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Association of Playing High School Football With Cognition and Mental Health Later in Life

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Editorial

Supplemental content

IMPORTANCE American football is the largest participation sport in US high schools and is a leading cause of concussion among adolescents. Little is known about the long-term cognitive and mental health consequences of exposure to football-related head trauma at the high school level.

OBJECTIVE To estimate the association of playing high school football with cognitive impairment and depression at 65 years of age.

DESIGN, SETTING, AND PARTICIPANTS A representative sample of male high school students who graduated from high school in Wisconsin in 1957 was studied. In this cohort study using data from the Wisconsin Longitudinal Study, football players were matched between March 1 and July 1, 2017, with controls along several baseline covariates such as adolescent IQ, family background, and educational level. For robustness, 3 versions of the control condition were considered: all controls, those who played a noncollision sport, and those who did not play any sport.

EXPOSURES Athletic participation in high school football.

MAIN OUTCOMES AND MEASURES A composite cognition measure of verbal fluency and memory and attention constructed from results of cognitive assessments administered at 65 years of age. A modified Center for Epidemiological Studies' Depression Scale score was used to measure depression. Secondary outcomes include results of individual cognitive tests, anger, anxiety, hostility, and heavy use of alcohol.

RESULTS Among the 3904 men (mean [SD] age, 64.4 [0.8] years at time of primary outcome measurement) in the study, after matching and model-based covariate adjustment, compared with each control condition, there was no statistically significant harmful association of playing football with a reduced composite cognition score (−0.04 reduction in cognition vs all controls; 97.5% CI, −0.14 to 0.05) or an increased modified Center for Epidemiological Studies' Depression Scale depression score (−1.75 reduction vs all controls; 97.5% CI, −3.24 to −0.26). After adjustment for multiple testing, playing football did not have a significant adverse association with any of the secondary outcomes, such as the likelihood of heavy alcohol use at 65 years of age (odds ratio, 0.68; 95% CI, 0.32-1.43).

CONCLUSIONS AND RELEVANCE Cognitive and depression outcomes later in life were found to be similar for high school football players and their nonplaying counterparts from mid-1950s in Wisconsin. The risks of playing football today might be different than in the 1950s, but for current athletes, this study provides information on the risk of playing sports today that have a similar risk of head trauma as high school football played in the 1950s.

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More than 1 million students played high school American football in 2014,[1] but, recently, many have questioned the safety of the sport[2,3] or even called for its ban.[4] These concerns have been driven partially by reports of chronic traumatic encephalopathy,[5,6] increased risks of neurodegenerative disease,[7] and associations between a history of concussion and cognitive impairment and depression later in life[8-10] among retired professional football players.

Although they are concerning, most reports of chronic traumatic encephalopathy among retired professional football players are based on posthumously donated brains and are potentially affected by referral bias. One exception, a study by Bieniek et al,[11] examined a larger, nonselected brain bank and found a higher rate of chronic traumatic encephalopathy among former athletes than nonathletes. However, they determined participation in contact sports by querying only medical records, potentially underestimating the true rate of participation and leading to information bias.[12] Without population-level samples, it is difficult to estimate the base rate of long-term dysfunction among professional football players, much less among high school players.

There has been limited work examining the association of playing high school football with cognitive impairment and depression later in life. One study found an association between increased exposure to head trauma and cognitive impairment and depression among former high school and college players.[13] A population-level study by Savica et al[14] found that high school football players were not at a higher risk of neurodegenerative disease than their male classmates who did not play football. Although they are informative, these studies have limitations for elucidating an association between playing football and cognitive impairment; the former study[13] used volunteer participants, and the latter[14] did not control for any potential confounders, such as adolescent IQ or family background.[15-18]

In the absence of a randomized clinical trial, the criterion standard for studying the association of an exposure with an outcome is a prospective longitudinal study that follows a population sample and measures many potential confounders.[19-21] We use data from such a study, the Wisconsin Longitudinal Study (WLS) of graduates from Wisconsin high schools in 1957,[22] to study the long-term association of playing high school football with cognitive impairment and depression. The WLS contains a rich set of baseline variables related to family background, adolescent characteristics including adolescent IQ, and educational level that all may be linked to health in later life,[15-18] high school football participation, and cognitive and psychological well-being assessments at 54, 65, and 72 years of age.

Key Points

Question Does playing high school football have a statistically and clinically significant adverse association with cognitive impairment and depression at 65 years of age?

Findings In this cohort study using data from the Wisconsin Longitudinal Study among men graduating high school in Wisconsin in 1957, there was no statistically or clinically significant harmful association between playing football in high school and increased cognitive impairment or depression later in life, on average.

Meaning For men who attended high school in the late 1950s, playing high school football did not appear to be a major risk factor for later-life cognitive impairment or depression; for current athletes, this study provides information on the risk of playing sports today that have a similar head trauma exposure risk as high school football played in the 1950s.

Methods

After constructing the participant matches but before examining the outcome data, we registered the study at clincialtrials.gov (identifier: NCT02833129) and posted our protocol with matching results online to arXiv (identifier: arXiv: 1607.01756), as recommended by Rubin.[23] The University of Pennsylvania institutional review board approved the protocol for this matched observational study, and WLS interviewers obtained oral informed consent from participants.

Study Population

In 1957, the WLS randomly sampled 10 317 Wisconsin high school graduates (one-third of all graduates) and has observed them since then.[22,24] Data on participation in football were recorded following systematic reviews of high school yearbooks between January 2005 and February 2011. Participation data were unavailable for 1018 of the 4991 men (20.4%) in the WLS. An additional 69 men (1.4%) played sports with a high incidence of head trauma (eg, soccer, hockey, wrestling, and lacrosse). The remaining 3904 men (78.2%) were eligible for this study. Of these men, primary outcomes were unavailable for 1212 (31.0%), who were removed from our primary analysis. Of the remaining 2692 men, 834 (31.0%) played football and 1858 did not. Further details of eligibility and inclusion criteria can be found in the eAppendix in the Supplement. The WLS data set does not include history of concussion and total exposure to football prior to high school. These factors have been associated with cognitive decline in later life,[8,9,13,25] but we were unable to explicitly control for them in our analysis.

Primary and Secondary Outcomes

We considered 2 primary outcomes measured at 65 years of age (mean [SD] age, 64.4 [0.8] years) related to depression and cognitive impairment. We measured depression with the WLS-modified Center for Epidemiological Studies' Depression Scale (CES-D).[26] We constructed a composite cognition measure by averaging the *z* scores from the Letter Fluency (LF) and Delayed Word Recall (DWR) tests. Of the measures of language and executive function and verbal memory attention in the WLS, these were the most consistent with the National Institute of Health's recommended Common Data Elements in Traumatic Brain Injury research.[27] A meta-analysis of the neuropsychological effects of mild traumatic brain injury identified LF as the task most sensitive to exposure.[28] Impairments in DWR may be particularly relevant to cognitive defects later in life associated with chronic head injuries because prior research has identified associations between sports-related concussions and preclinical Alzheimer disease.[8] For individuals missing either an LF or DWR score, we used the available *z* score instead of the mean of the 2 scores.

tj;3Secondary outcomes were the composite cognition score at 72 years of age, modified CES-D scores at 54 and 72 years of age, individual cognitive test scores, hostility indices, anxiety and anger indices derived from the State-Trait Anxiety Inventory[29] and State-Trait Anger Expression Inventory-II,[30] and whether the individual reported consuming 5 or more alcoholic drinks on at least 5 separate occasions in the month preceding the WLS interview at 54, 65, and 72 years of age.

Regular physical activity in early adulthood has been associated with slower rates of cognitive decline,[31] potentially mediating any negative association of playing football and cognitive impairment. Accordingly, we examined whether football players were more likely than controls to engage in such activity at 35 years of age. See the eAppendix in the Supplement for more details on the outcomes.

Statistical Analysis

Matching Methods

To control for potential confounding variables, we used full matching to create matched sets containing 1 football player and 1 or more controls or 1 or more football players and 1 control. These sets optimally balance the distribution of the baseline variables listed in **Table 1** between football players and controls.[32] Our full matching procedure first applies a propensity score caliper[33] and then minimizes the rank-based Mahalanobis distance between matched participants with similar propensity scores.[34] Our objective in matching is to achieve standardized differences between exposed participants and controls on baseline variables below 0.2 SDs. Regression-based covariate adjustment has been shown to remove biases due to covariate imbalance of this magnitude.[35,36]

Our control group consisted of all participants who did not play high school football (all controls). We also considered 2 subsets as alternative control groups: those who did not play any high school sports (nonsport controls) and those who played a noncollision sport but did not play football (noncollision sport controls); eTable 2 in the Supplement tabulates participation of eligible individuals by sport. These alternative control groups may differ along unmeasured characteristics, such as personality and fitness, that could affect our outcomes. A convincing study would show consistent evidence (or lack thereof) of an exposure association across comparisons with each control group. Comparability of the 2 alternative control groups would suggest that such unmeasured characteristics did not significantly influence the outcomes of interest.[37] To facilitate these 4 comparisons—football vs all controls, football vs noncollision sport controls, football vs nonsport controls, and noncollision sport vs nonsport controls—we built 4 separate full matches that were exactly matched on availability of LF, DWR, and modified CES-D scores at 65 years of age (eAppendix in the Supplement). Matching was performed prior to analysis between March 1 and July 1, 2017.

Attrition Analysis for the Availability of Outcome

eTable 3 in the Supplement shows the availability of primary outcomes. To examine whether playing high school football increased the likelihood of attrition from the WLS or the availability of outcomes at 65 years of age, we fitted logistic regressions to estimate the availability of the LF, DWR, and modified CES-D scores at 65 years of age using all baseline covariates and an exposure indicator.

Test Statistic for Exposure Association

For each continuous outcome, we fitted a multiple regression model using the same baseline covariates used in the matching, indicators for the matched sets, and an exposure indicator. We tested for an exposure association using a 2-tailed *t* test. $P < .05$ was considered significant. The combination of full matching and regression is robust and efficient.[37-40] An identical procedure was used for binary outcomes except we fitted a conditional logit regression model and reported the outcomes as odds ratios (ORs). For each outcome variable, we judged effect sizes by the popular criterion attributed to Cohen: 0.2 SDs for small effects, 0.5 SDs for medium effects, and 0.8 SDs for large effects.[41] For the combined cognition score, these cutoffs (on the absolute scale) are 0.16 for small effects, 0.41 for medium effects, and 0.65 for large effects; for the modified CES-D score, 2.56 for small effects, 6.41 for medium effects, and 10.25 for large effects.

Test for Unmeasured Confounding Using Postexposure Variables

Since acute cognitive dysfunction following concussions or mild traumatic brain injury resolves within 3 months in most patients,[42-46] we hypothesized that any medium-term differences in outcomes before 35 years of age between football players and controls would be due to unmeasured differences that existed prior to high school graduation. To assess the presence of these differences, we tested whether playing football was associated with several medium-term postexposure variables (military service, years of education, occupational prestige of job held in 1974, and earnings in 1974) at $\alpha = .05$, with no correction for multiple testing.

Ordered Hypothesis Testing

We tested each primary outcome at $\alpha = .025$ and reported 97.5% CIs so that the overall familywise error rate was 0.05. To perform the aforementioned comparisons with different control groups without losing power owing to multiple testing, we used an ordered testing procedure[47] (eAppendix in the Supplement).

Secondary Analyses

For testing the association of playing football with the secondary outcomes, we used only matched sets constructed using all controls. We adjusted for multiple testing of secondary outcomes with the Benjamini-Hochberg procedure,[48] controlling the false discovery rate at $\alpha = .05$.

Table 1. Comparison of Mean Baseline Covariates for Football Players vs All Controls, Before and After Matching[a]

Covariate	Football Players	All Controls[a]		Standardized Difference	
		Before Matching	After Matching	Before Matching	After Matching
Duncan socioeconomic index of job to which participant aspired in 1957	577.67	541.94	560.13	0.16	0.08
High school size, No.	134.86	188.12	139.01	−0.43	−0.03
High school rank (quantile)	48.81	45.12	47.45	0.14	0.05
Parental income in 1957 ($100)	69.38	62.53	65.22	0.10	0.06
Parental educational level, y					
Father	9.91	9.76	9.84	0.04	0.02
Mother	10.80	10.50	10.72	0.11	0.03
Duncan socioeconomic index of father's job in 1957	355.30	339.87	348.06	0.07	0.03
Planned future education, y	2.34	1.79	2.17	0.26	0.08
IQ	102.39	101.60	101.88	0.05	0.03
Considered an "outstanding student" by teacher, % (No./Total No.)	11.5 (96/834)	10.3 (191/1858)	12	0.04	−0.01
Participated in band, orchestra, chorus, or musical ensembles, % (No./Total No.)	33.7 (281/834)	28.5 (529/1858)	33	0.11	0.02
Participated in drama, speech, or debate, % (No./Total No.)	29.0 (242/834)	20.0 (371/1858)	28	0.21	0.02
Participated in school government, % (No./Total No.)	35.6 (297/834)	14.9 (276/1858)	30	0.49	0.14
Participated in school publications, % (No./Total No.)	23.0 (192/834)	14.9 (276/1858)	23	0.18	−0.01
Father was a farmer, % (No./Total No.)	18.2 (152/834)	18.6 (345/1858)	18	−0.01	0.00
Planned to serve in the military, % (No./Total No.)	26.7 (223/834)	27.1 (504/1858)	27	−0.01	0.00
Attended Catholic high school, % (No./Total No.)	6.6 (55/834)	11.3 (210/1858)	8	−0.17	−0.05
Lived with both parents, % (No./Total No.)	91.2 (759/832)	90.7 (1685/1857)	90	0.02	0.06
Mother working in 1957, % (No./Total No.)	36.7 (305/831)	35.8 (662/1847)	35	0.02	0.03
Teachers encouraged college, % (No./Total No.)	57.7 (464/804)	45.4 (807/1777)	55	0.25	0.05
Parents encouraged college, % (No./Total No.)	65.1 (530/814)	60.2 (1076/1788)	65	0.10	−0.01
Had friends who planned to go to college, % (No./Total No.)	42.7 (312/731)	36.4 (587/1611)	42	0.14	0.01
Extent to which participant discussed future plans with teachers, % (No./Total No.)					
Not at all	24.3 (199/820)	31.0 (561/1807)	26	−0.12	−0.04
Sometimes	65.6 (538/820)	61.2 (1105/1807)	64	0.08	0.03
Very much	10.1 (83/820)	7.8 (141/1807)	10	0.04	0.01
Extent to which participant discussed future plans with parents, % (No./Total No.)					
Not at all	2.1 (17/824)	2.3 (43/1839)	2	−0.01	0.01
Sometimes	42.0 (346/824)	45.7 (840/1839)	44	−0.07	−0.03
Very much	55.9 (461/824)	52.0 (956/1839)	54	0.07	0.03
Family wealth relative to community, % (No./Total No.)					
Considerably below average	0.5 (4/814)	0.5 (9/1790)	0	0.00	0.00
Somewhat below average	5.2 (42/814)	7.0 (126/1790)	7	−0.03	−0.04
Average	70.1 (571/814)	70.3 (1259/1790)	68	0.00	0.04
Somewhat above average	21.6 (176/814)	20.5 (367/1790)	22	0.02	0.00
Considerably above average	2.6 (21/814)	1.6 (29/1790)	2	0.02	0.00
Financial support from parents for college, % (No./Total No.)					
Cannot support	28.3 (208/735)	32.8 (526/1605)	31	−0.07	−0.05
Can support, with some sacrifice	58.0 (426/735)	54.4 (873/1605)	56	0.06	0.04
Easily support	13.7 (101/735)	12.8 (206/1605)	13	0.02	0.01
APOE ε4 variants, No.[b]	30	27	27	0.07	0.07

[a] Before matching control values are unweighted, and after matching control values are weighted according to the composition of the matched sets (eTable 1 in the Supplement).

[b] We did not explicitly match on the number of *APOE* ε4 variants, but we nevertheless assess the balance of this variable before and after matching.

Because physical activity at 35 years of age could mediate the association of playing football with the primary outcomes, we tested for football's association with physical activity at α = .05 using the same matches as the primary analysis.

The number of ε4 variants of the apolipoprotein E gene (*APOE* [OMIM 107741]), a risk factor for developing Alzheimer disease,[49] was available for a limited subset of participants. We assessed the balance of the number of ε4 variants and the availability of *APOE* data between football players and each control group. We repeated our primary analysis restricted to participants with *APOE* data and included the number of ε4 variants in the match. We then tested whether playing high school football and the presence of the *APOE* ε4 variant has an interaction association with long-term cognitive or mental health outcomes.

The availability of outcomes at multiple time points enabled us to compare rates of cognitive decline among football players and all controls. For each individual cognitive test and the modified CES-D score, we fitted a mixed-effects model with fixed effects for playing football, age, and their interaction, and a time-invariant random effect for each participant. We also included the covariates from Table 1 as fixed effects. This analysis without matching includes many of the 1212 individuals who were excluded from the primary analysis because they lacked LF, DWR, and modified CES-D scores at 65 years of age. We used a Benjamini-Hochberg correction to control the false discovery rate at α = .05.

Results

Attrition Analysis

Football players were not significantly more or less likely than controls to be missing the LF score (OR, 1.07; 97.5% CI, 0.90-1.28; *P* = .37), the DWR score (OR, 1.08; 97.5% CI, 0.91-1.29; *P* = .31), or the modified CES-D score (OR, 1.15; 97.5% CI, 0.96-1.39; *P* = .09) at 65 years of age.

Matching

Table 1 shows the standardized differences from matching football players with all controls. Before matching, the 2 groups were adequately balanced (standardized differences, <0.2) on all variables except high school size, participation in school government, and planned years of future education. After matching, all standardized differences were less than 0.2, so our covariate adjustment could remove remaining differences in the covariates.[35,36] The other matches were similar (eTables 4-6 in the Supplement). The distributions of IQ, planned years of future education, and parental income for football players and matched controls were very similar (eFigure in the Supplement). eTables 7 to 11 in the Supplement provide further details on the matching results.

Testing Unmeasured Confounding Using Postexposure Variables

After matching, we found that playing high school football was not significantly associated with serving in the military between 1957 and 1975 (OR, 1.05; 97.5% CI, 0.91-1.22; *P* = .42), years of education up to 1975 (1.04; 97.5% CI, 0.87-1.25; *P* = .62), occupational prestige of job held in 1974 (-6.86; 97.5% CI, -29.67 to 15.96; *P* = .50), or earnings in 1974 (10.30; 97.5% CI, -1.85 to 22.45; *P* = .06). The distributions of postexposure variables were similar across football players and each version of the matched controls (eFigure in the Supplement).

Primary Outcomes

The distributions of the primary outcomes for football players and each version of the matched controls were similar (**Figure 1**). **Table 2** shows the estimated treatment effect in each of the 4 comparisons.

Cognition

Football players did not have significantly different composite cognition scores than all controls (−0.04; 97.5% CI, −0.14 to 0.05; *P* = .37), and the 97.5% CI contained only effects smaller than the small effects cutoff (0.15) (Table 2). Compared with each control group, football players' composite cognition scores were not significantly different, although when compared with nonsport controls, the 97.5% CI contained some effects above the small-size cutoff but none above the medium-size cutoff (0.41). Noncollision sport controls and nonsport controls were also not significantly different (−0.09; 97.5% CI, −0.20 to 0.03; *P* = .10).

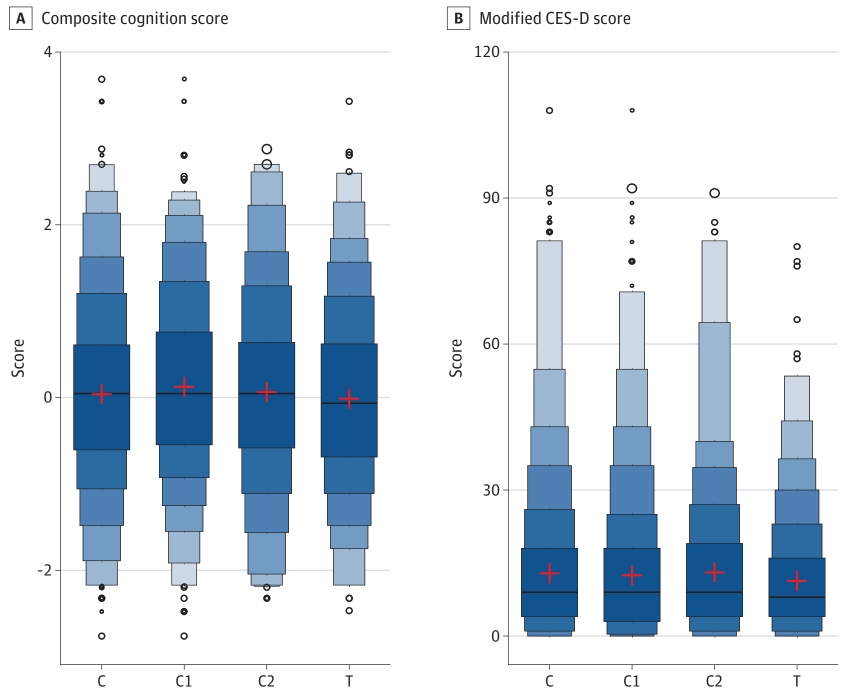
Depression

Football players' modified CES-D scores were significantly lower (−1.75; 97.5% CI, −3.24 to −0.26; *P* = .01) than all controls, meaning that they reported fewer depressive symptoms (Table 2). The 97.5% CI suggests that playing high school football could have a beneficial effect above the small-size cutoff (2.56) but not above the medium-size cutoff (6.4). Because the 97.5% CI contains only beneficial effects of football on depression, there is no evidence that football is associated with increased depression. Compared with each control group, we obtained similar findings, although the association of playing football with depression was not significant when compared with nonsport controls (−1.27; 97.5% CI, −2.89 to 0.35; *P* = .08). Noncollision sport controls and nonsport controls' modified CES-D scores were also significantly different (0.67; 97.5% CI, −1.19 to 2.52; *P* = .42).

Secondary Outcomes

Table 3 shows the estimated association of playing football with secondary outcomes when comparing football players with all controls.[50] After Benjamini-Hochberg correction, no estimated effects were significant. The estimates and 97.5% CIs for the association of playing football with cognitive impairment at 72 years of age (−0.01; 97.5% CI, −0.12 to 0.10) are similar to those at 65 years of age (−0.04; 97.5% CI, −0.14 to 0.05; *P* = .37). Relative to all controls, football players had lower modified CES-D scores at 54 years of age (−0.96; 97.5% CI, −2.65 to 0.73; unadjusted *P* = .20) and 72 years of age (−0.62; 97.5% CI, −2.78 to 1.53; unadjusted *P* = .52), but

Figure 1. Postmatching Distributions of Primary Outcomes



A, Postmatching distributions of the composite cognition score in 2003 for football players (T), all controls (C), nonsport controls (C1), and other sport controls (C2). B, Distributions of the modified Center for Epidemiological Studies' Depression Scale (CES-D) score in 2003. The lower limits of the boxes indicate the weighted, empirical second, third, sixth, 13th, and 25th percentiles (from bottom to top), and the upper limits indicate the 98th, 97th, 94th, 87th, and 75th percentiles (from top to bottom). The sizes of the outliers are proportional to their weights. The red cross indicates the weighted sample mean, and the black horizontal line indicates the weighted sample median. The points beyond are outliers beyond the 98th and second percentiles.

Table 2. Estimated Effect of Playing High School Football

	Estimated Effect (97.5% CI)			
Outcome	Football vs All Controls	Football vs Nonsport Controls	Football vs Noncollision Sport Controls	Noncollision Sport Controls vs Nonsport Controls
Combined cognition score	−0.04 (−0.14 to 0.05)	−0.09 (−0.20 to 0.02)	−0.02 (−0.14 to 0.10)	−0.09 (−0.20 to 0.03)
Modified CES-D score	−1.75 (−3.24 to −0.26)[a]	−1.27 (−2.89 to 0.35)	−1.78 (−3.50 to −0.06)	0.67 (−1.19 to 2.52)

Abbreviation: CES-D, Center for Epidemiological Studies' Depression Scale.

[a] Significant using the ordered testing procedure. For the composite cognition score, the cutoff for small effects is 0.16, for medium effects is 0.41, and for large effects is 0.65. For the modified CES-D score, the cutoff for small effects is 2.56, for medium effects is 6.41, and for large effects is 10.25.

the differences were not statistically significant, and the 97.5% CIs contained only values smaller than the small effect cutoff.

Apart from the Immediate Word Recall test, none of the 97.5% CIs for individual cognitive tests contained values larger than the small effect cutoff. After Benjamini-Hochberg correction, the difference in Immediate Word Recall test scores at 72 years of age between football players and all controls was not significant (0.20; 97.5 CI, −0.02 to 0.41; unadjusted P = .04) (Table 3). Football players' anger, anxiety, and hostility indices at all ages were not significantly different from all controls' indices. Football players were not significantly more likely than controls to consume a large amount of alcohol at 54 years of age (0.49; 97.5% CI, 0.21-1.14; unadjusted P = .06), 65 years of age (0.68; 97.5% CI, 0.32-1.43; unadjusted P = .25), and 72 years of age (1.11; 97.5% CI, 0.18-6.68; unadjusted P = .90).

Physical Activity

Compared with all controls and nonsport controls, at 35 years of age, football players were significantly more likely to engage in regular moderate to vigorous physical activity (all controls: OR, 1.23; 97.5% CI, 1.02-1.48; P = .02; nonsport controls: OR, 1.37; 97.5% CI, 1.11-1.70; P = .001). Football players were not significantly more or less likely to engage in such activity than noncollision sport controls. Noncollision sport controls were significantly more likely to engage in such activity than were nonsport controls.

Interaction of *APOE* ε4 Status With Playing High School Football

When we repeated our analysis using only individuals with available genotype data, our findings were similar (eTables 11-22 in the Supplement). The presence of an additional *APOE* ε4 variant does not significantly modify the association of playing high school football with modified CES-D scores (-1.49; 97.5% CI, -3.39 to 0.41; P = .08) or composite cognitive scores (0.01; 97.5% CI -0.11 to 0.14; P = .80) at 65 years of age (eTable 23 in the Supplement).

Mixed-Effects Models for Longitudinal Data

Figure 2 plots the longitudinal trajectories of mean scores for football players with mean covariate values as well as mean

Table 3. Estimated Effect of Playing Football Compared With All Controls for Secondary Outcomes

Outcome	Effect (97.5% CI)	Small Effect Cutoff	Unadjusted *P* Value[a]
Analogs of primary outcomes			
Composite cognition score (at 72 y)	−0.01 (−0.12 to 0.10)	0.17	.81
Modified CES-D score			
At 54 y	−0.96 (−2.65 to 0.73)	2.65	.20
At 72 y	−0.62 (−2.78 to 1.53)	2.80	.52
Individual cognitive test scores			
Letter Fluency score			
At 65 y	−0.20 (−0.77 to 0.38)	0.88	.44
At 72 y	−0.20 (−0.79 to 0.40)	0.84	.45
Delayed Word Recall score			
At 65 y	−0.11 (−0.37 to 0.15)	0.40	.36
At 72 y	−0.04 (−0.30 to 0.22)	0.33	.73
Digit Ordering score			
At 65 y	−0.05 (−0.44 to 0.34)	0.61	.77
At 72 y	−0.02 (−0.48 to 0.44)	0.55	.92
Similarity score			
At 54 y	−0.04 (−0.31 to 0.24)	0.56	.76
At 65 y	−0.03 (−0.29 to 0.22)	0.48	.76
At 72 y	−0.11 (−0.41 to 0.19)	0.48	.43
Immediate Word Recall score			
At 65 y	−0.05 (−0.26 to 0.17)	0.36	.64
At 72 y	0.20 (−0.02 to 0.41)	0.28	.04
Number Series score (at 72 y)	0.39 (−7.76 to 8.54)	11.88	.91
Behavioral and emotional outcomes			
Hostility score			
At 54 y	−0.16 (−0.47 to 0.15)	0.48	.25
At 65 y	−0.12 (−0.38 to 0.13)	0.43	.28
At 72 y	0.00 (−0.35 to 0.36)	0.46	.99
Speilberger Anger Index			
At 65 y	−0.29 (−0.84 to 0.26)	0.93	.23
At 72 y	0.34 (−0.42 to 1.11)	0.97	.32
Speilberger Anxiety Index			
At 65 y	−0.47 (−1.32 to 0.38)	1.45	.21
At 72 y	0.31 (−0.82 to 1.44)	1.45	.54
Heavy use of alcohol[b]			
At 54 y	0.49 (0.21 to 1.14)	1.50	.06
At 65 y	0.68 (0.32 to 1.43)	1.50	.25
At 72 y	1.11 (0.18 to 6.68)	1.50	.90

Abbreviation: CES-D, Center for Epidemiological Studies' Depression Scale.

[a] From testing whether the treatment effect is equal to zero.

[b] Effects on binary outcomes are reported on the odds ratio scale. The small effect size cutoff corresponding to the Cohen 0.2-SD threshold is 1.5.[50]

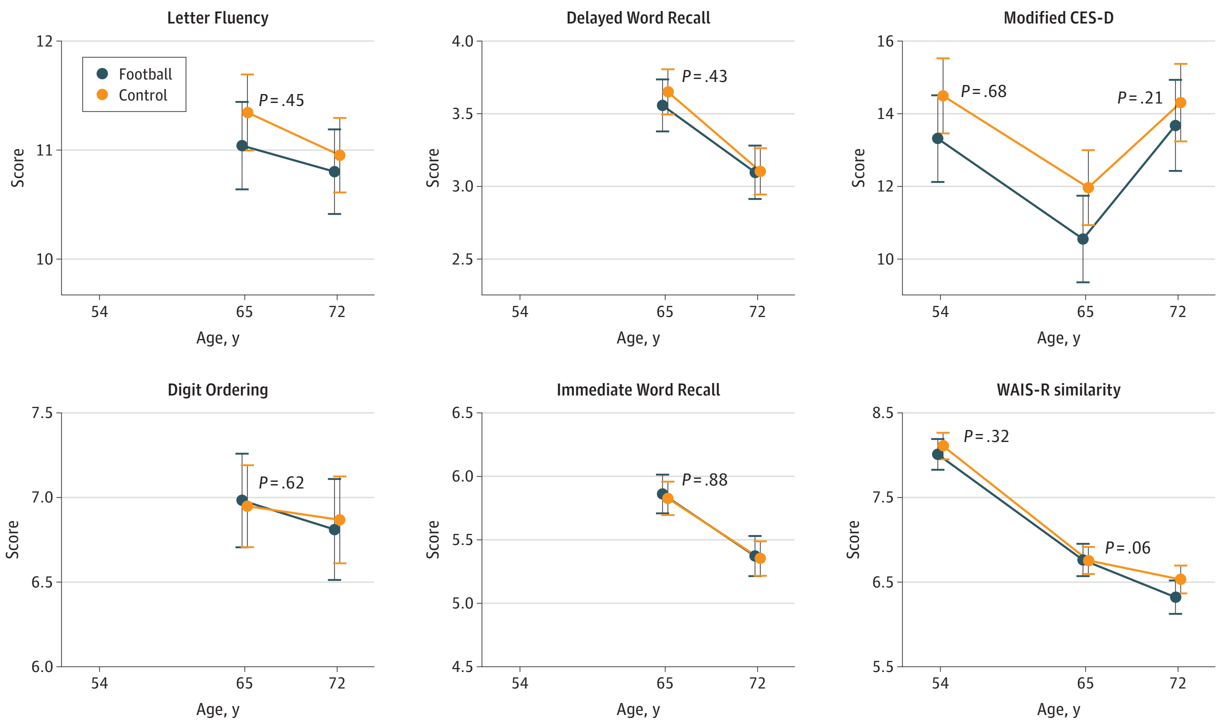
counterfactual scores for these same players had they not played football. After Benjamini-Hochberg correction, the association of playing football with these outcomes at all ages was not significant (eTable 24 in the Supplement). The changes in football players' and controls' test scores over time were not significantly different.

Discussion

Among men who graduated from Wisconsin high schools in 1957, playing high school football was not adversely associated with cognitive impairment or depression later in life. Furthermore, the corresponding 97.5% CIs contain only small positive and negative effect sizes. Our findings are consistent with those of Savica et al,[14] who found no differences in the incidence rates of neurodegenerative disease among football players and their non-football-playing classmates in a contemporaneous cohort.

Athletes and parents may consider our findings when weighing the potential risks and benefits of participation in high school athletics. Participation in high school sports, even contact sports with a high risk of head trauma, has potential benefits, including promoting physical activity, teamwork, and recreation. Indeed, in our cohort, playing any high school sport, football or otherwise, was associated with increased physical activity at 35 years of age. However, such participation is not without risk, and our findings do not speak to the benefits of

Figure 2. Longitudinal Trajectories of Outcomes Adjusted for Covariates



Longitudinal trajectories of estimated mean cognitive test and modified Center for Epidemiological Studies' Depression Scale (CES-D) scores for football players, with mean values of the covariates among football players (blue line) along with 95% CIs at each time point. Also shown are the counterfactual trajectories for the same individuals (ie, with mean values of the covariates among football players) had they not played football (orange line). *P* values are shown for testing the null hypothesis that the change in mean scores between successive ages for football players and controls, adjusted for covariates, are equal. WAIS-R indicates Wechsler Adult Intelligence Scale–Revised.

common-sense measures, such as improving concussion management protocols.

Strengths and Limitations

Our study has several strengths along with some limitations. Strengths include the use of prospectively collected longitudinal data from a large population sample and careful control for several important confounders, including adolescent IQ, high school rank, and parent's educational level. Using multiple control groups and comparing postexposure variables thought to be unaffected by playing football, we found no evidence of unmeasured confounding. However, because 31.0% of eligible participants were missing both primary outcomes, our results may be limited by selection bias. The attrition analysis found that football players were not significantly more or less likely to be missing either primary outcome, somewhat mitigating this concern.

Our findings may not generalize to current high school football players owing to changes in playing style, training technique, protective equipment, and rules aimed at improving safety. Although high school football today may be safer as a result of these changes, it is possible that the frequency and severity of head impacts have increased owing to the faster pace of the game, the larger body size of the players,[51] or an increased perception of safety.[52] Exposure to repeated head trauma before 12 years of age may lead to cognitive decline later in life,[53] but information on the age of first exposure is unavailable in the data set.

Although we did not find evidence of a large mean association of playing high school football with cognitive impairment and depression later in life, some subgroups of football players may have an elevated risk of dysfunction later in life. Several studies have found that a history of multiple concussions may have long-term cognitive and behavioral consequences[8,9,13,25] and that the frequency and severity of head impacts vary by team position (eg, quarterback, receiver).[54] Concussion history and position information were unavailable. Further research is needed to examine the risks for these subgroups.

Conclusions

Among men graduating from high school in Wisconsin in 1957, we did not find evidence that playing football had a negative long-term association with cognitive functioning and mental health at 65 and 72 years of age. Although our findings may not generalize to current high school football players, they may be relevant to current athletes playing contact sports with similar mean levels of head trauma as among the WLS football players. Repeating our analysis with a younger cohort as they reach 65 years of age may improve our understanding of how the risks of playing football have evolved over time.

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