Title

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TDP-43 Is as Important as Alzheimer's Disease Neuropathology in the Oldest Old (1407)

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Abstract

Objective: To highlight the high prevalence of TDP-43 pathology, also known as limbic predominant age related TDP-43 encephalopathy (LATE), and its strong association with dementia in the oldest old.

Background: The oldest old are the fastest growing segment of our population with the highest prevalence of dementia. By year 2050, more than 50% of dementia sufferers in the US will belong to this age group. TDP-43 pathology is a frequent but less studied pathology in this age. We describe findings from The 90+ Study, a longitudinal clinical and autopsy study of participants aged 90 years and older, that shows TDP-43 pathology might be as important as Alzheimer's disease (AD) in this age.

Design/Methods: 241 participants of the 90+ study with comprehensive clinical, neuropsychology, and neuropathology data were included. Dementia status, clinical syndrome, and impaired cognitive domains were determined at multi-disciplinary post-mortem conferences blind to autopsy data. AD neuropathology (ADNP) was defined as CERAD score for neuritic plaques ≥2 and Braak stage for neurofibrillary tangles ≥5. TDP-43 pathology was considered present in those with at least amygdala and hippocampal TDP-43. Logistic regression analyses adjusting for age, sex, and education, explored the association between ADNP, TDP-43, and dementia, clinical diagnosis of AD, and memory impairment.

Results: 125 participants (52%) died with dementia (Mean age at death: 98.1, 75% female). Of these, 33% had TDP-43 and 40% had ADNP. TDP-43 was as important a predictor of dementia and clinical diagnosis of AD at death as ADNP (For dementia outcome: TDP-43 OR: 3.0 vs. ADNP OR: 2.6; For clinical AD outcome: TDP OR: 3.5 vs. ADNP OR: 3.4). Both pathologies independently predicted memory impairment (TDP-43 OR: 4.7; ADNP OR: 4.1).

Conclusions: Our results suggest TDP-43 pathology is as important as ADNP in people over 90, the age group that will have the greatest number of dementia sufferers.

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