IS TAU MORE IMPORTANT THAN AMYLOID IN THE PATHOPHYSIOLOGY OF AD?

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Both meticulous neuropathological analyses and several recent functional imaging data challenge the cognitive impact of fibrillar amyloid deposits. In last decades, several autopsy studies using stereological principles demonstrated the absence of significant NFT-independent impact on cognition in brain aging. More recently, the progression of PIB-visualized deposits has been shown to be temporally and regionally unrelated to MRI/PET changes in AD. In particular, a striking stability of PIB-visualized deposits over time was found in clinically overt AD. In the same line, there is a substantial overlap in the amount of PIB-positive deposits as well as their regional between cases with mild cognitive impairment (MCI) and controls. Additional doubts about the cardinal role of fibrillar amyloid in cognitive decline come from the first data of vaccination trials indicating that the progression of dementia is not affected by the removal of Aß deposits. In contrast, the extent of NFT pathology and loss of pyramidal neurons in CA1 field of the hippocampus are the best pathological correlates of dementia in vascular pathology-free cases. Moreover, the loss of dendritic spines in the neocortex is an additional parameter that negatively impact cognitive performances. These pathological changes may explain as much as 50% of the cognitive variability. Based on neuropathological data in large hospital and community-based series, this presentation will discuss the role of tau-related pathology as a main determinant of cognitive deterioration in the elderly.