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# Neuropathological and neuropsychological associations in hippocampal sclerosis of aging; The 90+ study

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## Objective

- To identify the relationship between hippocampal sclerosis of aging and other common degenerative brain pathologies
- To identify the neuro-psychological deficits associated with HS

## Background

- In the oldest old, hippocampal sclerosis of aging (HS) is a stronger predictor of dementia than Alzheimer's disease (AD)
- HS pathological associations and neuro-psychologic signature remain poorly understood

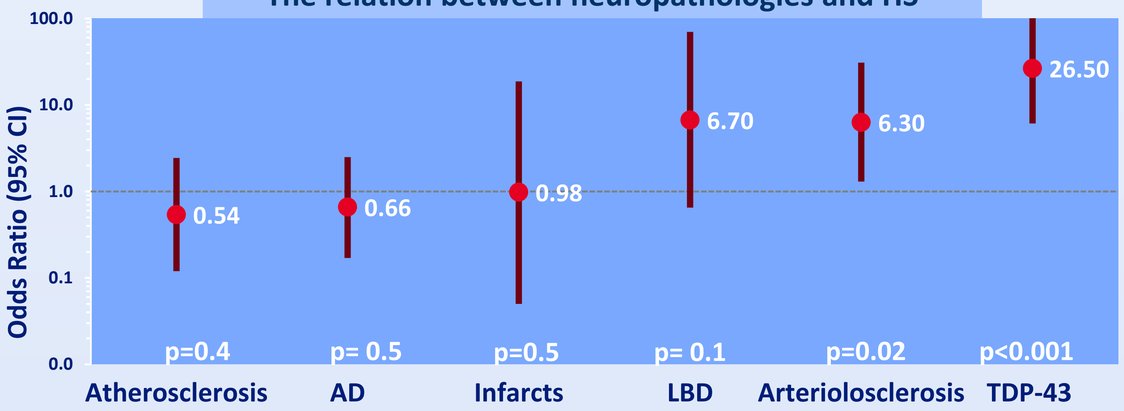
## Methods

- Post-mortem brain examination on 143 participants from ***The 90+ Study***, a study of aging and dementia in people aged 90 years and older
- Longitudinal neuropsychological assessments every 6 months (Average 6 visits, range 1-14)
- Modified mini-mental state (3MS), California verbal learning test long delay recall (CVLT-LD), Boston naming test (BNT), CERAD construction
- Neuropsychological data at the time of the first clinical diagnosis of cognitive impairment (for impaired) or death (for normal)
- Neuropathology data available for HS, AD, Lewy body disease (LBD), TDP-43, arteriolosclerosis, atherosclerosis, and infarcts (micro and large)
- Regression analyses adjusted for age, sex, interval between assessment and death, and education for the associations between HS and other pathologies (Logistic regression) and the effect of the neuropathologies on cognitive measures (Linear regression).

## Results

| | All participants (N=143) | Hippocampal sclerosis (N=22) | No hippocampal sclerosis (N=121) | p value |
|---|---|---|---|---|
| Age at death (Mean (SD)) | 98.2 (3.5) | 98.4 (4.1) | 98.1 (3.4) | 0.4 |
| Female | 71% | 82% | 69% | 0.2 |
| College graduate | 51% | 41% | 53% | 0.3 |
| Dementia at death | 51% | 96% | 43% | <0.001 |

### The relation between neuropathologies and HS




TDP-43 and arteriolosclerosis were independently associated with HS

### The relation between neuropathologies and cognitive measures

| | 3MS (/100) Estimate (p value) | CVLT-LD (/9) Estimate (p value) | BNT (/15) Estimate (p value) | Construction (/11) Estimate (p value) |
|---|---|---|---|---|
| HS | **-14.4 (<0.001)** | **-1.1 (0.02)** | **-1.6 (0.01)** | -0.54 (0.1) |
| AD | **-10.8 (<0.001)** | -0.39 (0.3) | **-1.1 (0.03)** | -0.1 (0.6) |
| TDP-43 | **-12.9 (<0.001)** | -0.66 (0.08) | **-1.4 (0.008)** | -0.36 (0.2) |

While HS, AD, and TDP-43 were all associated with lower scores in global cognition (measured by 3MS) and naming, only HS was associated with lower verbal recall (CVLT-LD)

## Conclusion

-TDP-43 and arteriolosclerosis were independently associated with HS

- HS pathology, but not AD, was associated with impaired verbal recall in the oldest old

## Discussion

- HS neuropathology was significantly associated with dementia in the oldest old
- Independent association of TDP-43 and arteriolosclerosis with HS suggests multiple pathways might lead to HS
- Given the lack of significant association with AD pathology, our study findings suggest the pathological underpinnings of memory impairment in the oldest old might be different compared to the younger age groups

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