The Protective Effect of Education on Cognition in Professional Fighters

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Abstract

Education has a protective effect against cognitive deficits following various forms of brain insult. Professional fighting (boxing and mixed martial arts) provides a model for assessing the impact of cumulative brain injuries on cognition and brain health. In the current cross-sectional observational study, we explore whether education would be protective against cognitive loss in fighters. We tested 141 professional fighters using a computerized neurocognitive battery, in addition to structural MRI. We used automated segmentation software to compute the volumes of various brain structures. We found fighters with high school education or less to show more associations between fight exposure and cognitive test scores. The relationship between brain structure volume and exposure did not differ based on education. These results are interpreted as putatively showing a protective effect of education on functional integrity in fighters, although longitudinal data and a larger sample size are required to further understand this relationship.

Keywords: Boxing; Mixed martial arts; Chronic traumatic encephalopathy; Thalamus; Hippocampus

Introduction

Professional fighting, such as boxing and mixed martial arts, involves repetitive head injury and, as a result, cognitive impairment (Heilbronner et al., 2009). In some cases, this progresses to dementia (Mendez, 1995) with pathological findings characteristic of chronic traumatic encephalopathy including changes in the limbic system and basal ganglia (Corsellis, Bruton, & Freeman-Browne, 1973). There have been few studies of cognition in active fighters and the results of studies that have been published are somewhat variable (Heilbronner et al., 2009). However, some of the larger studies demonstrate relationships between higher levels of exposure (more fights or more sparring) and reductions in attention, concentration, processing speed, and, in some cases, memory (Brooks, Kupshik, Wilson, Galbraith, & Ward, 1987; Jordan, Matser, Zimmerman, & Zazula, 1996). Importantly, a significant genetic risk factor for Alzheimer’s disease, possession of the ApoE e4 allele, has been shown to mediate the relationship between fighting and cognition; with e4 positive individuals showing poorer cognitive outcomes (Jordan et al., 1997). Here, we assess the effect of another mediating factor that has been associated with cognition in Alzheimer’s disease, as well as other forms of brain trauma, level of formal education.

The protective effect of education (and other factors including high verbal intelligence [Alexander et al., 1997] and occupational attainment [Stern et al., 1994]) on cognitive outcome to brain insult is often referred to as cognitive reserve (Stern, 2002; Stern, Alexander, Prohovnik, & Mayeux, 1992; Stern et al., 2003; Stern, Silva, Chaisson, & Evans, 1996). Early studies in Alzheimer’s disease pointed out a lack of a direct relationship between pathological load and cognition (Katzman et al., 1989). Later, it was suggested that there is active compensation or recruitment of alternative networks in some individuals, those with higher levels of education (or other factors that enhance cognitive reserve), which diminishes the impact of pathology. This is perhaps the strongest explanation for why individuals with higher levels of education tend to demonstrate cognitive decline later in Alzheimer’s disease. This pattern has also been shown in models of other brain insult, including traumatic brain injury.
Further, regional age-related changes in cortical volume have been found to be unassociated with education level (Coffey, Saxton, Ratcliff, Bryan, & Lucke, 1999), suggesting that it is the function, not the structure, of the brain that is protected by cognitive reserve.

The relationship between education and head injury is yet to be studied in professional fighting sports. This is important to study, since education may have a mediating effect on cognitive response to head injury. Since repetitive head injury in sports is receiving increased attention from scientists recently, it is important to understand how education might impact results. For example, a group of fighters with similar levels of exposure but from mixed educational backgrounds may not appear, on average, to be impacted by their injuries, but this could be due to less impairment in more educated fighters masking the impairments in less educated fighters.

This study utilizes initial cross-sectional data collected as part of a large-scale longitudinal study of brain health in professional fighters currently underway at our center. We are testing the hypothesis that the cognitive reserve hypothesis will hold in this population. Specifically, we expect that there will be no differences in the relationship between fight exposure and brain structure volume in fighters with different levels of education, but that there will be a more negative impact of higher levels of fight exposure on the cognitive scores of fighters with less education compared with those with more education.

**Methods**

The study cohort comes from the Professional Fighters Brain Health Study, a longitudinal study of professional combatants (both boxers and mixed martial arts fighters). Complete methods for the study have been detailed elsewhere (Bernick et al., 2013) so only details specific to the current study will be outlined here. A total of 141 fighters were included for analysis. All fighters gave informed consent and the protocol was approved by the Cleveland Clinic IRB. Subjects were divided into two groups based on years of formal education. We used 12 years as a cutoff since that is the number of years it generally takes to graduate high school.

All fighters underwent MRI scanning using a Siemens 3T Verio scanner with a 32 channel head coil (Siemens Medical Systems, Erlangen, Germany). Acquisition protocol details are TR/TE/T1 = 2300/2.98/900, flip angle = 9°, BW = 240 Hz/Px, Echo spacing = 7.1 ms, 240 × 256 matrix, 160 slices, voxel size = 1 × 1 × 1.2 mm, scan time: 9:14. Volume of the subcortical gray matter including hippocampus, amygdala, thalamus, caudate, and putamen were calculated on anatomical T1-weighted image using the automated full brain segmentation process in Freesurfer software (Fischl et al., 2002). The subcortical volumes were measured in each hemisphere separately.

Educational attainment and other demographic details were ascertained via structured interview. Fight exposure details were also collected during the interview and included total number of years of fighting, years of professional fighting, total number of fights, number of professional fights, type of fighter (boxer vs. MMA), and a composite score of the number of professional fights and number of professional fights/year (Bernick et al., 2013). This composite score was empirically derived and the process has been published previously. The composite index was derived by combining years of fighting and number of fights was also included as an exposure measure. This provides some measure of “intensity” of fight exposure above and beyond number and duration of fight exposure.

Cognitive testing was completed with the computerized CNS Vital Signs program (Gualtieri & Johnson, 2006). Raw summary scores were used for all analyses. Subtests administered were verbal memory (a word list recall task with immediate and delayed recall components), symbol digit coding, Stroop, and finger tapping tests. Results from these tests are used to make up scores in various clinical domains:

- **verbal memory:** Number of correct items on immediate and delayed recall
- **processing speed:** Correct responses on symbol digit coding minus errors
- **psychomotor speed:** Taps on finger tapping plus correct responses on symbol digit coding
- **reaction time:** A combination of scores from the Stroop test

The test battery was performed in the subject’s native language (English = 93%). These forms have established equivalency (Gualtieri & Johnson, 2006).

The primary goal of the study was to assess the effect of education on the relationship between cognitive test scores and fight exposure. Generalized linear models were constructed with cognitive test score as the dependent variable and education level, fight exposure variables, and their interaction as the independent variables of interest. Age (continuous variable) and race (categorized as Caucasian, African American, or other [Asian, Pacific Islander, American Indian, and Alaskan Native]) were also included in all models. Separate models were fit for each fight exposure variable considered: Type of fighter (boxer or mixed martial artist), total number of fights, number of professional fights, total number of years of fighting, and number of years of professional fighting, as well as the composite index. F-tests were used to evaluate the effect of the independent variables on cognition scores;
non-significant interaction terms were removed from the model. Thus, for each cognitive test score, six models were fit. A significance level of 0.05 was used.

Repeated-measures ANOVA was performed to test the association between brain volume and education, fight exposure, and their interaction. Five pairs of dependent variables were evaluated in separate models: Left and right thalamus, left and right hippocampus, left and right caudate, left and right putamen, and left and right amygdala. Models were adjusted for intracranial volume, age, and race. We omitted seven female fighters from the analysis, since our sample size was too small to include the additional covariates for appropriate gender adjustment. Least-squared means were calculated from the fitted models. When the left and right structures were not significantly different, the average of the least-squared means from the left and right sides was taken. We reported the percent difference between education levels, calculated as \((\text{least-squared mean for } \leq \text{HS} - \text{least-squared mean for } > \text{HS})/(\text{least-squared mean for all subjects}) \times 100\). All analyses were performed in SAS 9.2.

**Results**

Demographic details for the sample are given in Table 1. Among those with less than or equal to a high school education, 58.9% were boxers, and among those with more than a high school education, 32.4% were boxers. The difference is statistically significant \((p = .002, \chi^2\text{ test})\).

There is a possibility that our data are subject to a self-selection bias, since only those fighters motivated to be in our study participated (motivated in part by the offer of a free MRI, which is required for their license to fight in Nevada). To investigate this, we compared the ratio of wins:losses in our cohort with that of published data from all fights in Nevada (Nevada Athletic Commission) and found no significant differences between the participants in this study and the general population of fighters in Nevada.

**Education Level and Volume of Brain Structures**

Education level was not significantly associated with thalamus (adjusted percent mean difference in thalamus volume for \(\leq \text{HSD} \text{ vs. } > \text{HSD} \) is 1.2% \((p = .363)\)), hippocampus (0.2%, \(p = .844\)), caudate (1.0%, \(p = .581\)), putamen (1.3%, \(p = .376\)), or amygdala volumes (−1.2%, \(p = .471\)).

**Fight Exposure and Volume of Brain Structures**

In previous work (Bernick et al., 2012; C. Bernick et al., submitted), we found that the following variables were associated with significant reductions in caudate and thalamic volume and trended toward reduction in hippocampal and putamen volume: Boxers (when compared with MMA fighters), fighters with more professional fights, greater number of years of professional fighting, and greater composite index values. These associations, however, are not significantly modified by the fighter’s education level: The interaction of education and fight exposure on thalamus \((p \geq .114)\), hippocampus \((p \geq .186)\), caudate \((p \geq .190)\), putamen \((p \geq .197)\), and amygdala volumes \((p \geq .206)\).

**Processing Speed**

Processing speed: As the composite score increased \((p = .043)\) processing speed scores decreased. Processing speed scores of fighters with \(\leq 12\) years of education were lower than for fighters with more education \((p = .017)\). The interaction of composite score and education was not significant \((p = .152)\). The age-, race-, and fight exposure-adjusted mean difference in processing time scores for fighters with \(\leq 12\) years of education versus fighters with \(> 12\) years of education was −8.2% \((p = .043)\). Table 2 further summarizes processing time scores by professional fight exposure and education. Other fight exposure variables and the interaction of fight exposure and education were not significantly associated with processing speed score \((p \geq .152)\).

<table>
<thead>
<tr>
<th>Table 1. Demographic details for fighters</th>
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<tbody>
<tr>
<td>(\leq \text{HSD} (n = 73))</td>
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<tr>
<td># boxers (n [%])</td>
</tr>
<tr>
<td>Age (mean [SD])</td>
</tr>
<tr>
<td>Race: African American, Caucasian, and other</td>
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<tr>
<td>Age when started fighting: mean (SD) [range]</td>
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<tr>
<td>Years of education: mean (SD) [range]</td>
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</tbody>
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Notes: \(\leq \text{HSD}\) represents subjects with a high school diploma or who did not complete high school; \(> \text{HSD}\) represents subjects with some post-high school education.
Psychomotor speed: Higher education was associated with better scores on psychomotor speed (\( p = .021 \) for the interaction of total years of fighting and education). For less educated fighters, psychomotor speed scores declined with increasing years of fighting by an average of 4.6% per decade of fighting. For more educated fighters, psychomotor speed scores did not significantly change as the number of years of fighting increased (Fig. 1). In a post hoc analysis, we separated out the two components of the psychomotor speed scores; education level was associated with the finger tapping aspect (\( p = .015 \) for the interaction of total years of fighting and education), but not the symbol digit coding aspect (\( p = .545 \)).

Reaction time: There was a significant interaction between the type of fighter and education level (\( p = .006 \)) in predicting reaction times. Reaction time scores tended to be lower (i.e., slower) for MMAs with \( \leq 12 \) years of education versus more educated MMAs, though the difference was small (<1% difference). In contrast, reaction time scores were significantly higher for boxers with \( \leq 12 \) years of education compared with more educated boxers (adjusted mean difference of 13.1%). There was no association between reaction time and the quantitative measures of fight exposure.

Verbal memory scores: Neither education level nor exposure was significantly associated with verbal memory scores.

Discussion

There was no relationship in our exploratory study between education level and any of the brain structure volumes of interest. However, with increased exposure to fights, some of these structures appear to diminish in volume. There were relationships

<table>
<thead>
<tr>
<th>Exposure level</th>
<th>( \leq \text{HSD} )</th>
<th>( &gt; \text{HSD} )</th>
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<tbody>
<tr>
<td>Exposure level 1</td>
<td>—</td>
<td>+8.1%</td>
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<tr>
<td>Exposure level 2</td>
<td>—2.2%</td>
<td>+5.7%</td>
</tr>
<tr>
<td>Exposure level 3</td>
<td>—4.5%</td>
<td>+3.6%</td>
</tr>
<tr>
<td>Exposure level 4</td>
<td>—9.0%</td>
<td>—1.1%</td>
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</tbody>
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Notes: Estimates are from fitted model for 30-year-old Caucasian boxer as a function of education and professional fighting exposure, where both education level and exposure to professional fighting were independent predictors of processing time scores. The exposure levels correspond to no professional fights (level 1); \( \leq 15 \) professional fights and \( \leq 1 \) fight per year (level 2); \( \leq 15 \) professional fights but \( > 1 \) fight per year (level 3); and \( > 15 \) professional fights (level 4).

Fig. 1. Estimated psychomotor speed scores from the fitted model, after adjustment for age and race. Score are plotted against total years of fighting for those with less than or equal to a high school education versus those with more than a high school education.
between cognitive measures and fight exposure, and in some cases, these were more pronounced for fighters with less education. Specifically, the impact of exposure on psychomotor speed differed depending on education. Fighters with less education showed declines in psychomotor speed over fight exposure (e.g., year of fights), whereas those with higher education showed no relationship between psychomotor speed and increased fight exposure. These results seem to suggest a likely protective effect of education on the brain’s functioning but not on its structure, consistent with the cognitive reserve hypothesis.

Mental and motor slowing is a manifestation of the clinical precursor of CTE (Mendez, 1995). Hence, our findings might suggest that fighters with less education are more likely to progress to eventually develop this disorder. However, slowing is very non-specific and its reduction is consistent with repeated concussions (Collins et al., 1999; Peterson, Ferrara, Mrazik, Piland, & Elliott, 2003). Long-term outcome studies are necessary to understand the true relevance of slowed processing and psychomotor speed in these fighters.

We did not see any relationship between exposure and our more executive (labeled reaction time, but involving a Stroop task) or verbal memory measures. This is somewhat surprising but perhaps due to the relatively brief exposure that these fighters have had to fighting. It may be that retired fighters or fighters with longer histories would demonstrate decline in these factors with increased exposure or that the measures used did not capture any relationship: Future reanalysis of subtest scores may show such a relationship.

We found strong relationships between a decline in the volume of caudate and thalamus with increased exposure, and this is independent of educational level. Thalamic atrophy is a known feature of CTE (McKee et al., 2009). We also found an association with diminished caudate volume with more exposure, which is interesting in the light of our cognitive findings, since diseases that affect the caudate and its connections result in slowed processing speed (Maroof, Gross, & Brandt, 2011). We also found a trend toward hippocampal atrophy, and the lack of statistical significance of this finding is consistent with the absence of a relationship between verbal memory and exposure in our fighters. CTE is a clinicopathological diagnosis, and by death fighters, may have had longer exposure and would be older than our current sample; these factors might affect the volume of these structures post mortem.

The patterns seen in our data are consistent with the cognitive reserve findings, where similar levels of brain pathology are evident in less and more educated samples, but the lifetime manifestation of cognitive deficit is higher in the less educated group (Kesler et al., 2003; Stern 2002; Stern et al., 1992, 1996, 2003). This is the first paper to ascertain this relationship in a fighter population. Given the relative youth of our population, the fact that our findings were limited to only some aspects of cognition are perhaps not surprising. If we were assessing older populations, we might expect memory to be impacted by fighting to a greater degree and to be worse in those with less education. The current findings, however, might be the focus of future research to ascertain the predictive value of reduced test scores early in the career, as they may be a marker of decline. Future research from our group will assess this hypothesis. We will also use other neuroimaging modalities that are perhaps more sensitive to microstructural tissue integrity using diffusion tensor imaging.

There are several limitations of our study. Our sample size of 141 fighters was small for the number of relationships between fight exposure and outcome that we evaluated. We continue to actively recruit fighters for this study so that we can better model these relationships. Reanalysis of this larger group, as well as similar analyses in other contact sports populations, will be important in determining whether or not the current findings are robust and generalizable. We currently lack a non-fighting control group to ascertain the relationships between our cognitive measures and educational level. Control group data are soon to be collected, and comparisons will be available for future longitudinal analyses. Of course, we cannot speak to the development of CTE in our fighting group, as that would involve very long-term outcome studies, but the cognitive domains and brain regions affected in this study are consistent with those regions that atrophy and cognitive deficits seen in patients who are diagnosed with CTE following death. Furthermore, education serves as one proxy for cognitive reserve, but as mentioned above several additional factors, including overall intelligence and occupational attainment, also influence this phenomenon and were not probed in the current study. In addition, there may be differences in the type of fight (e.g., medical oversight at venue, or qualifications of the referee) or other fight factors selected by more educated, compared with less educated, fighters, and this was not taken into account in the current study. Finally, the use of summary scores from the CNS Vital Signs battery may be problematic, especially since there is some overlap between domains in terms of subtest scores included: When we reanalyze data once we have a larger group, we will also include the raw test scores from the subtests. At this point, we decided not to conduct such analysis, since it would increase the total number of analyses completed to an unacceptable degree.

Longitudinal data will allow us to answer more questions about this implied protective effect of education. The study currently underway will collect data annually for 4 years. Based on the current findings, we might expect to see cognitive changes in the less educated fighters at a more rapid rate than the more educated fighters. Data in other groups of contact sports athletes will determine whether our findings generalize to other groups.
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Conflict of Interest

None declared.

References


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