number of reported concussions	239 retired rugby players (median age = 52 y; IQR = 49–55.75 y) 138 other retired sportsmen (median age = 52 y; IQR = 49–55 y)	Rugby players = 3.1 ± 5.01 Other retired sportsmen = 0.68 ± 1.83	F–TICS–m	A higher rate of mild cognitive disorders was observed in retired rugby players (57%) than in other retired sportsmen (40%; $P = .005$).
Koerte et al[34] (2016)	Characterize, neuroimaging features of cavum septi pellucidi between former NFL players who present with cognitive, mood, and behavioral symptoms and asymptomatic noncontact-sport athletes	72 former NFL players (age = 54.53 ± 7.97 y) 14 former professional non-contact–sport athletes (age = 57.14 ± 7.35 y)	Not specified	BRI, BRIEF–A, NAB–LL, NAB–Map Reading, NAB–Naming, ROCFT, TMT–A and –B, WAIS–R, WCST, WRAT–4	Former professional NFL players demonstrated lower outcome scores in most tests of cognitive functioning and higher scores in behavioral evaluations.
Meehan et al[35] (2016)	Determine whether the exposure to the subconcussive blows that occur during National Collegiate Athletic Association Division III collision sports affect later-life neurobehavioral quality-of-life measures	3656 men and women Age < 40 y = 538 (14.7%), 40–44 y = 452 (12.4%), 45–49 y = 571 (15.6%), 50–54 y = 744 (20.4%), 55–59 y = 551 (15.1%), 60–64 y = 382 (10.5%), 65–70 y = 367 (10.0%), >70 y = 47 (1.3%)	Diagnosed concussion in collision-sport athletes = 283 (7.6%), contact-sport athletes = 121 (3.3%), noncontact-sport athletes = 177 (4.8%), nonathletes = 255 (6.9%) Undiagnosed concussion in collision-sport athletes = 396 (10.7%), contact sport athletes = 134 (3.6%), noncontact sport athletes = 102 (2.8%), nonathletes = 113 (3.1%)	Neuro–QoL, PROMIS	Athletes with a history of concussion had lower scores, indicating worse self-reported health, on measures of general concerns regarding cognition, executive function, and positive affect.
Coughlin et al[36] (2015)	Investigate cognitive, molecular, and structural markers in former NFL players	9 retired NFL players (age = 64.81 y) 9 controls (age = 58.33 y)	Retired NFL players: n = 12.90	CVLT–II	Former players had varied performance on a test of verbal learning and memory.

Table 1. Continued From Previous Page

Study or Subgroup	Objective(s)	Participants	No. of Concussions (Mean ± SD[b])	Cognitive Measures	Primary Findings
Stamm et al[37] (2015)	Determine the relationship between exposure to repeated head impacts through tackle football before age 12 y and later-life executive function, memory, and estimated verbal intelligence quotient	21 former NFL players AFE < 12 y (age = 51.95 ± 1.33 y) 21 former NFL players AFE ≥ 12 y (age = 52.33 ± 1.33 y)	AFE < 12 y = 392.00 ± 145.40 AFE ≥ 12 y = 370.30 ± 234.90	NAB–LL, WCST, WRAT–4	Former NFL players in the AFE <12 y group performed worse than the AFE ≥ 12 y group on all measures of the NAB–LL, WCST, and WRAT–4.
Koerte et al[38] (2015)	Evaluate neurochemistry by using magnetic resonance spectroscopy and neurocognitive performance in former professional soccer players without a known history of concussion but with a history of extensive heading and former noncontact-sport athletes	11 former soccer players (age = 52.0 ± 6.8 y) 14 former noncontact sport athletes (age = 46.9 ± 7.9 y)	Not specified	TMT–A and –B, ROCFT	All soccer players and controls tested within the normal range for age for TMT–A and –B and ROCFT.
Strain et al[39] (2015)	Assess the relationship of memory performance with hippocampal volume and concussion history in retired NFL athletes with or without a diagnosis of MCI	28 retired NFL athletes (MCI = 8; age = 58.1 ± 13 y) 27 controls (MCI = 6; age = 59 ± 12 y)	Retired NFL athletes MCI = 3.8 ± 3.5 Retired NFL athletes with MCI and concussion history = 4.6 ± 3.6	BNT, CVLT–II, ROCFT, SORT	No differences were found on the ROCFT. The CVLT–II scores were worse in athletes than controls (P = .002), athletes with no MCI than athletes with MCI (P < .001), and athletes with MCI than controls (P < .001).
Terry et al[40] (2015)	Examine neural activation, verbal memory, and behavioral scores on the fMRI paradigm between individuals who sustained at least 2 football-related concussions and controls	25 football players (age = 52.0 ± 8.05 y) 16 controls (age = 49.1 ± 8.3 y)	4.3 ± 3.7	CVLT–II, WMS–IV, WTAR	Concussive history was not associated with worse memory functioning on neuropsychological tests or worse behavioral performance.
Casson et al[41] (2014)	Perform clinical neurological, neuropsychological, and neuroradiologic examinations on a group of retired NFL players	45 retired NFL players (age = 45.6 ± 8.9 y)	6.9 ± 6.2	MMSE, ImPACT	Most retired players had normal clinical mental status and CNS neurologic examinations. Neuropsychological testing revealed isolated impairments in 11 players (24%), but none had dementia.
Tremblay et al[42] (2014)	Investigate white-matter integrity and cognitive and motor function in retired athletes with a history of concussions	15 retired athletes (age = 60.87 ± 7.51 y) 15 controls (age = 58.13 ± 5.28 y)	Retired athletes = 2.08 ± 1.31	EFT, MMSE, RAVLT, TMT–A and –B, SDMT, SRTT, TCFT	Most neuropsychological tests did not reveal clinically important differences between athletes and controls. Retired athletes showed reduced semantic verbal fluency (P = .04) and delayed recall (P = .03) and recognition conditions of the TCFT (P = .02).
Hart et al[43] (2013)	Assess for the presence of cognitive impairment and depression in aging former NFL players and identify neuroimaging correlates of these dysfunctions	34 retired NFL players (mean age = 61.8 y, range = 41–79 y) 26 controls (mean age = 60.1 y, range = 41–79 y)	32/34 Retired NFL players ≥ 1 (average = 4.0) Mean per participant for Grade 1 = 2.0, Grade 2 = 0.5, Grade 3 = 1.6	BNT, COWAT, CVLT–II, ROCFT, SORT, TMT–A and –B, WAIS–IV, WASI	Differences were found on BNT, CVLT–II, ROCFT, and SORT. No differences were found on the TMT, WAIS–IV, and COWAT.
Hampshire et al[44] (2013)	Evaluate the performances and brain activation patterns of retired NFL players relative to controls using an fMRI-optimized neuropsychological test of executive function	13 NFL alumni Controls were not specified	Not specified	CANTAB–TOTSPT	Behaviorally, the NFL alumni showed subclinical and modest performance deficits in executive function.

Table 1. Continued From Previous Page

Study or Subgroup	Objective(s)	Participants	No. of Concussions (Mean ± SD[b])	Cognitive Measures	Primary Findings
Pearce et al[45] (2014)	Investigate corticomotor excitability and inhibition, cognitive functioning, and fine-motor dexterity in retired elite and amateur Australian football players with a history of concussions	40 Australian football players: 20 elite players (age = 49.7 ± 5.7 y), 20 amateur players (age = 48.4 ± 6.9 y) 20 controls (age = 47.56 ± 6.85 y)	Elite players = 3.70 ± 2.89 Amateur players = 2.40 ± 1.56	CANTAB–PAL, CANTAB–RTI, CANTAB–SWM	Reaction time showed differences between the healthy control group and the combined Australian football groups ($P = .003$), with no differences between the 2 Australian football groups ($P = .06$). No differences were observed when comparing the healthy control group and the combined football groups on the CANTABL–PAL and –SWM. However, within the Australian football players, the amateur player group performed worse than the elite group.
Seichepine et al[46] (2013)	Examine executive function in current and retired collegiate and professional football players	64 retired collegiate and professional football players (age = 47 ± 13.6 y, range = 25–81 y)	56/64 Participants: 55 6/64 Participants: 100–140 1/64 Participants: approximately 350 1/64 Participants: approximately 20 000	BRIEF–A	Group differences were observed between football players and normative data for healthy adults on the BRIEF–A in the following areas: Global Executive Composite ($P < .05$), Metacognition Index ($P < .05$), and Behavioral Regulation Index ($P < .05$).
Randolph et al[47] (2013)	Explore the prevalence of cognitive impairment in a sample of retired NFL players	41 retired NFL players selected from 513 players who completed surveys from previous study (age = 64.2 ± 5.5 y) 41 cognitively normal participants extracted from RBANS normative data (age = 64 ± 5.8 y)	Not specified	RBANS	RBANS total mean score was lower for the NFL players than the healthy control sample ($P = .002$).
Tremblay et al[48] (2013)	Investigate the neuroimaging profile of former university athletes with concussions in relation to cognition	30 former university athletes 15 experiment group (age = 60.87 ± 7.51 y), 15 controls (age = 58.13 ± 5.28 y)	Experimental group = 24.00 ± 4.55 Controls = no history of concussion	Color Trails test (forms A and B), MMSE, RAVLT, SDMT, TCFT	Relative to controls, former athletes showed reduced semantic verbal fluency ($P = .040$) and altered episodic memory on both delayed-recall ($P = .026$) and recognition ($P = .015$) conditions of the TCFT, whereas performance on the copy trial did not differ across groups ($P > .15$).
Ford et al[49] (2013)	Examine long-term neural changes associated with multiple sport-related concussion using event-related fMRI	27 retired NFL players: 15 with low-level concussion history (age = 64.1 ± 6.8 y), 12 with high-level concussion history (age = 62.6 ± 5.0 y) 14 controls (age = 62.2 ± 6.3 y)	Low-level concussion history (≤2 concussions) = 1.07 ± 0.96 High-level concussion history (≥3 concussions) = 6.5 ± 5.1	BNT, COWAT, memory paradigm, MMSE, WAIS–III, WTAR, Telephone Interview for Cognitive Status, TMT–B	Both concussion groups demonstrated relational memory impairments relative to the age-matched group ($P < .05$).
Willeumier et al[50] (2012)	Investigate the effects of body mass as measured by waist-to-height ratio on regional cerebral blood flow using SPECT	76 retired NFL athletes: 38 healthy weight (age = 58 ± 9.6 y), 38 overweight (age = 58 ± 13.3 y)	Not specified	MicroCog	Between-groups differences were found in general cognitive proficiency and general cognitive function ($P < .025$). Overweight athletes had decreases in attention ($P = .01326$), general cognitive proficiency ($P = .012$), and memory ($P = .005$).

Table 1. Continued From Previous Page

Study or Subgroup	Objective(s)	Participants	No. of Concussions (Mean ± SD[b])	Cognitive Measures	Primary Findings
Amen et al[51] (2011)	Determine whether, compared with a healthy control group, a retired NFL players group would exhibit decreased regional cerebral blood flow consistent with previous brain trauma and compromised neuropsychological functioning	100 active and retired NFL players (age = 57.27 ± 12.37 y) 20 for SPECT control group (age = 50.0 ± 16.1 y)	Not specified Mean loss-of-consciousness episodes = 2.693 Loss-of-consciousness episodes: 0 episodes = 37, 1 episode = 15, 2 episodes = 15, 3–5 episodes = 18, >5 episodes = 14	CPT–II, MCIS, MicroCog	Players scored in the bottom half of the percentile placements on all measures, including general cognitive functioning, general cognitive proficiency, processing speed, processing accuracy, attention, reasoning, and memory and excepting spatial processing and reaction time, which were both in the top half of the percentile placements.
Hinton et al[52] (2011)	Determine the relative influence of current exercise and diet on the late-life cognitive health of former National Collegiate Athletic Association Division I collision-sport athletes (ie, football players) compared with non–collision-sport athletes and nonathletes	214 former Division I collision-sport athletes (football players) 136 former Division I non–collision-sport athletes (other athletes) 50 former nonathletes (nonathletes)	Not specified	CDS	Former football players reported more cognitive difficulties and worse physical and mental health than controls.
De Beaumont et al[53] (2009)	Investigate electrophysiological, motor, and cognitive measures in former athletes who sustained their last sport concussion > 30 y before the study	19 former Canadian university-level athletes (age = 60.79 ± 5.16 y) 21 controls (age = 58.89 ± 9.07 y)	Former Canadian university-level athletes: range = 1–5 Controls: no history of concussion or neurologic insult	MMSE, ROCFT	Former athletes with concussion obtained an equivalent total score on the MMSE to that of former athletes with no history of concussion ($P > .05$). Every participant from both groups scored within the normal range on the MMSE.
Thornton et al[54] (2008)	Examine the extent to which lifetime concussion exposure is associated with neurocognitive and symptomatic status in competitive versus recreational/retired rugby players and differential complications between groups	Male and female retired players 37 no heavy concussions (age = 32.14 ± 12.41 y), 29 1–2 heavy concussions (age = 28.72 ± 10.20 y), 35 ≥3 heavy concussions (age = 34.03 ± 12.06 y)	Divided participants into heavy concussion-exposure groups Sample size (female to male): grades 2 and 3: no heavy exposure to concussions = 37 (8:29), 1–2 heavy exposures = 39 (4:35), ≥3 heavy exposures = 35 (1:34)	CCFT, ETS Kit–V2 and –V3, PCSC, RAVLT, TMT–A and –B, WAIS–III, WCST, WMS–III	Participants with no heavy concussions reported fewer memory complaints ($d = -0.68$), less distress ($d = -0.76$), and fewer overall (total) postconcussion symptoms ($d = -0.65$) than those with ≥3 heavy concussions.
Guskiewicz et al[55] (2005)	Investigate the association between recurrent concussion and late-life cognitive impairment in retired professional football players	2552 retired professional footballers (age = 53.8 ± 13.4 y)	≥ 1 = 1513 ≥3 = 597	SF–36 (including MCS)	Retired players with ≥3 reported concussions had a 5-fold prevalence of MCI diagnosis and a 3-fold prevalence of reported substantial memory problems compared with retirees without a history of concussion.

Table 1. Continued From Previous Page

Study or Subgroup	Objective(s)	Participants	No. of Concussions (Mean ± SD[b])	Cognitive Measures	Primary Findings
Downs and Abwender[56] (2002)	Investigate neuropsychological function between older and retired soccer players and swimmers	32 male and female soccer players (15 men, 11 women; age = 19.81 ± 1.50 y) 6 older male soccer players (current/ retired professionals; age = 41.5 ± 9.77 y) Control groups: 22 male and female swimmers (7 men, 15 women; age = 19.50 ± 1.22 y), 7 adult male swimmers (age = 42.86 ± 15.09 y)	Not specified	CPT, PASAT, WCST	Soccer players performed worse than swimmers on tests of conceptual thinking. The older soccer group performed particularly poorly on measures of concentration, reaction time, and conceptual thinking.
Murelius and Haglund[57] (1991)	Analyze possible chronic brain damage in 47 former amateur boxers who started their careers after the introduction of stricter Swedish amateur boxing rules	25 high-match boxers (age = 30.5 ± 5.1 y) 25 low-match boxers (age = 32.3 ± 5.6 y) 25 soccer players (age = 33.0 ± 6.0 y) 25 track and field athletes (age = 33.4 ± 5.4 y)	Not specified	Synonyms test of verbal understanding, Block design test (Koh's cubes), TMT–A and –B, FTT, Claeson-Dahl Verbal Learning, Claeson-Dahl Verbal Retention, memory for designs, and motor functions of the hand	The groups differed on only 1 test. Boxers who had participated in a large number of bouts had slightly inferior finger-tapping performance. None of the boxers were considered to have definite signs of intellectual impairment.
Casson et al[58] (1984)	Dispute the claims that chronic encephalopathy occurs in only an occasional poorly skilled fighter or those who are poorly educated or abusing drugs and alcohol	18 Retired athletes: 13 former boxers, 2 active professional boxers, 3 active Golden Glove boxers (mean age = 36 y)	Not specified	BGT, DST, TMT, WMS	All former and active professional boxers had abnormal results on at least 2 of the 4 main test, and 8/17 had abnormal computed tomography scans; these had a higher mean impairment index on neuropsychological testing than those with normal computed tomography scans ($P < .001$).

Abbreviations: AFE, age of first exposure; CI, confidence interval; fMRI, functional magnetic resonance imaging; IQR, interquartile range; MCI, mild cognitive impairment; NA, not applicable; NFL, National Football League; SPECT, single photon emission computed tomography.

[a] Abbreviations of the cognitive measures are defined in Appendix 2.
[b] Unless otherwise indicated.
[c] Lafayette Instruments, Lafayette, IN.
[d] Cogstate Ltd, New Haven, CT.

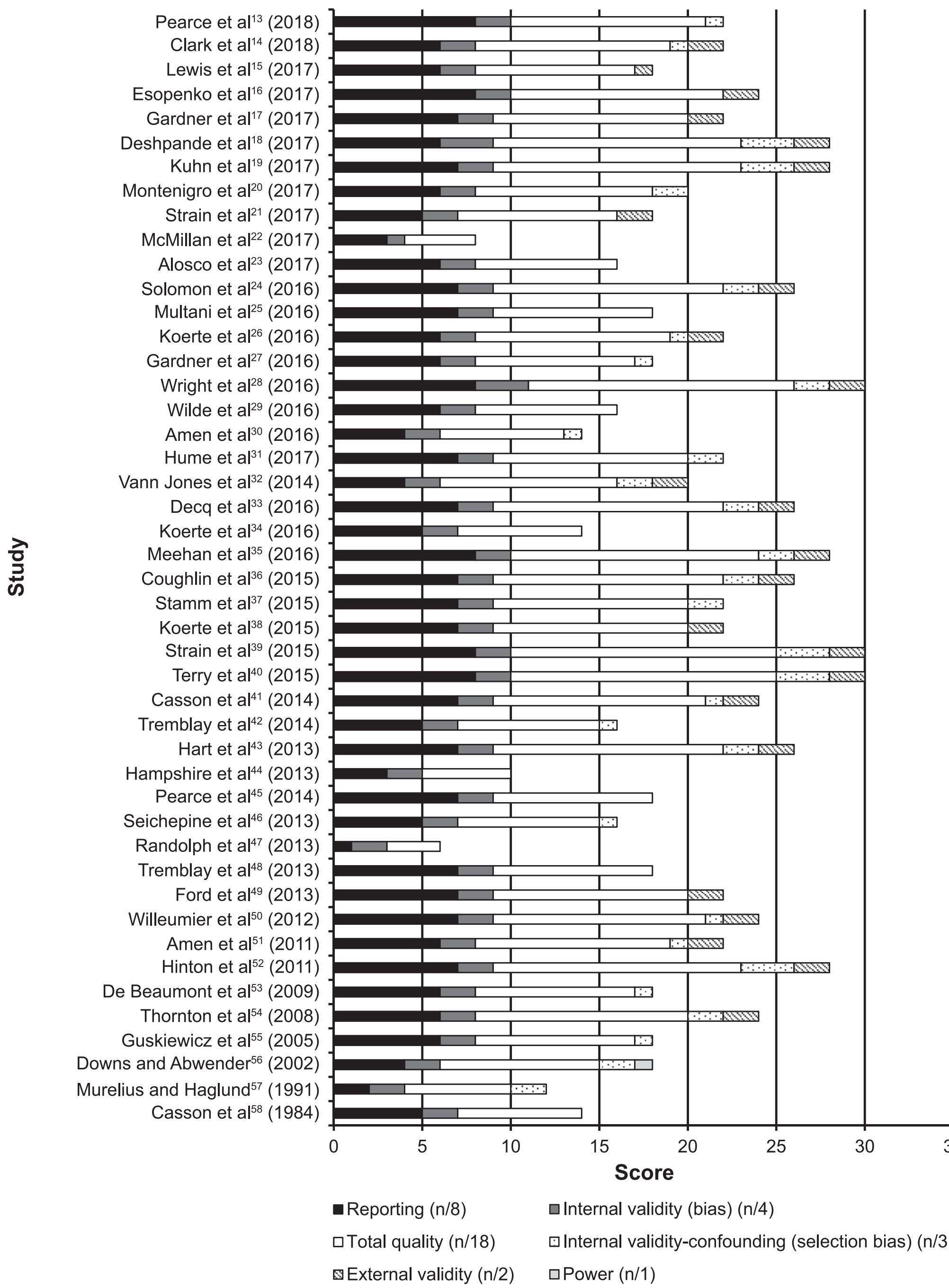


Figure 2. Summary of quality appraisal of the included studies using the Downs and Black checklist.

maining 9 studies¶ used a combination of objective and subjective tests. Cognitive tests were categorized according to the predominant cognitive domain assessed. The 9 cognitive domains assessed were global cognitive ability, attention, memory, executive function, language, psychomotor function, intelligence, perception, and self-reported cognitive functioning (Figure 3). Memory was the most commonly studied cognitive health outcome (n = 31, 67%), followed by attention (n = 17, 37%) and global cognitive ability (n = 16, 35%). The studies by Kuhn et al[19] and Tremblay et al[42] were excluded from the analysis, as the cognitive results were duplicates of those reported by Solomon et al[24] and Tremblay et al,[48] respectively. The cognitive results are shown in Table 3.

Cognitive Findings

Global Cognitive Ability. Global cognitive ability was assessed in 16 studies.# Individual cognitive tests are summarized in Table 2. Eleven of the 16 (69%) studies** showed no evidence for increased global cognitive difficulties in retired athletes compared with control participants or normative data, whereas the other 5 (31%)

¶*References 16, 17, 20, 22, 23, 25, 34, 47, 54.*

#*References 14, 16, 20, 22, 24, 27, 30, 31, 33, 41, 47–51, 53.*

***References 14, 16, 20, 22, 24, 27, 31, 41, 48, 49, 53.*

Table 2. Summary of Cognitive Tests Used Across Studies and Corresponding Cognitive Domains of Interest[a]

Domain (No. of Studies)	Domain Description	Cognitive Tests[b]	References
Global cognitive ability (16)	A broad array of cognitive domains	BTACT, Cambridge Brain Sciences, Cogstate,[c] CNS Vital Signs, F–TICS–m, ImPACT, MicroCog, MMSE, modified MMSE, MOCA, RBANS, WebNeuro	14,16,20,22,24,27,30,31,33,41,47–51,53
Attention (17)	Ability to concentrate and focus on specific stimuli; attention has multiple subprocesses specialized for different aspects of attentional processing and complex attention tasks, such as selective and divided attention	Color Trails Test (forms A and B), CPT–II, EFT, PASAT, SART, SDMT, SRTT, TMT, WAIS	14,16,17,22–24,26,28,29,31,38,41,43,48,49,54,57
Memory (31)	Involves the registration, storage, recognition, and retrieval of information	Animal fluency, BVMT–R, CANTAB–PAL, CANTAB–SWM, CVLT–II, DWR, LF, NAB–LL, NAB–Map Reading test, RAVLT, ROCFT, RVDLT, SOPT, SORT, TCFT, TOMM, TYM, VSRT, WMS–IV	13,16–18,22–26,28–32,34,36–41,43,45,48–51,53,54,57,58
Executive function (11)	Includes planning, decision making, working memory, responding to feedback, inhibition, and mental flexibility	CANTAB–IED, CANTAB–TOTSPT, D-KEFS, WCST	13,16,23,28,31,34,37,41,44,54,56
Language (8)	Includes object naming, word finding, fluency, grammar, syntax, and receptive language	BNT, COWAT, FAS, LF	16,17,21,23,24,39,43,49
Psychomotor function (6)	Relationship between cognitive functions and physical movements	CANTAB–VRT, CNS Vital Signs (motor speed domain), FTT, GPT, O'Connor Finger Dexterity test[d]	13,17,22,31,45,56
Intelligence (12)	Premorbid intelligence quotient refers to one's intellectual ability level before the onset of disorders, such as mild cognitive impairment and Alzheimer disease; estimating disease severity is important.	ACS–TOPF, CCFT, ETS Kit–V2 and –V3, WAIS–III and –IV, WASI, WRAT–4, WTAR	14,16,17,24,25,34,37,40,41,43,49,54
Perception (3)	Recognition and interpretation of sensory information from environment; includes response to this information for interacting with environment	B–SIT, JLO	16,22,23
Self-reported cognitive functioning (14)	The "self-experience" of cognition; a *self-report* is any method (eg, survey, questionnaire, or poll) that involves asking participant about feelings, attitudes, beliefs, etc	AD8, BRI, BRIEF–A, CDS, Cognitive Failures Questionnaire, cognitive self-report questionnaire, DQ, MCIS, Neuro–QoL, PCSC, PROMIS, RPQ, SF–36 (including MCS)	15–17,20,22,23,25,34,35,46,47,52,54,55

[a] The results of Kuhn et al[19] and Tremblay et al[42] were excluded, as the cognitive results were taken from Solomon et al[24] and Tremblay et al,[48] respectively.
[b] Abbreviations are defined in Appendix 2.
[c] Cogstate Ltd, New Haven, CT.
[d] Lafayette Instruments, Lafayette, IN.

studies did.[30,33,47,50,51] Decq et al[33] found that retired rugby players had a higher rate of mild cognitive disorders on a modified version of the Telephone Interview for Cognitive Status than players from a variety of other sports. However, the cognitive results were not associated with reported concussions. Amen et al[51] and Willeumier et al[50] assessed the same cohort of retired NFL players and reported decreases from normal values in cognitive functioning and proficiency. Amen et al[30] also studied a large number of the same participants and demonstrated relationships between position and body mass measured by waist-to-height ratio and cognitive function. Randolph et al[47] observed that retired NFL players scored worse than the healthy control sample on the Repeatable Battery for the Assessment of Neuropsychological Status ($P = .002$). The meta-analysis of 3 studies measuring global cognition using the Mini-Mental State Examination showed no difference between groups for this outcome (mean difference [MD] = 0.09; 95% confidence interval [CI] = –0.35, 0.54; $P = .68$; Figure 4A). Overall, most studies did not support decreased global cognitive ability or proficiency in retired athletes.

Attention. Tests of attention were administered in 17 (37%) of 46 investigations.†† In 3 studies,[23,28,31] investi-

††*References 14, 16, 17, 22–24, 26, 28, 29, 31, 38, 41, 43, 48, 49, 54, 57.*

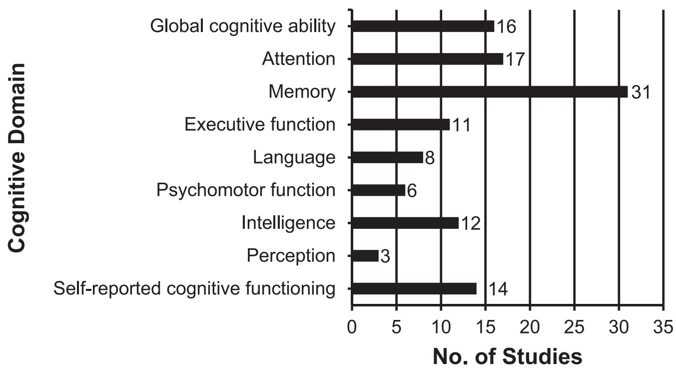


Figure 3. Summary of cognitive domains assessed in the included studies.

gators found that retired athletes had decreased attention scores. Alosco et al[23] reported that retired NFL players performed worse than controls on the Trail Making Test (TMT; $P = .005$). Wright et al[28] determined that retired NFL players had attentional and processing-speed deficits on the TMT and the Symbol Digit Modalities Test compared with normative values. Hume et al[31] noted that the elite rugby group performed worse on the Online Computerized Neurocognitive Assessment Software–Vital Signs test of complex attention than the noncontact-sport athletes (effect size = –0.67; 95% CI = –1.07, –0.26). Based on the variety of tests administered to investigate attention, the balance of the evidence did not support decreased functioning in retired athletes. The results from 6 studies that assessed attention using the TMT are illustrated in Figures 4B and 4C. Neither the TMT–A (MD = –0.52; 95% CI = –3.40, 2.36; $P = .72$) nor the TMT–B (MD = –1.41; 95% CI = –4.58, 1.76; $P = .38$) revealed between-groups differences when the findings were pooled.

Memory. Memory was assessed in 31 studies‡‡ using various tests (Table 2). The authors of 14 (45%) studies§§ reported normal functioning on memory tests. Seventeen (55%) studies|||| showed decreases in memory functioning among retired athletes compared with control participants or normative data. In 2 (6%) investigations,[39,43] researchers determined that retired NFL players performed worse than control participants on the California Verbal Learning Test. McMillan et al[22] identified worse performance on the Rey Auditory Verbal Learning Test by retired rugby players compared with the control group. Wilde et al[29] found that word-list recall on the Verbal Selective Reminding Test was worse in boxers than in control participants, whereas Koerte et al[34] observed that retired NFL players had decreased performance on a list-learning task. Tremblay et al[48] described decreased scores by retired American football athletes on the Rey Auditory Verbal Learning Test and Taylor Complex Figure Test. Using the Spatial Working Memory and Paired Associates Learning subtests to assess memory and reported differences, Pearce et al[13] noted that retired rugby players performed more poorly than the control group. Researchers in the remaining 4 studies[28,36,37,58] reported deficits in memory tests; however, no control groups were included. The same group of retired NFL players studied by Amen et al[51] and Willeumier et al[50] had decreases in memory on the MicroCog memory subset. Similar results were shown by Amen et al,[30] who studied a large proportion of the same players. In addressing relational memory impairments among retired athletes, Ford et al[49] described the multiple-concussion group as worse at recognizing intact pairs as "old" (intact-pair hits) than the age-matched group ($P < .05$). Overall, the results were mixed. However, preliminary evidence of memory decline exists in retired athletes. Our meta-analysis of 3 studies using the California Verbal Learning Test outcome measure indicated that retired athletes performed worse than control participants (MD = –6.48; 95% CI = –10.07, –2.88; $P < .001$; Figure 4D). Our meta-analysis of 5 studies that used the Rey-Osterreith Complex Figure Test outcome measure also showed that the control group outperformed retired athletes (Rey-Osterreith Complex Figure Test Copy and Immediate Recall: MD = –4.85; 95% CI = –7.15, –2.54; $P < .001$; and Rey-Osterreith Complex Figure Test Delayed Recall: MD = –5.36; 95% CI = –7.79, –2.94; $P < .001$; Figures 4E and 4F, respectively).

Executive Function. Tests of executive function were used in 11 investigations.¶¶ The most commonly used instrument was the Wisconsin Card Sorting Test.[16,34,37,54,56] Six (55%) studies[13,16,28,31,37,56] demonstrated decreased executive function in retired athletes, whereas the remaining 5 (45%) studies did not.[23,34,41,44,54] Three studies[16,37,56] showed decreased performance on the Wisconsin Card Sorting Test in retired athletes compared with control participants. Wright et al[28] found that retired NFL players displayed deficits in executive ability compared with normative data (Heaton system: 37.5%; Wechsler system: 20.0%). Pearce et al[13] reported that retired rugby players performed worse than the control group on the Cambridge Neuropsychological Test Automated Battery–Intra-Extra Dimensional Set Shift subtest. Hume et al[31] determined that the retired elite-rugby group performed worse on tests of executive function (effect size = –0.41; 95% CI = –0.80, –0.02) on the Online Computerized Neurocognitive Assessment Software–Vital Signs. Overall, the results were mixed. However, evidence of a decline in executive function in retired athletes exists.

Language. Eight groups[16,17,21,23,24,39,43,49] reviewed language tests, including tests of naming, speech production, and verbal fluency. The Boston Naming Test was used in 4 (50%) studies.[21,39,43,49] The mean Boston Naming Test *T* score of the retired athletes was lower than that of the control group in 2 of the 4 studies,[21,43] and no differences were found in the other 2 studies.[39,49] Esopenko et al[16] used the Phonemic Word List Generation (verbal phonemic fluency test) and found no differences between retired contact-sport athletes and control participants. The Controlled Oral Word Association Test was used in 5 investigations,[17,23,24,43,49] and no differences were identified between the retired athlete and control groups. Overall, our review showed mixed evidence of language deficits in retired athletes.

Psychomotor Function. Psychomotor function was assessed by 6 groups,[13,17,22,31,45,56] with 4 sets of researchers[13,17,22,45] reporting decreases in retired athletes compared

‡‡*References 13, 16–18, 22–26, 28–32, 34, 36–41, 43, 45, 48–51, 53, 54, 57, 58.*

§§*References 16–18, 23–25, 32, 36, 38, 40, 41, 45, 54, 57.*

||||*References 13, 22, 26, 28–31, 34, 37, 39, 43, 48–51, 53, 58.*

¶¶*References 13, 16, 23, 28, 31, 34, 37, 41, 44, 54, 56.*

with control participants. Pearce et al[13] used the Cambridge Neuropsychological Test Automated Battery–Visuomotor Reaction Time subtest and found that retired rugby players reacted more slowly to the stimulus than the control group ($P < .01$). McMillan et al[22] observed that retired rugby players had decreased fine motor coordination in the dominant hand on the Grooved Pegboard test, a measure of visual-motor coordination, whereas Gardner et al[17] reported worse scores for the nondominant hand ($P = .03$). Pearce et al[45] assessed fine motor control and learned that reaction time (both reaction to stimulus and movement time on the O'Connor Finger Dexterity Test) was better in the healthy control group than in the retired elite and amateur Australian football players ($P = .003$). The other 2 studies[31,56] did not support decreases in psychomotor function in retired athletes compared with control individuals. Evidence of difficulties in psychomotor functioning exists in retired athletes.

Intelligence. Premorbid intelligence was assessed in 12 studies.## A total of 9 studies*** showed no difference in intellectual ability in retired athletes compared with control groups. In 2 investigations,[16,34] retired athletes performed worse than control participants on intellectual function tests. Stamm et al[37] demonstrated that former NFL players exposed to tackle football before age 12 years performed worse on the Wide Range Achievement Test 4 than former NFL players exposed at age 12 or later. Overall, we did not find evidence of decreased intellectual functioning in retired athletes.

Perception. Alosco et al[23] used the Brief Smell Identification Test and reported scores that were lower among former NFL players than among noncontact control athletes. Visuospatial perception was assessed by 2 sets of researchers[16,22] who used the Judgment of Line Orientation test. No group differences were detected between retired athletes and control individuals.

Self-Reported Cognitive Functioning. In 14 studies,††† a variety of subjective self-reported cognitive functioning tests were used to compare retired athletes and control groups or normative data (Table 2). Eleven (79%) studies‡‡‡ identified increased subjective reports of cognitive difficulties experienced by former athletes. Authors of the remaining 3 studies[15,17,20] described no increase in self-reported concerns among retired athletes. We found evidence of increased sport-related cognitive concerns among retired athletes.

Rate of Mild Cognitive Impairment in Retired Athletes. Investigators in 3 studies[32,47,55] implemented self-reports rather than formal diagnoses to examine mild cognitive impairment (MCI) in retired athletes. Guskiewicz et al[55] determined that 35% of the retired NFL players self-reported cognitive difficulties, which were deemed consistent with MCI. Randolph et al[47] noted indications of possible cognitive impairment in retired NFL players: a subsample of the players was compared with a clinical sample of patients with MCI, revealing similar profiles of impairments. Conversely, Vann Jones et al[32] stated that the prevalence of possible MCI or dementia in former professional soccer players was not different from a large control sample. No association was demonstrated between low- and high-risk playing positions or length of playing career and a positive MCI screening result. Age was the only risk factor across both groups.

Pooled Summaries

Meta-analyses were conducted where possible for outcome measures using different scales and tools to assess the cognitive domains (Figure 5). The data were pooled using the standardized MD (SMD) and a random-effects model according to the Cochrane guidelines.[62] Global cognitive ability was almost different between groups (SMD = –0.14; 95% CI = –0.29, 0.00; $P = .05$; Figure 5A). The attention domain demonstrated no between-groups difference (SMD = 0.05; 95% CI = –0.14, 0.23; $P = .63$; Figure 5B). Retired players performed worse than control participants on tests of memory (SMD = –0.43; 95% CI = –0.59, –0.27; $P < .001$; Figure 5C). Assessment of executive function also revealed that control individuals outperformed retired athletes (SMD = –0.53; 95% CI = –0.78, –0.28; $P < .001$; Figure 5D). Tests of language (SMD = –0.38; 95% CI = –0.74, –0.02; $P = .04$; Figure 5E) and psychomotor function (SMD = –0.30; 95% CI = –0.50, –0.10; $P = .003$; Figure 5F) also favored control groups. The intelligence domain showed no between-groups difference (SMD = 0.01; 95% CI = –0.24, 0.26; $P = .91$; Figure 5G). Pooling of the self-report test results revealed that retired athletes reported more cognitive difficulties than control participants (SMD = –0.43; 95% CI = –0.66, –0.19; $P < .001$; Figure 5H).

Summary of Main Results

Our review focused on a qualitative synthesis of the included studies. The authors of 14 studies§§§ used a subjective, self-reported cognitive functioning test in mixed sporting populations, with 11 groups|||||| reporting increased subjective cognitive difficulties experienced by former athletes compared with control individuals or normative data. A synthesis of studies demonstrated more evidence for cognitive deficits in the areas of memory, executive function, psychomotor function, and self-reported cognitive functioning.

The balance of evidence to date did not support an association between cognitive deficits in retirement and concussion history and exposure to head impacts. Most studies (n = 33) did not identify any association between concussion history or exposure to head impacts and cognitive deficits. However, investigators in 13 (28%) of 46 studies¶¶¶ described a frequency-response relationship, with greater cognitive impairments (subjective or objective) in athletes with greater levels of exposure to head impacts or concussions. The cross-sectional nature of the studies included in this review and an insufficient number of longitudinal studies limited our ability to make causal inferences about the relationship between concussion and long-term cognitive outcomes.

##*References 14, 16, 17, 24, 25, 34, 37, 40, 41, 43, 49, 54.*

****References 14, 17, 24, 25, 40, 41, 43, 49, 54.*

†††*References 15–17, 20, 22, 23, 25, 34, 35, 46, 47, 52, 54, 55.*

‡‡‡*References 16, 22, 23, 25, 34, 35, 46, 47, 52, 54, 55.*

§§§*References 15–17, 20, 22, 23, 25, 34, 35, 46, 47, 52, 54, 55.*

||||||*References 16, 22, 23, 25, 34, 35, 46, 47, 52, 54, 55.*

¶¶¶*References 16, 20, 22, 29, 31, 37, 46, 49, 54–58.*

Table 3. Evaluation of Cognitive Outcome Measures by Cognitive Domain Effect Size (Mean Difference Interval Variance, Random Effects Model [95% Confidence Interval])[a] Extended on Next Page

Study or Subgroup	No. of Participants (Retired Athletes/ Controls)	Domain (Mean Difference [95% Confidence Interval])		
		Global Cognitive Ability	Attention	Memory
Pearce et al[13] (2018)	25/25	[b]	[b]	CANTAB–SWM: 2.20 (0.17, 4.23)[c]
Clark et al[14] (2018)	31/30	RBANS: 0.70 (−6.21, 7.61)[d]	RBANS: 7.50 (−1.27, 16.27)[d]	[b]
Lewis et al[15] (2017)	51/22	[b]	[b]	[b]
Esopenko et al[16] (2017)	33/18	Data not provided[d]	Data not provided[d]	Data not provided[d]
Gardner et al[17] (2017)	16/16	[b]	Composite cognition score[d]	Composite cognition score[d]
Deshpande et al[18] (2017)	3904/ND	[b]	[b]	No control group[d]
Montenigro et al[20] (2017)	93/ND	No control group[d]	[b]	[b]
Strain et al[21] (2017)	25/22	[b]	[b]	[b]
McMillan et al[22] (2017)	52/29	MOCA: −0.60 (−1.43, 0.23)[d]	TMT–B: 4.20 (−3.94, 12.34)[d]	RAVLT: −1.10 (−2.39, 0.19)[c]
Alosco et al[23] (2017)	95/28	[b]	TMT–A: −5.17 (−9.68, −0.66)[c]	NAB–LL: −3.81 (−8.16, 0.54)[d]
Solomon et al[24] (2016)	45/ND	No control group[d]	No control group[d]	No control group[d]
Multani et al[25] (2016)	18/17	[b]	[b]	RVDLT: 0.35 (−1.47, 2.17)[d]
Koerte et al[26] (2016)	15/15	[b]	TMT–B: −1.40 (−4.80, 2.00)[d]	ROCFT: −6.00 (−12.72, 0.72)[c]
Gardner et al[27] (2016)	17/17	MMSE: 0.00 (−2.45, 2.45)[d]	[b]	[b]
Wright et al[28] (2016)	40/ND	[b]	No control group[c]	No control group[c]
Wilde et al[29] (2016)	10/9	[b]	Data not provided[d]	Data not provided[c]
Amen et al[30] (2016)	161/ND	No control group[c]	[b]	No control group[c]
Hume et al[31] (2017)	301/65	CNS Vital Signs: 0.00 (−5.24, 5.24)[d]	CNS Vital Signs: 1.00 (−2.91, 4.91)[c]	CNS Vital Signs: −1.00 (−5.59, 3.59)[c]
Vann Jones et al[32] (2014)	92/ND	[b]	[b]	No control group[d]
Decq et al[33] (2016)	239/138	F–TICS–m: −1.02 (−1.76, −0.28)[c]	[b]	[b]
Koerte et al[34] (2016)	72/14	[b]	[b]	NAB–LL: −64.96 (−138.09, 8.17)[c]
Meehan et al[35] (2016)	1335/2321	[b]	[b]	[b]
Coughlin et al[36] (2015)	9/9	[b]	[b]	No control group[d]
Stamm et al[37] (2015)	21/21	[b]	[b]	NAB–LL: −2.48 (−4.44, −0.52)[c]
Koerte et al[38] (2015)	11/14	[b]	TMT–B: 1.00 (−2.72, 4.72)[d]	ROCFT: −5.30 (−15.82, 5.22)[d]
Strain et al[39] (2015)	28/27	[b]	[b]	CVLT–II: −7.74 (−11.71, −3.77)[c]
Terry et al[40] (2015)	25/16	[b]	[b]	CVLT–II: −1.30 (−8.29, 5.69)[d]
Casson et al[41] (2014)	45/ND	No control group[d]	No control group[d]	No control group[d]
Hart et al[43] (2013)	34/26	[b]	TMT–B: −2.20 (−11.32, 6.92)[d]	ROCFT: −4.30 (−12.43, 3.83)[c]
Hampshire et al[44] (2013)	13/NS	[b]	[b]	[b]
Pearce et al[45] (2014)	20/20	[b]	[b]	CANTAB–PAL: 1.07 (−1.27, 3.41)[d]
Seichepine et al[46] (2013)	64/ND	[b]	[b]	[b]
Randolph et al[47] (2013)	513/ND	No control group[c]	[b]	[b]
Tremblay et al[48] (2013)	15/15	MMSE: −0.20 (−0.91, 0.51)[d]	Color trails test (form B): 1.13 (−14.84, 17.10)[d]	RAVLT: −2.54 (−7.47, 2.39)[c]
Ford et al[49] (2013)	27/14	MMSE: 0.50 (−0.89, 1.89)[d]	TMT–B: 13.00 (−7.90, 33.90)[d]	Memory paradigm: −0.07 (−0.10, −0.04)[c]
Willeumier et al[50] (2012)	38/38	Data not provided[c]	[b]	Data not provided[c]
Amen et al[51] (2011)	100/ND	No control group[c]	[b]	No control group[c]
Hinton et al[52] (2011)	214/186	[b]	[b]	[b]
De Beaumont et al[53] (2009)	19/21	MMSE: 0.30 (−0.32, 0.92)[d]	[b]	ROCFT: −3.60 (−7.73, 0.53)[c]
Thornton et al[54] (2008)	74/37	[b]	WAIS–III: 0.98 (−2.96, 4.92)[d]	RAVLT: −3.54 (−7.43, 0.35)[d]
Guskiewicz et al[55] (2005)	2552/ND	[b]	[b]	[b]
Downs and Abwender[56] (2002)	38/22	[b]	[b]	[b]
Murelius and Haglund[57] (1991)	50/50	[b]	Data not provided[d]	Data not provided[d]
Casson et al[58] (1984)	18/ND	[b]	[b]	No control group[c]

Abbreviations: ND, normative data; NS, not specified.

[a] Kuhn et al[19] and Tremblay et al[42] were excluded because cognitive results were taken from Solomon et al[24] and Tremblay et al,[48] respectively.

[b] Test/domain.

[c] Athletes' results worse.

[d] Athletes' results not worse.

Table 3. Extended From Previous Page

Domain (Mean Difference [95% Confidence Interval])					
Executive Function	Language	Psychomotor Function	Intelligence	Perception	Self-Reported Cognitive Functioning
CANTAB–IED: 12.50 (4.64, 20.36)[c]	[b]	CANTAB–RTI: 15.46 (−22.39, 53.31)[c]	[b]	[b]	[b]
[b]	[b]	[b]	WAIS: −5.00 (−3.35, 13.35)[d]	[b]	[b]
[b]	[b]	[b]	[b]	[b]	RPQ: 3.50 (−2.51, 9.51)[d]
Data not provided[c]	Data not provided[d]	[b]	Data not provided[c]	Data not provided[d]	Data not provided[c]
[b]	Composite cognition score[d]	Composite cognition score[c]	Composite cognition score[d]	[b]	Composite cognition score[d]
[b]	[b]	[b]	[b]	[b]	[b]
[b]	[b]	[b]	[b]	[b]	No control group[d]
[b]	BNT: −9.40 (−15.58, −3.22)[c]	[b]	[b]	[b]	[b]
[b]	[b]	GPT: 6.20 (0.11,12.29)[c]	[b]	JLO: 0.10 (−0.88, 1.08)[d]	RPQ: 9.30 (4.14,14.46)[c]
D-KEFS: −1.40 (−2.55, −0.25)[d]	COWAT: −3.25 (−7.54, 1.04)[d]	[b]	[b]	Data not provided[c]	BRIEF-A: 1.32 (0.87, 1.78)[c]
[b]	No control group[d]	[b]	No control group[d]	[b]	[b]
[b]	[b]	[b]	WTAR: 1.93 (−3.02, 6.88)[d]	[b]	Data not provided[c]
[b]	[b]	[b]	[b]	[b]	[b]
[b]	[b]	[b]	[b]	[b]	[b]
No control group[c]	[b]	[b]	[b]	[b]	[b]
[b]	[b]	[b]	[b]	[b]	[b]
[b]	[b]	[b]	[b]	[b]	[b]
CNS Vital Signs: −5.00 (−8.80, −1.20)[c]	[b]	CNS Vital Signs: −2.00 (−5.93, 1.93)[d]	[b]	[b]	[b]
[b]	[b]	[b]	[b]	[b]	[b]
[b]	[b]	[b]	[b]	[b]	[b]
WCST: −46.16 (−106.31, 13.99)[d]	[b]	[b]	WAIS–R: −51.71 (−107.44, 4.02)[c]	[b]	BRI: 162.76 (157.58, 167.94)[c]
[b]	[b]	[b]	[b]	[b]	Data not provided[c]
[b]	[b]	[b]	[b]	[b]	[b]
WCST: −7.52 (−8.94, −6.10)[c]	[b]	[b]	WRAT–4: −8.55 (−10.06, −7.04)[c]	[b]	[b]
[b]	[b]	[b]	[b]	[b]	[b]
[b]	[b]	[b]	[b]	[b]	[b]
[b]	[b]	[b]	WTAR: 2.30 (−5.33, 9.93)[d]	[b]	[b]
No control group[d]	[b]	[b]	No control group[d]	[b]	[b]
[b]	BNT: −4.80 (−12.37, 2.77)[d]	[b]	Data not provided[d]	[b]	[b]
Data not provided[d]	[b]	[b]	[b]	[b]	[b]
[b]	[b]	CANTAB–RTI: 41.44 (8.52, 74.36)[c]	[b]	[b]	[b]
[b]	[b]	[b]	[b]	[b]	No control group[c]
[b]	[b]	[b]	[b]	[b]	No control group[c]
[b]	[b]	[b]	[b]	[b]	[b]
[b]	BNT: 0.80 (−3.36, 4.96)[d]	[b]	WAIS–III: 1.60 (−11.22, 14.42)[d]	[b]	[b]
[b]	[b]	[b]	[b]	[b]	[b]
[b]	[b]	[b]	[b]	[b]	[b]
[b]	[b]	[b]	[b]	[b]	CDS: 0.19 (0.03, 0.35)[c]
[b]	[b]	[b]	[b]	[b]	[b]
WCST: −2.11 (−5.65, 1.43)[d]	[b]	[b]	WAIS–III: −0.17 (−2.01, 1.67)[d]	[b]	PCSC: 4.31 (1.18, 7.44)[c]
[b]	[b]	[b]	[b]	[b]	No control group[c]
WCST: 27.50 (13.67, 41.33)[c]	[b]	PASAT: −10.60 (−31.10, 9.90)[d]	[b]	[b]	[b]
[b]	[b]	[b]	[b]	[b]	[b]
[b]	[b]	[b]	[b]	[b]	[b]

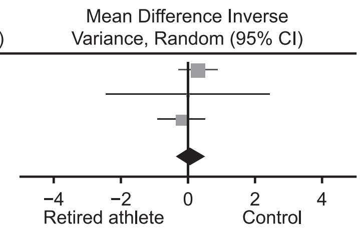
DISCUSSION

We appraised the literature regarding SRC and cognitive health outcomes in retired athletes. Our review was unique because we focused on clinical cognitive outcomes in living retired athletes. Findings suggested that certain areas of cognition may be affected by an SRC history. However, bias appeared to exist toward assessments of certain areas of cognition, such as global cognitive ability, attention, and

A

Study or Subgroup	Retired Athlete, score Mean ± SD	Retired Athlete, score Total	Control, score Mean ± SD	Control, score Total	Weight, %	Mean Difference Inverse Variance, Random (95% CI)
Clark et al[14] (2018)	29.3 ± 0.9	19	29 ± 1	21	57.6	0.30 (−0.29, 0.89)
De Beaumont et al[53] (2009)	26.5 ± 2.5	17	26.5 ± 4.5	17	3.3	0.00 (−2.45, 2.45)
Decq et al[33] (2016)	29.2 ± 0.86	15	29.4 ± 1.12	15	39.1	−0.20 (−0.91, 0.51)
Total		51		53	100.0	0.09 (−0.35, 0.54)

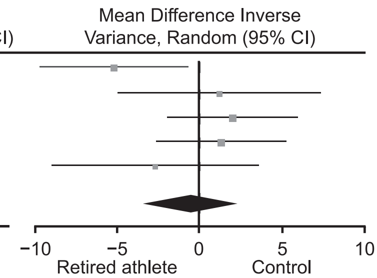
Heterogeneity: $\tau^2 = 0.00$; $\chi^2_2 = 1.13$, $P = .57$, $I^2 = 0\%$
Test for overall effect: $Z = 0.41$; $P = .68$



B

Study or Subgroup	Retired Athlete, score Mean ± SD	Retired Athlete, score Total	Control, score Mean ± SD	Control, score Total	Weight, %[a]	Mean Difference Inverse Variance, Random (95% CI)
Alosco et al[23] (2017)	49.01 ± 11.72	96	54.18 ± 10.37	28	21.6	−5.17 (−9.67, −0.67)
Hart et al[43] (2013)	50.2 ± 9.44	12	49 ± 7.92	26	14.8	1.20 (−4.95, 7.35)
Koerte et al[38] (2015)	102.6 ± 4.1	11	100.6 ± 5.3	11	24.5	2.00 (−1.96, 5.96)
Koerte et al[26] (2016)	103.9 ± 5.1	15	102.6 ± 5.9	15	24.6	1.30 (−2.65, 5.25)
Tremblay et al[42] (2014)	32.43 ± 6.43	15	35.13 ± 10.61	15	14.4	−2.70 (−8.98, 3.58)
Total		149		95	99.9	−0.52 (−3.40, 2.36)

Heterogeneity: $\tau^2 = 4.73$; $\chi^2_4 = 7.21$, $P = .13$, $I^2 = 45\%$
Test for overall effect: $Z = 0.35$; $P = .72$



C

Study or Subgroup	Retired Athlete, score Mean ± SD	Retired Athlete, score Total	Control, score Mean ± SD	Control, score Total	Weight, %[a]	Mean Difference Inverse Variance, Random (95% CI)
Alosco et al[23] (2017)	43.77 ± 15.86	96	52.75 ± 15.38	28	15.5	−8.98 (−15.50, −2.46)
Hart et al[43] (2013)	51.9 ± 11.02	12	54.1 ± 8.67	26	13.9	−2.20 (−9.27, 4.87)
Koerte et al[38] (2015)	108.4 ± 4.2	11	107.4 ± 5.3	11	26.2	1.00 (−3.00, 5.00)
Koerte et al[26] (2016)	108.5 ± 4.7	15	109.9 ± 4.8	15	29.6	−1.40 (−4.80, 2.00)
McMillan et al[22] (2017)	56.1 ± 18.5	52	51.9 ± 17.6	29	11.3	4.20 (−3.94, 12.34)
Tremblay et al[42] (2014)	73 ± 16.58	15	74.13 ± 26.86	15	3.6	−1.13 (−17.10, 14.84)
Total		201		124	100.1	−1.41 (−4.58, 1.76)

Heterogeneity: $\tau^2 = 5.84$; $\chi^2_5 = 8.41$, $P = .13$, $I^2 = 41\%$
Test for overall effect: $Z = 0.87$; $P = .38$

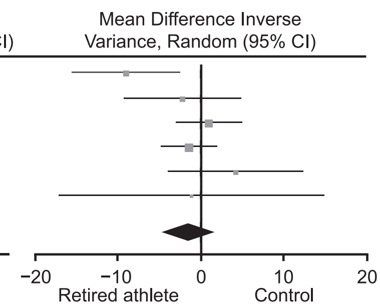


Figure 4. Forest plots of between-groups comparisons for cognitive outcomes. Retired athletes compared with control participants using the following: A, Mini-Mental State Examination. B, Trail Making Test–A. C, Trail Making Test–B. [a] The total does not equal 100% because percentages were rounded. **Continued on next page.**

memory, with neglect of other aspects of cognition, including language, psychomotor function, and perception. Furthermore, epidemiologic studies were confounded by individual differences in susceptibility to age-related neurocognitive decline or dementia-related pathologic conditions. Therefore, lifetime exposure to concussion is more than likely one of a myriad of environmental and predetermined risk factors for diminished cognitive reserve and early expression of neurocognitive decline. The researchers did not control for premorbid intellectual function and factors related to cognitive reserve. An important factor was the substantial overlap between a normal age-related neurocognitive downturn and the manifestation of SRC in later life.[63]

From this review, evidence of increased self-reported cognitive difficulties emerged. A substantial number of studies identified self-reported cognitive concerns among retired athletes (11 of 14 [79%] studies that tested for self-reported symptoms). However, conclusions drawn from self-reported data should be cautious, particularly in the absence of clear associations between self-reported symptoms and previous head-impact exposure or reported number of concussions and the potential recall bias that continues to be a limitation of all retrospective studies in this area. Furthermore, external factors, such as the media, may influence former players' reporting.[64,65] Among the investigations of objective and subjective cognition in retired athletes,### a lack of clear agreement existed between the measures. Most authors (n = 6 studies) did not support[16,17,20,22,25,54] the subjective reports with respect to neuropsychological test results. The clinical importance of the findings should be carefully considered in the overall context of the individual's performance on neuropsychological and cognitive testing and symptom self-report. The emerging disparity between subjective and objective tests may indicate that more sensitive cognitive test measures are required to recognize changes, which may then result in self-reported difficulties and translate to anomalies on cognitive tests.

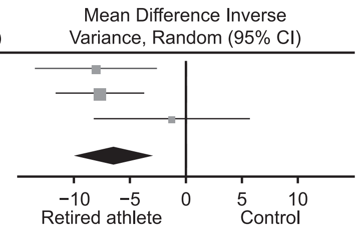
Our meta-analysis of the cognitive domains of memory, executive function, language, psychomotor function, and self-reported cognitive functioning revealed that retired athletes performed worse than control participants. However, the magnitudes of the effect sizes were small; therefore, whether the effect sizes were clinically meaningful is unclear. An additional methodologic shortcoming of the reviewed studies was a paucity of studies that used a prospective, longitudinal design and biased recruitment. The study designs also raised important concerns along with retrospective recall bias and failure to control for confounding variables: namely, failure to control for a history of non–sport-related concussion. A

###References 16, 17, 20, 22, 23, 25, 34, 47, 54.

D

Study or Subgroup	Retired Athlete, score Mean ± SD	Retired Athlete, score Total	Control, score Mean ± SD	Control, score Total	Weight, %	Mean Difference Inverse Variance, Random (95% CI)
Hart et al[43] (2013)	52.1 ± 8.18	12	60.2 ± 7.58	26	31.2	−8.10 (−13.57, −2.63)
Strain et al[39] (2015)	52.5 ± 8	28	60.24 ± 7	27	47.4	−7.74 (−11.71, −3.77)
Terry et al[40] (2015)	55.7 ± 10.4	25	57 ± 11.6	16	21.4	−1.30 (−8.29, 5.69)
Total		65		69	100.0	−6.48 (−10.07, −2.88)

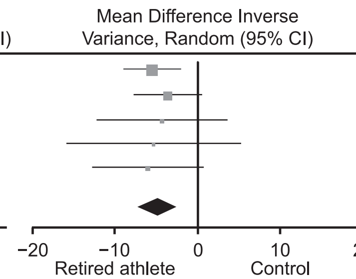
Heterogeneity: $\tau^2 = 3.00$; $\chi^2_2 = 2.80$, $P = .25$, $I^2 = 29\%$
Test for overall effect: $Z = 3.53$; $P < .001$



E

Study or Subgroup	Retired Athlete, score Mean ± SD	Retired Athlete, score Total	Control, score Mean ± SD	Control, score Total	Weight, %[a]	Mean Difference Inverse Variance, Random (95% CI)
Alosco et al[23] (2017)	47.91 ± 9.93	95	53.39 ± 7.69	28	43.8	−5.48 (−8.96, −2.00)
De Beaumont et al[53] (2009)	19.4 ± 6.7	19	23 ± 6.6	21	31.1	−3.60 (−7.73, 0.53)
Hart et al[43] (2013)	46.3 ± 11.65	12	50.6 ± 10.38	22	8.5	−4.30 (−12.19, 3.59)
Koerte et al[38] (2015)	48.7 ± 11	11	54 ± 15.8	14	4.8	−5.30 (−15.82, 5.22)
Koerte et al[26] (2016)	48.9 ± 10.9	15	54.9 ± 7.6	15	11.7	−6.00 (−12.72, 0.72)
Total		152		100	99.9	−4.85 (−7.15, −2.54)

Heterogeneity: $\tau^2 = 0.00$; $\chi^2_4 = 0.62$, $P = .96$, $I^2 = 0\%$
Test for overall effect: $Z = 4.12$; $P < .001$



F

Study or Subgroup	Retired Athlete, score Mean ± SD	Retired Athlete, score Total	Control, score Mean ± SD	Control, score Total	Weight, %	Mean Difference Inverse Variance, Random (95% CI)
Alosco et al[23] (2017)	48.43 ± 11.01	95	55 ± 7.88	28	43.8	−6.57 (−10.23, −2.91)
De Beaumont et al[53] (2009)	18.9 ± 6.5	19	22.4 ± 6.4	21	36.6	−3.50 (−7.50, 0.50)
Hart et al[43] (2013)	56.6 ± 13.38	12	58.3 ± 13.42	22	6.6	−1.70 (−11.12, 7.72)
Koerte et al[38] (2015)	47.8 ± 14.8	11	55 ± 11.5	14	5.2	−7.20 (−17.82, 3.42)
Koerte et al[26] (2016)	47.7 ± 14.7	15	56.9 ± 8.8	15	7.8	−9.20 (−17.87, −0.53)
Total		152		100	100.0	−5.36 (−7.79, −2.94)

Heterogeneity: $\tau^2 = 0.00$; $\chi^2_4 = 2.70$, $P = .61$, $I^2 = 0\%$
Test for overall effect: $Z = 4.34$; $P < .001$

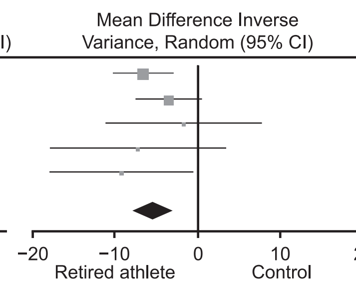


Figure 4. Continued from previous page. D, California Verbal Learning Test. E, Rey-Osterreith Complex Figure Test Copy and Immediate Recall. F, Rey-Osterreith Complex Figure Test Delayed Recall. [a] The total does not equal 100% because percentages were rounded.

further factor was the lack of suitable control groups. Important aspects associated with professional team sports, such as high levels of physical fitness, high income, and potential drug use (eg, opioid analgesics), were not considered. The late effect upper limb orthopaedic injuries may have had on psychomotor tests was also overlooked. A total of 13 studies**** did not include a control group, which greatly limited the conclusions that could be drawn because of a lack of context with respect to population normative data. Among the investigations that included a control group (n = 33), only a small number (n = 8) included an appropriate noncontact-athlete control cohort[15,26,31,34,35,38,56,57]; most researchers (n = 22 studies)†††† did not accurately match control individuals with retired noncontact athletes. In addition, a large proportion of investigators (n = 19) did not provide a definition of *concussion*,‡‡‡‡ which reduced the validity of player recall.[66] Others[67,68] noted both underreporting (eg, lack of understanding about concussion) and exaggeration of head impacts. The inability to accurately quantify participants' exposure to subconcussive blows was a further difficulty.

Just over 50% of the studies (n = 24)§§§§ controlled for a history of neurologic or psychiatric conditions. A history of head-impact exposure or concussion is one of myriad factors that may lead to neurocognitive decline in retired athletes; therefore, inclusion and exclusion criteria must be robust, and these factors must be appropriately controlled in research. Individuals with premorbid psychiatric or other health problems or life stressors are more likely to experience postconcussion syndrome.[69,70] Similarly, only a minority of authors (n = 14 studies)‖‖‖‖ reported past or present alcohol or drug use. Downs and Abwender[56] described screening for alcohol abuse but did not provide these findings in their "Results" section. Some investigators[17,22,33,35] noted higher alcohol consumption among retired athletes than among control individuals, which could have negatively influenced cognitive performance on certain cognitive tests. Substance abuse has been associated with sustained deficits in executive functioning, especially inhibition.[71] Long-term, high-dose anabolic steroid exposure may cause cognitive deficits, notably in visuospatial memory.[72]

Authors of epidemiologic and intervention studies[73,74] have suggested that overall physical activity preserves or improves cognitive function during aging; therefore, the

*****References 18–20, 24, 28, 30, 32, 41, 46, 47, 51, 55, 58.*

††††References 13, 16, 17, 21–23, 25,27, 29, 30, 33, 36, 39, 40, 42–44, 47–49, 51, 53.

‡‡‡‡References 15, 17–19, 26, 27, 29, 32–34, 38, 41, 44, 47, 49, 52, 56–58.

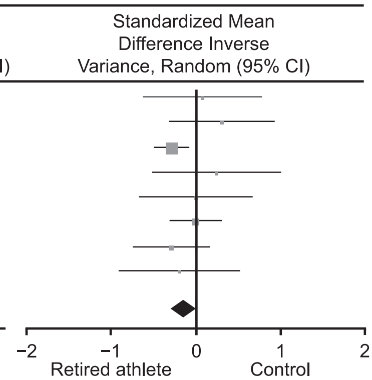
§§§§References 13, 14, 17, 19, 22, 24–26, 28, 29, 33, 34, 38, 40–43, 45, 48, 49, 52–54, 58.

‖‖‖‖References 16, 18, 19, 23, 31, 33, 35, 37, 40–42, 48, 53, 58.

A

Study or Subgroup	Retired Athlete, score Mean ± SD	Retired Athlete, score Total	Control, score Mean ± SD	Control, score Total	Weight, %	Standardized Mean Difference Inverse Variance, Random (95% CI)
Clark et al[14] (2018)	97.1 ± 11.2	15	96.4 ± 8.07	16	4.2	0.07 (−0.63, 0.77)
De Beaumont et al[53] (2009)	29.3 ± 0.9	19	29 ± 1	21	5.3	0.31 (−0.32, 0.93)
Decq et al[33] (2016)	30.24 ± 3.54	239	31.26 ± 3.56	138	46.8	−0.29 (−0.50, −0.08)
Ford et al[49] (2013)	27.6 ± 1.2	12	27.1 ± 2.4	15	3.6	0.25 (−0.52, 1.01)
Gardner et al[17] (2016)	26.5 ± 2.5	17	26.5 ± 4.5	17	4.6	0.00 (−0.67, 0.67)
Hume et al[31] (2017)	98 ± 17	103	98 ± 16.8	65	21.5	0.00 (−0.31, 0.31)
McMillan et al[22] (2017)	27.4 ± 2.3	52	28 ± 1.5	29	10.0	−0.29 (−0.75, 0.17)
Tremblay et al[48] (2013)	29.2 ± 0.86	15	29.4 ± 1.12	15	4.0	−0.19 (−0.91, 0.52)
Total		472		316	100.0	−0.14 (−0.29, 0.00)

Heterogeneity: $\tau^2 = 0.00$; $\chi^2_7 = 6.56$, $P = .48$, $I^2 = 0\%$
Test for overall effect: $Z = 1.94$; $P = .05$



B

Study or Subgroup	Retired Athlete, score Mean ± SD	Retired Athlete, score Total	Control, score Mean ± SD	Control, score Total	Weight, %[a]	Standardized Mean Difference Inverse Variance, Random (95% CI)
Alosco et al[23] (2017)	49.01 ± 11.72	95	54.18 ± 10.37	28	14.9	−0.45 (−0.87, −0.02)
Clark et al[14] (2018)	107 ± 10.3	15	99.5 ± 14.4	16	6.1	0.58 (−0.14, 1.30)
Ford et al[49] (2013)	87 ± 34.1	12	74 ± 15.9	15	5.4	0.49 (−0.28, 1.27)
Hart et al[43] (2013)	51.9 ± 11.02	12	54.1 ± 17.33	26	5.7	−0.14 (−0.82, 0.55)
Hume et al[31] (2017)	100 ± 10.6	103	99 ± 13.7	65	23.4	0.08 (−0.23, 0.39)
Koerte et al[38] (2015)	108.4 ± 4.2	11	107.4 ± 5.3	14	5.1	0.20 (−0.59, 0.99)
Koerte et al[26] (2016)	108.5 ± 4.7	15	109.9 ± 4.8	15	6.1	−0.29 (−1.01, 0.43)
McMillan et al[22] (2017)	56.1 ± 18.5	52	51.9 ± 17.6	29	13.4	0.23 (−0.23, 0.68)
Thornton et al[54] (2008)	38.39 ± 7.77	33	37.41 ± 9.06	37	12.4	0.11 (−0.36, 0.58)
Tremblay et al[48] (2013)	74.13 ± 26.86	15	73 ± 16.58	15	6.2	0.05 (−0.67, 0.77)
Total		363		260	100.1	0.05 (−0.14, 0.23)

Heterogeneity: $\tau^2 = 0.01$; $\chi^2_9 = 10.60$, $P = .30$, $I^2 = 15\%$
Test for overall effect: $Z = 0.48$; $P = .63$

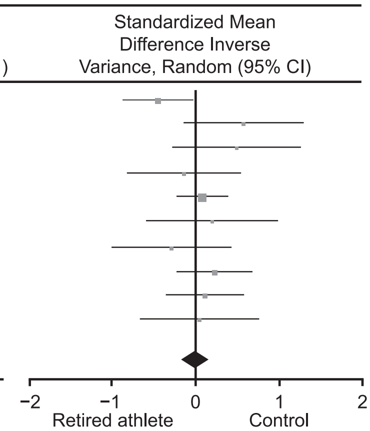


Figure 5. Forest plots of between-groups comparisons for cognitive domains. Retired athletes compared with control participants in the following areas: A, Global cognitive ability. B, Attention. [a] The total does not equal 100% because percentages were rounded. Continued on next page.

failure to control for current activity levels among retired players versus control groups in most research presented a potential bias. However, only a minority of studies[26,35,38,42,48,52] controlled for the modifiable risk factors, such as diet and physical activity, that accounted for physical activity engagement and exercise frequency. Similarly, only a small proportion of investigators[22,23,28,30,50–52] examined factors such as body mass index, weight-to-height ratio, or cardiovascular health. These factors may affect cognitive functioning: a meta-analysis[75] indicated that being categorized in the overweight or obese range in midlife was a risk factor for dementia later in life. A large proportion of the studies (n = 20) included retired NFL players. Given the propensity toward being overweight in this population,[76] the risk of cognitive impairment may be elevated.[77] Hinton et al[52] found that dietary fat intake was more associated with self-reported cognitive difficulties than was exposure to football alone among former collegiate football players. Wright et al[28] reported that body mass index was associated with cognitive-reserve outcomes in retired NFL players.

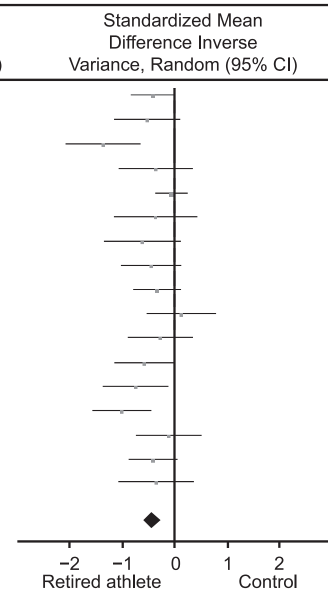
Aside from the proposed negative relationship between concussion and cognitive function, the potential causes of cognitive concerns in retired athletes are diverse. Factors including genetics,[78] diet and nutrition,[79] exercise,[80] obesity,[81] chronic pain and life stress,[82] childhood adversity,[83] personality factors,[84] family history of neurologic conditions,[85] steroid use,[86] drug and alcohol use,[87] depression and anxiety,[88] general medical history (eg, hypertension, diabetes, heart disease),[89] and neurodegenerative diseases (eg, Alzheimer disease, Parkinson disease, and amyotrophic lateral sclerosis)[90–92] have been implicated in exacerbated cognitive decline with aging. Most authors did not control for these variables. Parental socioeconomic status, race, and medical history independently predicted baseline memory scores among collegiate athletes, whereas concussion history and years exposed to sport did not.[93] None of the investigators accounted for socioeconomic status during childhood, which could affect cognitive reserve later in life and may account for differences among athlete groups with a history of concussion or head-impact exposure versus control participants or normative data. The importance of premorbid information; intellectual level; and learning disabilities, such as attention-deficit/hyperactivity disorder, which is known to exist at a high level among athletes, should also be considered. Athletes with a history of multiple concussions and a premorbid learning disability are vulnerable to neurocognitive impairment.[94]

Individual differences in baseline intelligence and education status have not been addressed in most studies. Stamm et al[37] reported that 14% of the group younger than 12 years and 0% of the group older than 12 years had a learning disability and displayed differences in premorbid intellectual functioning (ie, Wechsler Test of Adult Reading scores), with the younger group representing those who were exposed to tackle football before age 12 and the older group representing those who were not

C

Study or Subgroup	Retired Athlete, score: Mean ± SD	Retired Athlete, score: Total	Control, score: Mean ± SD	Control, score: Total	Weight, %[a]	Standardized Mean Difference Inverse Variance, Random (95% CI)
Alosco et al[23] (2017)	39.19 ± 8.45	96	43 ± 10.82	28	8.9	−0.42 (−0.84, 0.00)
De Beaumont et al[53] (2009)	19.4 ± 6.7	19	23 ± 6.6	21	5.0	−0.53 (−1.16, 0.10)
Ford et al[49] (2013)	0.84 ± 0.05	27	0.91 ± 0.05	14	4.1	−1.37 (−2.09, −0.66)
Hart et al[43] (2013)	46.3 ± 11.65	12	50.6 ± 11.39	22	4.2	−0.37 (−1.08, 0.34)
Hume et al[31] (2017)	102 ± 15.8	103	103 ± 14.1	65	12.5	−0.07 (−0.38, 0.24)
Koerte et al[38] (2015)	48.7 ± 11	11	54 ± 15.8	14	3.5	−0.37 (−1.17, 0.43)
Koerte et al[26] (2016)	48.9 ± 10.9	15	54.9 ± 7.6	15	4.0	−0.62 (−1.36, 0.11)
Koerte et al[34] (2016)	418.611 ± 144.342	72	483.571 ± 124.258	14	5.8	−0.46 (−1.03, 0.12)
McMillan et al[22] (2017)	10.5 ± 3.6	52	11.6 ± 2.3	29	8.1	−0.34 (−0.80, 0.12)
Multani et al[25] (2016)	10.11 ± 3.3	18	9.76 ± 2.1	17	4.7	0.12 (−0.54, 0.79)
Pearce et al[45] (2014)	−5.74 ± 4.49	20	−4.67 ± 2.89	20	5.2	−0.28 (−0.90, 0.35)
Pearce et al[13] (2018)	−4.3 ± 4.12	25	−2.1 ± 3.15	25	6.0	−0.59 (−1.16, −0.02)
Stamm et al[37] (2015)	40.81 ± 2.95	21	43.29 ± 3.5	21	5.1	−0.75 (−1.38, −0.12)
Strain et al[39] (2015)	52.5 ± 8	28	60.24 ± 7	27	6.0	−1.01 (−1.58, −0.45)
Terry et al[40] (2015)	55.7 ± 10.4	25	57 ± 11.6	16	5.1	−0.12 (−0.75, 0.51)
Thorton et al[54] (2008)	53.43 ± 8.64	35	56.97 ± 8.17	37	7.8	−0.42 (−0.88, 0.05)
Tremblay et al[48] (2013)	52.33 ± 5.79	15	54.87 ± 7.83	15	4.1	−0.36 (−1.08, 0.36)
Total		594		400	100.1	−0.43 (−0.59, −0.27)

Heterogeneity: $\tau^2 = 0.03$; $\chi^2_{16} = 21.67$, $P = .15$, $I^2 = 26\%$
Test for overall effect: $Z = 5.28$; $P < .001$



D

Study or Subgroup	Retired Athlete, score: Mean ± SD	Retired Athlete, score: Total	Control, score: Mean ± SD	Control, score: Total	Weight, %	Standardized Mean Difference Inverse Variance, Random (95% CI)
Downs and Abwender[56] (2002)	−50.2 ± 31.9	38	−22.7 ± 22.5	22	15.9	−0.94 (−1.49, −0.39)
Hume et al[31] (2017)	96 ± 15	103	101 ± 10.1	65	33.8	−0.37 (−0.69, −0.06)
Koerte et al[34] (2016)	399.552 ± 98.372	72	445.714 ± 106.317	14	14.9	−0.46 (−1.04, 0.12)
Pearce et al[13] (2018)	−23.3 ± 18.17	25	−10.8 ± 8.48	25	14.7	−0.87 (−1.45, −0.29)
Thornton et al[54] (2008)	14.46 ± 7.89	37	16.57 ± 7.42	35	20.7	−0.27 (−0.74, 0.19)
Total		275		161	100.0	−0.53 (−0.78, −0.28)

Heterogeneity: $\tau^2 = 0.02$; $\chi^2_4 = 5.54$, $P = .24$, $I^2 = 28\%$
Test for overall effect: $Z = 4.14$; $P < .001$

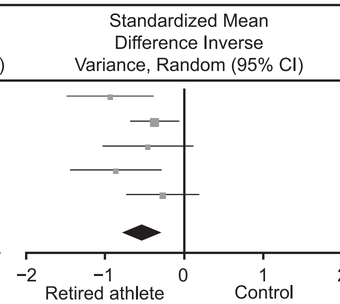


Figure 5. Continued from previous page. C, Memory. D, Executive function. [a] The total does not equal 100% because percentages were rounded. Continued on next page.

exposed until a later age. This casts doubt on whether the group differences reflected premorbid impairment as opposed to the effects of concussion. Many authors included in control groups participants who were exposed to considerable concussion risk, albeit a lower risk of head impacts. The control groups of Alosco et al[23] and Murelius and Haglund[57] included participants with a history of playing soccer, and Alosco et al[23] included 1 participant with a history of amateur wrestling; McMillan et al[22] included a control group in which 34% of participants had a history of concussion and rugby participation. The inclusion of current and retired athletes in some studies, without distinguishing between them, may have skewed the results,[46,54] as the results may have reflected the effects of recent concussions or current head-impact exposure.

The assessment of cognition should ideally capture all of its domains. The tests used varied greatly among studies, and only a small proportion of the authors used a comprehensive battery that explored all aspects of cognitive functioning. Most studies focused on specific domains, such as tests of attention, memory, and executive function. Furthermore, many of the assessments used were designed to detect gross cognitive impairments and may have failed to uncover subtle changes in cognitive function. Given the media interest in concussion and public perceptions, studies with negative findings are potentially less likely to be published. We did not assess publication bias in this review; it was not possible to perform a funnel plot due to the heterogeneity of the outcome measures used. Large-scale, prospective longitudinal studies with a high level of control of confounding factors are required to confirm the effects of aging with a history of concussion on cognitive functioning in retired athletes.

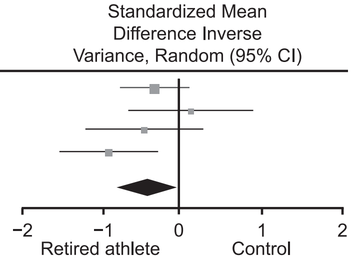
STUDY LIMITATIONS AND FUTURE WORK

The self-selected convenience samples limited the conclusions that could be drawn. This concern was exacerbated in some investigations because the inclusion criteria were limited to retired NFL players with a minimum 6-month history of self-reported complaints of cognitive, behavioral, and mood symptoms[23,34,37] and players presenting to memory clinics with cognitive or behavioral symptoms.[27] Self-selected participants may not have represented the retired athlete population. Given the retrospective nature of the studies, the possible long-term sequelae of concussion were influenced by methodologic biases, making it difficult to draw conclusions. A large proportion of the studies (n = 43) were based on retired male athletes; only 3 groups of authors[35,54,56] recruited retired female athletes. Alumni of the NFL

E

Study or Subgroup	Retired Athlete, score Mean ± SD	Retired Athlete, score Total	Control, score Mean ± SD	Control, score Total	Weight, %	Standardized Mean Difference Inverse Variance, Random (95% CI)
Alosco et al[23] (2017)	48.96 ± 11.38	95	52.21 ± 9.8	28	38.0	−0.29 (−0.72, 0.13)
Ford et al[49] (2013)	52.5 ± 6.1	12	51.7 ± 4.6	15	17.7	0.15 (−0.61, 0.91)
Hart et al[43] (2013)	48.6 ± 9.92	12	53.4 ± 11.86	21	19.3	−0.42 (−1.14, 0.30)
Strain et al[21] (2017)	43.2 ± 11.4	25	52.6 ± 10.2	22	25.0	−0.85 (−1.45, −0.25)
Total		144		86	100.0	−0.38 (−0.74, −0.02)

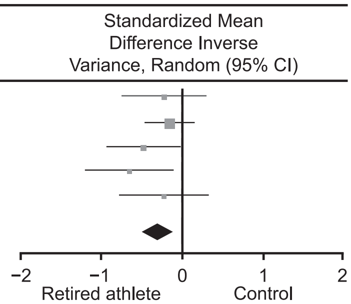
Heterogeneity: $\tau^2 = 0.04$; $\chi^2_3 = 4.38$, $P = .22$, $I^2 = 32\%$
Test for overall effect: $Z = 2.04$; $P = .04$



F

Study or Subgroup	Retired Athlete, score Mean ± SD	Retired Athlete, score Total	Control, score Mean ± SD	Control, score Total	Weight, %[a]	Standardized Mean Difference Inverse Variance, Random (95% CI)
Downs and Abwender[56] (2002)	158.8 ± 56.3	38	169.4 ± 23.9	22	14.3	−0.22 (−0.75, 0.31)
Hume et al[31] (2017)	101 ± 13.8	103	103 ± 11.9	65	41.0	−0.15 (−0.46, 0.16)
McMillan et al[22] (2017)	−74.9 ± 12.3	52	−68.7 ± 14	29	18.7	−0.48 (−0.94, −0.01)
Pearce et al[45] (2014)	−378.2 ± 64.08	40	−336.76 ± 59.9	20	13.1	−0.65 (−1.20, −0.10)
Pearce et al[13] (2018)	−336.66 ± 73.79	25	−321.2 ± 62.26	25	12.8	−0.22 (−0.78, 0.33)
Total		258		161	99.9	−0.30 (−0.50, −0.10)

Heterogeneity: $\tau^2 = 0.00$; $\chi^2_4 = 3.16$, $P = .53$, $I^2 = 0\%$
Test for overall effect: $Z = 2.92$; $P = .003$



G

Study or Subgroup	Retired Athlete, score Mean ± SD	Retired Athlete, score Total	Control, score Mean ± SD	Control, score Total	Weight, %	Standardized Mean Difference Inverse Variance, Random (95% CI)
Clark et al[14] (2018)	118 ± 13.3	15	113 ± 10.1	16	12.8	0.41 (−0.30, 1.13)
Ford et al[49] (2013)	115.6 ± 19.5	12	114 ± 12.9	15	11.3	0.10 (−0.66, 0.86)
Koerte et al[34] (2016)	469.718 ± 94.127	72	521.429 ± 97.968	14	18.6	−0.54 (−1.12, 0.04)
Multani et al[25] (2016)	113.87 ± 6.6	18	111.94 ± 8.2	17	14.4	0.25 (−0.41, 0.92)
Terry et al[40] (2015)	110.6 ± 11.6	25	108.3 ± 12.5	16	16.0	0.19 (−0.44, 0.82)
Thornton et al[54] (2008)	35.21 ± 11.6	34	35.38 ± 3.93	37	26.9	−0.02 (−0.49, 0.45)
Total		176		115	100.0	0.02 (−0.24, 0.29)

Heterogeneity: $\tau^2 = 0.01$; $\chi^2_5 = 5.61$, $P = .35$, $I^2 = 11\%$
Test for overall effect: $Z = 0.18$; $P = .85$

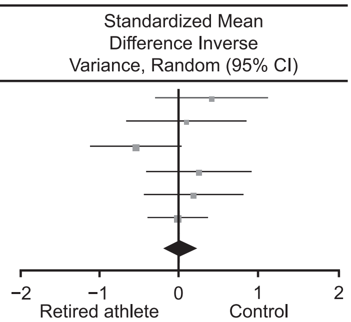


Figure 5. Continued from previous page. E, Language. F, Psychomotor function. G, Intelligence. [a] The total does not equal 100% because percentages were rounded. Continued on next page.

accounted for a large number of participants in many of the studies (n = 20). The career paths and levels of head-impact exposure make it impossible to infer results beyond this unique cohort. Aside from the level of head-impact exposure, a host of factors separate NFL players from the population at large, including income, education level, and various lifestyle aspects. Large gaps exist in our knowledge of the effect of concussion on female athletes (because of potential sex influences on concussion recovery[95,96]) and on people who participate at other sporting levels.

A further limitation was that concussions were often not well documented in the past. Therefore, all researchers relied on the athletes' self-reported history of concussion, making this information subject to retrospective recall bias. Only Wright et al[28] corroborated patients' self-reported history with verifiable reports. Relying solely on players' self-reported history of concussion and retired athletes' responses to a survey-based questionnaire regarding subjective memory difficulties is potentially unreliable. This is compounded by the fact that SRCs that occurred in the past may have been overlooked by clinicians unless loss of consciousness occurred.[97] A history of non–sport-related concussion, which accounts for most concussions,[98,99] needs to be considered in future study designs.

CONCLUSIONS

A total of 46 studies evaluated 9 aspects of cognitive functioning. Relative to the control groups or normative data, 5 areas showed declines: memory, executive function, language, psychomotor function, and self-reported cognitive functioning. The 4 other areas—global cognitive ability, attention, intelligence, and perception—were, on balance, neutral. The preliminary evidence of a dose-response association between cognitive health outcomes and past concussion exposure warrants further examination to determine the complex interaction between previous head-impact exposure and factors that may influence cognitive health in the aging retired athlete. As detailed throughout this review, confounding variables, case ascertainment, recall bias on behalf of the participants, and publication bias in the SRC field at large may have inflated these findings.

ACKNOWLEDGMENTS

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SUPPLEMENTAL MATERIAL

Supplemental Table. Detailed quality appraisal for the 46 studies.

Found at DOI: http://dx.doi.org/10.4085/1062-6050-297-18.S1

H

Study or Subgroup	Retired Athlete, score Mean ± SD	Retired Athlete, score Total	Control, score Mean ± SD	Control, score Total	Weight, %	Standardized Mean Difference Inverse Variance, Random (95% CI)
Hinton et al[52] (2011)	−1.71 ± 0.65	214	−1.52 ± 0.5	49	56.3	−0.30 (−0.61, 0.01)
Lewis et al[15] (2017)	−11.8 ± 8.4	23	−8.3 ± 11.8	22	15.7	−0.34 (−0.93, 0.25)
McMillan et al[22] (2017)	−9.6 ± 11.1	18	−0.3 ± 0.8	7	6.5	−0.94 (−1.86, −0.02)
Thornton et al[54] (2008)	−27.06 ± 7.44	32	−22.75 ± 5.11	32	21.5	−0.67 (−1.17, −0.16)
Total		287		110	100.0	−0.43 (−0.66, −0.19)

Heterogeneity: $\tau^2 = 0.00$; $\chi^2_3 = 2.77$, $P = .43$, $I^2 = 0\%$
Test for overall effect: $Z = 3.59$; $P < .001$

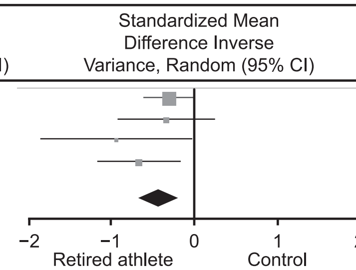

Figure 5. Continued from previous page. H, Self-reported cognitive functioning.

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Address correspondence to Joice Cunningham, BSc, Trinity Centre for Health Sciences, St James Hospital, James's Street, Dublin, Leinster D08 W9RT, Ireland. Address e-mail to cunninj1@tcd.ie.

Appendix 1. Search Strategy Continued on Next Page

Database	Search Strategy	Results
EMBASE	1. “cognitive defect”/exp 2. “depression”/exp 3. ((Cogniti* OR neuropsychological OR neurocognitive OR executive OR brain) NEAR/3 (impairment OR defect* OR function* OR dysfunction* OR process* OR symptom* OR factor* OR Deficit* OR disorder*)):ti,ab 4. (Neuropsychological NEAR/3 test*):ti,ab 5. Depressi*:ti,ab 6. 1 OR 2 OR 3 OR 4 OR 5 7. “athlete”/exp 8. ((Athlete* OR “sports person” OR sportswomen OR sportswoman OR sportsman OR sportsmen OR rugby OR player* OR box* OR “contact-sport”) NEAR/5 (retire* OR former)):ti,ab 9. 7 OR 8 10. 6 AND 9	1792
PsychINFO	1. DE “Cognitive Impairment” OR DE “Depression (Emotion)” OR DE “Executive Function” 2. TI ((Cogniti* OR neuropsychological OR neurocognitive OR executive OR brain) N3 (impairment OR defect* OR function* OR dysfunction* OR process* OR symptom* OR factor* OR Deficit* OR disorder*)) OR AB ((Cogniti* OR neuropsychological OR neurocognitive OR executive OR brain) N3 (impairment OR defect* OR function* OR dysfunction* OR process* OR symptom* OR factor* OR Deficit* OR disorder)) 3. TI (Neuropsychological N3 test*) OR AB (Neuropsychological N3 test*) 4. TI Depressi* OR AB Depressi* 5. S1 OR S2 OR S3 OR S4 6. DE “Athletes” 7. TI ((Athlete* OR “sports person” OR sportswomen OR sportswoman OR sportsman OR sportsmen OR rugby OR player* OR box* OR “contact- sport”) N5 (retire* OR former)) OR AB ((Athlete* OR “sports person” OR sportswomen OR sportswoman OR sportsman OR sportsmen OR rugby OR player* OR box* OR “contact-sport”) N5 (retire* OR former)) 8. S6 OR S7 9. S5 AND S8	783
MEDLINE/PubMed	1. (MH “Cognition Disorders+”) OR (MH “Neurocognitive Disorders+”) OR (MH “Mild Cognitive Impairment”) OR (MH “Depression”) OR (MH “Depressive Disorder+”) 2. TI ((Cogniti* OR neuropsychological OR neurocognitive OR executive OR brain) N3 (impairment OR defect* OR function* OR dysfunction* OR process* OR symptom* OR factor* OR Deficit* OR disorder*)) OR AB ((Cogniti* OR neuropsychological OR neurocognitive OR executive OR brain) N3 (impairment OR defect* OR function* OR dysfunction* OR process* OR symptom* OR factor* OR Deficit* OR disorder)) 3. TI (Neuropsychological N3 test*) OR AB (Neuropsychological N3 test*) 4. TI Depressi* OR AB Depressi* 5. S1 OR S2 OR S3 OR S4 6. (MH “Athletes”) 7. TI ((Athlete* OR “sports person” OR sportswomen OR sportswoman OR sportsman OR sportsmen OR rugby OR player* OR box* OR “contact-sport”) N5 (retire* OR former)) OR AB ((Athlete* OR “sports person” OR sportswomen OR sportswoman OR sportsman OR sportsmen OR rugby OR player* OR box* OR “contact-sport”) N5 (retire* OR former)) 8. S6 OR S7 9. S5 AND S8	459
CINAHL	1. (MH “Cognition Disorders+”) OR (MH “Depression+”) 2. TI ((Cogniti* OR neuropsychological OR neurocognitive OR executive OR brain) N3 (impairment OR defect* OR function* OR dysfunction* OR process* OR symptom* OR factor* OR Deficit* OR disorder*)) OR AB ((Cogniti* OR neuropsychological OR neurocognitive OR executive OR brain) N3 (impairment OR defect* OR function* OR dysfunction* OR process* OR symptom* OR factor* OR Deficit* OR disorder)) 3. TI (Neuropsychological N3 test*) OR AB (Neuropsychological N3 test*) 4. TI Depressi* OR AB Depressi* 5. S1 OR S2 OR S3 OR S4 6. (MH “Athletes”) 7. TI ((Athlete* OR “sports person” OR sportswomen OR sportswoman OR sportsman OR sportsmen OR rugby OR player* OR box* OR “contact- sport”) N5 (retire* OR former)) OR AB ((Athlete* OR “sports person” OR sportswomen OR sportswoman OR sportsman OR sportsmen OR rugby OR player* OR box* OR “contact-sport”) N5 (retire* OR former)) 8. S6 OR S7 9. S5 AND S8	239

Appendix 1. Continued from Previous Page

Database	Search Strategy	Results
Cochrane Central Register of Controlled Trials	1. [mh "Cognition Disorders"] OR [mh "Neurocognitive Disorders"] OR [mh "Mild Cognitive Impairment"] OR [mh "Depression"] OR [mh "Depressive Disorder"] 2. ((Cogniti* or neuropsychological or neurocognitive or executive or brain) near/3 (impairment or defect* or function* or dysfunction* or process* or symptom* or factor* or Deficit* or disorder*)):ti,ab,kw 3. (Neuropsychological NEAR/3 test*):ti,ab,kw 4. Depressi*:ti,ab,kw 5. {OR 1–4} 6. [mh "Athletes"] 7. ((Athlete* OR "sports person" OR sportswomen OR sportswoman OR sportsman OR sportmen OR rugby OR player* OR box* OR "contact- sport") NEAR/5 (retire* OR former)):ti,ab,kw 8. {OR 6, 7} 9. {AND 5, 8}	14
Web of Science	1. TS=((Cogniti* or neuropsychological or neurocognitive or executive or brain) NEAR/3 (impairment or defect* or function* or dysfunction* or process* or symptom* or factor* or Deficit* or disorder*)) OR TS =((Neuropsychological NEAR/3 test*)) OR TS=(Depressi*) 2. TS=((Athlete* OR "sports person" OR sportswomen OR sportswoman OR sportsman OR sportsmen OR rugby OR player* OR box* OR "contact-sport") NEAR/5 (retire* OR former)) 3. 2 AND 1	179

Appendix 2. List of Abbreviations and Acronyms

Abbreviation or Acronym	Name
ACS–TOPF	Advanced Clinical Solutions Test of Premorbid Functioning[a]
AD8	Eight-Item Informant Interview to Differentiate Aging and Dementia[b]
AMNART	American version of the National Adult Reading Test
BGT	Bender Visual-Motor Gestalt Test[a]
BNT	Boston Naming Test[a]
BRI	Behavioral Regulation Index[c]
BRIEF–A	Behavior Rating Inventory of Executive Function–Adult Version[c]
B–SIT	Brief Smell Identification Test
BTACT	Brief Test of Adult Cognition by Telephone
BVMT–R	Brief Visuospatial Memory Test–Revised[c]
CANTAB–IED	Cambridge Neuropsychological Test Automated Battery–Intra-Extra Dimensional Set Shift[d]
CANTAB–PAL	Cambridge Neuropsychological Test Automated Battery–Paired Associates Learning[d]
CANTAB–RTI	Cambridge Neuropsychological Test Automated Battery–Reaction Time[d]
CANTAB–SWM	Cambridge Neuropsychological Test Automated Battery–Spatial Working Memory[d]
CANTAB–TOTSPT	Cambridge Neuropsychological Test Automated Battery–One Touch Spatial Planning Task
CANTAB–VRT	Cambridge Neuropsychological Test Automated Battery–Visuomotor Reaction Time
CCFT	Cattell Culture Fair Intelligence Test
CDS	Cognitive Difficulties Scale
CFQ	Cognitive Failures Questionnaire
CNS	Central nervous system
CNS Vital Signs	Online computerized neurocognitive assessment software[e]
COWAT	Controlled Oral Word Association Test
CPT	Conners Continuous Performance Test[f]
CPT–II	Conners Continuous Performance Test, second edition[f]
CVLT–II	California Verbal Learning Test, second edition[a]
D-KEFS	Delis-Kaplan Executive Function System
DQ	Dysexecutive Questionnaire
DST	Digit Symbol Test
DWR	Delayed Word Recall
EFT	Eriksen Flanker Task
ETS Kit–V2 and –V3	Educational Testing Service Kit V2 and V3 vocabulary items
FAS	Verbal phonemic fluency test
F–TICS–m	French version of the modified Telephone Interview for Cognitive Status
FTT	Finger tapping test
GPT	Grooved Pegboard Test[g]
ImPACT	Immediate Post-Concussion Assessment and Cognitive Testing[h]
JLO	Judgment of Line Orientation[c]
LF	Letter Fluency task
MCIS	Mild Cognitive Impairment Screen
MCS	Mental Component Summary
MicroCog	MicroCog: Assessment of Cognitive Functioning[a]
MMSE	Mini-Mental State Examination[c]
MOCA	Montreal Cognitive Assessment[i]

Appendix 2. Continued

Abbreviation or Acronym	Name
NAB	Neuropsychological Assessment Battery[c]
NAB–LL	Neuropsychological Assessment Battery List Learning test
Neuro–QoL	Quality of Life in Neurological Disorders
PASAT	Paced Auditory Serial Addition Test
PCSC	Postconcussion Syndrome Checklist
PROMIS	Patient-Reported Outcomes Measurement Information System
RAVLT	Rey Auditory Verbal Learning Test
RBANS	Repeatable Battery for the Assessment of Neuropsychological Status[a]
RCFT	Rey Complex Figure Test
ROCFT	Rey-Osterreith Complex Figure Test
RPQ	Rivermead Post Concussion Symptoms Questionnaire
RVDLT	Rey Visual Design Learning Test
SART	Sustained Attention to Response Task
SDMT	Symbol Digit Modalities Test[j]
SF–36 (including MCS)	36-Item Short Form Health Survey[k]
SOPT	Self-Ordered Pointing Task
SORT	Semantic Object Retrieval Test
SRTT	Serial Reaction Time Test
TCFT	Taylor Complex Figure test
TMT	Trail Making Test
TMT–A	Trail Making Test part A
TMT–B	Trail Making Test part B
TOMM	Test of Memory Malingering[a]
TYM	Test Your Memory
VRST	Verbal Selective Reminding Test
WAIS	Wechsler Adult Intelligence Scale[a]
WAIS–III	Wechsler Adult Intelligence Scale, third edition[a]
WAIS–IV	Wechsler Adult Intelligence Scale, fourth edition[a]
WAIS–R	Wechsler Adult Intelligence Scale, revised version[a]
WASI	Wechsler Abbreviated Scale of Intelligence[a]
WCST	Wisconsin Card Sorting Test[c]
WMS	Wechsler Memory Scale[a]
WMS–III	Wechsler Memory Scale, third edition[a]
WMS–IV	Wechsler Memory Scale, fourth edition[a]
WRAT–4	Wide Range Achievement Test, fourth edition[j]
WTAR	Wechsler Test of Adult Reading[a]

[a] Pearson Education, Inc, London, United Kingdom.
[b] Washington University, St Louis, MO.
[c] PAR, Inc, Lutz, FL.
[d] Cambridge Cognition Ltd, Bottisham, Cambridge, United Kingdom.
[e] CNS Vital Signs, Morrisville, NC.
[f] MHS Inc, North Tonawanda, NY.
[g] Lafayette Instrument, Lafayette, IN.
[h] ImPACT Implications, Inc, Pittsburgh, PA.
[i] Ziad Nasreddine, MoCA Test Inc, Greenfield Park, Québec, Canada.
[j] WPS, Torrance, CA.
[k] QualityMetric Incorporated, Lincoln, RI.