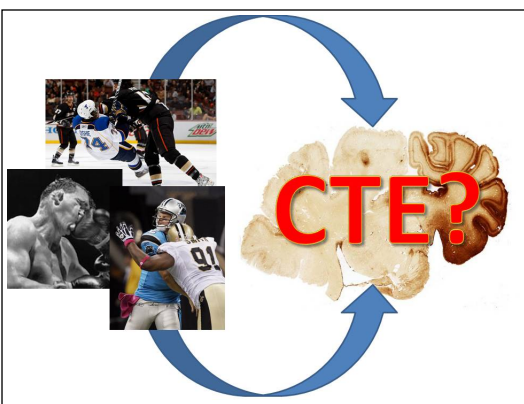


Risk Factors for Chronic Traumatic Encephalopathy

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Introduction

Chronic traumatic encephalopathy (CTE) is a neurodegenerative disease believed to be consequence of repetitive head trauma. Although initially believe to effect only boxers, the at-risk population for CTE has recently expanded to encompass a much wider demographic, resulting in considerable media attention and public concern for the potential neurodegenerative effects of repetitive head trauma. This review compiles all neuropathologically confirmed cases of CTE in the medical literature to date in order to analyze our current understanding of CTE and better identify the at-risk population.



Methods

The literature reviewed was obtained via PubMed and MEDLINE. Search criteria included terms such as "chronic traumatic encephalopathy," "dementia pugilistica," "repetitive mTBI." Duplicate cases were excluded in our collection.

Neuropathologically Confirmed Cases of CTE (n = 153)

Primary TBI Exposure	Pro	Amateur	Not Specified	Total	%
Boxing	43	11	15	69	45.1%
Football	47 ²	16 ³	-	63	41.2%
Hockey	4	1	-	5	3.3%
Wrestling	3	-	-	3	2.0%
Military	-	-	6	6	3.9%
Misc. ¹	-	-	7	7	4.6%
Total	97	28	28	153	

¹Misc. TBI exposure include physical abuse, self-injury behavior, circus clown, amateur soccer
²Pro football category includes 41 Former NFL, 4 CFL, and 1 Semi-Pro Football player(s)
³The amateur football category includes 9 collegiate and 7 high school football players

Table 1. Confirmed Cases of CTE

Results and Discussion

The literature review yielded 153 unique cases of neuropathologically confirmed CTE, making this the largest series to date of CTE case reports reported in the medical literature. Cases include boxers, football players, veterans, hockey players, wrestlers, and miscellaneous cases (Table 1).

Although head trauma appears to be the only widely recognized major risk factor for CTE, severity and number of injuries varied greatly with no apparent threshold for CTE development.

Apolipoprotein E (ApoE) genotyping data was available across all demographics for 80 cases (Table 2), but the data did not vary significantly from the ApoE data of the general population, suggesting ApoE may not be a significant risk factor for the onset of CTE.

The age of death was available for 150 cases (Table 3) and did not appear to be a major risk factor associated with CTE. However, symptoms and neuropathologies generally appeared more pronounced in aged subjects.

Incidence of Substance Abuse, Age of Death, and ApoE Genotype

ApoE Genotype	Number of Cases	%
0 x ε4	53	66.3%
1 x ε4	22	27.5%
2 x ε4	5	6.3%

Table 2. ApoE Genotype Data

Age Range	Number of Cases	%	Primary TBI Exposure		
			Number of Cases	%	
10-19	3	2.0%	Boxers	9	14.3%
20-29	16	10.7%	Football	13	18.8%
30-39	9	6.0%	Hockey	3	60.0%
40-49	21	14.0%	Wrestling	2	66.7%
50-59	21	14.0%	Military	2	33.3%
60-69	39	26.0%	Misc.	1	14.3%
70-79	26	17.3%	Total	30	19.6%
80-89	12	8.0%			
90-99	3	2.0%			

Table 3. Age of Death Data

Table 4. Incidence of Substance Abuse

Results and Discussion (cont.)

Cause of death was identified in 118 cases and classified as natural, accidental, or suicide. Despite the recent publicity of CTE and the suicides of professional athletes, the majority of deaths found from this review were due to be from natural causes.

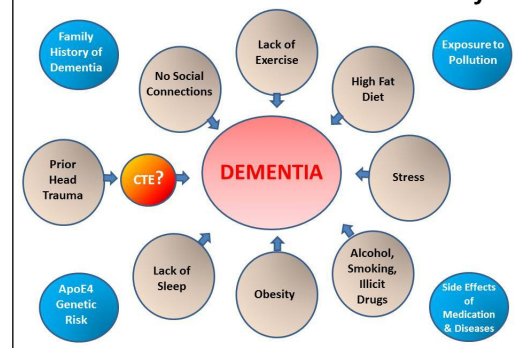
Thirty cases were found positive for a history of substance abuse (Table 4). Although rarely recognized as a potential contributing factor to neuropathologies of CTE, studies have demonstrated that substance abuse alone can enhance the development of neuropathological changes, such as elevated levels of hyperphosphorylated tau, white matter rarefaction, and microglia activation, which are all common pathologies observed in CTE.

Mood and anxiety disorders are commonly observed in this cohort CTE positive subjects. The relationship between the neurochemical changes associated with these mood disorders and the onset of CTE is unknown.

Conclusion

Although recent studies have strongly suggested the neuropathologies seen in CTE to be consequence of repetitive head trauma, only 153 neuropathologically confirmed cases have been reported to date. Additionally, numerous risk factors beyond mTBI may play a role in the development of the symptoms and neuropathologies associated with CTE.

Risk Factors for Dementia in NFL Players



Additional blinded non-selective studies investigating large groups of athletes in a variety of sports are still needed before any comprehensive risk identification and prevention policy can be implemented for addressing CTE in contact sports.

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