

SYNAPTIC PROTEINS PREDICT COGNITIVE DECLINE IN ALZHEIMER'S DISEASE AND LEWY BODY DEMENTIA

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Background: Initial work suggests that the loss of synapses is more robustly correlated with cognitive decline than the traditional markers of Alzheimer's disease (AD) pathology. Our objective was to compare the levels of three synaptic proteins involved in different steps of the synaptic transmission: Rab3A, SNAP25 and neurogranin, in three common forms of dementia: AD, dementia with Lewy bodies (DLB) and Parkinson's disease dementia (PDD).

Methods: 129 post-mortem human brain tissues from PD, DLB, AD and non-demented controls were analyzed using ELISA and Western blots in brain regional specific manner exploring their associations with morphological changes and cognitive decline.

Results: We have observed robust changes reflecting synaptic dysfunction in all studied dementia groups. Decreased Rab3A and SNAP25 levels correlated with increased rate of cognitive decline in DLB and AD as well as with neuropathological markers.

Discussion: Our results suggest that stabilization of synaptic protein levels such as Rab3A may represent an important treatment strategy in DLB patients, while SNAP25 could be a new marker in the progression of AD. These findings indicate that the proposition that synaptic markers can predict cognitive decline in AD, should be extended to Lewy body diseases.

