Human and mouse Alzheimer's seeds differentially affect amyloid and tau aggregates in aged mice

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Alzheimer's disease (AD) is a complex neurodegenerative proteinopathy in which Aβ and tau misfold and aggregate into entities that structurally unsettle native proteins, mimicking a prion-like or "seeding" process. These Aβ and tau "seeds" can arrange in different conformations or strains that might display distinct pathogenic properties. Furthermore, recent evidence suggest that microglia play a key role in the amyloidogenic event and can modulate the propagation and aggregation processes. Here, we investigated whether amyloid seeds from human AD brains compared to those from transgenic mice (3xTg-AD) are more prone to induce Aβ and tau aggregates *in vivo*, as well as potential differences in the microglial response to the plaque pathology. We employed histological and molecular approaches to determine the Aβ/tau pathology and Aβ-seeding capacity of brain extracts derived from postmortem AD cortex versus aged 3xTg-AD mice (25-month-old). Brain homogenates were injected into the hippocampus of 3xTg-AD mice and examined at 17-18 months of age. The seeds from the human AD brain induced more aggressive amyloid pathology compared to seeds from aged 3xTg-AD mice. However, the AD seeds from aged transgenic mice triggered more tau pathology. Interestingly, such mice seeds impaired microglial clustering around plaques leading to more severe neuritic pathology. These results suggest that multiple variables such as the AD seed, recipient model and time, are critical factors that can modulate the amyloid pathology onset and progression. Thus, more profound understanding on these factors will provide key insight on how amyloid pathology progresses in AD.