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183. Cognitive Impairment and Risk Factors of LATE, a Novel Degenerative Pathology

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Background: Limbic predominant age related TDP-43 encephalopathy (LATE) is a newly proposed term to denote the contribution of transactive response DNA-binding pro-tein of 43 kDa (TDP-43) pathology to dementia at older age. The aim of this work was to study the role of LATE in cognitive impairment and its risk factors in the oldest old (those ≥ 90years old).

Methods: 240 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 case conferences blind to autopsy data. Alzheimer's disease neuropathology (ADNP) was defined as CERAD neuritic plaque score≥2 and Braak neuro-fibrillary tangle stage≥5. We defined LATE as those with at least amygdala and hippocampal TDP-43 pathology (stage>2). We explored the association of LATE and of ADNP with cognition measures by logistic regression ana-lyses adjusting for age, sex, and education. We separately explored the association between medical histories (as potential risk factors) and LATE and ADNP as outcomes adjusting for the above covariates.

Results: 52% of the participants (N=125) died with dementia and of those, 33% were LATE positive (compared to 40% ADNP positive). There was no association between LATE and sex, age at death, or education. Compared with ADNP, LATE was as important a predictor of dementia (OR: 2.9 for ADNP vs. 3.3 for LATE) and clinical diagnosis of Alzheimer's at death (OR: 3.7 for ADNP vs 3.9 for LATE). Both pathologies were significantly associated with impaired memory, language, visuospatial ability, and orienta-tion. Only ADNP (OR=2.1), but not LATE, was associated with impaired executive function. Lower likelihood of LATE was associated with histories of hypertension (but not hyper-tension medications), cataract, alcohol use (median 1 drink/day), and macular degeneration (trended toward significant association). History of COPD was significantly associated and history of autoimmune conditions (thyroid or rheumato-logical diseases) trended towards an association with a higher likelihood of LATE. None of the above relationships were seen for ADNP.

Discussion: LATE is an important degenerative pathology in the oldest old comparable to ADNP in its relation to dementia and clinical diagnosis of Alzheimer's dementia. The intriguing associations of LATE with other health conditions warrant further investigation of the potential effect of autoim-munity, reduced brain perfusion, and chronic hypoxia in its development.