Association of performance on the Cogstate Brief Battery with ptau217 in cognitively unimpaired older adults

Karra D Harrington, Annie Aitken, Svenja Wacker, Paul Maruff, Kaycee M Sink, and the A4 study team
Cogstate Ltd, New Haven CT

Cogstate

Background

- Digital cognitive assessments (DCA) offer a scalable strategy for identifying and staging early Alzheimer's disease (AD), particularly when combined with AD biomarkers.
- The Cogstate Brief Battery (CBB) has demonstrated sensitivity to cognitive dysfunction in preclinical and early symptomatic AD, particularly when the individual test scores are combined into cognitive domain specific composite scores[1,2].

Aim:

- To examine the relationship between performance on the CBB with the ptau217 blood-based biomarker among cognitively unimpaired (CU) older adults.

Method

Sample:

- Data were drawn from CU participants (n = 1515, mean (SD) age = 71.4 (4.7) years, 59.7% female), that had CBB and ptau217 results from the baseline visit of the A4 and LEARN studies.

Measures:

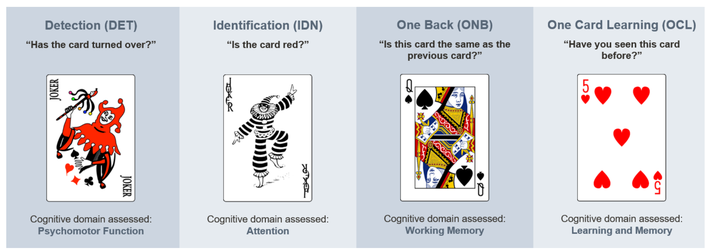
ptau217:

- ptau217 levels were measured using an electrochemiluminescent immunoassay, with sample preparation automated by the Tecan Fluent workstation and detection performed on the MSD Sector S Imager 600MM by the Lilly Clinical Diagnostics Laboratory.
- Scores were classified as low (<0.2), medium (0.2 – 0.28), and high (>0.28) using established cut scores from the A4 cohort.

Cognition:

- Figure 1 summarizes the Cogstate Brief Battery tests and the cognitive domains measured by each test.
- Individual test scores were standardized to z-scores using age-matched normative data and then averaged to derive Psychomotor/Attention (PSA) and Learning/Working Memory (LWM) composite scores.

Figure 1: Cogstate Brief Battery

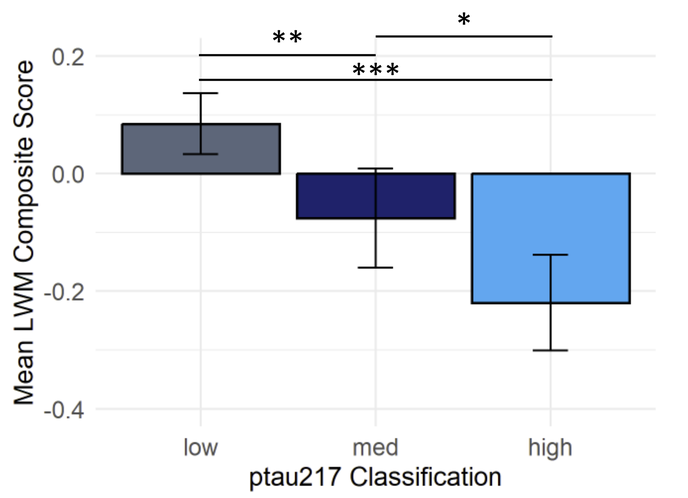


Results

Table 1: Sample Demographics

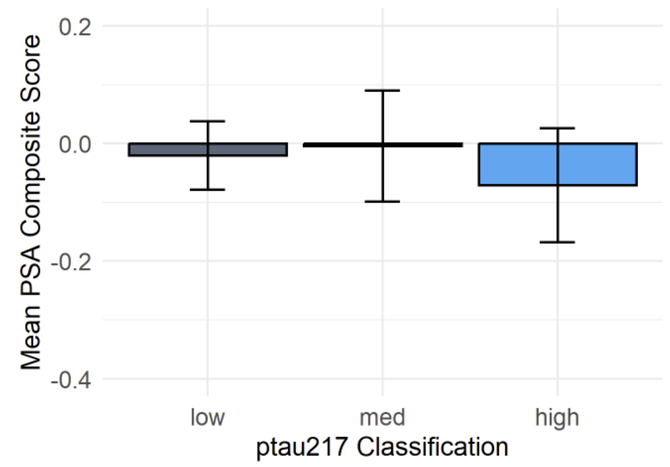
	Low ptau217 (n=803)	Mid ptau217 (n=351)	High ptau217 (n=361)
Age	70.49 (4.24)	71.59 (4.78)	73.35 (4.96)
% (n) Female	60.0% (n=482)	57.5% (n=202)	60.9% (n=220)
% (n) APOE4 Carrier	34.0% (n=273)	62.4% (n=219)	63.7% (n=230)
Years of Education	16.76 (2.69)	16.40 (2.76)	16.46 (2.87)
Race: White	93.5% (n=751)	95.2% (n=334)	96.4% (n=348)
PSA composite	-0.02 (0.84)	0.00 (0.90)	-0.07 (0.94)
LWM composite	0.08 (0.75)	-0.08 (0.80)	-0.22 (0.79)

Figure 2: Mean (95% CI) Learning/Working Memory Performance by ptau217 level



$^{*}p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$

Figure 3: Mean (95% CI) Psychomotor Speed/Attention Performance by ptau217 level



Analyses & Results

Analyses:

- Correlations between continuous ptau217 level and each of the CBB composite scores
- Comparison of performance on each of the CBB composite scores between the low, medium, and high ptau217 groups using ANOVA with post-hoc pairwise comparisons.
- Examination of group mean and 95% confidence intervals (CI) relative to age-adjusted normative mean of each ptau217 group on each of the CBB composite scores

Results:

- Ptau217 was correlated significantly with LWM (Spearman's ρ = -0.19, p < .001), but not with PSA (ρ = -0.01, p = .701).
- There was a significant difference between ptau217 groups for LWM (p < .001) but not for PSA (p = .553).
- The LWM composite was significantly below the age-adjusted normative mean for the high ptau217 group (z = -0.22 [95% CI = -0.30, -0.14]), but not for the low (z = 0.08 [95%CI = 0.03, 0.14]) or medium (z = -0.08 [95%CI = -0.16, 0.01]) groups (Figure 2).
- There was no difference from age-adjusted normative performance on the PSA composite for any of the ptau217 groups (Figure 3).

Conclusion

- In CU adults, increased ptau217 is associated with poorer learning and working memory, but not with psychomotor speed or attention.
- In CU adults with abnormal ptau217 levels, subtle dysfunction in learning and working memory is evident relative to age-adjusted normative data.
- DCAs that can detect subtle impairment in learning and working memory could provide a useful method for identification and staging of individuals with early AD.

References

1. White et al. Sensitivity of Individual and Composite Test Scores from the Cogstate Brief Battery to Mild Cognitive Impairment and Dementia Due to Alzheimer's Disease. J Alzheimers Dis. 2023;96(4):1781-1799. doi: 10.3233/JAD-230352. PMID: 38007647.
2. Lim et al. Relationships Between Performance on the Cogstate Brief Battery, Neurodegeneration, and Aβ Accumulation in Cognitively Normal Older Adults and Adults with MCI, Arch Clin Neuropsychol. 2015; 30(1), 49–58, doi:10.1093/arclin/acu068

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