The relationship between traumatic brain injury and the neuropathology of dementia

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BACKGROUND

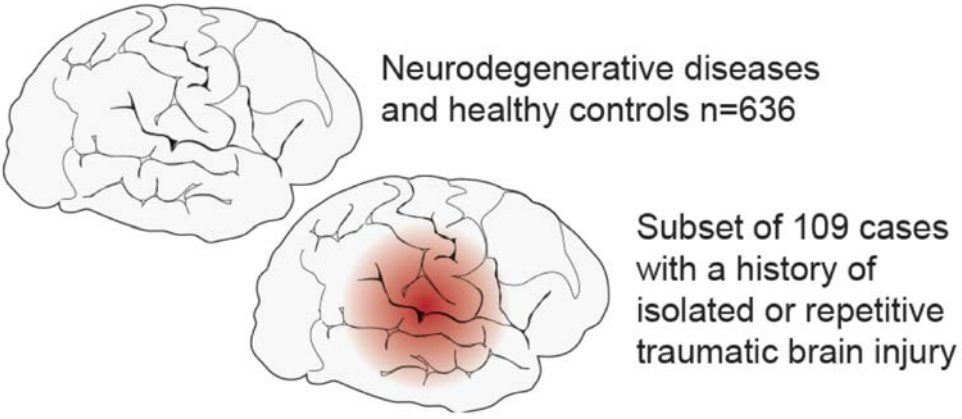
Clinical studies indicate that traumatic brain injury (TBI) is linked to an increased risk of dementia during life[1,2]. This includes large observational studies of populations and meta-analyses of some of these studies (only a small subset of references shown below).

However, the smaller number of studies involving neuropathologically-confirmed cases have so far shown conflicting results[3-5].

AIMS

We assessed a large brain bank cohort to identify any association between TBI and the presence of pathologies underlying the most common dementias- Alzheimer's disease (AD) and Lewy body disease (LBD).

METHODS



Mean case age (in years) 76±12.

1/3 of cases had a primary classification of AD or dementia dominant LBD. Many cases with other primary classifications also had AD and LBD pathological features present as an age-related or secondary finding.

Cases with a history of TBI were identified using donor records held at the Sydney Brain Bank. TBI cases included those with a history of single or multiple TBI, as well as repetitive mild neurotrauma that may be subconcussive (contact or combat sports participants).

The definition of TBI was kept intentionally broad to identify the largest sample of cases that might be at risk for a higher frequency of neurodegenerative change.

METHODS

Amyloid plaque and alpha synuclein pathologies were identified by immunohistochemistry. Neurofibrillary tangles were identified using modified Bielschowsky silver staining (Figure 1).

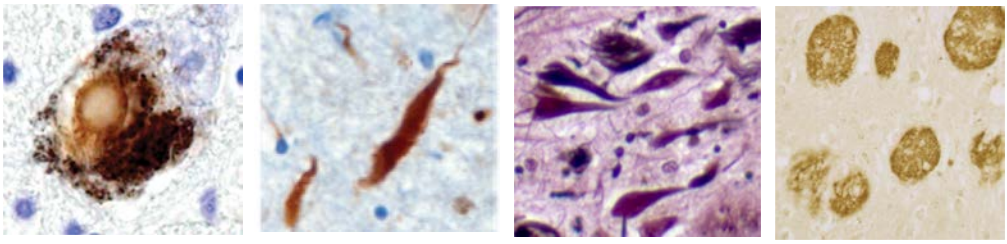


Figure 1- Lewy body (A), Lewy neurites (B), neurofibrillary tangles (C) and beta-amyloid plaques (D)

Pathology was assessed and staged according to current neuropathological diagnostic criteria[6,7,8].

Multivariate regression statistics were used to assess the effect of TBI, age and gender on amyloid plaque (A score), neurofibrillary tangles (B score) and Lewy pathology stages.

RESULTS

TBI was not significantly associated with increased amyloid (p=0.06) or Lewy pathology stages (p=0.7) (Table 1).

The odds of having a higher neurofibrillary tangle stage increased by 79% in the TBI group (p=0.006)(Table 1).

Gender was not a significant predictor of amyloid (p=0.28), neurofibrillary tangle (p=0.91) or Lewy pathology (p=0.15) (Table 1).

Not unexpectedly, age was a significant predictor of AD pathologies- for every year of increasing age (compared to the group mean) the odds of having a higher ß-amyloid stage (A score) increased by 4.3% (p=<0.0000001) and a higher neurofibrillary tangle stage (B score) by 3.4% (p=0.00002). Age was not a significant driver of Lewy body pathology (p=0.11) (Table 1).

Pathology		OR (95% CI)	p-value
A score (amyloid)	Gender	1.21 (0.85-1.71)	0.28
	Age	1.04 (1.03-1.06)	**0.0000001**
	TBI	1.49 (0.98-2.29)	0.06
B score (tangles))	Gender	1.02 (0.72-1.44)	0.91
	Age	1.03 (1.01-1.05)	**0.00002**
	TBI	1.79 (1.18-2.72)	**0.006**
Braak Lewy body score	Gender	0.76 (0.52-1.10)	0.15
	Age	1.01 (0.99-1.03)	0.11
	TBI	1.09 (0.69-1.71)	0.7

Table 1. Odds ratios with 95% confident intervals for gender, post-mortem delay, age and TBI on individual pathologies using multinomial regression.

CONCLUSIONS

In this elderly neurodegenerative cohort, age remains a risk factor for AD, but not LBD pathology.

Gender did not have a significant association with these pathologies in this cohort.

TBI increased the frequency of neurofibrillary tangles, suggesting that abnormal tau protein accumulation following TBI is an important long-term consequence that may contribute to poor brain aging and the development of future neurodegeneration.

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