Exposure to traumatic brain injury and risk of frontotemporal dementia: a systematic review and meta-analysis

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Introduction: Frontotemporal dementia (FTD) is a neurodegenerative disorder involving frontal and anterior temporal lobes, anterior cingulate and insular cortex. It is the third most frequent type of dementia and the first one in patients younger than 65 years. The underlying neuropathology is mainly characterized by intracellular inclusions of proteins, neuronal death and gliosis. FTD symptoms are heterogeneous and include progressive deficits in behavior, executive function, or language. Traumatic brain injury (TBI) has been known as a risk factor for several types of dementia and other neurodegenerative conditions for a long time. Several studies have investigated the possible association between TBI and FTD.

Methods: As objective of the PREV-ITA-DEM project, a large-scale study funded in 2022 by the Italian Ministry of Health under the National Recovery and Resilience Plan (PNRR-MAD-2022-12375822), we searched Pubmed, Embase and Scopus for studies exploring the association between TBI and risk of developing FTD. Both case control and cohort studies were included. Results from selected studies were pooled separately according to their type. Risk of bias of included articles was evaluated with Newcastle-Ottawa scale.

Results: We screened 651 abstracts and included six studies; four of them had a case-control design and provided odds ratios (ORs) as effect size, the other two were retrospective cohort studies and provided hazard ratios (HRs). Case control studies encompassed 1512 cases of FTD and 3244 healthy controls; cohort studies included 42062 participants with a TBI history. Summary OR was 2.14, with confidence interval 0.85 - 5.39; summary HR was 1.45, with confidence interval 0.6 - 12.96. Both groups of studies showed significant heterogeneity (I2 statistic of 89.97% and 93.13% respectively).

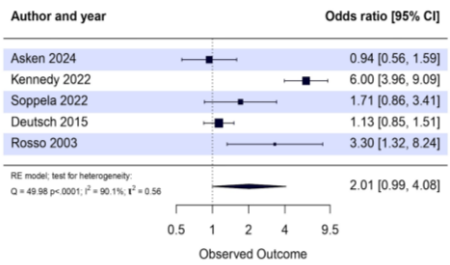

Figure 1. Forest plot for metanalysis of case-control included studies

Discussion and conclusion: Our results show that TBI may increase the risk of FTD, but the trend to a greater risk of FTD in people with a history of TBI did not reach statistical significance in our analyses, probably because of the high heterogeneity of included studies. In fact, when considering studies with a less clear correlation between FTD and TBI, it could be observed that they provide other types of results in this sense, for example in terms of dose-response associations or in terms of significant association between severe head trauma and FTD. To conclude, results of our meta-analyses are not enough to exclude an influence of TBI over the risk of this type of dementia and wider observational studies will be necessary in future to get more robust evidence.

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