## Correlating common TDP-43 and Tau pathologic patterns in the aged human hippocampus

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**INTRODUCTION/BACKGROUND:** TDP-43 and tau pathology are both implicated in numerous neurodegenerative states, but the relationship between TDP-43 and tau pathology is still incompletely understood. In particular, hippocampal sclerosis of aging (HS-Aging) is strongly linked to aberrant TDP-43 pathology and many cases of HS-Aging show some degree of tau pathology; yet it is unclear whether or not there is interaction between these two commonly seen brain changes. Our study aims to elucidate the following: whether TDP-43 pathology is more severe with increasing Braak stage; whether argyrophilic grains are more likely to be present in cases with, versus without, TDP-43 pathology; and whether hippocampal TDP-43 affects hippocampal neurofibrillary tangle (NFT) distribution.

**METHODS:** Data were analyzed from the University of Kentucky Alzheimer's Disease Center (UK-ADC) autopsy series with detailed neuropathological observations to study the association between TDP-43 pathology and tauopathy. Two-hundred and forty-seven cases were included from the UK-ADC cohort. TDP-43 immunoreactivity in the hippocampus was graded in a 3-tier scheme: 0 (no TDP-43 deposition), 1 (mild), and 2 (moderate to severe). Tau pathology was graded based on Braak staging with complementary quantitative assessment. Argyrophilic grains were graded on a 0-3 scale in multiple medial temporal lobe regions.

**RESULTS:** The average age of death among included patients was 88.4 years, with 63% of cases demonstrating TDP-43 grade of 0, 6.9% with a grade of 1 and 30% with a grade of 2. There was enrichment for TDP-43 pathology in advanced Braak stages (stages V-VI) compared to cases with lower Braak stages (stages <= IV). There was not a strong trend in terms of association between TDP-43 pathology and argyrophilic grains.

**CONCLUSION:** TDP-43 pathology appears to be more severe in correlation with increasing Braak stage, whereas argyrophilic grains do not appear to have a strong correlation with TDP-43 pathology in this data set.