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HUMAN NEUROPATHOLOGY

Neuropathology in the LifeAfter90 Study: 2023 update on an Ethnically Diverse Cohort Study of Oldest-Old

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Abstract

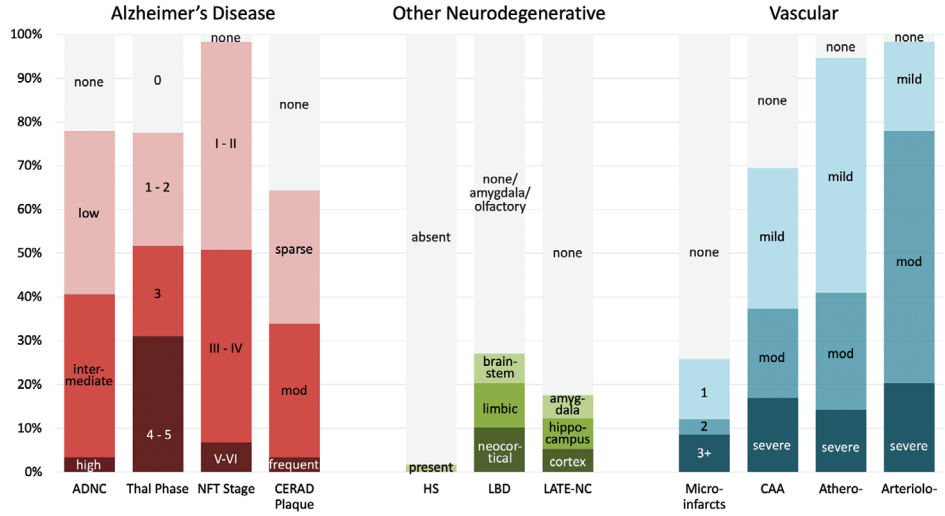
Background: Neuropathology studies of the oldest-old have significantly advanced our understanding of the multiple etiologies late in very late life. Most studies, however, have limited ethnoracial diversity with almost exclusively White decedents. Our goal was to characterize neuropathology in a cohort of ethnically and racially diverse oldest-old decedents.

Method: The LifeAfter90 study is an ongoing cohort study of Kaiser Permanente Northern California members, aged 90+ with targeted recruitment of individuals across different racial/ethnic groups with no prior diagnosis of dementia in their medical record. Interviews and cognitive assessments occur approximately every 6 months. Brain donation was available to all interested consenting participants. Neuropathology was assessed using the National Alzheimer's Coordinating Center Neuropathology form v.10 and used NIA-AA guidelines for Alzheimer's diagnoses. As of January 2023, 304 participants (40%) were enrolled in autopsy (20% Asian, 18% African American, 17% Latino, 9% Multiracial/Other, and 36% White).

Result: Of the 304 participants, 59 had died and neuropathological evaluations were completed. The median age of death was 93 years (range 90-105), 33 (56%) were female, 8 Asian, 5 Black, 10 Latino, 31 White, and 5 Multiracial/Other. At final clinical exam, 17 participants had dementia (29%), 25 questionable/mild cognitive impairment (42%), and 16 were cognitively normal (27%). Alzheimer disease (AD) and vascular pathologies were the most frequent findings (Figure). Twenty two percent of participants did not have AD, one lacked neurofibrillary tangles (NFT). The most severe distributions/densities of NFTs and plaques were infrequent, with high likelihood of AD in two participants. For vascular pathologies, 98% had some level of arteriolosclerosis, 97% had atherosclerosis, 70% had amyloid angiopathy, and 26% had at least one old microinfarct. Other pathologies were less common: 27% had Lewy bodies, 18% had TDP-43 deposits, and only one had Hippocampal sclerosis. Although data is sparse to test for associations, the proportion of individuals with dementia tended to increase with increasing pathology severity especially for AD pathologies.

Conclusion: This diverse cohort of oldest-old individuals reveal numerous brain pathologies are present with advanced age, with AD and select vascular pathologies being the most common. Future analyses will investigate their role with cognitive impairment.

Figure. Frequency of Neuropathologies in the ***Life After 90 Study*** (N=59)



ADNC=Alzheimer's Disease Neuropathologic Change; NFT=Neurofibrillary Tangles; HS=Hippocampal Sclerosis; LBD=Lewy Body Disease; LATE-NC=Limbic Predominant Age Related TDP-43 Encephalopathy-Neuropathologic Change; CAA=Cerebral Amyloid Angiopathy; Athero=Atherosclerosis; Arteriolo=Arteriolosclerosis