Change in body mass index and neurocognitive effects in retired NFL players

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Thesis

CHANGE IN BODY MASS INDEX AND NEUROCOGNITIVE EFFECTS IN RETIRED NFL PLAYERS

by

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CONTACT SPORT ATHLETES CAN EXPERIENCE THOUSANDS OF REPEATED HEAD IMPACTS (RHI) IN THEIR CAREER. RETIRED NFL PLAYERS HAVE BEEN FOUND TO BE SUFFERING FROM DEPRESSION, MOOD/BEHAVIOR CHANGES, AND COGNITION DEFICITS THAT ARE LINKED TO UNDERLYING NEUROLOGICAL IMPAIRMENT FROM RHIs, INCLUDING THE NEURODEGENERATIVE DISEASE, CHRONIC TRAUMATIC ENCEPHALOPATHY (CTE). RESEARCHERS AT BOSTON UNIVERSITY SCHOOL OF MEDICINE RECEIVED FUNDING FROM THE NATIONAL INSTITUTES OF HEALTH TO CREATE THE DETECT STUDY TO EXAMINE METHODS OF DIAGNOSING CTE DURING LIFE AND TO EXAMINE THE POSSIBLE RISK FACTORS FOR CTE AND OTHER LONG-TERM CONSEQUENCES OF RHI. THIS STUDY EXAMINED THE ASSOCIATION BETWEEN CHANGE IN BODY MASS INDEX (BMI) AND COGNITIVE IMPAIRMENT IN RETIRED NFL PLAYERS. THE COHORT WAS 95 RETIRED NFL PLAYERS BETWEEN THE AGES OF 40-69 WHO HAVE A MINIMAL 12 YEARS OF FOOTBALL EXPERIENCE AND MINIMAL 2 YEARS IN THE NFL. THE PARTICIPANTS UNDERWENT A 2-3 HOUR NEUROPSYCHOLOGICAL BATTERY. CHANGE IN BMI WAS FROM THE TIME OF RETIREMENT (HEIGHT AND WEIGHT AVAILABLE ON THE NFL WEBSITE ARCHIVE OF HISTORICAL PLAYERS) AND FROM TIME OF THE DETECT STUDY VISIT (HEIGHT AND WEIGHT RECORDED BY NURSES ON DIGITAL SCALES). THE RESULTS FOUND SIGNIFICANCE BETWEEN GREATER CHANGE IN BMI AND DECLINE IN PSYCHOMOTOR SPEED/EXECUTIVE FUNCTIONING (p=0.038). THERE WAS ALSO SIGNIFICANCE BETWEEN WAIS DIGIT SYMBOL CODING TEST AND BMI CHANGE (p=0.043). THE RESULTS SHOW THAT GREATER POSITIVE CHANGE IN BMI HAVE NEGATIVE CONSEQUENCES ON RETIRED NFL PLAYER’S COGNITIVE FUNCTIONING.
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LIST OF ABBREVIATIONS

AD ............................................................Alzheimer’s Disease
BMI ............................................................Body Mass Index
B-SIT ....................................................Brief Smell Identification Test
BQSS .....................................................Boston Qualitative Scoring System
BU ...........................................................Boston University
COWAT ...........................................Controlled Oral Word Association Test
CTE .....................................................Chronic Traumatic Encephalopathy
CVD .......................................................Cardiovascular Disease
DECTECT ...Diagnosing and Evaluating Traumatic Encephalopathy Using Clinical Tests
DLPFC ..................................................Dorsolateral Prefrontal Cortex
fMRI ......................................................Functional Magnetic Resonance Imaging
FTD .....................................................Frontotemporal Dementia
LTD .......................................................Long Term Depression
LTP .......................................................Long Term Potential
mTBI ....................................................Mild Traumatic Brain Injury
NAB .....................................................Neuropsychological Assessment Battery
NFL .......................................................National Football League
NFTs .....................................................Neurofibrillary Tangles
NINDS .................................................National Institute of Neurologic Diseases and Stroke
PCS .......................................................Post-concussive Syndrome
RHI .....................................................Repetitive Head Impact
ROCF……………………………………………Rey-Osterrieth Complex Figure
TES ......................................................Traumatic Encephalopathy Syndrome
TMT………………………………………………….Trail Making Tests
WAIS-R…………………………………Wechsler Adult Intelligence Scale-Revised version
WCST……………………………………………….Wisconsin Card Sorting Test
WMT…………………………………………………….Word Memory Test
WRAT-4…………………………………….Wide Range Achievement Test, 4th edition
INTRODUCTION

Football is a dangerous sport for more reasons than just overt physical injuries, such as broken bones or torn ligaments. Specifically, American football has a high rate of concussive and subconcussive injuries, also known as repetitive head impacts (RHI). Concussions are defined as a blow to the head that is accompanied by specific symptoms; namely, blurred or double vision, seeing stars, sensitivity to light or noise, headache, dizziness, nausea, trouble sleeping, fatigue, confusion, memory, concentration problems, or loss of consciousness (Seichepine et al., 2013). These symptoms can occur for any length of time to be defined as a concussion. There is much variability in the reported prevalence of concussions in football due to lack of knowledge as to what classifies as a concussion, lack of historical record keeping, or the social stigma among football players to ignore the symptoms. Even so, there are an estimated 0.61 concussions per professional football game and the number varies depending upon the position played (Nathanson et al., 2016).

Concussion symptoms are typically acute, but can persist and last months or even greater than one year. Post-concussive syndrome is the occurrence of at least three concussive symptoms that persist three months after the head injury incident (APA). These symptoms include fatigue, headache, dizziness, or disturbed sleep. There may also be behavioral changes such as irritability or aggression, changes in personality, apathy, anxiety and depression. Post-concussive syndrome can also be seen using neuroimaging techniques. After neuropsychological evaluation in combination with neuroimaging,
neuropsychological tests show that a patient may be experiencing memory problems or reading/comprehension difficulties shortly after the time of concussion. At the time of return-visit, patients are no longer exhibiting neuropsychological deficits, their fMRI nevertheless may not have returned to fully functional. Patient fMRIs may continue to show alterations for months after injury, even though patients present with no clinical symptoms (McAllistort et al., 1999). The underlying brain injuries that occur with no clinical symptoms are potentially dangerous to current athletes who return to play without being completely healed from concussions.

Subconcussive injuries include hits to the head at enough force to cause axonal injury, but do not clinically manifest (Talavage et al., 2014). Crisco et al. (2010) estimated that offensive lineman can be exposed to over 1,000 subconcussive hits within one playing season. These subconcussive hits may not result in concussive symptoms, but the injuries can be seen in fMRI neurological imaging. Johnson et al., (2014) performed a study on collegiate rugby players. They had fMRI scans pre and post game to compare the changes in brain activity. After one game, athletes who did not report a concussion were found to have altered functional connectivity in the certain brain regions.

The cumulative effects of RHI (both subconcussive and concussive) may increase risk for long-term neurological impairment. Chronic Traumatic Encephalopathy (CTE) is a unique distinct neurodegenerative disease associated with a history of exposure to RHI (McKee et al., 2009; McKee et al., 2013; McKee et al., 2016). CTE can only currently be diagnosed using recently defined neuropathological criteria (McKee et al., 2016). It is pathologically characterized by the perivascular deposition of hyperphosphorylated tau (p-
tau) in an irregular pattern at the depths of the cerebral sulci, a pattern unique from other tauopathies such as Alzheimer’s disease (AD) and frontotemporal dementia (FTD). Neurofibrillary tangles (NFTs) are typically present in the superficial layers (II and III) of the cerebral cortex and are often most noticeable in the temporal cortex. McKee et al. developed a 4 stage classification system to describe the pathological severity and progression of CTE. Stage I is characterized by perivascular p-tau NFL and AT in sulcal depths of the superior and dorsolateral frontal cortices. With limited axonal varicosities are observed in the frontal cortex. As the disease progresses into stage II, the p-tau spreads to the adjacent cortex and white matter, medial temporal lobes, and diencephalon. Stage III CTE is characterized by a significant degree of brain atrophy. The distribution of p-tau is more extensive than in stage I and II with spreading to olfactory bulbs, mammillary bodies, and hypothalamus. The last stage, Stage IV, has significant decrease in brain weight, severe p-tau abnormalities, and neuronal loss in the cortex. Macroscopic changes in CTE are typically unremarkable in the early stages of the disease, but in more advanced stages there is enlargement of the lateral and third ventricles, cerebral atrophy, cavum septum pellucidum, and depigmentation of locus coeruleus and substantia nigra (McKee et al., 2013). Other pathological features of CTE includes TDP-43 inclusions, axonal injury, and chronic neuroinflammation. Unlike Alzheimer’s disease (AD), amyloid beta deposition in CTE is sparse and diffuse and associated with aging and APOE e4 allele (Stein et al., 2015).

Although the neuropathological features of CTE are now well defined, the clinical features of CTE remains in its infancy. Indeed, because CTE cannot currently be
diagnosed during life, the epidemiology of this disease remains unknown. To date, all neuropathologically-confirmed cases of CTE have had a history of RHI, making RHI a necessary but not sufficient feature for CTE. Importantly, 16% of documented cases of CTE do not have a reported history of concussion (Stein et al., 2015). This statistic may be indicative of a substantial risk of developing neurodegeneration by means of recurrent subconcussive trauma.

The mean age of onset of symptoms is around 43 years of age and occurs approximately 8 years after retirement from the NFL. There are often clinical symptoms that correspond with certain stages of CTE. It is demonstrated that the longer the individual engaged in contact sports and the older the person, the more pronounced the symptoms (Daneshvar et al., 2011, Mckee et al., 2013). Early clinical symptoms of CTE may include headaches, attention and/or concentration problems, aggression, explosive issues and depression. Memory problems may not be noticeable in early stages (I and II) of CTE. As the disease progresses into stage III some of the clinical symptoms can remain but, there is an increased prevalence of memory problems. Stage IV CTE demonstrates more dramatic attention and concentration problems, language deficits, and executive function impairment. Most notably, all stage IV individuals suffered from dementia (McKee et al., 2013).

The first categorization for the clinical presentations of CTE were grouped into two categories based on the clinical phenotype. The first category are individuals with symptoms of CTE that begin at a young onset and are marked by behavioral and mood disturbances (explosivity, inappropriate behavior, physical/verbal abusive tendencies, and
depression), but not accompanied by many cognitive or motor complications at that time. Second, those with an older onset of symptoms show cognitive impairment (memory impairment, executive function, language complications, etc.) and may be associated motor disturbances (Stern et al., 2013). The individuals in the first group may develop cognition problems as they age and the disease progresses, but those in the second category are less likely to experience mood and behavioral problems over-time. It is important to note that most clinical symptoms of CTE are not self-reported. The behavior, mood, and cognitive problems have been reported by a family member or loved one of the deceased. There are currently no methods to diagnose CTE in the living and the diagnosis requires a postmortem brain autopsy.

The above findings led to the development of classifying clinical symptoms of CTE under Traumatic Encephalopathy Syndrome (TES) guidelines. TES is a proposed diagnosis for individuals who have a history of RHI, are not suffering from other neurological disorders (such as Post Concussive Syndrome), and are experiencing cognitive, behavior, or mood disturbances (Montenigro et al., 2014). If an individual meets these requirements, the TES guidelines will then group them into one of four subtypes. The fours subtypes are 1) TES behavioral/mood variant (TES-BMv), individuals that experience behavioral and/or mood disturbances without the presence of cognitive problems 2) TES cognitive variant (TES-COGv), the presentation of cognitive features and negative behavior/mood variant 3) TES mixed variant (TES-MIXv), a presentation of both cognition and mood/behavioral variants and 4) TES dementia (TES-D) in which a person is experiencing progressive cognitive impairments, clinician diagnosis of functional
impairment, or the clinical presentation of symptoms cannot be distinguishable from another neurological disease (i.e. dementia from AD). The development of the TES diagnosis is intended to be used in conjunction with in vivo biomarkers (once available) for future clinician to be able to diagnosis patients with ‘possible,’ ‘probable,’ or ‘unlikely’ diagnosis of CTE.

Not everyone exposed to RHI develops CTE, so it is likely RHI interact with other potential risk factors in athletes. The present study chose to examine a symptomatic physical and cognitive epidemic in the United States that is also prevalent in American Football: Obesity.

**Obesity and neurocognitive impairment**

Obesity is now a well-established risk factor for cognitive impairment. A systematic review of relationships between cognitive tasks and obesity has demonstrated that everyday mental efforts can become more difficult with increasing body mass index (BMI) (Prickett et al., 2015). Prickett et al found that the results of the meta-analysis review differ due to study qualities, there were significant changes between BMI groups and cognitive tests. The inclusion criteria of the studies included participants between 18-65, a group with participant’s BMI ≥ 30 kg/m², and and normative/non-obese control group. The cognitive tests that resulted in differences between normal weight, overweight, and obese BMIs included: the WAIS Digit Symbol test measuring psychomotor speed (Cournot et al., 2006), Trail Making A and B measuring visual attention and psychomotor speed (A) and cognitive response set (B) (Fergenbaum et al., 2009), Rey-Osterrieth
Complex Figure copy and recall measuring visual construction and visual memory (Boeka and Lokken, 2008), and list learning test finding differences between obese persons and normal weight people in verbal memory (Gunstad et al., 2006; Cournot et al., 2006). The two tests that found a positive correlation between obesity and executive functioning were the Wisconsin Card Sorting Test (WCST) (Chelune et al., 1986) and the Stroop test (Fagundo et al., 2012), both measures of executive functioning. These tests examine mental tasks used every day are being affected by the presence of high levels of adiposity.

The above meta-analysis shows that obesity can alter a person’s mental performance in everyday life in significant but small degrees during adult life. A dangerous side-effect of obesity is its association between midlife obesity and the development of dementia. A 27 year longitudinal study found that overweight middle aged individuals had a 35% increased risk of a dementia diagnosis compared to normal weight persons. Individuals who were obese at midlife had a 74% increased risk of being diagnosed with dementia in later life (Whitmer et al., 2005).

While midlife obesity may increase a person’s risk of developing dementia, late-life obesity is negatively associated with memory impairments. The longitudinal Cardiovascular Health Cognition Study examined close to 3,000 adults with a mean age of 75 years. They calculated BMI at the time of the study and used self-reported weights from age 50 to estimate BMI. The study's results found that those who reported midlife obesity at age 50 had a greater risk of having dementia during follow-up visits to the study. The risks were reversed in old age. Those who were underweight in old age had an increased risk of dementia while those who were obese in old age had a reduced chance in the
development of the disease (Fitzpatrick et al., 2009). These findings are now thought of as the “obesity paradox” and may suggest there is a protective nature of adiposity in old age.

**Obesity and neuroimaging**

Neuroimaging can also show researchers the effects obesity have directly on brain integrity. Gazdinski et al., (2008) found that an increased BMI is associated with axonal and/or myelin differences in the frontal lobe white matter compared to individuals with lower BMIs. The study’s results suggest that increased BMI and high levels of adiposity can have an accelerated aging effect in the brain and ultimately, poses a greater likelihood for the development of Alzheimer’s disease.

The prolonged effect of obesity (i.e., years of classifying as obese), may be more detrimental to the overall health of the brain. Brain atrophy occurs in individuals with high BMIs, but also in those who maintained high BMIs (those that classify as overweight or obese) over a five year period showed increased brain shrinkage in participants 65 years of age and older (Raji et al., 2010). The participants of said study did not show signs cognitive decline over the five year period. Further neuroimaging evidence correlating BMI and altered brain integrity was reported via a personal communication from Singh (2014) to Montenegro (2015) that as BMI increased, hippocampal MRI volume decreased in a football player population (Singh et al., 2014; Montenegro et al., 2015).

**Potential Mechanisms of cognitive impairment**

An explanation for the higher prevalence of dementia in obese populations can be explained, in part, by vascular problems commonly associated with obesity. Obesity is
often comorbid with diabetes, high blood pressure, and unhealthy levels of cholesterol. The longitudinal study, the Framingham Heart Study, evaluated the effects of hypertension on cognitive outcomes. Using data over an 18 year testing period, the Framingham Heart Study concluded that men who suffered only from hypertension performed worse on cognitive functioning than their healthy counterparts. To further the point of obesity affecting cognition, they also found that hypertension combined with obesity was the group that had the poorest outcomes on cognitive testing (Elias et al., 2002). Kivipelto et al., (2005) has also found that the combination of obesity and its comorbidities increases the likelihood of being diagnosed with dementia and AD in the future. They found that the prevalence of dementia or AD increased in individuals that suffered from vascular risk factors (high blood pressure, diabetes, cardiovascular disease, etc.). The risk percentage of later-life dementia rose with each added complication.

CVD may be used as a predictor of dementia and AD, but it can also have effects on people before they are diagnosed with a memory disorder. Rostamin et al., (2015), found participants who scored in the lowest percentile for executive function had the highest prevalence of CVD risk-factors. This was compared to those who scored in the lowest percentile in memory did not have correlations to CVD at that time. The findings of executive functioning declining before memory by point researchers to establish a timeline between CVD and its effects on the brain. It may be due to the areas of the brain CVD effects first and the physiological elements of the disease.

The mechanisms of the clinical presentation of cognitive decline may be explained by CVD causing inflammation of blood vessels that impair normal blood flow. CVD has
been linked to a reduction of blood flow and velocity of blood flow to the brain. Pase et al., (2012) found that as CVD risk rose in otherwise healthy middle-aged people, blood flow to the brain decreased. The blood vessels affected by CVD included the common carotid artery and middle cerebral artery. The reduction of blood flow may help explain the decline in cognitive function persons affected with CVD risks (Kaffashian et al., 2011). Similar results of decreased cerebral blood flow is seen in people with Alzheimer’s disease (Sabayan et al., 2012).

Obesity may also be a risk factor in the presence of good cardiovascular health and in those with increased muscle mass. Some people think that obesity is not detrimental to their health if they engage in regular exercise claiming they can be “fat but fit.” Hogström et al., (2015) found that obese persons are less likely to show benefits from physical fitness on overall health. Those who are overweight (BMI of 25-29.99) can benefit from aerobic fitness reducing their risk of death, but obese persons (BMI over 30) who participated in aerobic exercise did not reduce their risk of all-cause death. Interestingly, normal weight persons (BMI of 18.5-24.99) who did not engage in regular cardiovascular activity have lower all-cause mortality than physically active obese persons. These finding are an attempt to dispel the “fat but fit” argument which has been applied to the professional football players with the greatest BMIs.

**Obesity in Football**

Obesity is an issue in football players even before they reach the NFL. Young boys (9 to 14 years old) who played American football are twice as likely to be obese than the
general age matched sample (Malina et al., 2007). Obesity is a growing problem in our nation’s youth. As children get heavier they may be more inclined to play sports that value their size, not realizing they may be increasing their chances of developing neurocognitive deficits by starting football at a younger age (Stamm et al., 2015). In football, the offensive line consists of crucial positions that protect the quarterback. Without these positions, the quarterback would not be able to get any plays running, hence no scoring. Because these players contribute to the success of the game their size has become an asset. The bigger (taller and heavier) the player the more of a barrier they can create for their quarterback. These reasons may be why we see an increase in player size in younger populations. In the 2015 football season, Arkansas University’s offensive line had the heaviest average players in all of football, beating out all of the professional football teams (ESPN, 2015). These players are in the 17-22 age range and yet they are heavier than grown men who have had many years of training and muscle building. The average weight of offensive line is now around 330 lbs. for the heaviest teams. Even if a player was six foot ten inches, their BMI would soar into the obese category, putting their overall health at risk even though they take part in some of the most elite athletic training programs.

**Change of BMI in NFL Players**

NFL players are typically larger than the average male, apparent to anyone watching a game of football on the television. They also tend to be larger after their retirement and into middle age. In the general population, 32.1% of men between the ages of 30-49 have a BMI over 30 which signify obesity. Within the same age range (30-49)
56.0% of retired NFL players have a BMI over 30 points. This trend continues into older adults as well. In the general population of 50 and older men, 28.5% of men are likely to be obese compared to 49.3% of NFL retirees over 50 who are obese. The percentages get smaller for both groups when the BMI is raised to 35+ (11.6% of males 30-49 years old; 9.1% of males over 50; 20.7% of retired NFL players 30-49 years old; 12.4% of retired NFL players over 50 years old) (Weir et al., 2009). This midlife obesity in retired professional football players may contribute to some neurocognitive decline in their future.

**Obesity and cognitive functioning in football**

As a first assumption, we would not expect to see cognitive impairment in persons with high levels of physical activity, due to the positive effects of exercise on cognition (Loprinzi and Kane, 2015). Nonetheless, Division I athletes that have higher BMIs project small but, significant negative correlations for cognitive functioning in verbal and visual memory and visual motor speed (Fedor and Gunstad, 2013). These results show that even during personal elite levels of cardiovascular fitness, a measure a good health, high BMIs are affecting the complex brain functions. It is important to note that in the study the Division I athletes with the highest BMIs were the football players.

The previous studies have only used BMI to find a correlation between obesity and cognitive functioning. It is important to point out that another study established overweight athletes have a significant decrease in cognitive function. This study used waist-to-hip measurement to establish relationships between attention, cognitive proficiency, and memory in football players (Willeumier et al., 2012). The overweight athletes were noted as having reduced blood flow to Brodmann areas 8, 9, and 10 on fMRI scans. The reduced
blood flow to brain areas thought to be involved in attention, reasoning, and executive function. The study by Wileumier et al., included two interesting aspects that may strengthen the argument of weight affects cognition. First, the use of waist-to-hip ratio rather than BMI is a more widely validated tool for overall healthy fat levels. The second aspect of the study was the recruitment of active athletes. The study saw differences between waist-to-hip ratio and cognition in active athletes, because these athletes are fulfilling their exercise requirements there must be other underlying causes of cognitive impairment in heavy athletes.

Cardiovascular disease (CVD) and its risk factors (hypertension, diabetes, high total cholesterol, etc.) can be associated with an increased risk of dementia and cognitive decline (Kaffashian et al., 2011). Larger athletes may be at a greater risk later in life than their healthy weight counterparts due to the complications associated with their large stature. Active NFL players have been noted to have a higher prevalence of hypertension compared to age-matched healthy men (23-35 years old). The study also found that BMI of both groups (players and controls) was positively correlated with presence of CVD risk-factors (Tucker et al., 2009).

**Objective of the Current Study**

Taken together, obesity may be a key risk factor for later-life cognitive impairment in former NFL players. However, no study to date has examined the relationship between obesity and later-life neurocognitive impairment in former NFL players presumably at high
risk for CTE (based on duration of football played, position played, and being currently symptomatic).

The generalization of men in the NFL are athletes in their peak fitness levels, but most are also obese or overweight according to their Body Mass Index. BMI is a simple calculation that divides a person’s weight by their height squared (in the metric system). BMI is an easy tool for the majority of people to calculate if they are in a normal healthy weight or if they fall above or below this predetermined average weight. For an athlete with high muscle content, the formula is often skewed and will likely push them to obese even though they are likely to have more lean muscle mass than fat. This has led to the argument that BMI is not a valid tool for athletes. There have been reported discrepancies between high BMI and healthy fat levels in athletes (Nevill et al., 2006; Kruschiz et al., 2013). While BMI may not be the best tool to evaluate health of all NFL players, there was a rise in unhealthy fat levels in some positions. For example, the professional offensive line has the highest and least healthy rates of body fat (Kramer et al., 2005). This group also has the highest BMI and these finding enhance the accuracy in BMI classifications for the larger football players. Notably, this group also experiences the most subconcussive hits per season (Crisco et al., 2010). While they start out as the heaviest players on the field, it may be unhealthy remain obese into retirement given the extent of receptive head injuries they may have sustained.

The purpose of the present study was to identify an association between cognitive impairment and the dramatic change of weight seen in retired NFL players. The men of our study all participated at least two years in the NFL and majority played positions that
are associated with high weights. Because that entire sample was above normal weight, the examination of change in BMI was intended to separate those who stayed close to their normal height and weight and those who gained more weight after retirement. Most studies examining cognition are limited to participant visits that may show change of weight over a few years or a decade. An advantage from working with retired NFL players, was having a database of athletes’ height and weight available for all players. Another advantage was having the weights from when people were in the prime of their physical capabilities.

Using the method of comparing early weights to participant current weight, it was hypothesized that change of BMI may be a risk factor for later-life cognitive impairment in retired football players. More specifically, the current study hypothesized the greater increase in BMI (from football retirement to the DETECT study) would result in a higher prevalence of cognitive decline (i.e. memory, executive functioning, and language impairment).
METHODS

Participants

The present study cohort was from the Diagnosing and Evaluating Traumatic Encephalopathy Using Clinical Tests (DETECT) study at Boston University School of Medicine funded by the National Institute of Neurologic Diseases and Stroke (NINDS). The study lasted four years and was concluded in October of 2015. The cohort included 96 former NFL players. Study inclusion criteria included men aged 40-69 years, a minimum of two years active play in the NFL and a combined twelve years of play in organized tackle football (youth, high school, college and/or semi-pro), and at least two complaints about their cognitive functioning (problems in episodic memory, executive function, or attention) and about their behavior (suffering from a short-fuse, verbal and/or physical aggression, disinhibition of actions), and one or more complaints in mood (depression, anxiety, or apathy). Symptoms must have been present for a minimum of six months. These symptoms were confirmed by receiving medical treatment, self-reporting or the reports of family or friends.

All subjects underwent comprehensive examinations during a three day outpatient visit. These tests included: neurological evaluation, neuropsychological testing, a psychiatric and history interview, neuroimaging, cerebrospinal fluid analysis, and genetic testing. Only neuropsychological and physical data taken by nurses are relevant to the current study. All protocols were approved by the Boston University Medical Center Institutional Review Board. Subjects gave written consent prior to participation and were provided a copy of all signed consent forms.
Neuropsychological Battery

Participants completed an approximately 2-3 hour long neuropsychological battery conducted by trained graduate students or employees of the center. The test battery assessed all of the major cognitive domains, including premorbid IQ/intelligence, effort, executive function, olfactory function, attention/psychomotor speed, visuospatial function, visual memory, working memory, verbal memory, and language. The selected neuropsychological tests were included based on their extensive use in neurodegeneration research and for their reliability and validity. These tests include:


Effort: Word Memory Test (WMT) (Green et al., 2003).

Executive Function: Wisconsin Card Sorting Test (WCST) percent perseverative responses and percent perseverative errors (Heaton et al., 1993); Trail Making Test Part B (Reitan R.M., 1992); DKEFS Inhibition/Switching completion time (Delis et al., 2001); Controlled Oral Word Association Test (COWAT) (Lezak M.D., 2012); Boston Qualitative Scoring System (BQSS) for the Rey-Osterrieth Complex Figure (ROCF) organization score. (Stern et al., 1999)

Olfactory Function: The Brief Smell Identification Test (B-SIT) (Doty et al., 1989; Doty et al., 1995)

Attention/Psychomotor Speed: Trail Making Test (TMT) Part A (Reitan, 1992); Wechsler Adult Intelligence Scale-Revised version (WAIS-R) Digit Span
(Wechsler D., 1997); Delis-Kaplan Executive Function System (DKEFS): Color Naming and Word Reading. (Delis et al., 2001)

**Visuospatial function:** Neuropsychological Assessment Battery (NAB) Map Reading (Stern et al., 2003); BQSS ROCF Copy, Presence, and Accuracy. (Stern et al., 1999)

**Visual Memory:** BQSS ROCF Immediate, Delay, Immediate Retention, Delayed Retention (Stern et al., 1999).

**Working Memory:** WAIS-R Digit Symbol Test (Wechsler D., 1997)

**Verbal Learning:** NAB List and Story Learning and Memory (Stern et al., 2003).

**Language:** Animal Fluency (Lezak M.D., 2012) and NAB Naming. (Stern et al., 2003)

**Statistical Analysis**

Participant descriptive demographics were performed with SPSS software and reported as minimum, maximum, mean with standard deviation for the continuous variables: age, years of football played, age of first starting football, and years since retirement. The results are also reported for BMI factors: BMI at retirement, BMI at study visit, and change in BMI.

**BMI calculations**

Each study visit included a physical health check. The nurses in Boston University’s General Clinical Research Unit weighed each participant on a digital scale with shoes off. The nurses also measured the height of the participants with their shoes
off. From these data points BMI was calculated in an excel spreadsheet with the equation:

$$\text{BMI} = \frac{\text{weight (lb)}}{\text{height (in)}^2} \times 703.$$ 

The choice to use pounds and inches over the more scientific, meters and kilograms, was because the nurses scales/measures recorded both and the NFL database only reported in pounds and inches. Keeping the two variables consistent helped reduced errors in conversion.

The NFL has a long history of recording the physical statistics of their players. Access to the NFL Historical Database posted on the NFL website at [http://www.nfl.com/players](http://www.nfl.com/players) allowed our study to look up players by last name to find the recorded height and weight from their profile. Each profile had one height and weight even if the player was active for many years. It has to be assumed that these parameters remained relatively constant during their active years. To calculate the BMI, the same equation from above was used.

The DETECT sample was a sample of 96 men that had varying years of play in the NFL and varying years of time after retirement. One participant had to be removed from the sample due to the fact that the NFL database did not have him listed as a historical player; therefore there was no record of height and weight at retirement. Reasons may have included professional football in the Canadian league or being part of an NFL team, but never seeing professional game time.

The equation used to find change in BMI was BMI from study visit minus BMI from retirement. This formula did result in both positive and negative variables. The positive variables being points of increased BMI and the negative variables were found in those who lost weight since retirement of the NFL.
**Exposure Measures**

Exposure measures were included based on predetermined exposure factors that can influence neurocognitive results. These include: years of football exposure (Mckee et al., 2009), number of concussions (McKee et al., 2009), and age of first exposure (AFE) <12 years old or >12 years old (Stamm et al., 2015). The exposure measures were analyzed by using SAS software and performing an independent multivariable regression for each exposure metric. These results were reported as a point estimate, standard error, t-value, and p-value. The log of concussions is used to reduce outliers and normalize the number of concussions that can be skewed.

**BMI change on selected factors**

Participant scores from the neuropsychological battery were converted to age and education appropriate T-scores from published normative data. The tests that required a T-score included: WCST, Trails A and B, ROCF, NAB Story, Grooved Pegboard, NAB list learning, NAB Map, COWAT, Animal Fluency, and NAB naming. Standard scores were used for the WRAT, BSIT, Digit Span and Digit Symbol tests. Tests were evaluated individually and as factor composite derived from Principal Component Analysis (PCA). The PCA model used measures from the neurocognitive testing and from participants’ behavior/mood completed questionnaires. The PCA generated rotated factor composite scores for all of the tests from the DETECT visit in order to group the tests into neurological factors based on an iterative method. The iterative criteria included: 1) Only factors with an eigenvalue >1 were retained; and 2) following a VARIMAX rotation, input variables with a loading of 0.5 were removed and the PCA was repeated until both criteria were
satisfied. The tests that remained in the model were the following neurocognitive measures were: Trail Making Test A, WAIS-R Digit Symbol Coding, Trail Making Test B, WCST Percent Preservative Errors, DKEFS Color Word: Inhibition/Switching completion time, total score COWAT FAS, Rey Osterrieth Immediate, Rey Osterrieth Delay, NAB Story Immediate, NAB Story Delay, NAB List Short Delay, NAB List Long Delay, NAB Map, NAB Naming, Rey Osterrieth Copy Presence & Accuracy. The included behavior and mood tests were: Hamilton Depression Rating Scale (HDRS), Modified Scale for Suicide Ideation (MSSI), Beck Hopelessness (BHS), Center for Epidemiologic Studies Depression Scale (CES-D), Apathy-Evaluation Scale (AES), Barratt impulsivity scale, Brown-Goodwin lifetime history of aggression, Buss-Durkee Inventory, Behavior Rating Inventory of Executive Function (BRIEF).

BMI change was hypothesized to affect participant neurocognitive scores. Using SAS software to perform a mixed effect regression model to account for multiple observations per subject, BMI change was evaluated on its neurological deficits in participants’ mood/behavior, psychomotor speed/executive functioning, verbal memory, and visual memory. BMI change was also tested for association between each individual neurocognitive test and controlled for years of play. Statistical reporting of estimation, standard error, degrees of freedom, t-value, partial correlation and p-value (Pr > |t|) are shown. Statistical significance was determined from a 0.05 alpha level and effect size based on partial correlation.
RESULTS

Demographics

The average exposure demographics are depicted in Table 1. The average age of participants was 55 ± 7.942 years. The average years of playing football was 18.5 ± 3.491. Most participants began playing football around 11.89 years of age ± 2.56 years. The mean year of retirement was in 1986. At the time of retirement the mean BMI = 30.27 ± 3.37. This BMI mean rose to mean = 33.34 ± 5.04 at the time the participants came to the DETECT study. The mean change in BMI points was 3.07 ± 4.09. The maximum change in BMI was 14 points and the minimum was a reduction of 7 BMI point (Table 2).

Table 1. DETECT participant demographics among exposure factors: age, total years of football participation, age of first exposure, and the years since retirement. The data is presented as minimum (min.), maximum (max.), mean, and standard deviation.

<table>
<thead>
<tr>
<th>DETECT Demographics</th>
<th>Min.</th>
<th>Max.</th>
<th>Mean</th>
<th>Standard Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at DETECT Visit</td>
<td>40</td>
<td>69</td>
<td>55.06</td>
<td>7.94</td>
</tr>
<tr>
<td>Total years playing football</td>
<td>12</td>
<td>26</td>
<td>18.25</td>
<td>3.49</td>
</tr>
<tr>
<td>Age started playing football</td>
<td>6</td>
<td>17</td>
<td>11.89</td>
<td>2.56</td>
</tr>
<tr>
<td>Year since retirement</td>
<td>8</td>
<td>45</td>
<td>26.40</td>
<td>9.30</td>
</tr>
</tbody>
</table>
Table 2. Changes in BMI in DETECT. This table shows the average BMIs between the time of retirement to the time of the DETECT visit with the average BMI points of change. The data is presented as minimum (min.), maximum (max.), mean, and standard deviation.

<table>
<thead>
<tr>
<th></th>
<th>Min.</th>
<th>Max.</th>
<th>Mean</th>
<th>Standard Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI at Retirement</td>
<td>24</td>
<td>42</td>
<td>30.27</td>
<td>3.37</td>
</tr>
<tr>
<td>BMI at DETECT Visit</td>
<td>25</td>
<td>52</td>
<td>33.34</td>
<td>5.04</td>
</tr>
<tr>
<td>BMI Change since retirement</td>
<td>-7</td>
<td>14</td>
<td>3.07</td>
<td>4.09</td>
</tr>
</tbody>
</table>

The World Health Organization uses the most thoroughly verified Body Mass Index classification system. The normal range of BMI is 18.5 - 24.99. Overweight is 25.00 - 29.99. Obese is anything about 30 points. Obesity class 1: 30.00 - 34.99, class 2: 35.00 - 39.99 and class 3: is any BMI over 40.00 points (World Health Organization). Many of the individuals in the DETECT sample were in the overweight and obese stage 1 categories while playing professional football (N=39 and N=46 respectively). Only 7 players were above stage 1 obesity. After varying years of retirement those numbers change dramatically. At the time of the DETECT study the number of retired football players above obesity 1 cut off were 31 individuals (See table 3).
Table 3. Change in BMI Classification among retired NFL sample

<table>
<thead>
<tr>
<th>BMI Classification</th>
<th>Number of players at Retirement</th>
<th>Number of players at DETECT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underweight (&lt;18.5)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Normal Weight (18.5-24.9)</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Overweight (25.0-29.9)</td>
<td>39</td>
<td>20</td>
</tr>
<tr>
<td>Class 1 Obesity (30.0-34.9)</td>
<td>46</td>
<td>44</td>
</tr>
<tr>
<td>Class 2 Obesity (35.0-39.9)</td>
<td>6</td>
<td>21</td>
</tr>
<tr>
<td>Class 3 Morbidly Obese (&gt;40)</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td>Total</td>
<td>95</td>
<td>95</td>
</tr>
</tbody>
</table>

Exposure measures

Exposure measures were based on predetermined factors that can influence degree of impairment in retired NFL players. There was no statistical significance between change of BMI and level of exposure (Table 4). This could be explained by the similar nature of the cohort. Majority of the DETECT cohort were in linemen position and might have been exposed to reasonably similar amount of exposure factors. They were also all large men with a mean BMI=33 which would classify the average participant as obese. These similar factors may have contributed to the lack of significance among exposure factors.
Table 4. Effect of BMI change on exposure variables.

| Predictor                          | Estimate | Standard Error | t Value | Pr > |t| |
|-----------------------------------|----------|----------------|---------|-------|---|
| Years playing football            | -0.16    | 0.12           | -1.31   | 0.20  |
| Concussions (log)                 | 0.30     | 0.21           | 1.40    | 0.17  |
| AFE (<12 vs >=12)                 | -0.40    | 0.92           | -0.44   | 0.66  |
| Starting age for playing football | 0.31     | 0.170          | 1.85    | 0.07  |

Principal Component Analysis

The iterative model selection for PCA resulted in four factors. Tests were included in a factor if they had a high-factor loading >0.5 (Table 5). The four factors were 1) behavior/mood which included tests: HDRS, BHS, CES-D, AES, Barratt impulsivity scale, Brown-Goodwin Lifetime History of Aggression, the Buss Durkee Inventory, and the BRIEF, 2) psychomotor speed/executive function including: Trail Making Tests Parts A and B, WAIS-R Digit Symbol Coding, DKEFS Color Word Inhibition/Switching, and FAS, 3) verbal memory: NAB Story and List Immediate and Long Delayed Recall, and 4) visual memory: ROCF Immediate and Delayed Recall.

Change of BMI and factors

The association between change in BMI and each of the four PCA factors are shown in Table 6. There was a statistical significance (based on a 0.05 alpha level) between change in BMI and psychomotor speed/executive function (p=0.038). The higher the change in BMI the lower the participants scored in psychomotor speed and executive function domains. The effect size was low based on a partial correlation value =-
0.14. There were no significant differences between change in BMI and mood/behavior, visual memory, or verbal memory (Table 6). Higher values with the mood/behavior domain represent higher dysfunction while higher scores in the other factors represent higher functioning among participants.
Table 5. Results of PCA model, Rotated Factor Pattern. Factors were determined by a load >0.5

<table>
<thead>
<tr>
<th>Rotated Factor Pattern</th>
<th>Mood/Behavior</th>
<th>Psychomotor speed/EF</th>
<th>Verbal Memory</th>
<th>Visual Memory</th>
</tr>
</thead>
<tbody>
<tr>
<td>attime</td>
<td>Trails A Time - T-score</td>
<td>-0.067</td>
<td><strong>0.685</strong></td>
<td>0.104</td>
</tr>
<tr>
<td>wdsctt</td>
<td>Total scaled score</td>
<td>-0.197</td>
<td><strong>0.612</strong></td>
<td>0.086</td>
</tr>
<tr>
<td>btttime</td>
<td>Trails B Time - T-score</td>
<td>-0.128</td>
<td><strong>0.719</strong></td>
<td>0.111</td>
</tr>
<tr>
<td>inswscale</td>
<td>Inhibition/ Switching completion time - Scaled score</td>
<td>-0.187</td>
<td><strong>0.547</strong></td>
<td>0.255</td>
</tr>
<tr>
<td>tofast</td>
<td>Total (F+A+S): T-score</td>
<td>0.056</td>
<td><strong>0.513</strong></td>
<td>0.196</td>
</tr>
<tr>
<td>roipt</td>
<td>Immediate Presence &amp; Accuracy - T-score</td>
<td>-0.059</td>
<td>0.141</td>
<td>0.191</td>
</tr>
<tr>
<td>rodelrt</td>
<td>Delayed Presence &amp; Accuracy - T-score</td>
<td>-0.098</td>
<td>0.211</td>
<td>0.160</td>
</tr>
<tr>
<td>nstput</td>
<td>Phrase Unit (1 &amp; 2) Immediate Recall - T-score</td>
<td>-0.052</td>
<td>0.235</td>
<td><strong>0.814</strong></td>
</tr>
<tr>
<td>nstpudrt</td>
<td>Phrase Unit Delayed Recall - T-score</td>
<td>-0.181</td>
<td>0.293</td>
<td><strong>0.825</strong></td>
</tr>
<tr>
<td>nlsdt</td>
<td>List A Short Delay - T-score</td>
<td>-0.01485</td>
<td>0.47087</td>
<td><strong>0.51500</strong></td>
</tr>
<tr>
<td>nlldt</td>
<td>List A Long Delay - T-score</td>
<td>-0.08155</td>
<td>0.45074</td>
<td><strong>0.53657</strong></td>
</tr>
<tr>
<td>hamtot</td>
<td>Hamilton total score</td>
<td><strong>0.77803</strong></td>
<td>-0.15275</td>
<td>0.05806</td>
</tr>
<tr>
<td>beckhope</td>
<td>Hopelessness total score</td>
<td><strong>0.75848</strong></td>
<td>-0.13137</td>
<td>0.07294</td>
</tr>
<tr>
<td>bartotal</td>
<td>Total Score</td>
<td><strong>0.78772</strong></td>
<td>-0.08533</td>
<td>-0.14525</td>
</tr>
<tr>
<td>bdtotal</td>
<td>Total Score</td>
<td><strong>0.73752</strong></td>
<td>-0.06948</td>
<td>-0.11300</td>
</tr>
<tr>
<td>brit</td>
<td>Behavioral Regulation Index (BRI) - T-score</td>
<td><strong>0.83198</strong></td>
<td>-0.11018</td>
<td>-0.14593</td>
</tr>
<tr>
<td>cesdtot</td>
<td>CES-D total score</td>
<td><strong>0.87535</strong></td>
<td>-0.16607</td>
<td>-0.01699</td>
</tr>
<tr>
<td>aestot</td>
<td>AES total score</td>
<td><strong>0.81218</strong></td>
<td>-0.15718</td>
<td>-0.08490</td>
</tr>
<tr>
<td>maxaggsum</td>
<td>Brown-Goodwin Max Aggression Sum</td>
<td><strong>0.54178</strong></td>
<td>0.08858</td>
<td>-0.04616</td>
</tr>
</tbody>
</table>
BMI change on individual neurocognitive tests

Participant scores on individual tests were also evaluated based on change of BMI (Table 7). Most of the selected tests did not show significance between test scores and change in BMI. There was a significance between change in BMI and the WAIS-R Digit coding test (p-value = 0.04). But, the effect size was low (partial correlation = -0.06). The results reflect the greater the BMI change, the worst the participant would perform on this test based on an alpha level 0.05.

Table 6. Change of BMI on cognitive and performance factors. * indicates statistical significance based on a 0.05 alpha level.

| Factor                        | Estimate | Standard Error | DF  | t Value | partial correlation | Pr > |t| |
|-------------------------------|----------|----------------|-----|---------|--------------------|-------|---|
| Mood/Behavior                 | 0.03     | 0.02           | 239 | 1.35    | 0.09               | 0.180 |
| Psychomotor speed/Executive Function | -0.04    | 0.02           | 239 | -2.08   | -0.14              | 0.038*|
| Verbal Memory                 | 0.01     | 0.02           | 239 | 0.5     | 0.03               | 0.617 |
| Visual Memory                 | 0.01     | 0.02           | 239 | 0.4     | 0.03               | 0.691 |
Table 7. Change of BMI on individual cognitive tests. * indicates statistical significance based on a 0.05 alpha level. The data is presented as standard error (S.E.), partial correlation (P.R.).

| Scores                           | Estimate | S.E. | DF   | t Value | p.c. | Pr > |t| |
|----------------------------------|----------|------|------|---------|------|------|---|
| Animal Fluency                   | -0.43    | 0.30 | 1253 | -1.44   | -0.04| 0.15 |
| BSIT                             | -0.01    | 0.04 | 1253 | -0.18   | -0.01| 0.85 |
| NAB List Immediate               | 0.09     | 0.22 | 1253 | 0.41    | 0.01 | 0.68 |
| NAB Map Reading                  | -0.21    | 0.26 | 1253 | -0.79   | -0.02| 0.43 |
| NAB Story Delay                  | 0.05     | 0.20 | 1253 | 0.25    | 0.01 | 0.80 |
| NAB naming                       | -0.10    | 0.30 | 1253 | -0.35   | -0.01| 0.73 |
| ROCF Copy Presence & Accuracy    | 0.05     | 0.30 | 1253 | 0.15    | 0.00 | 0.88 |
| ROCF Delayed Presence & Accuracy | 0.07     | 0.26 | 1253 | 0.26    | 0.01 | 0.79 |
| Total (F+A+S)                    | -0.47    | 0.28 | 1253 | -1.67   | -0.05| 0.10 |
| Trails A                         | -0.55    | 0.29 | 1253 | -1.93   | -0.05| 0.05 |
| Trails B                         | -0.07    | 0.39 | 1253 | -0.17   | 0.00 | 0.86 |
| WAIS Digit span total score      | -0.09    | 0.06 | 1253 | -1.59   | -0.04| 0.11 |
| WAIS-R Digit Symbol Coding       | -0.10    | 0.05 | 1253 | -2.02   | -0.06| 0.04*|
| WCST learning to learn score     | -1.44    | 1.31 | 1253 | -1.11   | -0.03| 0.27 |
| WRAT-4                           | -0.15    | 0.30 | 1253 | -0.49   | -0.01| 0.62 |
DISCUSSION

The current study examined the association of change in BMI and current cognitive functioning in former NFL players. After the scores were adjusted for age, education, and years of football participation, results indicated that greater changes in BMI have a negative effect on an individual’s psychomotor speed and executive functioning. There was one significant result between change in BMI and a specific neurocognitive test, the WAIS-R Digit Symbol Substitution Test. The results from Table 7 may seem inconsistent with previous studies that demonstrate there is a negative correlation between obesity and other cognitive testing (Benito-León et al., 2013). The important difference in our study is that the entire cohort was overweight or obese. The use of controls may have shown that there is a difference in BMI on cognitive tests, but that would be difficult to separate from RHI exposure within the NFL cohort and no exposure in controls. That is the main reason the study used change in BMI from retirement, to observe if there are any differences in neurocognitive dysfunction with greater variations of weight in at-risk populations. The results are the first to examine the change of BMI in NFL players on cognitive functioning.

Executive functioning/psychomotor speed

Executive functioning and psychomotor speed have been grouped together based on their neuropsychological processes and estimated brain regions. Executive functioning is thought to include cognitive functions such as cognitive flexibility (Greve et al., 2002) and working memory (Dunbar and Sussman, 1995). Cognitive flexibility can include set
shifting, planning, and abstract thinking. These processes are thought to take place in the frontal lobe of humans (Alvarez and Emory, 2006).

Anatomical divisions of the frontal lobe include the dorsolateral, ventromedial, and orbitofrontal prefrontal regions. These subdivisions have been preferentially associated with specific cognitive functions. The dorsolateral prefrontal cortex (DLPFC) is thought to control most of the executive functioning tasks mentioned previously. The ventromedial and orbitofrontal prefrontal lobes appear to be more involved in emotional and behavioral aspects of humans. Lesions in the ventromedial lobe have been reported to produce apathy and psychomotor dysfunction in patients (Sbordone, 2000). When the orbitofrontal cortex has been lesioned, patients have been observed to experience a lack of socially accepted behavior including greater disinhibition, impulsivity and antisocial tendencies (Cummings, 1995).

These brain regions share an important trait that may help to explain the executive functioning and psychomotor speed deficits in our cohort. These brains regions are situated anteriorly in the brain. When some football players set themselves up for a play, they squat down into a typical three-point stance meaning that they place one hand on the ground and prepare to propel themselves forward in a low, linear plane. Rowson et al., (2009) found that these linear hits are mostly small hits, but some can be greater than 40 g in collegiate level of play. This is common in both offensive and defensive linemen position. The majority of the hits from a three-point stance will be to the front of the helmet hitting an opponent’s shoulder pad or, even more dangerous, a helmet to helmet contact. These hits may be preferentially affecting the frontal lobe. Talavage et al., (2014)
reported that all individuals who had sustained subconcussions (positive fMRI scans) with no clinically observational symptoms showed altered fMRI activation of the DLPFC and deficits in working memory. The study is important because it shows the DLPFC can be altered while athletes are active in their sport, not retired like the sample for the study.

The results from the cognitive domain deficits in our study match reasonably well with observed pathological findings of CTE. McKee et al., (2013) found that CTE tends to affect the superior, dorsolateral and lateral frontal cortices first. The anatomical location and functional properties of these affected areas are consistent with many of the pathological and clinical features of CTE such as decline in executive function, disinhibition, and apathy.

Weight alone can also contribute to executive functioning deficits. Gunstad et al., (2007) performed a study on obese populations and executive functioning. They excluded any participant who had a comorbid health complication (hypertension, CVD, diabetes, etc.). They also excluded any individual who has suffered from a traumatic brain injury. With this exclusion and controlling for age, the study found that normal weight individuals outperformed overweight and obese participants in tests of executive functioning. This study can strengthen the argument that weight alone has the potential to negatively influence function in select cognitive processes. The study can also be taken to indicate that some of these cognitive declines are preventable. In most cases obesity is reversible and healthy weight can be achieved from a healthy diet and an increase in physical exercise.
Older obese individuals may feel that it would not be beneficial for them to lose weight at an old age; but research has shown that exercise intervention in obese elderly (over 65) has had promising results. In a randomized controlled trial, research participants completed either: 52 weeks of exercise intervention, just diet intervention, diet and exercise intervention, or control group. When cognitive tests were administered after the intervention period, elderly adults who were in the intervention groups showed positive increase in cognitive functioning in the trail making tests, word fluency tests and, arguably most important, quality of life. Those who participated in the diet-exercise and exercise groups saw the most positive effects (Napoli et al., 2014). These results show us that by changing lifestyle, we may be able to reverse some cognitive decline and therefore increase quality of life in aging adults.

As people age, they may feel it is easier to continue a sedentary lifestyle than implement an exercise regimen, even if all the research results argue in favor of changing. Daly et al., (2014) observed an interesting bidirectional relationship between exercise and executive functioning. While Daly and colleagues agree that exercise can increase a person’s level of executive functioning, they also found that the participants who began with low levels of executive functioning were more likely to have reduced physical exercise overtime. This may be because of lack of motivation and the difficulties in starting and sticking to a new exercise routine. In contrast, those who participated in sports and exercised to exhaustion tended to retain higher levels of executive functioning. This phenomenon can be applied to healthy retirement protocols in the NFL cohort. It may be the case that if NFL players are given plans and guidance to retain an exercise regimen
similar to the level that they are used to in training, they may have the opportunity to retain executive functioning skills and experience fewer hardships from RHI.

**Conclusion**

Looking at change in BMI may reveal important insights in the aftermath of a professional NFL career. If we see that individuals with the biggest increases in weight are dealing with more severe cognitive deficiencies, this would seem a strong hint on the importance of better retirement care of our NFL players. The results show us that the exposure risk factor of number of concussions do not vary with changes in BMI. The amount of concussions a participant may have sustained has been noted to play a role in cognitive dysfunction. It is difficult to separate the exposure risk and weight because the bigger guy tends to have a higher chance of playing a high exposure position. These results show that managing BMI may be beneficial in the management of symptoms associated with TES and CTE. While we cannot erase the repetitive traumatic brain injury once it occurs, helping individuals live a healthy lifestyle may have positive effects on their overall wellbeing.

Results from our study may also have more implication into the future. Anzell et al., (2013) found that each year between 1942-2011, body composition (percent body fat) of linemen rose between 0.046%-0.275%. The data used for the present study’s cohort averaged a retirement year from 1986. That has allowed contemporary linemen 30 years of body composition growth. Also, to reiterate a point from the introduction, some college football offensive line athletes are the heaviest in all football players. The implications of
weight on CTE may be more significant than we could even imagine at this point. When the players from 2016 retire, we may be seeing exacerbated cognitive decline based on weight and future weight gain. This may not be due to weight alone, but may be from increased exposure risks. While the offensive line is the heaviest position, it would make sense for teams to pair their largest defensive players against them for an even fight. This may increase exposure and increase the force of the hits.

The study has been limited in participant variation. Many of the participants played the same positions in football. There were no quarterbacks in our sample. It may be beneficial for future studies to include a wide range of positions to be able to differentiate exposure factors from other potential risk factors. Also, this population cohort tended to have players in the largest positions. Having more variation of positions would give more data of BMI change among a better representation of retired football players.

Future studies may benefit from performing intervention experiments with the retired NFL cohort. There has been significant evidence that exercise interventions can benefit cognitive functioning and it would be interesting to see if these observations can be seen in men who have been exposed to repetitive head injuries. It would also be interesting to observe more time points for changes of weight as well as associated CVD risk-factors. To extend these individuals into a longitudinal study can give more validity and time points to observe weight and cognition changes.

The importance of the present study was the unique method of examining BMI affects in an unusually large cohort. It may have been possible to find results from comparing overweight, obese stage 1, obese stage 2, etc. But, the benefit of using change
in BMI gave a new perspective on retirement life after the NFL. Retired professional football players may continue to have many complications in behavior, mood, and cognition. It is important that we identify means for America’s top athletes to alleviate their physical and emotional burden.
LIST OF JOURNAL ABBREVIATIONS

Alzheimers Res Ther…………………………………Alzheimer’s Research and Therapy

JAMA……………………………………The Journal of the American Medical Association
REFERENCES


CURRICULUM VITAE

Alyssa M. Schmitt
Year of Birth: 1990
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Boston, MA 02127
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EDUCATION

Boston University School of Medicine: Boston, MA August 2014 - Expected, May 2016
Master of Science, Anatomy and Neurobiology

Clemson University: Clemson, South Carolina August 2009 - December 2012
Bachelor of Science, Psychology - Cum Laude

AWARDS AND HONORS

Cum Laude graduation honors, Clemson University, Clemson, SC 2012
President’s List and Dean’s List, Clemson University, Clemson, SC 2011-2012
Alcatel-Lucent CWA/IBEW Academic Scholarship 2009-2012
Alcatel-Lucent Scholar Award 2011-2012

RESEARCH EXPERIENCE

Graduate Research Assistant, CTE Center: Boston, MA February 2015-Present
Primary administrator of neuropsychological assessment to research participants. Working as part of the DETECT team to help evaluate cognitive function in order to work towards a goal of detecting Chronic Traumatic Encephalopathy in living persons.

Thesis: Change in BMI and cognitive functioning in retired NFL players

Research Intern, Resources for Human Development: Philadelphia, PA Summer 2012
Assisted in ongoing research exploring effective methods for group therapy, terms of stay policy, and safety intervention in substance abuse facilities and half-way homes for homeless population.

Participant of Mentor Guided Research Experience: Clemson, SC Fall 2011-Spring 2012
Participated in a program for junior level psychology students to develop individual research from start to end with the guidance of a faculty mentor. Developed and implemented a research study to examine the effects of food choices on college aged students’ self-esteem.

BUSINESS EXPERIENCE

Sales/Brand Ambassador, First Aid Shot Therapy: Boston, MA July 2015-Present
Promote a new brand to the New England Region by informing the public of the merchandise and benefits of the innovative Over-the-Counter products. Contact local small business and sell the merchandise through excellent communication and presentation.

**OFFICE EXPERIENCE**

**Warranty Clerk (Temporary), Rolex: New York, NY** May 2014-August 2014
Involved various office duties such as: accuracy checking thousands of individual warranty cards for mistakes or blemishes, data entry for missing warranty cards, organizing and filing statements from jewelry facilitators, creating and implementing a more efficient system for warranty card replacement.

**Medical Secretary, Hospital for Special Surgery: New York, NY**
September 2013-May 2014
Assisted physician and medical support staff with patient relations by answering multiple phone lines, organizing and ordering diagnostic testing, and scheduling patient appointments. In charge of patient check out, keeping records of receipts and inputting data into Excel. Learned various medical billing, coding, proofreading, scanning and data entry.

**RESEARCH SKILLS**
- Writing IRB Proposals
- Developing Study design
- VNC Viewer/Terminal
- Neuropsychological assessment
- Research subject recruitment
- MATLAB/SPSS
- EEG administration, Brainscope
- Psychological Survey design

**VOLUNTEER WORK AND ORGANIZATIONS**

**Mentor, EDUCAN at Boston University School of Medicine** 2016-currently
Established a relationship with grade-school students to implement successful mindsets in students to increase self-esteem, learn from failure, and embrace challenges.

**Social Chair, Student Advisory Committee for Anatomy and Neurobiology** 2015-2016
Had original ideas to better the department cohesion by implementing a successful series of mini-lectures from laboratories to students. Planned social events for students.

**Shelter Assistant, Animal Rescue Fund**
Seneca, SC: 2010-2012

**Volunteer Youth Cheerleading Coach**, Medford Youth Athletic Association
Medford, NJ

**OTHER INTERESTS**

**Oversea travel**: Have spent various months and weeks backpacking in Europe

**Long distance running**: Completed Philadelphia Half-Marathon, On track to complete Plymouth Half-Marathon

**Beach volleyball and intramural softball**

**Creative writing**

**Nutrition**