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An Exploratory Study of Mild Cognitive Impairment of Retired Professional Contact Sport Athletes

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Abstract

Objective—To test the hypothesis that Mild Cognitive Impairment (MCI) rates are higher among retired professional contact sport athletes compared to non-contact athlete controls and compare history of contact sports to other MCI risk factors.

Setting—University Concussion Management Clinic

Participants—21 retired National Football League (NFL) and National Hockey League (NHL) players and 21 aged matched non-contact athlete controls.

Designs—Case-control

Main Measures—Comprehensive Criteria was used to assess MCI based on Wisconsin Card Sorting Test, Delis-Kaplan Executive Function System, Trail Making Part A and B, Wechsler Adult Intelligence Scale-Third Edition subtests, Neuropsychological Assessment Battery Memory Module List Learning, Story Learning, and Naming subtests, and Controlled Oral Word Association Test. The Wide Range Achievement Test was used as a proxy measure for IQ.

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Atherosclerotic cardiovascular disease risk factors were self-reported and blood cholesterol were measured. Depression was measured by Beck Depression Inventory-II (BDI).

Results—Eight contact sport athletes (38%) and three non-contact athletes (14%) met MCI criteria ($p=0.083$). Contact sport athletes' scores were significantly worse on Letter Fluency and List B Immediate Recall. Contact athletes were more obese, had more vascular risk factors, and had higher scores on the BDI than Controls.

Conclusion—Athletes with a history of playing professional contact sports had more vascular risk factors and higher depression scores. MCI rates were somewhat higher, though not significant.

Keywords

cerebral concussion; athletics; mild cognitive impairment; cognitive reserve; neuropsychology tests; risk factors

INTRODUCTION

Much attention has been given to Chronic Traumatic Encephalopathy (CTE) as a cause of behavioral, mood, and cognitive changes among retired professional contact sport athletes. Other competing hypotheses for these changes have received less attention. Vascular, mood, and other disease etiologies leading to Mild Cognitive Impairment (MCI) may explain some of the cognitive changes among aging professional athletes. A study using post-mortem analysis shows that up to 99% of retired NFL players had chronic traumatic encephalopathy (CTE) with 71% having severe CTE and it is suggested that MCI is present in CTE.¹ The definition of MCI has changed since its inception more than twenty years ago.² It is distinguishable from normal aging and may be a precursor to dementia.³ A patient with MCI may be aware of cognitive difficulties and able to function independently.⁴ The DSM-V diagnostic criteria for Mild Neurocognitive Disorder (a broader term which includes MCI) states that it includes a modest impairment in cognitive performance, preferably documented by standardized neuropsychological testing.⁵ Some studies of retired NFL players have not found evidence for cognitive, mood, and behavioral changes that would be consistent with CTE. Randolph et al.⁶ studied a subsample of 513 retired football players over 50 whose spouse completed a screening interview for MCI. They identified players with probable MCI and compared this group to age-matched healthy controls and a sample diagnosed with MCI. The cognitive profile of the NFL MCI group was milder although similar to the profile of the clinical MCI group. There was no association between years of play and cognitive scores. They concluded that their results supported diminished cognitive reserve (process of adapting to deterioration by using cognitive processing resources to compensate for deficits) rather than CTE as an explanation for MCI.

Alosco et al.⁷ studied 25 professional football players (mean age at death = 65 years) with autopsy confirmed stage III or IV CTE using next-of-kin interviews. They found that all 25 had cognitive symptoms and their age of cognitive decline was inversely related to their cognitive reserve. Unfortunately, this study did not compare the football players with a control population. Hart et al.⁸⁸ studied 34 retired football players, aged 41 to 79 years (mean 61.8), and found that 14 of 34 (41%) demonstrated cognitive deficits. Eight of 34

were identified with MCI which the authors note is slightly higher than the proportion in the general population, but not significant. McMillan et al.⁹ studied mental health and cognitive functioning in 52 retired professional rugby players aged 53.5 years (26 – 79) and compared them to age-matched healthy controls. Despite a high number of concussions in the rugby players, no differences in mental health or cognitive functioning were found later in life.

Other hypotheses for MCI in retired contact-sport athletes have received less attention. Willeumier et al.¹⁰ studied 38 over-weight and 38 healthy-weight retired National Football League (NFL) players (mean age = 57 years, range 25 – 82) and showed that players with higher body mass had significantly worse neuropsychological test scores compared to the healthy-weight players. Hart et al.⁸ showed that differences in regional blood flow using arterial spin labeling in retired NFL players corresponded to regions associated with impaired cognitive performance. Other etiologies, like depression, have been associated with MCI in the non-athlete population and may explain some of the cognitive changes among aging former professional athletes.^{11,12} Due to the controversy present in the literature, we wanted to study a sample of retired professional contact sport athletes and compare them to non-contact sport athlete controls on rates of MCI, cognitive scores, and other etiologies of MCI like vascular disease and depression. We hypothesized that the contact sport athletes would have higher rates of MCI, lower neurocognitive scores, and more vascular and depression risk factors.

METHODS

The current case-control study was completed as part of a larger study of retired athletes (*cite overview paper*) at the University at Buffalo. Approval was obtained prior to the study from the University at Buffalo IRB committee.

Study Participants

The contact sport athlete group was composed of former NFL and National Hockey League (NHL) players who were contacted and ultimately recruited through their respective local alumni associations (N=21, mean age 56.7). The non-contact athlete control group was composed of people who participated in non-contact sports (N=21, mean age 55.4) and were contacted through associations of athletic clubs that included older athletes on their roster. Detailed inclusion and exclusion criteria are presented in the *overview paper*.

Measures

Neurocognitive Measures—Executive function was assessed with the Wisconsin Card Sorting Test (WCST)¹³ and the Delis-Kaplan Executive Function System (D-KEFS).¹⁴ Five subtests for the WCST (perseverative, non-perseverative, and conceptual level responses, perseverative and total errors) and two subtests for the DKEFS (inhibit and switch) were selected based on their relevance to the long term effects of multiple concussions. Attention was assessed with the Wechsler Adult Intelligence Scale, Third Edition (WAIS-III) using the Standardization Sample norms for Scaled Scores for the subtest of Digit Span¹⁵ and the Trail Making Test Part A.¹⁶ Memory was assessed with the Neuropsychological Assessment Battery (NAB) Memory Module including the four primary scores for immediate and

delayed recall from the List Learning test and immediate and delayed recall for phrases for the Story Learning test, using the same parallel form across participants.¹⁷ Language was assessed using Controlled Oral Word Association Test (COWAT) and NAB Naming Test.^{18–20} For the COWAT, the FAS form was used for phonemic fluency and the Animal Naming task was used to measure category or semantic fluency.

Finally, the domain of perceptual motor skills was assessed with the WAIS-III Scaled Scores for the Digit Symbol subtest¹⁵ and Trail Making, Part B.^{16,21} IQ was estimated using standard scores from a proxy measure for IQ, the WRAT-4 Word Reading achievement test.^{21,22} Each of the scores for the tests noted above were converted to T-scores in order to provide a common metric for the subtests of each of the measures. All of the tests were performed under the supervision of the same experienced neuropsychologist.

Criteria for MCI—To define MCI we used the Jak. et al.²³ publication which provided several approaches to quantifying cognitive impairment that use test scores in multiple cognitive domains. The cognitive domains are based on norm-referenced neuropsychological test scores in attention, memory, executive function, language, and visuospatial domains. They recommend the Comprehensive criteria to classify individuals as MCI or normal. The criteria include (1) two test scores below 1 standard deviation (SD) in one domain or (2) at least one test score below 1 SD in three domains. Subtypes of MCI have been based on test scores below 1 or 1.5 standard deviations in one versus multiple domains and in memory versus non-memory domains. The four currently recognized subtypes include: memory, one domain; memory, multiple domains; non-memory, one-domain; and non-memory, multiple domains.^{24,25} At least two neuropsychology tests were included for each domain. For tests with more than one score per test, we included 2 to 5 primary scores for that test.

Depression—Beck Depression Inventory-II (BDI-II) was used to assess depression in both groups. It is a validated 21-item instrument that rates depression in the following categories: none, mild, moderate, and severe.²⁶

Vascular Risk Factors—Participants reported on vascular risk factors, including a history of: high blood pressure, diabetes, smoking, elevated cholesterol, and obesity. One or more vascular risk factors were compared to no vascular risk factors. Serum cholesterol levels and supine blood pressures were obtained. The Framingham Heart Study atherosclerotic cardiovascular disease (ASCVD) risk calculator was used to estimate the 10-year primary risk of ASCVD for people aged 40 to 79.²⁷ Patients are considered to be at “elevated” risk if the Pooled Cohort Equations predicted risk is $\geq 7.5\%$.²⁸ The factors used in calculating risk include: age, gender, race, total cholesterol, high density lipoproteins, systolic blood pressure, diastolic blood pressure, history of high blood pressure, history of diabetes, and smoking.

Statistical Analysis

According to the systematic review and meta-analysis by Karr et al.²⁹, an estimated effect size of 0.80 was used for the power analysis. Based on the computed power analysis, the results indicated that in order to achieve a power of 0.80 with a one sided test at level 0.05, a

total of 20 participants in each group was required. Independent two sample t-tests were used to compare neuropsychology test scores in each of five domains between the contact sport athletes and non-contact sport athletes with statistic, p-value, Cohen's d effect size and 95% confidence interval is reported. Most of the normative reference scores for the neuropsychology tests included adjustment for education with the exception of one measure in each of the attention, executive function, and visuospatial domains. Since IQ and education (and therefore cognitive reserve) was significantly different between contact sport athletes and non-contact sport athletes, we compare neuropsychology test scores in each of the five domains in a full model containing IQ and group as explanatory variables and a reduced model only containing group as the explanatory variable with test score as response. The full model and reduced model were compared using a partial F-test. Similarly, two sample t-tests (unequal variation) were conducted to examine vascular risk factors, BDI scores, and MCI in Athletes and Controls. All analyses were performed using the R programming language.³⁰

RESULTS

The neurocognitive test results are summarized in Table 1. Using a proxy measure of IQ, the WRAT-4 Word Reading achievement test standard score, the contact sport athletes scored significantly lower on this measure of estimated IQ ($p < 0.001$). Contact sport athletes did not significantly differ from non-contact sport athletes on most of the primary scores in the five domains. Only the Letter Fluency, NAB Naming, and List B Immediate Recall scores were significant, but after adjusting for IQ, only Letter Fluency ($p = 0.01$) and List B Immediate Recall ($p = 0.03$) were significant.

Table 2 presents contact sport athletes and non-contact athletes who qualified as MCI along with self-reported vascular risk factors, BDI categories, and number of years played (only for the contact sport athlete group). Eight contact sport athletes (38%) versus 3 non-contact controls (14%) met the criteria for MCI ($p = 0.083$). Although close, this did not reach significance. Of the 8 contact sport athletes who met the Comprehensive criteria for MCI; 7 were considered memory MCI, multiple domains; and 1 was considered memory MCI, one domain. Of the 3 non-contact sport athletes who met the criteria; 2 were considered memory MCI, multiple domains; and 1 was considered non-memory MCI, one domain. In a sub-analysis of contact athletes, the number of playing years was not associated with meeting the MCI criteria ($p = 0.66$).

Table 3 presents the vascular risk factors and depression scores for contact sport athletes and non-contact sport athletes. The ASCVD risk for one contact sport athlete could not be calculated because he was 36 years old. BMI ($p < 0.001$) and one or more reported vascular risk factors ($p = 0.005$) was significantly higher in contact sport athletes and HDL Cholesterol ($p = 0.017$) was significantly higher in non-contact sport controls. No other vascular risk factors were significantly different. Table 3 also presents the depression scores of the contact athlete and non-contact control groups as assessed by the BDI. The contact sport athlete group scored significantly higher ($p = 0.04$) than the non-contact control group in the BDI raw scores, but were not significantly different ($p = 0.078$) when comparing minimal risk for depression (13 or below on BDI) to mild depression or higher (14 or above on BDI).

DISCUSSION

The purpose of our study of retired athletes was to extensively evaluate the cognitive and behavioral characteristics of athletes who had professional careers playing contact sports that may have left them vulnerable to CTE.^{31–39} The research on CTE and extensive media attention, have given the impression that most former contact sport athletes will experience early onset dementia marked by cognitive impairment, even though the high rate of findings of CTE occurred in a very selected population of athletes involved in contact sports. The former NFL and NHL athletes we recruited and evaluated in this study were convinced that early signs of dementia had already happened, or was about to happen, which was their primary reason for participating in our study.

Contrary to expectations, our results provide little evidence of early onset dementia. The control group, with whom the contact sport athletes were compared, were healthier due in part to their continued athletic activities, better education level, had a higher estimated IQ, and a reduced likelihood of dementia.^{40,41} Despite the substantial advantage, we did not find many differences in cognitive abilities (except those that could easily be explained by the differences in education and IQ).

The rates of MCI were higher in the contact sport athlete group but this did not reach significance. We found that 38% of our contact sport athletes had MCI vs 14% of our non-contact sport controls which is similar to earlier studies,^{6,8,9} but lower than studies with similar sample sizes. Tremblay et al.⁴² found reduced semantic verbal fluency and altered episodic memory on both delayed recall and recognition among a sample of 15 retired contact sport athletes aged 51 to 75. De Beaumont et al.⁴³ found decreased episodic memory and response inhibition performance that correlated with slowed motor speed and delayed event-related potentials among 19 retired athletes compared to 21 controls. Stern et al.⁴⁴ conducted a retrospective post-mortem analysis of 36 athletes with confirmed CTE (mostly former NFL athletes and a few former NHL athletes). Three were asymptomatic, 11 had recognizable cognitive dysfunction, 13 had behavior alterations that gradually became mood disturbance, and 10 were diagnosed with dementia. Guskiewicz et al.⁴⁵ found that more than 3 reported concussions resulted in a five-fold increase in MCI among their sample of retired NFL players. Larger studies from the Boston University group have identified the range of pathologies of CTE. Post-mortem analysis of professional NFL players suggest that almost every individual who plays contact sports will have cognitive impairment and develop CTE, but they also provide a cautionary note.¹ Simply stated, one cannot expect that an autopsy based case series is representative of the total population of athletes that play contact sports since families of individuals with cognitive deficits are far more likely to donate the brain of their deceased family member for study.

When comparing other risk factors for developing MCI, we found that BMI, presence of one or more vascular risk factors, and depression score differences approached significance. HDL cholesterol was higher in the non-contact sport athletes. The higher BMI is easily explained by the fact that contact sport athletes were much heavier builds,⁴⁶ and our non-contact athlete controls were currently active in aerobic activities. Both the contact sport athletes and non-contact sport athletes controls had vascular risk factors (71% vs 43%), but

the contact athletes were significantly higher risk because of obesity. Although not significantly different, both contact sport athletes and non-contact sport athletes had a high risk of a cardiovascular event according to the Framingham Heart Study risk calculator. This could be due to the older ages of both groups, which is a strong modifier of vascular risk. HDL Cholesterol is considered to be the “good” cholesterol and is associated with lower BMI and exercise, which was higher in the non-contact control group.⁴⁷

Our rate of MCI among the athletes using the Comprehensive criteria ($8/21 = 38\%$) was higher than that found in the Hart et al⁸ study ($8/34 = 24\%$), which the authors note was slightly higher than the general population.

There are a number of limitations of the current study. Most notable, we were unable to ascertain with confidence, the number of concussions experienced by each athlete. The contact sport athlete group studied did play a substantial amount of time in their respective professional leagues with an average career length of 8.7 years. Several of these athletes are hall of fame members. The years played does not account for the number of concussive or sub-concussive hits directly nor does it account for the years of contact and potential head injuries sustained in junior and college playing years. All members of the non-contact athlete group continue to remain physically active in their sports of cycling, running or swimming. The continued physical activity is important to note as physical activity has been shown to reduce the risk of developing dementia.^{40,41} They also had higher education levels which is an indicator of higher cognitive reserve. Also, the impact of head injuries on cognitive reserve is related to education⁴⁸ and our non-contact athlete control group had much higher education, on average.

We realize that studies that report no significant differences between groups are often underpowered to make such claims. However, when we began this study we too were influenced by the media reports and reports of high rates of CTE among former NFL and NHL athletes. We hypothesized that these former contact sport athletes would be significantly impaired cognitively compared with an above average non-contact group of athletes and concluded that the likelihood of type II error would be reduced. Still, our sample size is small and the study results need to be replicated. Future studies of retired contact sport athletes can continue to examine alternate influences on cognition with aging. Examples could include nutrition, exercise/activity, chronic pain, sleep disturbance, current and previous substance abuse, and a history of performance enhancing drugs.

CONCLUSION

According to the results of our study, contact sport athletes do not have a significantly higher rate of mild cognitive impairment when compared to age-matched, non-contact sport control athletes. Other risk factors for mild cognitive impairment, such as vascular risk factors, depression, and lower cognitive reserve, are present in contact sport athletes and could explain some of the cognitive issues thought to be present in retired athletes due to chronic traumatic encephalopathy.

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References

1. Mez J, Daneshvar DH, Kiernan PT, et al. Clinicopathological Evaluation of Chronic Traumatic Encephalopathy in Players of American Football. *Jama*. 2017; 318(4):360–370. [PubMed: 28742910]
2. Lopez OL. Mild cognitive impairment. *Continuum: Lifelong Learning in Neurology*. 2013; 19(2 Dementia):411. [PubMed: 23558486]
3. Petersen RC. Mild cognitive impairment as a diagnostic entity. *Journal of internal medicine*. 2004; 256(3):183–194. [PubMed: 15324362]
4. Knopman DS, Petersen RC. Mild cognitive impairment and mild dementia: a clinical perspective. Paper presented at: Mayo Clinic Proceedings; 2014.
5. Association AP. Diagnostic and statistical manual of mental disorders (DSM-5®). American Psychiatric Pub; 2013.
6. Randolph C, Karantzoulis S, Guskiewicz K. Prevalence and characterization of mild cognitive impairment in retired national football league players. *Journal of the International Neuropsychological Society*. 2013; 19(08):873–880. [PubMed: 23902607]
7. Alosco ML, Mez J, Kowall NW, et al. Cognitive Reserve as a Modifier of Clinical Expression in Chronic Traumatic Encephalopathy: A Preliminary Examination. *The Journal of neuropsychiatry and clinical neurosciences*. 2017; 29(1):6–12. [PubMed: 27539377]
8. Hart J, Kraut MA, Womack KB, et al. Neuroimaging of Cognitive Dysfunction and Depression in Aging Retired National Football League Players A Cross-sectional Study *Neurobiology of Aging NFL Players*. *JAMA neurology*. 2013; 70(3):326–335. [PubMed: 23303193]
9. McMillan T, McSkimming P, Wainman-Lefley J, et al. Long-term health outcomes after exposure to repeated concussion in elite level: rugby union players. *Journal of Neurology, Neurosurgery & Psychiatry*. 2016 jnnp-2016-314279.
10. Willeumier K, Taylor D, Amen D. Elevated body mass in National Football League players linked to cognitive impairment and decreased prefrontal cortex and temporal pole activity. *Translational psychiatry*. 2012; 2(1):e68. [PubMed: 22832730]
11. Ganguli M, Fu B, Snitz BE, Hughes TF, Chang C-CH. Mild cognitive impairment Incidence and vascular risk factors in a population-based cohort. *Neurology*. 2013; 80(23):2112–2120. [PubMed: 23658380]
12. Geda YE, Roberts RO, Mielke MM, et al. Baseline neuropsychiatric symptoms and the risk of incident mild cognitive impairment: a population-based study. *American Journal of Psychiatry*. 2014; 171(5):572–581. [PubMed: 24700290]
13. Heaton RK. Wisconsin card sorting test: computer version 2. Odessa: Psychological Assessment Resources; 1993.
14. Delis DC, Kaplan E, Kramer JH. Delis-Kaplan executive function system (D-KEFS). Psychological Corporation; 2001.
15. Wechsler D. The Psychological Corporation. 1997. Wechsler Adult Intelligence Scale.
16. Tombaugh TN. Trail Making Test A and B: normative data stratified by age and education. *Archives of clinical neuropsychology*. 2004; 19(2):203–214. [PubMed: 15010086]
17. Stern RA, White T. NAB, Neuropsychological Assessment Battery: Administration, Scoring, and Interpretation Manual. Psychological Assessment Resources; 2003.
18. Loonstra AS, Tarlow AR, Sellers AH. COWAT metanorms across age, education, and gender. *Applied neuropsychology*. 2001; 8(3):161–166. [PubMed: 11686651]

19. Rodriguez-Aranda C, Martinussen M. Age-related differences in performance of phonemic verbal fluency measured by Controlled Oral Word Association Task (COWAT): a meta-analytic study. *Developmental neuropsychology*. 2006; 30(2):697–717. [PubMed: 16995832]
20. Tombaugh TN, Kozak J, Rees L. Normative data stratified by age and education for two measures of verbal fluency: FAS and animal naming. *Archives of clinical neuropsychology*. 1999; 14(2): 167–177. [PubMed: 14590600]
21. Strauss E, Sherman EMS, Spreen O. A compendium of neuropsychological tests: Administration, norms, and commentary. Oxford University Press; 2006.
22. Wilkinson GS, Robertson G. Wide Range Achievement Test 4 (WRAT4). Psychological Assessment Resources, Inc; Lutz, FL: 2006.
23. Jak AJ, Bondi MW, Delano-Wood L, et al. Quantification of five neuropsychological approaches to defining mild cognitive impairment. *The American Journal of Geriatric Psychiatry*. 2009; 17(5): 368–375. [PubMed: 19390294]
24. Clark LR, Delano-Wood L, Libon DJ, et al. Are empirically-derived subtypes of mild cognitive impairment consistent with conventional subtypes? *Journal of the International Neuropsychological Society*. 2013; 19(06):635–645. [PubMed: 23552486]
25. Busse A, Hensel A, Gühne U, Angermeyer M, Riedel-Heller S. Mild cognitive impairment long-term course of four clinical subtypes. *Neurology*. 2006; 67(12):2176–2185. [PubMed: 17190940]
26. Beck AT, Steer RA, Brown GK. Beck depression inventory-II. San Antonio. 1996; 78(2):490–498.
27. Goff DC, Lloyd-Jones DM, Bennett G, et al. 2013 ACC/AHA guideline on the assessment of cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Journal of the American College of Cardiology*. 2014; 63(25_PA)
28. Stone NJ, Blum CB, Eckel FRH, et al. 2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults. 2015
29. Karr JE, Garcia-Barrera MA, Areshenkoff CN. Executive functions and intraindividual variability following concussion. *Journal of clinical and experimental neuropsychology*. 2014; 36(1):15–31. [PubMed: 24283964]
30. Team RC. R: A language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing; 2013. URL <http://www.R-project.org>
31. McKee AC, Cantu RC, Nowinski CJ, et al. Chronic traumatic encephalopathy in athletes: progressive tauopathy after repetitive head injury. *J Neuropathol Exp Neurol*. 2009; 68(7):709–735. [PubMed: 19535999]
32. McKee AC, Stein TD, Kiernan PT, Alvarez VE. The neuropathology of chronic traumatic encephalopathy. *Brain pathology (Zurich, Switzerland)*. 2015; 25(3):350–364.
33. McKee AC, Stern RA, Nowinski CJ, et al. The spectrum of disease in chronic traumatic encephalopathy. *Brain: a journal of neurology*. 2013; 136(Pt 1):43–64. [PubMed: 23208308]
34. Omalu BI, Bailes J, Hammers JL, Fitzsimmons RP. Chronic traumatic encephalopathy, suicides and parasuicides in professional American athletes: the role of the forensic pathologist. *Am J Forensic Med Pathol*. 2010; 31(2):130–132. [PubMed: 20032774]
35. Riley DO, Robbins CA, Cantu RC, Stern RA. Chronic traumatic encephalopathy: Contributions from the Boston University Center for the Study of Traumatic Encephalopathy. *Brain injury*. 2015; 29(2):154–163. [PubMed: 25587744]
36. Stamm JM, Bourlas AP, Baugh CM, et al. Age of first exposure to football and later-life cognitive impairment in former NFL players. *Neurology*. 2015; 84(11):1114–1120. [PubMed: 25632088]
37. Seichepine DR, Stamm JM, Daneshvar DH, et al. Profile of self-reported problems with executive functioning in college and professional football players. *Journal of neurotrauma*. 2013; 30(14): 1299–1304. [PubMed: 23421745]
38. Stern RA, Daneshvar DH, Baugh CM, et al. [Accessed 13, 81] Clinical presentation of chronic traumatic encephalopathy; *Neurology*. 2013. 1122–1129. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/23966253>
39. Gavett BE, Stern RA, McKee AC. Chronic traumatic encephalopathy: a potential late effect of sport-related concussive and subconcussive head trauma. *Clin Sports Med*. 2011; 30(1):179–188. xi. [PubMed: 21074091]

40. Elwood P, Galante J, Pickering J, et al. Healthy lifestyles reduce the incidence of chronic diseases and dementia: evidence from the Caerphilly cohort study. *PloS one*. 2013; 8(12):e81877. [PubMed: 24349147]
41. Larson EB, Wang L, Bowen JD, et al. Exercise is associated with reduced risk for incident dementia among persons 65 years of age and older. *Annals of internal medicine*. 2006; 144(2):73–81. [PubMed: 16418406]
42. Tremblay S, De Beaumont L, Henry LC, et al. Sports Concussions and Aging: A Neuroimaging Investigation. *Cerebral Cortex*. 2012
43. De Beaumont L, Theoret H, Mongeon D, et al. Brain function decline in healthy retired athletes who sustained their last sports concussion in early adulthood. *Brain: a journal of neurology*. 2009; 132(3):695–708. [PubMed: 19176544]
44. Stern RA, Daneshvar DH, Baugh CM, et al. Clinical presentation of chronic traumatic encephalopathy. *Neurology*. 2013; 81(13):1122–1129. [PubMed: 23966253]
45. Guskiewicz KM, Marshall SW, Bailes J, et al. Association between recurrent concussion and late-life cognitive impairment in retired professional football players. *Neurosurgery*. 2005; 57(4):719–726. [PubMed: 16239884]
46. Jonnalagadda SS, Skinner R, Moore L. Overweight athlete: fact or fiction? *Current sports medicine reports*. 2004; 3(4):198–205. [PubMed: 15231223]
47. Gordon B, Chen S, Durstine JL. The effects of exercise training on the traditional lipid profile and beyond. *Current sports medicine reports*. 2014; 13(4):253–259. [PubMed: 25014391]

Table 1
Sub-Domains of Neurocognitive Measures Associated with Mild Cognitive Impairment using T-scores

Domain	Primary Variable	Mean Contact Sport Athletes T-score mean (SD)	Mean Non-Contact Sport Athletes T-score mean (SD)	T-test score	p-value	Cohen effect (95% CI)	Intercept Shift in Contact Athletes relative to Controls	p-value ²
Proxy IQ	WRAT Word Reading / achievement test	49.29 (±6.76)	57.57 (±8.82)	3.44	0.01	1.06 (3.43, 13.2)		
	Letter Fluency (FAS Total Score) *	52.95 (±10.98)	47.43 (±6.83)	1.96	0.06	0.6 (−0.03, 1.24)	8.9742	0.01
	Animal Naming Total *	49.95 (±11.59)	49.14 (±10.39)	0.24	0.81	0.07 (−0.55, 0.70)	−2.3015	0.55
Visual-spatial	NAB- ² Naming **	49.33 (±8.49)	53.33 (±1.68)	−2.12	0.05	−0.65 (−1.29, −0.01)	−2.7477	0.21
	WAIS-III Digit Symbol ***	55 (±9.98)	53.38 (±8.38)	0.57	0.57	0.18 (−0.45, 0.80)	2.6053	0.43
	Trails B ****	48.52 (±23.06)	53.38 (±9.95)	−0.89	0.38	−0.27 (−0.9, 0.35)	−5.2625	0.41
Attention	WAIS-III Digit Span ***	54.9 (±11.67)	57.33 (±9.65)	−0.73	0.47	−0.23 (−0.85, 0.40)	0.5543	0.88
	Trails A ****	55.52 (±13.12)	54.9 (±10.2)	0.17	0.87	0.05 (−0.57, 0.68)	2.8804	0.49
	DKEFS Color-Word Interference ⁴ Inhibition ***	57.67 (±4.64)	57.19 (±8.29)	0.23	0.82	0.07 (−0.55, 0.69)	2.5044	0.28
Executive Function	DKEFS Color-Word Interference Inhibition/ Switching ***	59.14 (±5.86)	56.48 (±8.1)	1.22	0.23	0.38 (−0.25, 1.01)	4.6449	0.06
	WCST- ⁵ Total Errors ***	49.43 (±9.89)	52.45 (±6.3)	−1.17	0.25	−0.36 (−1, 0.27)	−2.9522	0.33
	WCST Perseverative Responses ****	49.95 (±9.46)	51.3 (±6.06)	−0.55	0.59	−0.17 (−0.8, 0.46)	−1.2879	0.66
	WCST Perseverative Errors ****	49.95 (±9.82)	51.75 (±6.25)	−0.70	0.49	−0.22 (−0.85, 0.42)	−1.5971	0.59
	WCST Non-Perseverative Errors ****	48.29 (±9.74)	51.65 (±6.76)	−1.29	0.21	−0.4 (−1.04, 0.24)	−4.1909	0.17
	WCST Conceptual Level Responses ****	49.71 (±10.35)	52.7 (±6.33)	−1.12	0.27	−0.35 (−0.98, 0.29)	−3.1447	0.32
Memory	List A Immediate Recall **	54.48 (±10.21)	56.71 (±8.99)	−0.75	0.46	−0.23 (−0.86, 0.39)	−2.6561	0.44
	List B Immediate Recall **	50.9 (±9.93)	57.24 (±10.44)	−2.01	0.05	−0.62 (−1.26, 0.02)	−8.2536	0.03
	List A Short Delay **	53.48 (±10.85)	57.33 (±8.3)	−1.29	0.2	−0.4 (−1.03, 0.23)	−4.2227	0.23
	List A Long Delay **	56.1 (±11.48)	59.38 (±8.12)	−1.07	0.29	−0.33 (−0.96, 0.30)	−2.2336	0.53

Domain	Primary Variable	Mean Contact Sport Athletes T-score mean (SD)	Mean Non-Contact Sport Athletes T-score mean (SD)	T-test score	p-value	Cohen effect (95% CI)	Intercept Shift in Contact Athletes relative to Controls	p-value ²
	STL ¹ 6 Phrase Immediate Recall ^{**}	41.71 (±9.72)	45.57 (±9.66)	-1.29	0.2	-0.4 (-1.03, 0.23)	-3.9058	0.26
	STL Phrase Delayed Recall ^{**}	45.1 (±8.81)	48.19 (±8.43)	-1.16	0.25	-0.36 (-0.99, 0.27)	-2.2176	0.47

¹Wide Range Achievement Test-4 Word Reading;

²Adjustment for Estimated IQ;

³Neuropsychological Assessment Battery;

⁴Delis-Kaplan Executive Function System;

⁵Wisconsin Card Sorting Test;

⁶Story Learning Trial;

* Age, Education, and Ethnicity Normative T-Scores;

** Age, Education, and Gender Normative T-Scores;

*** Age Normative T-Scores;

**** Age and Education Normative T-Scores

Table 2

MCI Classification, Reported VRF, and AHA Risk in Contact Sport Athletes and Non-Contact Sport Controls

	Contact Sport Athletes (n=21)							Non-Contact Athletes (n=21)			
Case #	Sport	Age	MCI ¹	VRF ²	BDI ³	Years Played	Sport	Age	MCI	VRF	BDI
1	Football	62	X	X	-	2	Running	72	X	X	-
2	Hockey	64	X	X	-	13	Running	49	X	-	-
3	Football	64	X	X	1	9	Cycling	61	X	-	-
4	Hockey	71	X	X	-	6	Running	57	-	X	-
5	Hockey	58	X	X	2	2	Running	42	-	-	-
6	Hockey	52	X	-	3	18	T & F	72	-	-	-
7	Hockey	36	X	-	-	2	Running	64	-	X	-
8	Football	69	X	X	-	2	Running	59	-	-	-
9	Hockey	45	-	X	-	19	Cycling	47	-	-	-
10	Football	72	-	-	-	5	Cycling	61	-	X	-
11	Hockey	45	-	-	-	16	Running	67	-	X	-
12	Football	71	-	X	-	2	Running	65	-	X	-
13	Hockey	50	-	X	-	9	Cycling	62	-	-	-
14	Hockey	66	-	X	-	15	Running	61	-	X	-
15	Hockey	59	-	-	-	13	Triathlete	61	-	-	-
16	Football	57	-	X	1	5	Running	59	-	X	-
17	Football	57	-	X	-	6	Running	55	-	X	1
18	Hockey	52	-	X	-	18	Cycling	45	-	-	-
19	Football	51	-	X	-	4	Cycling	45	-	-	-
20	Hockey	41	-	X	2	4	Triathlete	44	-	-	-
21	Hockey	40	-	-	-	12	Running	43	-	-	-

¹Comprehensive criteria: at least 2 test scores in 1 cognitive domain or 1 test score in 3 domains fall 1 SD below normative reference values, X = Yes, - = No;²VRF's = Vascular risk factors, presence of one or more of BMI ≥ 30 (criteria for obesity), history of high blood pressure, diabetes, smoking, or high cholesterol, X = Yes, - = No;³BDI = Becks Depression Inventory, - = minimal, 1 = mild, 2 = moderate, 3 = severe

Table 3

Contact Sport Athletes and Non-Contact Sport Athletes vs Vascular Risk Factors and Depression

	Contact Athletes (n=21)	Non-Contact Athletes (n=21)	p-value	Cohen effect (95% CI)
AHA/ACC Risk				
Mean (SD)	14.11 (± 10.60)	10.36 (± 8.44)	0.223	0.39 (−9.89, 2.37)
Elevated Risk ¹	70% (n = 14/20 [*])	62% (n = 13/21)	0.747	0.10 (−0.35, 0.26)
Body Mass Index				
Mean (SD)	29.67 (± 3.64)	24.52 (± 2.55)	<0.001	1.63 (−7.10, −3.19)
Obese (BMI > 30)	42.8% (n = 9)	0% (n = 0)	<0.001	1.19 (−0.65, −0.21)
One or More Reported VRF²	71.4% (n = 15)	42.9% (n = 9)	0.005	0.57 (−0.59, 0.017)
History of High Blood Pressure	38.0% (n = 8)	19.0% (n = 4)	0.18	0.41 (−0.47, 0.092)
History of Diabetes	-	-	-	-
History of High Cholesterol	9.5% (n = 2)	19.0% (n = 4)	0.39	0.25 (−0.13, 0.32)
History of Smoking	33.3% (n = 7)	23.8% (n = 5)	0.506	0.19 (−0.38, 0.19)
Total Cholesterol (SD)	189.4 (± 30)	182.8 (± 25)	0.44	0.24 (−23.8, 10.5)
LDL ³ Cholesterol (SD)	106.9 (± 39)	103.3 (± 33)	0.753	0.09 (−26.0, 19.0)
HDL ⁴ Cholesterol (SD)	42.6 (± 8)	49.8 (± 11)	0.017	0.76 (1.37, 13.1)
Beck Depression Inventory				
Mean Score (SD)	10.2 (± 8.1)	3.9 (± 5.3)	0.004	0.92 (−10.6, −2.09)
Mild Depression or Higher ⁵	23.8% (n = 5)	4.8% (n = 1)	0.078	0.59 (−0.78, 0.025)

* One participant < 40 years of age;

¹ AHA/ACC Risk 7.5;

² Vascular Risk Factors;

³ Low Density Lipoprotein;

⁴ High Density Lipoprotein;

⁵ Fourteen or higher on Beck Depression Inventory