Debate: is snap a preclinical state of alzheimer`s disease (ad)? Yes.

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Suspected non-Alzheimer disease (AD) pathophysiology /SNAP) is a biomarker-based concept denoting AD-like neurodegeneration in clinically normal elderly individuals or those with mild cognitive impairment without brain amyloid-β (Aβ-) but positive neurodegeneration markers (ND+). It does not fall into the stages of preclinical AD as defined by the NIA-AA, but may have tau on PET scan in temporal lobes. Both SNAP and PART (characterized by NFTs - Braak stage ≤4, and Thal Aβ phase ≤2 or 0) cases have a low prevalence of ApoE ε4 and a greater conversion rate to dementia than Aβ-/ND-individuals [1]. Autopsy studies revealed low level AD (neuritic plaque score 0), AGD, PART or white matter lesions, indicating comorbid pathologic features rather than early evolving AD [2]. SNAP may be a heterogenous condition which may overlap with PART considered an Aβ-independent subgroup of AD or may be related to severe hippocampal atrophy [3]. From the perspective that SNAP is not AD, however, it is consistent with the concept of preclinical AD, although there is a debate as to whether PART is an early stage or a variant of AD. According to a recent autopsy study PART differs considerably from typical AD [4]. Further studies should subclassify the SNAP group and determine the biological correlates of ND markers among Aβ-negative individuals and their relations to PART and atypical AD. References: 1. Jack CR, Jr., et al., Nat Rev Neurol 2016;12:117-124 2. Gordon BA, et al., JAMA Neurol 2016;73:1192-1200 3. Mormino EC, et al., JAMA Neurol 2016;73:1185-1191 4. Josephs KA, et al., Acta Neuropathol 2017; submitted