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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 Aβ 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