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Disordered APP metabolism in trauma and aging: dual risk for chronic neurodegenerative disorders

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Highlights

- Traumatic brain injury (TBI), advanced age, and cerebral vascular disease are major factors conferring increased risk for Alzheimer's disease (AD)
- We discuss evidence supporting TBI and aging as dual, interacting risk factors for AD, and the role of disordered APP metabolism and cerebral vascular dysfunction in this relationship
- Evidence is discussed that amyloid- β is involved in chronic neuronal and synaptic loss after TBI, and that these effects are potentiated by aging and impaired cerebral vascular function
- Both severe TBI and repetitive mild TBI result in complex polypathologies, with A β and tau changes occurring in different proportions at different time points after injury, and with variable involvement of other protein aggregates linked to chronic neurodegenerative diseases

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