IS TAU MORE IMPORTANT THAN AMYLOID IN THE PATHOPHYSIOLOGY OF AD: NO

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When discussing the pathogeny of Alzheimer's disease (AD) we formally seek for a prime abnormal event, which eventually determine all others. However, it might happen there is not such an event, or maybe various changes do not take place in the same order in all cells. Moreover, during several phases of evolution of AD different pathogenic events might have the predominant role. The hallmark pathologic lesions in AD brain are senile plaques (composed of aggregated beta-amyloid) and neurofibrillary tangles (NFT - intracellular aggregates of hyperphosphorylated microtubule associated protein tau) and therefore the permanent debate in AD was and is which of these too is responsible for disease-progression. One of the main arguments for the tau theory is that NFT correlate with the degree of cognitive loss and NFT distribution is used as well by Braak neuropathological staging of AD. However, it has been shown as well for beta-amyloid levels in the brain that they do correlate with cognitive decline. Moreover, in the triple transgenic mice, which reproduce both NFT and plaques, an increase in intracellular beta-amyloid precedes the hyperphosphorylation of tau and in vitro studies demonstrate that treatment with beta-amyloid 1-42 increases the activity of GSK-3beta, the main kinase responsible for tau phosphorylation. In conclusion, there are probably a lot of interactions between amyloid precursor protein processing and beta-amyloid clearing and tau hyperphosphorylation and axonal transport deficits, with many more factors involved (vascular factors, inflammation, metals deposition and clearance, etc.) in mediation of the disease progression.