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Association of Retrospectively Reported Concussion Symptoms with Objective Cognitive Performance in Former American-Style Football Players

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Abstract

Objective: Sustaining concussions has been linked to health issues later in life, yet evidence for associations between contact sports exposure and long-term cognitive performance is mixed. This cross-sectional study of former professional American-style football players tested the association of several measures of football exposure with later life cognitive performance, while also comparing the cognitive performance of former players to nonplayers.
Methods: In total, 353 former professional football players ($M_{age} = 54.3$) completed both (1) an online cognitive test battery measuring objective cognitive performance and (2) a survey querying demographic information, current health conditions, and measures of past football exposure, including recollected concussion symptoms playing professional football, diagnosed concussions, years of professional play, and age of first football exposure. Testing occurred an average of 29 years after former players' final season of professional play. In addition, a comparison sample of 5,086 male participants (nonplayers) completed one or more cognitive tests.
Results: Former players' cognitive performance was associated with retrospectively reported football concussion symptoms ($r_p = -0.19$, 95% CI -0.09 to -0.29; $p < 0.001$), but not with diagnosed concussions, years of professional play, or age of first football exposure. This association could be due to differences in pre-concussion cognitive functioning, however, which could not be estimated based on available data.
Conclusions: Future investigations of the long-term outcomes of contact sports exposure should include measures of sports-related concussion symptoms, which were more sensitive to objective cognitive performance than other football exposure measures, including self-reported diagnosed concussions.

Keywords: Head injury; traumatic brain injury; Executive functions; Attention; Learning and memory; Assessment

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Introduction

Acute concussion symptoms typically resolve within several weeks (Harmon et al., 2019; McCrory et al., 2017). However, repeated concussion exposure has been associated with later life neural abnormalities (Strain et al., 2015) and health problems (Chrisman & Richardson, 2014; Didehbani, Munro Cullum, Mansinghani, Conover, & Hart, 2013; Grashow et al., 2019a; Guskiewicz et al., 2007; Montenigro et al., 2017; Roberts et al., 2019). In addition, some previous studies have demonstrated associations between sports-related head injuries and long-term cognitive performance (Guskiewicz et al., 2005; Hume et al., 2017; Montenigro et al., 2017; Strain et al., 2015), although others have not found evidence for this relationship (Broglio, Ferrara, Piland, Anderson, & Collie, 2006; Bruce & Echemendia, 2009; Casson, Viano, Haacke, Kou, & LeStrange, 2014; Collie, McCrory, & Makdissi, 2006; Rosenblum et al., 2020). The mixed findings regarding the association between sports-related concussions and long-term cognitive performance likely occur for several reasons, including differences in how cognitive performance is assessed, variations in sample characteristics, and inconsistencies in how concussion history is documented. In particular, studies finding an association between concussions and cognitive performance often measure concussion exposure using concussion symptom history (Guskiewicz et al., 2005; Hume et al., 2017) or estimates of cumulative head impact (Montenigro et al., 2017), whereas studies failing to find such an association often ask participants to report the precise number of sports-related concussions they experienced (Broglio, Ferrara, Piland, Anderson, & Collie, 2006; Bruce & Echemendia, 2009; Collie, McCrory, & Makdissi, 2006; Rosenblum et al., 2020). Reporting an accurate number of concussions may be challenging due to underdiagnosis of concussions (Kerr et al., 2015; McCrea, Hammeke, Olsen, Leo, & Guskiewicz, 2004; Meehan, Mannix, O'Brien, & Collins, 2013), which can occur due to athletes hiding concussions (Kerr et al., 2015) or being unaware of what symptoms are consistent with having sustained a concussion (LaBotz, Martin, Kimura, Hetzler, & Nichols, 2005; Robbins et al., 2014). Thus, measures that query previous concussion symptoms, rather than a specific number of concussions, have the potential to be more sensitive to cognitive performance.

To address the discrepancies among previous studies that examine associations between sports-related concussion exposure and long-term cognitive performance, we recruited former National Football League (NFL) players to complete multiple measures of football exposure and objective cognitive performance. These former players were recruited as part of the Harvard Football Players' Health Study, a large and comprehensive study (Roberts et al., 2019; Zafonte et al., 2019) of former players who participated in the NFL after 1960, when most players began using hard plastic helmets. The present study recruited the largest sample to date to investigate the relationship between various measures of football exposure and objective cognitive function in former NFL players, allowing a relatively highly powered analysis of whether concussion exposure is associated with long-term cognition, although larger studies have assessed this association in other populations (Bruce & Echemendia, 2009; Collie, McCrory, & Makdissi, 2006). Importantly, we selected cognitive assessments sensitive to variations in cognitive performance in the normal, and not just impaired, range. Finally, we compared former players' cognitive performance to a sample of nonplayers from the general population.

Methods

Participants

Former American-style football players. All study procedures were approved by the Institutional Review Board of the Harvard faculty of Medicine and participants provided informed consent prior to participation. The study was advertised as an effort to better understand the health and well-being of former NFL players. All former players who received compensation from the NFL after 1960 were eligible to participate (Roberts et al., 2019). In an initial data collection effort from 2015 to 2019 (Roberts et al., 2019), 15,454 former players were asked to complete a 76-item health questionnaire that included 10 questions about signs and symptoms of a concussion following a blow to the head while playing football, hereafter referred to as "recollected football concussion symptoms." One hundred six former players who completed five or fewer of these questions were excluded. In total, 3,975 former players completed the questionnaire and responded to at least six football concussion symptom questions as of December, 2019; as reported elsewhere (Roberts et al., 2019), questionnaire respondents began their professional careers earlier and played more seasons of professional football than non-responders. These 3,975 former players were later asked to complete a remote, unsupervised battery of eight computerized cognitive tests using the TestMyBrain.org platform (Germine et al., 2012); the present study's sample was a self-selected subset of these former players who completed the cognitive test battery using a computer or laptop between 2018 and 2019 ($n = 353$, $M_{age} = 54.3$, $SD_{age} = 13.4$, range$_{age}$ = 25–81; 6.5% attended college but did not graduate, 41.6% graduated college, 32.9% pursued education beyond college, 19.0% were missing education information; see Table 1 for additional demographic information); three former players who completed the cognitive tests using a phone or tablet were excluded from the present study (Passell et al., 2021). On average, former players completed the battery

Table 1. Characteristics of former player who were study participants and non-participants

Characteristic	Non-participants ($n = 3{,}619$) n (%)	Participants ($n = 353$) n (%)
Age***		
<40	971 (26.8%)	61 (17.3%)
40–59	1,506 (41.6%)	145 (41.0%)
60+	1,142 (31.6%)	147 (41.6%)
Race***		
Black	1,443 (39.9%)	70 (19.8%)
White	2,023 (55.9%)	269 (76.2%)
Other	110 (3.0%)	11 (3.1%)
Missing	43 (1.2%)	3 (0.8%)
Position		
Defensive back	534 (14.8%)	42 (11.9%)
Defensive line	465 (12.8%)	32 (9.1%)
Kicker/punter	108 (3.0%)	14 (4.0%)
Linebacker	550 (15.2%)	56 (15.9%)
Offensive line	771 (21.3%)	89 (25.2%)
Quarterback	165 (4.6%)	20 (5.7%)
Running back	340 (9.4%)	28 (7.9%)
Special teams only	31 (0.9%)	2 (0.6%)
Tight end	277 (7.7%)	31 (8.8%)
Wide receiver	378 (10.4%)	39 (11.0%)
Total seasons in the NFL		
1	173 (4.8%)	22 (6.2%)
2–4	1,056 (29.2%)	105 (29.7%)
5–6	706 (19.5%)	72 (20.4%)
7–9	834 (23.0%)	81 (22.9%)
10+	848 (23.4%)	73 (20.7%)
Missing	2 (0.1%)	0 (0.0%)
Self-reported cognition-related difficulties***		
Mild	1,851 (51.2%)	222 (62.9%)
Moderate	1,291 (35.7%)	106 (30.0%)
Severe	472 (13.0%)	24 (6.8%)
Missing	5 (0.1%)	1 (0.3%)
High depressive symptoms***		
No	3,111 (86.0%)	324 (91.8%)
Yes	508 (14.0%)	29 (8.2%)
High anxiety symptoms**		
No	3,079 (85.1%)	321 (90.9%)
Yes	540 (14.9%)	32 (9.1%)

**$p < 0.01$ ***$p < 0.001$ *Note*: p-values from Chi-square tests of independence comparing non-participants and participants

of cognitive tests 29.2 years ($SD = 13.6$, range = 1–58) after their final season of professional play. See Fig. 1 for a summary of the recruitment of former players. Due to the sensitive nature of this study, data are not available for public distribution.

Nonplayer comparison group. To help characterize the cognitive performance of the sample of former players, data were obtained from a normative sample of male participants (nonplayers; N = 5,086, $M_{age} = 44.9$ years, $SD_{age} = 15.4$, range$_{age}$ = 25–81, 3.3% black, 66.0% white, 11.7% other, 19.0% race unreported, 8.1% did not attend college, 19.4% attended college without graduating, 57.4% graduated college, 15.1% education unreported) who completed one or more of the eight cognitive tests completed by former players through the online neuropsychology platform TestMyBrain.org (TMB; Germine et al., 2012). This sample was drawn from the normative databases that are widely used in conjunction with TMB tests (Singh et al., 2021). These databases are shared widely with the research community and include participant-level cognitive test scores and basic demographic data, as part of TMB's open science mission. Nonplayer participants were a subset of the TestMyBrain.org normative sample who (1) reported being male, (2) were between the ages of 25–81, (3) completed testing within the United States, (4) completed testing using a computer or laptop (Passell et al., 2021), and (5) completed the exact form of at least one cognitive test completed by former players. Test-specific nonplayer demographics are presented in Table 3. Nonplayer participants were recruited to complete cognitive tests on TestMyBrain.org for the prospect of self-discovery via percentile performance feedback. Importantly, this nonplayer sample was meant to serve as a broadly normative comparison group, but

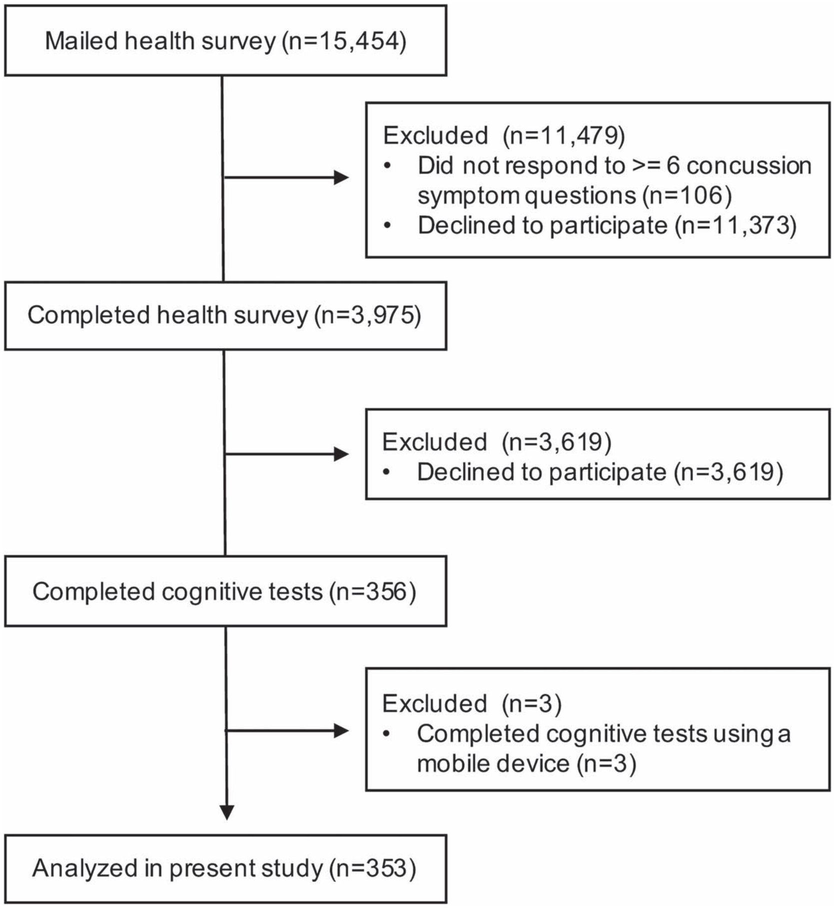

Fig. 1. Recruitment of former players.

was not demographically matched to the sample of former players. Thus, the nonplayer group differed from the former player group in ways other than professional football exposure (see Results). In addition, nonplayer participants were not queried about their previous football or head injury exposure. Thus, the nonplayer sample cannot be considered a "healthy" comparison sample, as it is possible that some comparison participants previously experienced head injuries, potentially biasing results towards null findings when comparing former players and nonplayers.

Concussion and football exposure

Recollected football concussion symptoms were assessed with: "While playing or practicing football, did you experience a blow to the head, neck, or upper body followed by: headaches, nausea, dizziness, loss of consciousness, memory problems, disorientation, confusion, seizure, visual problems, or feeling unsteady on your feet?" Participants responded to each of the 10 symptom questions separately by selecting one of the following options: none, once, 2–5 times, 6–10 times, or 11 times or more. This measure has been used and validated in previous studies looking at concussion symptoms and other health outcomes in former players (Grashow et al., 2019a; Roberts et al., 2019; Roberts et al., 2021; Roberts et al., 2022). Unlike measures querying a specific number of head injuries or diagnosed concussions, this measure was designed to capture both minor and severe head injuries that produced symptoms, while also being sensitive to differences in injury severity. However, some prior studies have found that individuals with mild traumatic brain injury report more symptoms than those with more severe traumatic brain injury, potentially limiting this approach (e.g., Gordon, Haddad, Brown, Hibbard, & Sliwinski, 2000). Notably, the wording of the recollected football concussion symptoms question is ambiguous as to whether it requests the specific number of head/neck/upper body injuries that caused concussion symptoms, or the total number of times symptoms occurred. Nevertheless, scores on this concussion symptom measure have previously been associated with cognition-related quality of life (Roberts et al., 2019) and sexual dysfunction (Grashow et al., 2019a), providing support for its utility despite its

Table 2. Former player demographics by recollected football concussion symptom quartile

Characteristic	Football Concussion Symptom Quartile (Score Range)			
	1 (0.0–11.0) *n* (% of Quartile)	2 (11.5–22.0)	3 (22.7–41.0)	4 (42.0–117.0)
Age				
<40	15 (16.9%)	17 (18.9%)	14 (16.3%)	15 (17.0%)
40–59	24 (27.0%)	33 (36.7%)	41 (47.7%)	47 (53.4%)
60+	50 (56.2%)	40 (44.4%)	31 (36.0%)	26 (29.5%)
Race				
Black	15 (16.9%)	11 (12.2%)	21 (24.4%)	23 (26.1%)
White	72 (80.9%)	76 (84.4%)	60 (69.8%)	61 (69.3%)
Other	2 (2.2%)	2 (2.2%)	4 (4.7%)	3 (3.4%)
Missing	0 (0.0%)	1 (1.1%)	1 (1.2%)	1 (1.1%)
Position				
Defensive back	8 (9.0%)	5 (5.6%)	18 (20.9%)	11 (12.5%)
Defensive line	7 (7.9%)	6 (6.7%)	11 (12.8%)	8 (9.1%)
Kicker/punter	8 (9.0%)	2 (2.2%)	4 (4.7%)	0 (0.0%)
Linebacker	13 (14.6%)	14 (15.6%)	10 (11.6%)	19 (21.6%)
Offensive line	16 (18.0%)	26 (28.9%)	20 (23.3%)	27 (30.7%)
Quarterback	4 (4.5%)	13 (14.4%)	1 (1.2%)	2 (2.3%)
Running back	11 (12.4%)	5 (5.6%)	8 (9.3%)	4 (4.5%)
Special teams only	0 (0.0%)	1 (1.1%)	1 (1.2%)	0 (0.0%)
Tight end	6 (6.7%)	9 (10.0%)	7 (8.1%)	9 (10.2%)
Wide receiver	16 (18.0%)	9 (10.0%)	6 (7.0%)	8 (9.1%)
Total seasons in NFL				
1	9 (10.1%)	9 (10.0%)	1 (1.2%)	3 (3.4%)
2–4	26 (29.2%)	21 (23.3%)	37 (43.0%)	21 (23.9%)
5–6	15 (16.9%)	18 (20.0%)	19 (22.1%)	20 (22.7%)
7–9	21 (23.6%)	19 (21.1%)	18 (20.9%)	23 (26.1%)
10+	18 (20.2%)	23 (25.6%)	11 (12.8%)	21 (23.9%)
Self-reported cognition-related difficulties				
Mild	78 (87.6%)	67 (74.4%)	48 (55.8%)	29 (33.0%)
Moderate	10 (11.2%)	21 (23.3%)	37 (43.0%)	38 (43.2%)
Severe	1 (1.1%)	2 (2.2%)	1 (1.2%)	20 (22.7%)
Missing	0 (0%)	0 (0%)	0 (0%)	1 (1.1%)
Education				
Some college	5 (5.6%)	4 (4.4%)	5 (5.8%)	9 (10.2%)
Graduated college	43 (48.3%)	38 (42.2%)	34 (39.5%)	32 (36.4%)
More than college	27 (30.3%)	37 (41.1%)	27 (31.4%)	25 (28.4%)
Missing	14 (15.7%)	11 (12.2%)	20 (23.3%)	22 (25.0%)

specific wording, reliance on retrospective report, and inability to account for non-symptomatic head injuries. See Table 2 for the distribution of football, demographic, and health-related variables by recollected football concussion symptom quartile.

In addition to overall concussion symptoms scores, loss of consciousness score was defined using participants' responses to the loss of consciousness symptom question described above, one of the 10 questions used to assess recollected football concussion symptoms. History of diagnosed concussions was assessed by asking: "Were you ever diagnosed by a medical professional with a concussion? If yes, please write the approximate number of diagnosed concussions you sustained." Thirteen former players who did not report their history of diagnosed concussions were excluded from analyses involving this variable. Seasons of professional play was assessed by asking, "How many seasons did you actively practice or play professional football?" In addition, former players reported the first and last calendar year in which they played professional football. Data on playing years from four participants with missing data were obtained from Pro-Football-Reference.com (Sports Reference LLC). Finally, former players reported the age at which they started playing organized football—five former players who did not report their age when they started playing organized football were not included in analyses involving this exposure variable.

Tests of cognitive performance

Former players completed a remote, unsupervised battery of eight cognitive tests on TestMyBrain.org, which included TestMyBrain's (TMB) digital versions of measures of processing speed (TMB Trails A & B, TMB Digit Symbol Matching),

Table 3. Nonplayer demographics for each cognitive test

Characteristic	Cognitive Test							
	TMB Trails A	TMB Trails B	TMB Digit Symbol Matching	TMB Multiple Object Tracking	TMB Digit Span	TMB Visual Paired Associates	TMB Verbal Paired Associates	TMB Vocabulary
Sample size	212	185	2,587	622	1,084	534	572	363
Age in years; *M* (*SD*)	45.5 (15.5)	45.7 (15.7)	45.1 (15.5)	48.3 (14.3)	44.3 (15.8)	48.9 (14.1)	40.6 (14.0)	43.9 (15.6)
Age group; *n* (%)								
<40	101 (47.6%)	88 (47.6%)	1,162 (44.9%)	194 (31.2%)	513 (47.3%)	153 (28.7%)	330 (57.7%)	181 (49.9%)
40–59	61 (28.8%)	52 (28.1%)	845 (32.7%)	272 (43.7%)	329 (30.4%)	244 (45.7%)	172 (30.1%)	110 (30.3%)
60+	50 (23.6%)	45 (24.3%)	580 (22.4%)	156 (25.1%)	242 (22.3%)	137 (25.7%)	70 (12.2%)	72 (19.8%)
Race; *n* (%)								
Black	2 (0.9%)	2 (1.1%)	94 (3.6%)	12 (1.9%)	41 (3.8%)	12 (2.2%)	18 (3.1%)	7 (1.9%)
White	136 (64.2%)	136 (73.5%)	1,745 (67.5%)	452 (72.7%)	686 (63.3%)	396 (74.2%)	352 (61.5%)	242 (66.7%)
Other	19 (9%)	19 (10.3%)	281 (10.9%)	61 (9.8%)	101 (9.3%)	54 (10.1%)	123 (21.5%)	44 (12.1%)
Missing	55 (25.9%)	28 (15.1%)	467 (18.1%)	97 (15.6%)	256 (23.6%)	72 (13.5%)	79 (13.8%)	70 (19.3%)
Education; *n* (%)								
No college	13 (6.1%)	13 (7.0%)	213 (8.2%)	43 (6.9%)	82 (7.6%)	37 (6.9%)	58 (10.1%)	25 (6.9%)
Some college	33 (15.6%)	33 (17.8%)	514 (19.9%)	112 (18.0%)	205 (18.9%)	95 (17.8%)	123 (21.5%)	78 (21.5%)
Graduated college	64 (30.2%)	64 (34.6%)	755 (29.2%)	173 (27.8%)	285 (26.3%)	160 (30.0%)	184 (32.2%)	115 (31.7%)
More than college	55 (25.9%)	55 (29.7%)	751 (29.0%)	218 (35.0%)	287 (26.5%)	188 (35.2%)	154 (26.9%)	96 (26.4%)
Missing	47 (22.2%)	20 (10.8%)	354 (13.7%)	76 (12.2%)	225 (20.8%)	54 (10.1%)	53 (9.3%)	49 (13.5%)

Table 4. Cognitive test descriptive statistics

Sample and Test	Units	Mean	*SD*	Range	Skewness	Kurtosis	Correlation with Age
Former Players							
TMB Trails A	Hits/min	49.1	19.1	3.5–105.7	0.23	-0.40	-0.61***
TMB Trails B	Hits/min	33.5	14.3	2.8–77.2	0.50	-0.02	-0.61***
TMB Digit Symbol Matching	Total correct	41.5	12.1	6–87	0.35	0.85	-0.69***
TMB Multiple Object Tracking	Total correct	54.9	7.5	26–72	-0.41	0.69	-0.43***
TMB Digit Span	Span length	6.5	1.7	1–11	0.13	0.43	-0.23***
TMB Visual Paired Associates	Total correct	13.8	4.7	3–24	0.10	-0.58	-0.35***
TMB Verbal Paired Associates	Total correct	7.6	4.3	2–25	1.63	2.97	-0.31***
TMB Vocabulary	Total correct	26.1	3.0	8–30	-2.48	8.94	0.10
Nonplayers							
TMB Trails A	Hits/min	62.9	20.8	16.9–121.8	0.17	-0.51	-0.55***
TMB Trails B	Hits/min	41.8	15.4	6.0–88.6	0.40	-0.10	-0.48***
TMB Digit Symbol Matching	Total correct	52.2	14.3	3–119	0.53	1.17	-0.52***
TMB Multiple Object Tracking	Total correct	57.2	7.1	29–72	-0.24	-0.04	-0.42***
TMB Digit Span	Span length	6.8	1.7	1–11	-0.12	0.32	-0.17***
TMB Visual Paired Associates	Total correct	15.6	4.6	3–24	-0.02	-0.79	-0.36***
TMB Verbal Paired Associates	Total correct	11.2	5.6	0–25	0.65	-0.32	-0.28***
TMB Vocabulary	Total correct	25.9	3.5	6–30	-2.32	7.65	0.21***

***$p < 0.001$ *Note*: *p*-values correspond to Pearson correlation between participants' test scores and age

attention (TMB Multiple Object Tracking), working memory (TMB Digit Span), episodic memory (TMB Verbal Paired Associates, TMB Visual Paired Associates), and vocabulary (TMB Vocabulary). Participants comprising the nonplayer participant group completed one or more of the eight cognitive tests. See Supplementary Methods 1 for descriptions and demonstrations of each cognitive test.

Self-reported health symptoms

Anxiety, depression, and self-reported cognition-related difficulties have previously been associated with worse cognitive performance (Beaudreau & O'Hara, 2008; Hammar & Årdal, 2009; Mantella et al., 2007; McIntyre et al., 2013; Snyder, 2013) and head injury exposure (Chrisman & Richardson, 2014; Didehbani, Munro Cullum, Mansinghani, Conover, & Hart, 2013;

Table 5. Age-adjusted performance differences between former players and nonplayers

Test	Partial correlation (95% CI)	β	SE	t	p
TMB Trails A	−0.19 (−0.27 to −0.11)	-0.32	0.07	-4.51	< 0.001
TMB Trails B	−0.13 (−0.21 to −0.04)	-0.22	0.08	-2.92	0.004
TMB Digit Symbol Matching	−0.16 (−0.20 to −0.13)	-0.42	0.05	-8.93	< 0.001
TMB Multiple Object Tracking	−0.07 (−0.14 to −0.01)	-0.14	0.06	-2.28	0.02
TMB Digit Span	−0.01 (−0.06–0.04)	-0.02	0.06	-0.36	0.72
TMB Visual Paired Associates	−0.13 (−0.19 to −0.06)	-0.25	0.06	-3.86	< 0.001
TMB Verbal Paired Associates	−0.18 (−0.25 to −0.12)	-0.39	0.07	-5.68	< 0.001
TMB Vocabulary	−0.03 (−0.11 to −0.04)	-0.07	0.08	-0.91	0.36

Note: All statistics reflect group differences (players vs. nonplayers) while adjusting for age. 95% CI = 95% confidence interval; β = standardized beta coefficient; SE = standard error of standardized beta coefficient

Guskiewicz et al., 2007; Montenigro et al., 2017; Roberts et al., 2019). We measured these health-related variables and examined their association with objective cognitive performance and head injury exposure (see Supplementary Methods 2).

Covariates

To adjust for potential confounders that might be associated with football exposure or cognitive performance, we included age as a covariate in our primary analyses. Race (Houck et al., 2020; Houck, Asken, Clugston, Perlstein, & Bauer, 2018), education, health-related variables, and playing position were included as covariates in supplementary analyses (see Supplementary material online, *Figure S2*). All participants were asked to provide their current age (in years), race, and ethnicity; responses to the race and ethnicity questions were used to code each participant's race as White, Black, or Other. To determine playing position, former players selected the position(s) they played most frequently; former players who selected multiple positions were assigned to the position with the highest risk for mild traumatic brain injury (Pellman et al., 2004). Health-related variables that could be downstream effects of concussions (e.g., depression and anxiety) were not included as covariates in our primary analyses. For completeness, however, we include analyses of the association between football exposure and cognitive performance while adjusting for health-related variables in Supplementary material online, *Figure S3*. Education was not included as a covariate in our primary analyses, as all the former players in our sample who reported their education level attended college (Weir, Jackson, & Sonnega, 2009).

Statistical analyses

Measures of football exposure. For each of the 10 football concussion symptom questions, concussion symptom frequency responses of none, once, 2–5 times, 6–10 times, or 11 or more were coded as 0, 1, 3.5, 8, and 13, respectively, following the procedure of a prior study using the same concussion symptom questionnaire (Grashow et al., 2019a). These coded scores for each symptom were then summed to create a recollected football concussion symptom score. This score was then divided into quartiles to minimize the influence of outliers (see Supplementary material online, *Figure S1* for results without dividing scores into quartiles). One or more missing football concussion symptoms were imputed for 19 former players (5.4%) using multiple imputation (Honaker, King, & Blackwell, 2011); of these 19 former players, 14 were missing data for one symptom, two were missing data for two symptoms, two were missing data for three symptoms, and one was missing data for four symptoms.

A loss of consciousness score was created using responses to the football concussion symptom item querying the frequency of losing consciousness following a head injury while playing professional football. To create this score, responses to the loss of consciousness question were rank ordered from 1 (no events leading to loss of consciousness) to 5 (11 or more events leadings to loss of consciousness). No data were missing for the loss of consciousness symptom question. See Supplementary material online, *Figure S1* for results using numerically coded loss of consciousness responses instead of rank ordering.

Like recollected concussion symptom scores, number of diagnosed concussions were divided into quartiles to minimize the influence of outliers (see Supplementary material online, *Figure S1* for results without dividing responses into quartiles). Participants in the lowest quartile reported 0 diagnosed concussion, those in the second quartile reported one diagnosed concussion, those in the third quartile reported either two or three diagnosed concussions, and those in the highest quartile reported four or more diagnosed concussions.

Predictors of cognitive performance in former players. For analyses testing the association of football exposure with cognitive performance (Fig. 2), former players' scores on each cognitive test were converted to z-scores, with the z-score representing

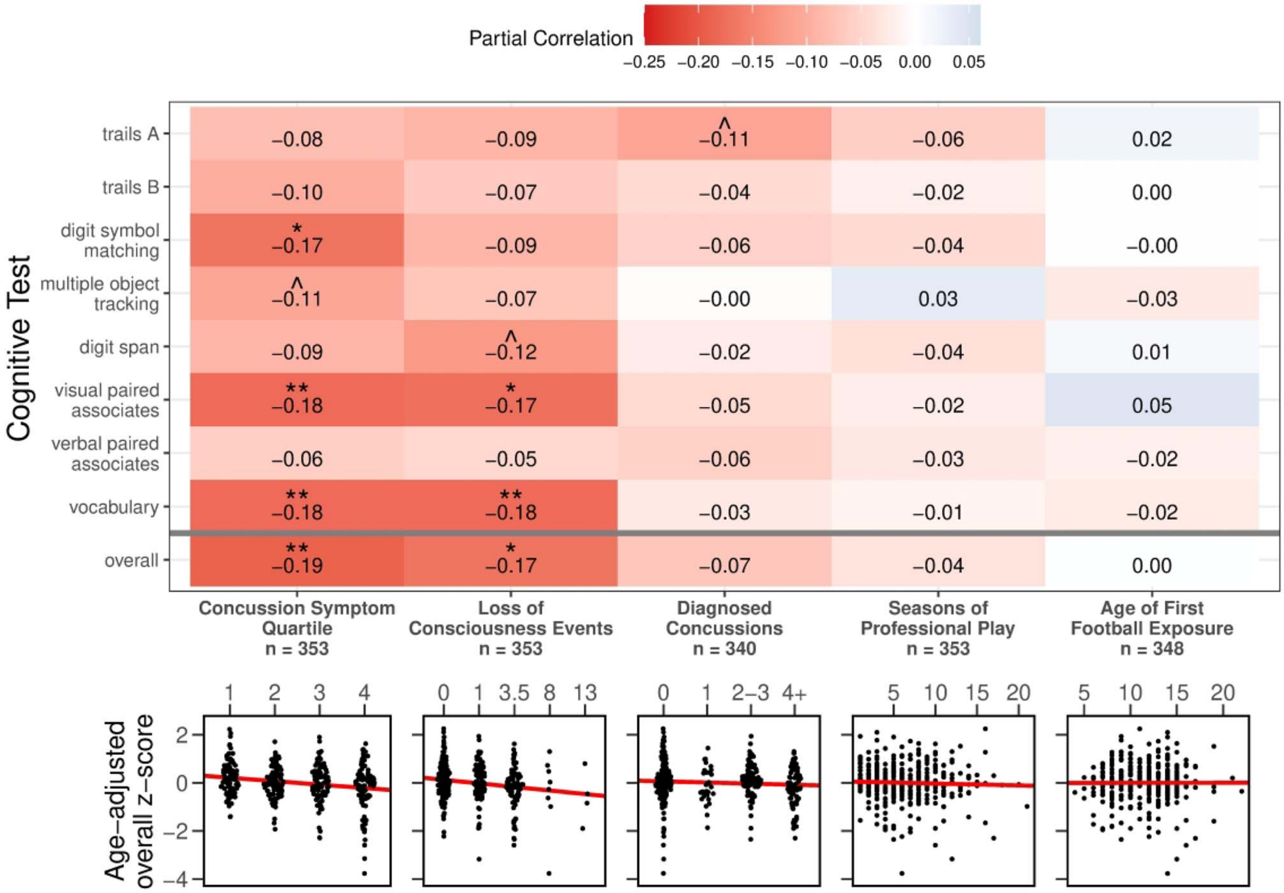

Fig. 2. Association of football exposure and cognitive performance. (Top) Partial correlations of cognitive test performance with concussion and football exposure measures. (Bottom) Partial residual plots showing relationship between overall cognitive performance (averaged across tests) and each exposure variable. $^{**}p < 0.001$, $^{*}p < 0.00556$, $^{\wedge}p < 0.05$. Associations with p-values <0.00556 survive correction for nine comparisons within each exposure variable.

performance relative to other former players. Converting scores to z-scores allowed calculation of composite performance across cognitive tests. Although the test battery was intended to cover a variety of cognitive constructs, using an exploratory factor analysis, both Kaiser's criteria (Kaiser, 1960) and scree-plot acceleration (Cattell, 1966) suggested that cognitive test scores were best explained by a single latent factor. Participants' factor scores on this single factor were nearly perfectly correlated with the equally weighted average of z-scores across the eight cognitive tests ($r = 0.98$). For ease of interpretation, therefore, we computed composite cognitive performance as the mean z-score across the eight cognitive tests, which was then scaled to have a standard deviation of 1.

Associations between cognitive performance and football exposure variables were assessed using multiple regression. Separate models were created to predict performance on each cognitive test, as well as the composite of all tests, from each individual football exposure measure. Age was included as a covariate in these models.

Former American-style football players versus nonplayers. For analyses comparing the cognitive performance of former players and nonplayers (Fig. 3), scores from the two groups on each cognitive test were aggregated and converted to z-scores, with the z-scores representing performance relative to all participants (both former players and nonplayers). The association of group (former players vs. nonplayers) with performance on each cognitive test was assessed using multiple regression adjusting for age by including age as a continuous covariate; additionally, we adjusted for age using inverse probability weighting in sensitivity analyses.

Effect sizes. Effect sizes throughout are reported as partial correlations (r_p): the correlation of the exposure and outcome measure while adjusting for covariates. Correlation values of 0.1, 0.3, and 0.5 are often considered cutoffs for small, medium, and large effect sizes, respectively (Cohen, 1988).

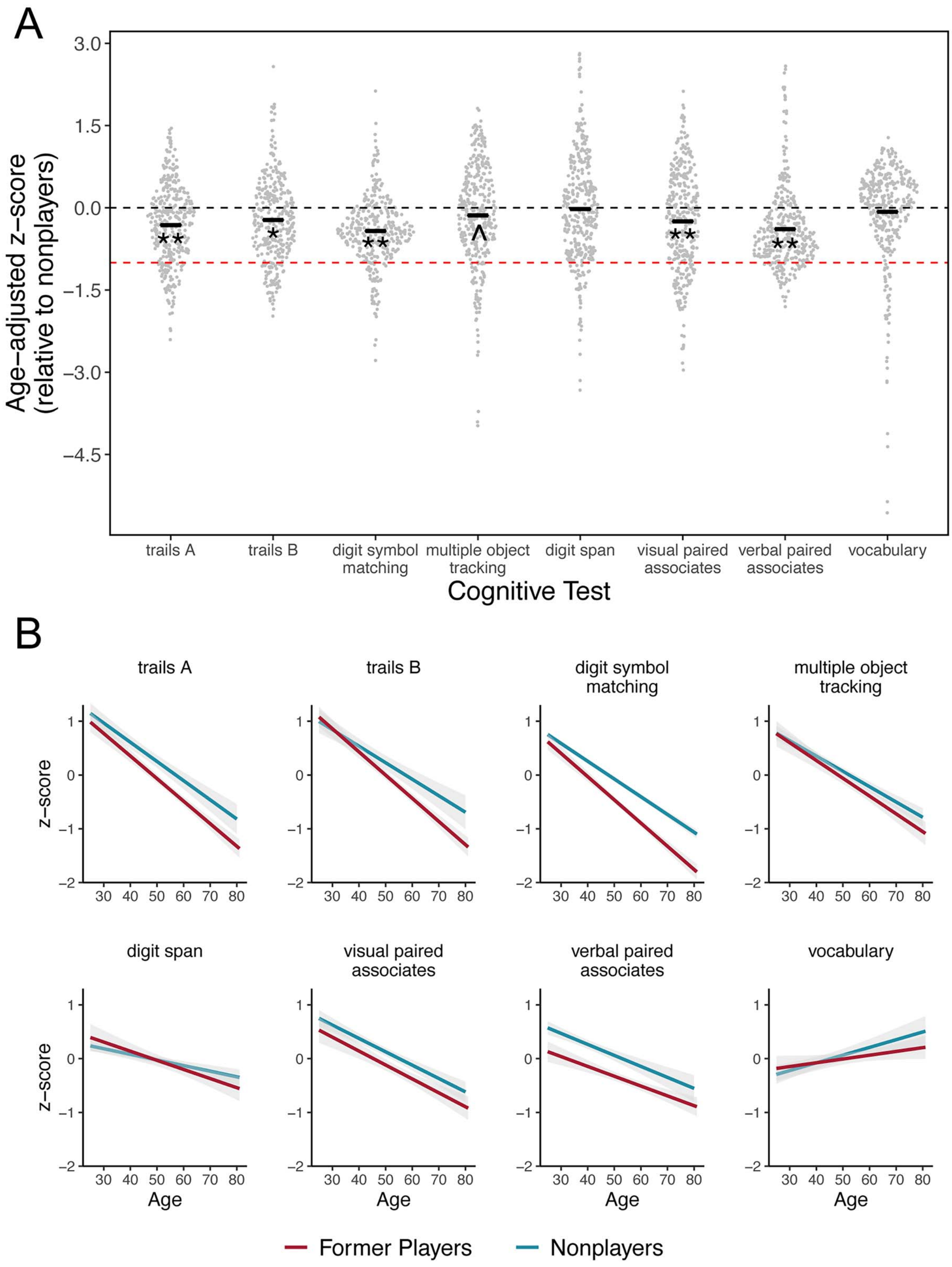

Fig. 3. Cognitive performance of former players and nonplayers. (A) Age-adjusted *z*-scores of football players (gray dots) on each cognitive test relative to mean performance of nonplayers (dashed black line). Stars represent significant group differences between former players and nonplayers. Solid black lines depict mean performance of former players on each test. Dashed red line depicts one standard deviation below nonplayer mean. **$p < 0.001$, *$p < 0.00625$, ^$p < 0.05$. *p*-values <0.00625 survive correction for eight comparisons. (B) Best-fit linear regression lines of *z*-standardized cognitive performance versus age, separately for former players and nonplayers on each cognitive test. Shaded regions represent 95% confidence intervals of regression lines.

Adjusting for multiple comparisons. Throughout the results section, original p-values are presented before adjusting for multiple comparisons. The association of each football exposure variable was tested with eight cognitive tests and the composite of the eight tests, for a total of nine statistical tests for each exposure variable. Therefore, an adjusted significance level of $0.05/9 = 0.00556$ is necessary for surviving nine comparisons for these analyses of former players (Fig. 2). Comparisons between former players and nonplayers were performed across eight cognitive tests; therefore, an adjusted significance level of $0.05/8 = 0.00625$ is necessary for surviving eight comparisons when comparing former players and nonplayers (Fig. 3).

Results

Compared with former players who completed the questionnaire but did not complete the battery of cognitive tests ($n = 3{,}619$), the participants in the present study ($n = 353$) were older ($p < 0.001$), less racially diverse ($p < 0.001$), less likely to report cognition-related difficulties ($p < 0.001$), and less likely to report high levels of depression ($p = 0.003$) and anxiety symptoms ($p = 0.004$; Table 1). Self-reported cognition-related difficulties, depression symptoms, and anxiety symptoms were each associated with worse overall cognitive performance and more recollected football concussion symptoms (see Supplementary Methods 2).

Table 4 shows the psychometric characteristics of each cognitive test separately for the former player and nonplayer samples, as well as the association of age with performance on each test. Consistent with prior reports, older age was associated with worse performance on each cognitive test except for vocabulary (Hartshorne & Germine, 2015). Notably, a large negative skew indicative of ceiling effects was present for the vocabulary test in both samples, whereas a large positive skew indicative of floor effects was present for the verbal paired associates test in the former player sample.

Models adjusting for age revealed an association between recollected football concussion symptoms and overall cognitive performance in former players ($r_p = -0.19$, 95% confidence interval [CI] = −0.09 to −0.29, B = −0.14, standard error of standardized beta coefficient [SE] = 0.04, $t = 3.61$, $p < 0.001$; Fig. 2). Recollected football concussion symptoms were specifically associated with worse performance on the TMB Digit Symbol Matching, TMB Visual Paired Associates, and TMB Vocabulary tests. In addition, a concussion symptom score reflecting the number of times former players endorsed loss of consciousness following a blow to the head was significantly associated with worse overall cognitive performance ($r_p = -0.17$, 95% CI = −0.07 to −0.27, B = −0.15, SE = 0.05, $t = 3.21$, $p = 0.001$). The relationship between recollected football concussion symptoms and cognitive performance remained after further adjusting for race, education, and playing position (Supplementary material online, *Figure S2*). This relationship was largely attenuated when additionally adjusting for reported anxiety and depression symptoms, as recollected football concussion symptoms did not predict significant variance in cognitive performance over and above anxiety and depression symptoms (ps > 0.05). This relationship was still significant, however, when adjusting for all other health-related variables (e.g., obesity, hypertension; Supplementary material online, *Figure S3*).

In contrast to the association between overall cognitive performance and recollected football concussion symptoms, overall cognitive performance was not associated with a binary classification of whether former players reported any previous concussion diagnosis ($r_p = -0.04$, 95% CI = 0.06 to −0.15, B = −0.07, SE = 0.09, $t = 0.81$, $p = 0.42$), self-reported number of diagnosed concussions ($r_p = -0.07$, 95% CI = 0.03 to −0.17, B = −0.05, SE = 0.04, $t = 1.28$, $p = 0.20$), professional play duration ($r_p = -0.04$, 95% CI = 0.07 to −0.14, B = −0.01, SE = 0.01, $t = 0.68$, $p = 0.50$), or age of first football exposure ($r_p = 0.0008$, 95% CI = 0.11 to −0.10, B = 0.0002, SE = 0.01, $t = 0.02$, $p = 0.99$). See Supplementary material online, *Figure S4* for position-specific associations between concussion exposure measures and overall cognitive performance.

Group-level differences in cognitive performance between former players and nonplayers were tested using multiple linear regression predicting cognitive test performance by group (former players vs. nonplayers) while adjusting for age. When using a significance threshold of $p < 0.00625$ to account for multiple comparisons, former players displayed worse age-adjusted performance than nonplayers on five tests: TMB Trails A, TMB Trails B, TMB Digit Symbol Matching, TMB Visual Paired Associates, and TMB Verbal Paired Associates (see Table 5 and Fig. 3A). Although the group-level performance of former players was worse than nonplayers on these tests, the effect sizes of performance differences were small (Cohen, 1988). As a sensitivity analysis, we adjusted for age differences between the player and nonplayer samples using inverse probability weighting (stabilized weights with 5% truncation; Thoemmes & Ong, 2016). Consistent with our initial analysis, this approach revealed better group-level performance for nonplayers on the same five cognitive tests (all ps < 0.001).

We next tested age-related variation in cognitive performance among players and nonplayers using models predicting test performance by age, group (players vs. nonplayers), and the interaction of age and group (Fig. 3B). Significant age × group interactions revealed larger differences in performance between younger and older former players than between younger and older nonplayers for TMB Trails B ($r_p = 0.11$, 95% CI = 0.02–0.19, $t = 2.52$, $p = 0.01$) and TMB Digit Symbol Matching ($r_p = 0.05$, 95% CI = 0.02–0.09, $t = 2.96$, $p = 0.003$); note, however, that the interaction for TMB Trails B failed to reach the $p < 0.00625$ significance threshold used to account for multiple comparisons. As a sensitivity analysis, we adjusted for age differences between the player and nonplayer samples using inverse probability weighting (stabilized weights with 5% truncation; Thoemmes & Ong, 2016). Using this approach, age × group interactions again revealed larger differences in performance between younger and older former players than between younger and older nonplayers for TMB Trails B ($p = 0.01$) and TMB Digit Symbol Matching ($p = 0.002$).

Discussion

Predictors of cognitive performance in former players

Here, we report the largest study to date characterizing the association between head injury exposure and objectively assessed cognitive function in former American-style professional football players. Retrospectively reported football concussion symptoms were associated with worse performance on a battery of cognitive tests, including assessments of episodic memory, sustained attention, processing speed, and vocabulary, taken on average 29 years after last playing football. In contrast, self-reported number of diagnosed concussions, professional play duration, and age of first football exposure were not significantly associated with overall cognitive performance. Many head injuries that cause concussion symptoms are not ultimately diagnosed as concussions (Kerr et al., 2015; McCrea, Hammeke, Olsen, Leo, & Guskiewicz, 2004), which may make diagnosed concussions a less sensitive measure of head injury exposure than symptom-based measurements and might explain the mixed findings of prior studies investigating associations between diagnosed concussions and cognitive performance. Previous studies have also provided mixed support for associations of cognitive performance with seasons of play (Fields, Didehbani, Hart, & Cullum, 2020; Hart et al., 2013; Randolph, Karantzoulis, & Guskiewicz, 2013; Roberts et al., 2019) and age of first football exposure (Alosco et al., 2017; Solomon et al., 2016; Stamm et al., 2015). In the present study, these measures of football exposure were less sensitive than recollected football concussion symptoms for predicting cognitive performance, suggesting that future studies assessing the association between prior head injuries and health outcomes may benefit from using a measure that captures specific symptoms experienced following a hit to the head. Querying the number of football injuries that resulted in loss of consciousness may be particularly useful, as this individual concussion symptom was sensitive to cognitive performance in the present study.

Notably, recollected football concussion symptoms did not predict significant variance in cognitive performance over and above anxiety symptoms and depression symptoms (Supplementary material online, *Figure S3*), due to anxiety and depression symptoms being associated with both cognitive performance and recollected football concussion symptoms. There are several possible explanations for this finding, which cannot be differentiated with our cross-sectional, retrospective study design. One possibility is that poorer cognitive performance, anxiety, and depression are all downstream effects of football injuries that produce concussion symptoms. Although this possibility is consistent with prior studies reporting associations between concussion exposure and mental health symptoms (Chrisman & Richardson, 2014; Didehbani, Munro Cullum, Mansinghani, Conover, & Hart, 2013; Guskiewicz et al., 2007; Montenigro et al., 2017; Roberts et al., 2019), drawing causal links between these variables is challenging without a well-documented concussion symptom history, which was not available for participants in the present study. A second possibility is that former players experiencing anxiety and depression symptoms at the time of being surveyed were biased to retrospectively report more football concussion symptoms, along with displaying worse cognitive performance than former players who were not experiencing such symptoms. Finally, a third possibility is that individuals experiencing or at high-risk for mental health symptoms may be more likely to experience concussion symptoms. Studies that help clarify the complex relationship between concussion symptoms, mental health symptoms, and cognitive performance will likely be critical for addressing the many negative health outcomes associated with concussion exposure (Broshek, De Marco, & Freeman, 2015; Solomon, Kuhn, & Zuckerman, 2016). Better understanding the relationship between these variables in today's professional football players may be possible by better documenting football-related injuries and their symptoms (e.g., by combining structured interviews with head impact sensor technology; Rowson & Duma, 2020), closely tracking mental and physical health symptoms, and repeatedly measuring both subjective and objective cognitive performance throughout players' careers.

Although prior reports have demonstrated that the measures used in the present study's testing battery measure distinct cognitive constructs (e.g., processing speed vs. working memory; Singh et al., 2021; Treviño et al., 2021), an exploratory factor analysis indicated that cognitive performance in former players was best explained by a single "general cognition" factor, rather than loading onto distinct latent factors as in prior studies. This result suggests that cognitive variation in the former player sample was largely domain-general, potentially due to football exposure and health-related variables being broadly associated with overall cognitive performance. Therefore, future work is needed to clarify whether football exposure and health-related variables are differentially associated with distinct cognitive constructs, or more broadly are associated with general cognitive performance.

Comparisons of cognitive performance in former players to nonplayers

Age-adjusted cognitive performance was generally worse for former players than for our nonplayer comparison sample (Fig. 3). In addition, for two tests of processing speed (TMB Trails B and TMB Digit Symbol Matching), age-related differences in cognitive performance were larger among the former player group than the nonplayer group (Fig. 3B). There are several possible explanations for this result, which our cross-sectional design cannot differentiate between. One possibility is that football exposure accelerates age-related declines in processing speed, producing cognitive disadvantages for former players relative to nonplayers at older ages, despite former players' similar or better performance at younger ages. A second possibility is that improved head injury prevention and management over time (e.g., by incorporating head impact sensor technology; Rowson & Duma, 2020) has lessened the impact of football exposure on cognitive performance, sparing younger former players from processing speed disadvantages displayed by older former players. Finally, a third possibility is that sampling biases may have differed between former players and nonplayers (Euser, Schram, Hofman, Westendorp, & Breteler, 2008). Although we adjusted for age differences between the former player and nonplayer groups, this adjustment does not remedy all potential biases related to age; for example, our study may have been biased to include only high-functioning older participants in the nonplayer group. Future longitudinal studies that closely match former player and nonplayer participants are needed to differentiate between these possibilities. Importantly, however, the observed differences in age-related cognitive performance between former players and nonplayers cannot be attributed solely to age differences between the groups, as we adjusted for age in our models by including age as a continuous covariate (rather than binning participants into discrete age groups); furthermore, these results were consistent when using inverse probability weighting to account for differences between the player and nonplayers groups.

Limitations

The biggest limitation of this study was our lack of information about former player's premorbid or pre-injury cognitive functioning. Although we had data on education level, previous work has found years of education to be an unreliable proxy for educational quality or experience (Glymour & Manly, 2008). For example, differential school quality that follows racial/ethnic lines (e.g., due to structural inequalities) means that a year of education is not necessarily comparable across schools (Avila et al., 2021). Indeed, baseline cognitive differences (where available) can explain post-injury cognitive differences among athletes with sports-related concussion (Wallace, Beidler, Covassin, Hibbler, & Schatz, 2021). Premorbid estimates of cognitive ability are therefore critical for interpreting post-injury cognitive differences (Carvalho et al., 2015).

Vocabulary scores remain relatively stable when assessing the acute effects of traumatic brain injury (Green et al., 2008). Thus, vocabulary can be a useful measure of premorbid cognitive performance when tested relatively soon after severe head injuries. In this study, we did not use vocabulary scores to estimate premorbid cognitive performance for two reasons. First, cognitive test scores were highly intercorrelated in our sample, with variations in scores best explained by a single latent factor that included vocabulary scores, making it statistically inappropriate to use vocabulary as a covariate. Second, our sample had a nearly 40-year gap (on average) between age of first football exposure and age of testing. Scores on the TMB Vocabulary test (adapted from the General Social Survey "wordsum" task; Cor, Haertel, Krosnick, & Malhotra, 2012) are more than one standard deviation higher among 55 year olds as compared with 15 year olds (Hartshorne & Germine, 2015). TMB Vocabulary scores among former players therefore likely reflect both word knowledge accumulated prior to playing football and decades of word learning thereafter. Given that head injury impacts vocabulary acquisition (Turkstra, Politis, & Forsyth, 2015), these scores may not reflect pre-football cognitive performance independent of football or concussion exposure (Maroon et al., 2015; Stamm et al., 2015). Our inability to estimate premorbid or baseline cognitive functioning is a significant limitation of the current work. Without such an estimate we cannot rule out the possibility, for example, that individuals with worse cognitive function may have been more likely to experience or report concussion symptoms playing professional football; doing so would require cognitive measures recorded before the start of football exposure (e.g., elementary academic achievement test scores).

Our study adds to the literature on sports-related concussion exposure and cognitive performance (Manley et al., 2017), as we recruited 353 former professional football players to complete eight objective measures of cognitive performance selected for their sensitivity to subtle differences in cognitive function. To obtain a larger sample of former players spanning a wide age range, we relied on retrospective reports of concussion exposure and remote, unsupervised assessment of cognitive performance, which introduced some notable limitations. First, concussion symptoms experienced playing football and history of diagnosed concussions were self-reported, which may have led to recall bias. Second, unsupervised cognitive assessment has many theoretical limitations (e.g., the possibility of poor effort; Kraut et al., 2004). Although some cognitive test scores may not accurately reflect cognitive performance due to these limitations, it is unclear how these limitations would result in our primary finding: recollected concussion symptoms being a more sensitive predictor of cognitive performance than other measures of football exposure in a group of former professional football players. In addition, consistent with prior reports (Hartshorne & Germine, 2015), older age was associated with worse performance on each cognitive test except for vocabulary, supporting the validity of test scores in the present study. Third, our nonplayer sample from the general population was not strictly matched to our sample of former football players, which prohibits strong conclusions about differences in cognitive performance between the two groups. Fourth, because the nonplayer sample for each cognitive test was different, test-specific variability in performance between former players and nonplayers could potentially be attributable to differences in the demographics of each test's nonplayer sample. Thus, although we adjusted for age, it is possible that other unmeasured variables associated with cognitive performance (e.g., anxiety and depression symptoms) differed between test-specific nonplayer samples. Finally, because this study tested associations between professional football exposure and cognitive performance in former NFL players, our results may not be generalizable to other populations at risk for head injury exposure, including female athletes.

Importantly, our study had a self-selection bias resulting in the exclusion of many former players in poor health. Our sample was a subset of former players who completed both a health questionnaire and, at a later date, a battery of cognitive tests. Consistent with previous investigations of health and attrition rates (Chatfield, Brayne, & Matthews, 2005; Euser, Schram, Hofman, Westendorp, & Breteler, 2008), our sample was less likely to report cognition-related difficulties than former players who completed only the health questionnaire (Table 1). In addition, a sensitivity analysis (Supplementary Methods 3) revealed that the association between recollected football concussion symptoms and self-reported cognition-related difficulties was weaker in our sample than in former players who did not complete the battery of cognitive tests. Due to the lack of participation of many of the most affected former players, our study likely underestimates the relationship between recollected football concussion symptoms and later life cognitive performance. Although our measure of football concussion symptoms was more sensitive than other football exposure variables for predicting cognitive performance, the clinical significance of this association, which had a small effect size, cannot be determined from this study. Still, our measures of objective cognitive performance were associated with self-reported cognition-related difficulties, demonstrating that our tests are at the very least sensitive to variation in self-perceived cognitive functioning, even with a self-selection bias of former players in relatively good health compared with non-participants. Although selection biases towards healthy individuals are often unavoidable (Grashow et al., 2019b), future studies might target former players with poorer health to estimate how self-selection biases influence associations between cognitive performance and measures of football exposure.

Despite including a 76-item health questionnaire and eight different cognitive tests, this study has limitations in the health-related variables and cognitive constructs it addresses. For example, age of first football exposure was operationalized as age when first playing organized football, which may be less sensitive than age when first playing tackle football for predicting cognitive performance. In addition, our questionnaire asked players to report only the frequency of concussion symptoms experienced after an injury playing professional football, and thus cannot capture variability in cognitive performance associated with other potential head injuries, including those sustained playing high school and college football (Montenigro et al., 2017). Furthermore, although we cannot account for all possible device-related differences between participants, we excluded participants who completed cognitive tests using mobile devices (Passell et al., 2021). Finally, our cognitive test battery assessed recognition-based memory, but did not include tests measuring free-recall; such tests are difficult to administer using remote, unsupervised assessments. Despite these limitations, the remote cognitive testing platform used in the present study has previously been found to produce results similar to in-person assessments (Germine et al., 2012), allowing us to collect reliable data while increasing participation.

Conclusions

We found that objective cognitive performance in former professional football players was associated with retrospectively reported football concussion symptoms, but not self-reported diagnosed concussions, years of professional play, or age of first football exposure. Lack of information about premorbid cognitive abilities limits interpretability, however, as associations may be due to differences in cognitive functioning prior to concussion or football exposure. Future investigations of the long-term effects of contact-sports exposure may benefit from including measures of recollected concussion symptoms following an injury.

Supplementary material

Supplementary material is available at *Archives of Clinical Neuropsychology* online.

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Conflict of Interest

Laura Thi Germine, Ph.D., is President and Director of the 501c3 nonprofit Many Brains Project, Inc., that supports open source cognitive tests for research. She previously served as Scientific Advisor to Sage Bionetworks, Inc., a 501c3 nonprofit that supports research studies. Douglas Terry, Ph.D., serves as a scientific advisor for HitIQ. He previously consulted for REACT Neuro, Inc. He has a consulting practice in forensic neuropsychology, including expert testimony, involving individuals who have sustained mild TBIs (including former athletes).

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