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SET translocation is associated with increase in caspase cleaved amyloid precursor protein in CA1 of Alzheimer and Down syndrome patients

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Abstract

Caspase cleaved amyloid precursor protein (APPcc) and SET are increased and mislocalized in the neuronal cytoplasm in Alzheimer Disease (AD) brains. Translocated SET to the cytoplasm can induce tau hyperphosphorylation. To elucidate the putative relationships between mislocalized APPcc and SET, we studied their level and distribution in the hippocampus of 5 controls, 3 Down syndrome and 10 Alzheimer patients. In Down syndrome and Alzheimer patients, APPcc and SET levels were increased in CA1 and the frequency of both localizations in the neuronal cytoplasm was high in CA1, and low in CA4. As the increase of APPcc is already present at early stages of AD, we overexpressed APPcc in CA1 and the dentate gyrus neurons of adult mice with a lentiviral construct. APPcc overexpression in CA1 and not in the dentate gyrus induced endogenous SET translocation and tau hyperphosphorylation. These data suggest that increase in APPcc in CA1 neurons could be an early event leading to the translocation of SET and the progression of AD through tau hyperphosphorylation.

Lien vers l'article