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Title

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Permalink

<https://escholarship.org/uc/item/2h02z2gv>

Journal

NEUROLOGY, 94(15)

ISSN

0028-3878

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Publication Date

2020-04-14

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

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First published April 14, 2020,

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.

Disclosure: Dr. Sajjadi has received personal compensation for consulting, serving on a scientific advisory board, speaking, or other activities with Grand round speaker (CME activity). Dr. Corrada has nothing to disclose. Dr. Phelan has nothing to disclose. Dr. Kawas has nothing to disclose.