Is amyloid deposition a non-specific manifestation of aging?

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High amyloid brain load, mainly in amyloid plaques (APs), together with high intra-cerebral load of intracellular tau-enriched neurofilament tangles (NFTs) and brain atrophy, as the pathological landmarks of Alzheimer's disease (AD). Indeed, the 2011 (and currently being revised) NIA/AA diagnostic criteria for research purposes postulate that the presence of biomarker- based evidence of the above neuro-pathological findings are key criteria for the diagnosis of AD. Of note, most of the current drug discovery and development programmes of the pharmaceutical industry are targeting amyloid cascade key components as the amyloid hypothesis is thought to represent the core aetiological pathway of this otherwise multi-factorial disease. However, increasingly emerging longitudinal and case- control studies suggest that up to 30% of clinically probable AD patients have below-threshold amyloid load. On the other hand, high amyloid load, as documented by amyloid positron emission tomography (PET) or in cerebrospinal fluid (CSF) studies is found in ~ 40-50& of patients with mild cognitive impairment (MCI) and 15-30% in cognitively healthy volunteers of a similar age group. These figures increase with increasing age and several studies in older old individuals show increased amyloid load with increasing age. Furthermore, population based neuro-pathological studies confirm the presence of high levels of post mortem APs and NFTs in the brains of individuals with no history of significant cognitive decline, in particular those who are APOE4 carriers. These findings and discrepancies prompted the hypothesis of this debate. Our two speakers, both well- known experts in the field, will outline the pro and con arguments, leading to a wider discussion among the audience on this very important issue.