Introduction

- Chronic traumatic encephalopathy (CTE) is a debilitating and enigmatic neurodegenerative disorder associated with repetitive traumatic brain injuries (TBI), often sustained through prior contact/collision sport participation or military-related exposure.1,2
- The clinical presentation of CTE (“traumatic encephalopathy syndrome”) includes a spectrum of neurological and psychiatric symptoms encompassing cognitive dysfunction, emotional dysregulation, behavioral change, and motor disturbance.3
- Neuropathological consensus criteria for the diagnosis of CTE define the underlying pathognomonic lesion as hyperphosphorylated tau aggregates in neurons, astrocytes, and cell processes around small vessels in an irregular pattern at the depths of the cortical sulci.4
- Given that approximately 28 million children (<15 years old), 8 million high school athletes and 500,000 collegiate athletes participate in organized sports programs in the United States annually,5 research regarding whether playing specific sports (especially at the amateur level) is associated with an increased risk of developing CTE pathology is imperative.

Abstract

Objective: Understanding the etiology of CTE requires examination of risk factors at both the population (environment: type of sport, age/level of participation, etc.) and individual (genes: single nucleotide polymorphisms, neuroanatomical expression, etc.) levels.

Methods: CTE pathology was screened for in cortical autopsy tissue from 300 athletes and 450 non-athletes via tau immunohistochemistry. Tissue microarrays (TMA) of 21 CTE+ athletes and 7 CTE- athletes were sampled and immunostained. Multiplex gene expression analysis (800 gene targets) will be performed on TMA samples through NanoString Technologies’ nCounter molecular barcoding panels.

Results: Of 477 male (ages 12-99; median 66) and 273 female (ages 7-100; median 67) subjects, 42 individuals (98% male) had pathology consistent with, or features of, CTE. Football participation, but not participation in other contact sports (including baseball, basketball, hockey, soccer and wrestling), was associated with an increased odds of occurrence of CTE in males (OR=2.62, P=0.005). For multiplex gene expression (experimental optimization ongoing), it is anticipated that specific pathway annotations (i.e., “Disease Association”, “Axon and Dendrite Structure”, etc.) and genes (i.e., MAPT, NEFL, GFAP, etc.) associated with tauopathies and/or TBI will demonstrate marked alterations in gene expression in CTE cases relative to other targets.

Materials and Methods

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<th>Study Cohort</th>
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<th>CTE Screen</th>
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<tr>
<td>REP + MCTR N = 2,566</td>
<td>Baseball, football - youth/high school</td>
<td>Tau HIC</td>
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Figure 1: Study workflow. Obituary and yearbook records were queried for 2,566 individuals in the Mayo Clinic Tissue Registry to identify 300 contact sport athletes (various sports) and 450 non-contact sport controls. Tau immunohistochemistry (AT8, 1:2500) was performed on 3 neocortical regions for all 750 cases to screen for CTE pathology.

Results (continued)

- 42 cases (5.6% cohort) with CTE pathology (21/42 Features of CTE).
- Interestingly, 15 cases had no documented contact sports exposure.
- Football only sport with increased odds of CTE in males (OR=2.62, P=0.005) especially exposure post-high school (OR=13.23, P<0.001).
- Participating in multiple sports did not increase odds of CTE.

Future Directions (Figure 4)

Conclusion

In assessing a variety of contact sports, we identified specific athletic activities, such as American football, that were more strongly associated with CTE pathology compared to other sports, and within football, a dose-response relationship between exposure and CTE pathogenesis. CTE pathology observed in non-athletes warrants further research.8

References