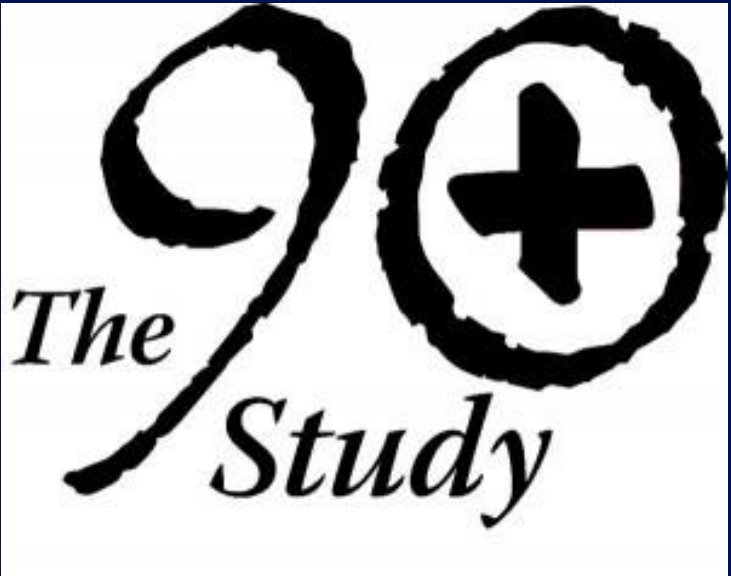




Functional decline in the oldest old is linked to LATE-NC, but not ADNC: The 90+ Study



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BACKGROUND

Alzheimer’s Disease Neuropathological Changes (ADNC) and Limbic-predominant age-related TDP-43 encephalopathy neuropathological changes (LATE-NC) have similar cognitive presentations, but it is unclear whether functional decline is also similar.

OBJECTIVE

To examine longitudinal trajectories of functional decline in relation to ADNC and LATE-NC at autopsy.

METHODS

- **Participants:** from *The 90+ Study*, a longitudinal study of aging with evaluations every 6 months.
- **Outcome – Functional decline assessment:**
12-item Functional Activities Scale (FAS), including
 - Activities of daily living (ADLs): scored 0 (normal) to 3 (dependent)¹
 - Instrumental ADLs: scored 0 (normal) to 3 (dependent)²
 - FAS composite summing all items: scored 0 to 36
 - Analyzed each item as 3 - FAS score and composite as 39 - FAS score
- **Predictor - neuropathological changes assessment:**
 - **ADNC**³: intermediate/high vs. none/low
 - **LATE-NC**⁴: present in the amygdala, hippocampus, cortex vs absent
- **Statistical analysis:**
To examine the longitudinal association of ADNC and LATE-NC with functional decline for the FAS composite and each item, we used linear mixed regression models adjusted for sex, age at death, and education.

RESULTS

Characteristics of participants	N = 459
Age at baseline, years (range)	93 (90-110)
Follow up time, years (range)	4 (1-14)
Age at death, years (range)	98 (91-111)
Female (n, %)	305 (66%)
White race (n, %)	452 (99%)
College education or higher (n, %)	236 (51%)
Community dwelling (n, %)	376 (82%)
ADNC (interm./high) (n, %)	327 (71%)
LATE-NC (amygdala, hippocampus, cortex) (n, %)	167 (36%)

¹Katz, Sidney. "The index of ADL: a standardized measure of biological and psychosocial function." *J Am Med Assoc* 185 (1963): 914-919.

²Pfeffer, R. I., Kurosaki, T. T., Harrah Jr, C. H., Chance, J. M., & Filos, S. Measurement of functional activities in older adults in the community. *Journal of gerontology*. 1982;37(3), 323-329.

³Montine TJ, Phelps CH, Beach TG, et al. National Institute on Aging-Alzheimer’s Association guidelines for the neuropathologic assessment of Alzheimer’s disease: a practical approach. *Acta Neuropathol*. 2012;123(1):1-11.

⁴ Nelson PT, Dickson DW, Trojanowski JQ et al.TDP-43 encephalopathy (LATE): consensus working group report. *Brain*. 2019;142(6):1503-1527.

In individuals 90 years and older:

- **LATE neuropathological changes** were associated with faster **functional decline**.
- **AD neuropathological changes** were **NOT** associated with faster **functional decline**.

LATE-NC

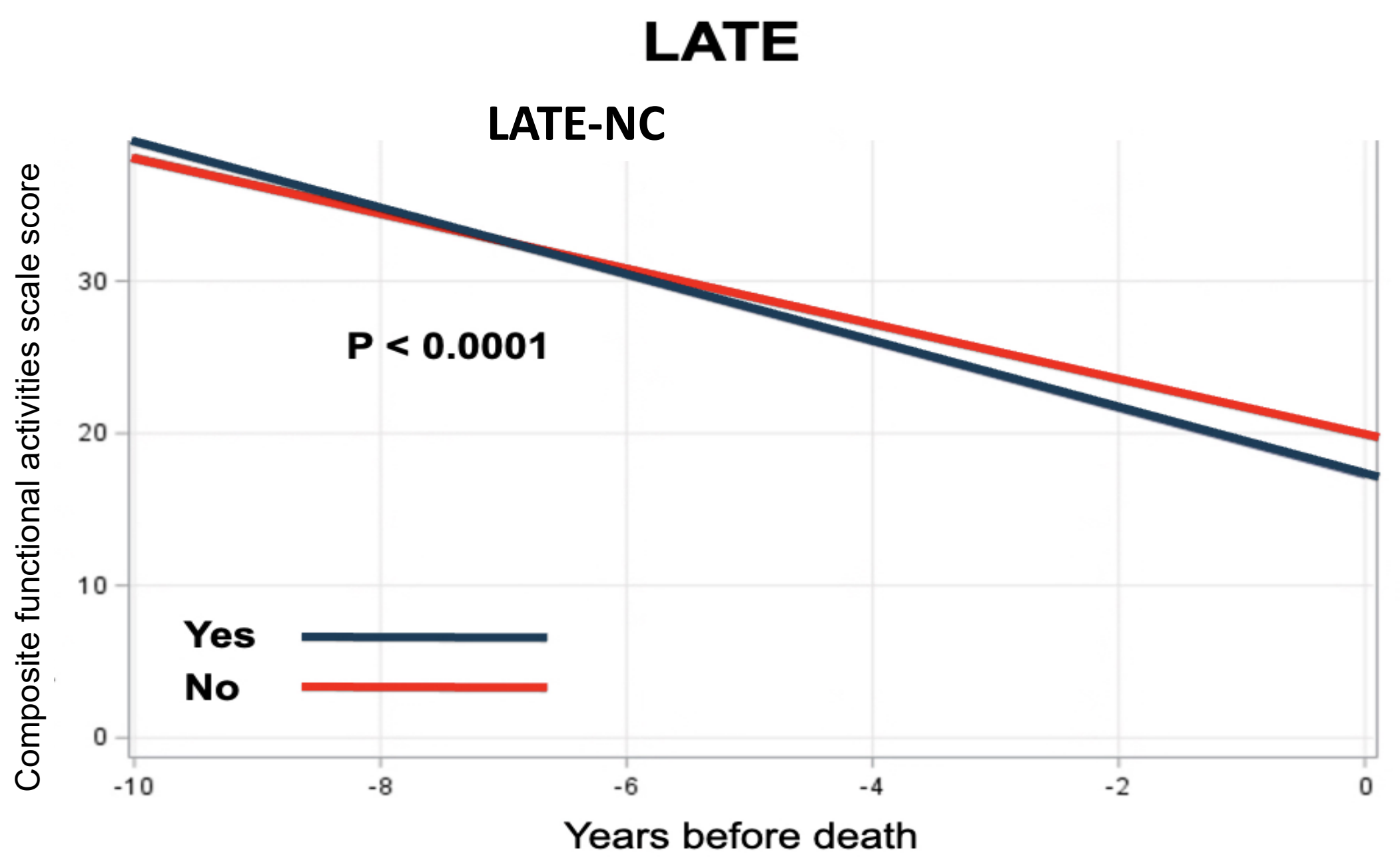
Functional Activities Scale	Average functional decline per year			95% Confidence intervals	P-value
	With LATE-NC	Without LATE-NC	Difference		
Composite	2.19	1.73	0.46	0.26-0.66	<0.001
Paying bills	0.23	0.21	0.02	-0.01-0.04	0.15
Shopping	0.23	0.22	0.01	-0.01-0.03	0.37
Keeping track of current events	0.18	0.11	0.07	0.05-0.09	<0.001
Traveling	0.23	0.23	0.00	-0.03-0.03	0.93
Feeding	0.09	0.06	0.03	0.01-0.05	0.002
Bathing	0.21	0.18	0.03	0.01-0.05	0.03
Dressing	0.19	0.15	0.04	0.02-0.07	<0.001
Transferring	0.15	0.13	0.02	0.002-0.5	0.03
Toileting	0.15	0.12	0.03	0.003-0.5	0.03
Continence	0.14	0.07	0.07	0.04-0.09	<0.001
Moving about indoors	0.17	0.14	0.03	0.01-0.05	0.004
Taking Meds	0.25	0.19	0.06	0.04-0.1	<0.001

Functional decline was faster in participants with LATE-NC vs those without in the composite FAS and in 9/12 ADLs and IADLs.

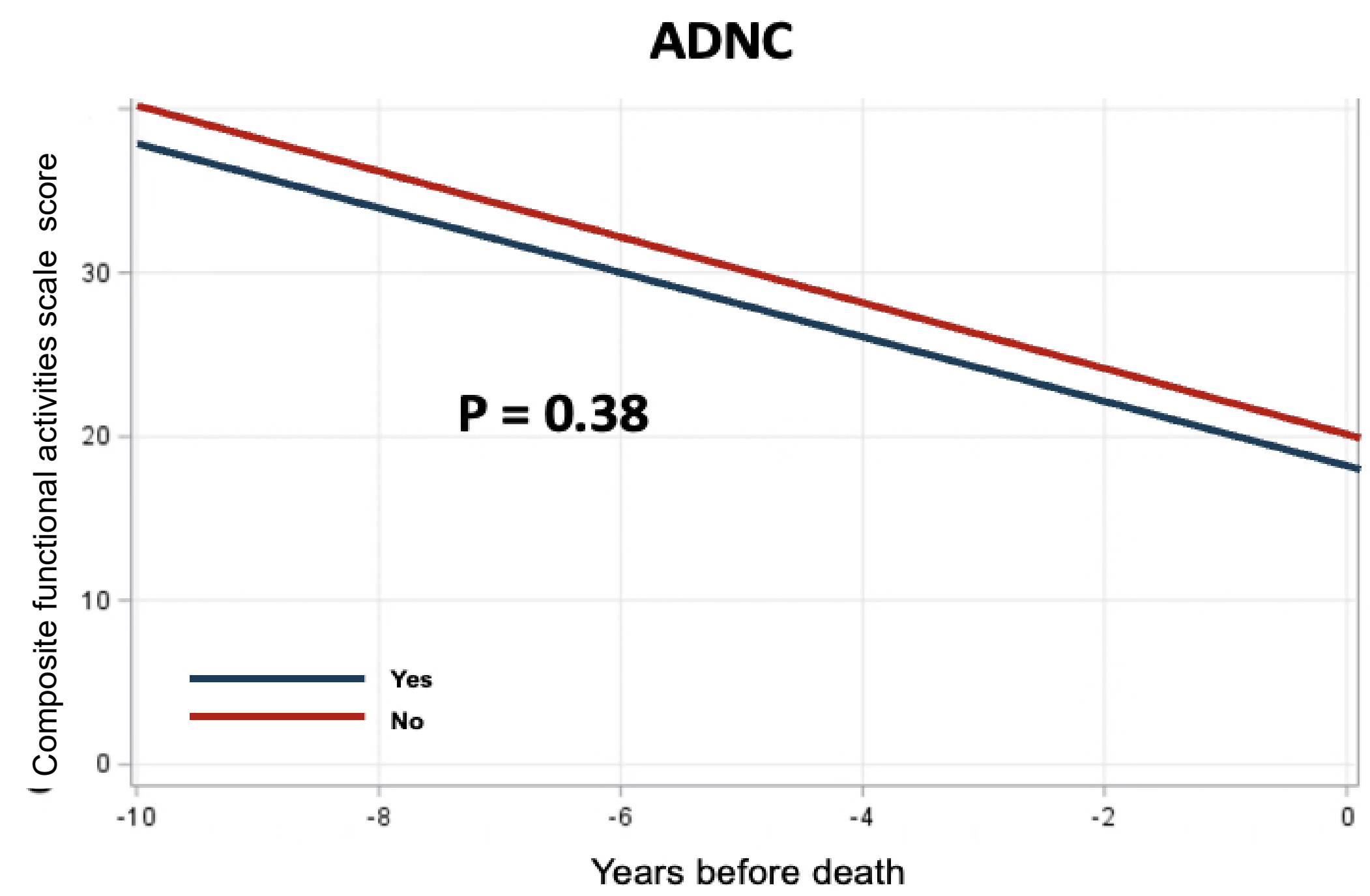
ADNC

Functional Activities Scale	Average functional decline per yar			95% Confidence intervals	P-value
	With ADNC	Without ADNC	Difference		
Composite	1.87	1.97	-0.10	-0.32-0.12	0.38
Paying bills	0.21	0.23	-0.02	-0.04-0.01	0.27
Shopping	0.22	0.24	-0.02	-0.04-0.01	0.20
Keeping track of current events	0.15	0.11	0.04	0.02-0.07	<0.001
Traveling	0.23	0.24	-0.01	-0.04-0.02	0.62
Feeding	0.07	0.07	0.00	-0.03-0.01	0.42
Bathing	0.19	0.20	-0.01	-0.03-0.01	0.45
Dressing	0.16	0.17	-0.01	-0.04-0.01	0.22
Transferring	0.13	0.15	-0.02	-0.04-0.01	0.22
Toileting	0.13	0.15	-0.02	-0.05-0.01	0.27
Continence	0.10	0.09	0.01	-0.01-0.04	0.22
Moving about indoors	0.15	0.14	0.01	-0.01-0.03	0.49
Taking Meds	0.21	0.21	0.00	-0.04-0.03	0.93

Functional decline was faster in the composite FAS in participants with ADNC vs those without. Functional decline was faster in only 1/12 ADLs/IADLs, keeping track of current events.



Participants with LATE-NC demonstrated faster functional decline compared with those without LATE-NC



Participants with ADNC did not demonstrate faster functional decline compared with those without LATE-NC

DISCUSSION / CONCLUSIONS

- LATE-NC, but not ADNC, are significantly associated with faster functional decline in the oldest old.
- Despite similar cognitive presentations of LATE-NC and ADNC, functional manifestations are distinct.
- This research contributes to our understanding of the differences in clinical presentation between LATE-NC and ADNC.

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