Elevated Temporal Tau PET Signal Is Associated with Lower Cognitive Performance in Cognitively Unimpaired Older Adults

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Background

- In cognitively unimpaired (CU) older adults, abnormal cerebral β-amyloid (Aβ+) indicates Alzheimer's disease (AD) has begun and is termed preclinical AD.
- Despite CU status, adults with preclinical AD show subtle impairment in memory and other cognitive functions, with emerging evidence indicating these occur once tau pathology spreads into temporal regions.
- The Cogstate C3 digital cognitive battery has previously been shown to be sensitive to amyloid-related cognitive decline in preclinical AD, particularly when using composite scores from the individual tests in the battery[1,2,3].

Aim:

- To investigate relationships between temporal tau PET burden and cognition in a well characterized sample of individuals with preclinical AD.

Method

Sample:

- Data were drawn from the baseline visits of the A4 and LEARN studies for participants who had undergone both amyloid and tau PET. See Table 1 for demographics.
- Participants were classified into three neuropathologic stages, A−/T− (N=54), A+/T− (N=283), and A+/T+ (N=105).

Measures:

Amyloid PET: 18F-florbetapir PET with established thresholds was used to define A+.

Tau PET: 18-F Flortaucipir tau PET, with temporal lobe PET tau burden defined using a temporal meta-ROI[4]. T+ was defined as SUVR for the temporal meta-ROI exceeding 2 SD above the mean of CU Aβ− group[4].

Cognition: Cogstate C3 Battery was used to assess cognitive function. The tests included in the battery are shown in Figure 1. Three composites were derived from the battery;

- C3 Composite (All tests)
- Learning/Working Memory (LWM; comprising OCL & ONB)
- Psychomotor/Attention (PSA; comprising DET & IDN) .
- All composites were expressed as age standardized z-scores relative to normative data

Analyses:

Between group differences were evaluated with:

- Linear regression model with A-T- as the reference group.
- ANOVA F-test from the same model to assess overall group effects.
- Cohen's d for between-group effect sizes.

Results

Table 1: Sample Characteristics

	A-T-	A+T-	A+T+
Age	69.6 (4.3)	71.8 (4.7)	73.1 (5.1)
Female	57% (n=31)	57% (n=162)	59% (n=62)
Race: White	94% (n=51)	92% (n=259)	93% (n=98)
Years of Education	16.5 (2.5)	16.1 (2.3)	16.2 (2.5)
Amyloid SUVR	1.02 (0.06)	1.29 (0.13)	1.38 (0.17)
Tau SUVR	1.09 (0.05)	1.11 (0.05)	1.27 (0.08)
C3	0.13 (0.50)	0.01 (0.48)	-0.23 (0.58)
LWM	0.17 (0.66)	-0.07 (0.78)	-0.28 (0.84)
PSA	0.07 (0.83)	0.07 (0.76)	-0.03 (0.95)

Figure 1: Cogstate C3 Digital Cognitive Battery

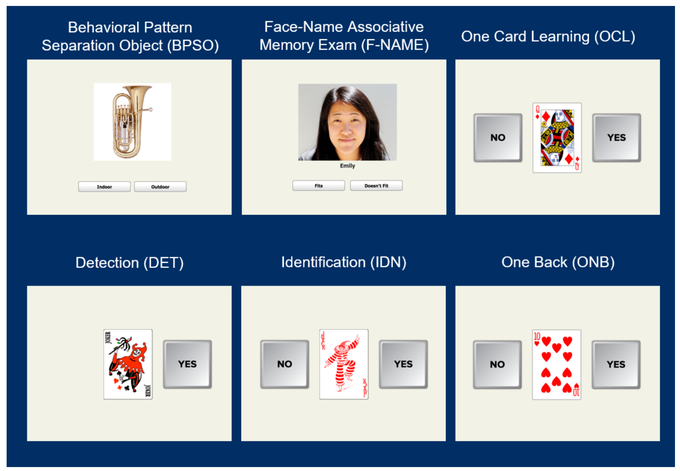
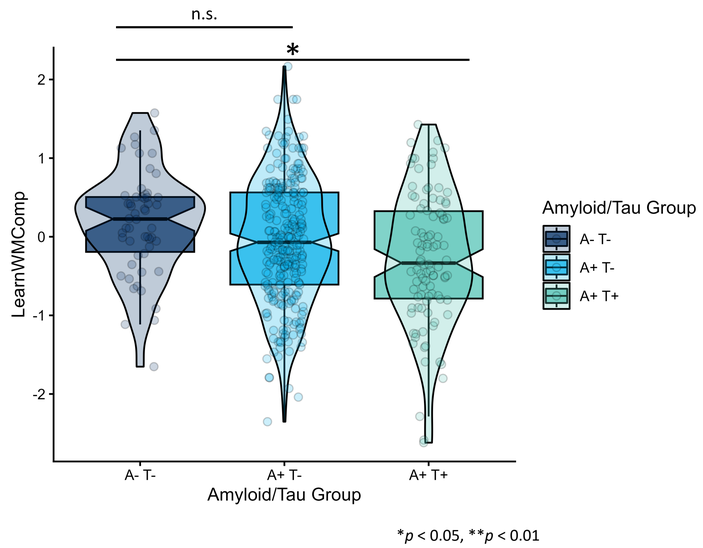


Figure 2: Learning/Working Performance by Group

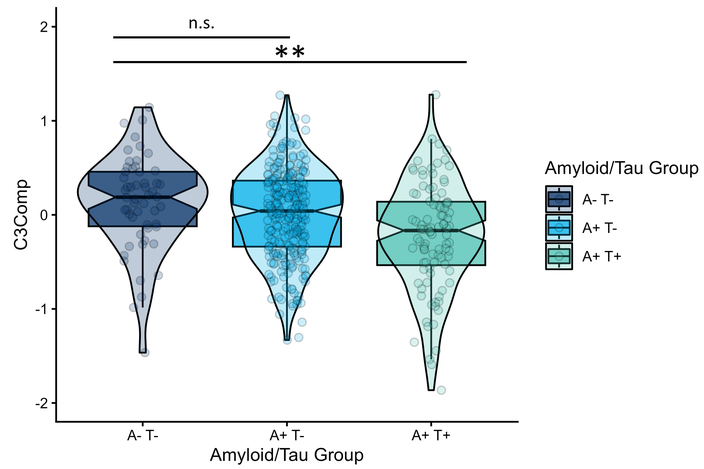


*p < 0.05, **p < 0.01

Results

- Neuropathologic stage was associated with differences in LWM (F (2, 419) = 6.63, p<0.002) and C3 performance (F (2, 404) = 12.21, p<0.001), but not PSA performance.
- For the LWM composite, the A+/T+ group performed significantly worse than the A-/T- group (p=0.03, d=0.60), but the A+/T− group did not significantly differ from the A-/T- group (p=0.23, d=0.33). See Figure 2.
- For the C3 composite, the A+/T+ group performed significantly worse than the A-/T- group (p=0.006, d=0.66), but the A+/T− group did not significantly differ from the A-/T- group (p=0.52, d=0.24). See Figure 3.

Figure 3: C3 Performance by Group



*p < 0.05, **p < 0.01

Conclusion

- In preclinical AD, higher temporal tau burden was associated with moderate magnitude impairment in learning/working memory, and on the C3 composite.
- Temporal tau levels were unrelated to psychomotor speed and attention.
- These findings suggest that sensitive digital cognitive assessments can detect subtle domain-specific cognitive dysfunction in preclinical AD.

References

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