

Combining Cognitive Screening with ALZpath pTau217 Levels to Identify Cognitive Impairment in a Primary Care Setting

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BACKGROUND

- Detection of cognitive impairment (CI) in primary care remains challenging, with many cases of Alzheimer’s disease (AD) going undiagnosed.
- Blood biomarkers—particularly phosphorylated tau at threonine 217 (pTau217)—have demonstrated strong reliability in identifying AD pathology.
- Brief cognitive screening tools such as the Quick Mild Cognitive Impairment (Qmci) screen can efficiently detect early cognitive changes.
- **Aim:** To evaluate the utility of combining Qmci screening with plasma pTau217 levels to identify CI in a real-world primary care cohort.

METHODS

Participants

- 111 adults aged 60 and older
 - Average age (yrs) = 69.3 (SD=5.4)
 - Average education (yrs) = 16.9 (SD=2.3)
 - 68% female
 - 77% non-Hispanic white
 - 23% APOE ε4 positive

- No prior dementia diagnosis

Procedures

- Participants completed:
 - Qmci, a short (<5 min) cognitive screening test
 - Six subtests: Orientation, Word Registration, Clock Drawing, Delayed Word Recall, Verbal Fluency, and Logical Memory.
 - Scores range from 0 to 100
 - <67 indicative of MCI
 - Blood draw to measure pTau217 levels
 - Neuropsychological test battery (NTB)
 - *Language* (Boston Naming Test, phonemic fluency/FAS, and Animal Naming)
 - *Memory* (Hopkins Verbal Learning Test-Revised Immediate Recall, Delayed Recall, and Recognition Discrimination)
 - *Executive functioning* (EF; Trail Making Test and Southwest Assessment of Processing Speed, a digit symbol substitution test)
 - *Global functioning:* Average T score across all cognitive tests

METHODS (cont.)

Analyses

- Participants were placed into pTau217 groups based on the following plasma concentration levels.
 - Negative: < 0.34 ng/L
 - Intermediate: 0.34-0.63 ng/L
 - Positive: > 0.63 ng/L
- Participants were classified as CI if:
 - ≥2 T scores < 40 within a domain
OR
 - ≥1 T score < 40 in each of the three domains.
- Descriptive statistics were used to characterize the study sample and dependent variables.
- Pearson *r* was computed to examine relationships between pTau217 plasma concentrations and cognitive performance.
- Parametric and non-parametric tests were used to assess group differences using covariates as needed.

RESULTS

- 23 (21%) screened positive on Qmci
- 35 (32%) were classified as CI on NTB
- pTau217 levels:
 - Elevated: 13 (12%)
 - Intermediate: 30 (27%)
 - Negative: 68 (61%)
- Better cognitive performance was significantly associated with lower pTau217 levels.
 - Qmci: *r* = −0.43 (*p* < .001)
 - Global T: *r* = −0.30 (*p* = .002)
 - Memory T: *r* = −0.30 (*p* = .002)
 - EF T: *r* = −0.21 (*p* = .03)
- Patients with elevated pTau217 levels performed significantly worse than those in the negative group on the Qmci and Memory domain (see Table 1).

Table 1: Cognitive Test Score Means (SD) by pTau217 Group

Cognitive Measure	Negative (n=68)	Intermediate (n=30)	Elevated (n=13)
Qmci*	77.9 (9.3) ^a	74.2 (9.6) ^a	65.7 (9.9) ^b
Global T score	50.0 (5.9)	48.6 (4.4)	45.1 (9.5)
Language T score	54.7 (6.9)	52.9 (6.5)	51.2 (8.5)
Memory T score	48.4 (8.9) ^a	45.6 (8.2) ^{a,b}	41.7 (10.5) ^b
EF T score	46.9 (7.2)	47.5 (6.2)	42.4 (12.0)

Note: SD = standard deviation; Qmci = Quick Mild Cognitive Impairment screen; EF = executive functioning
*Groups with different subscripts are significantly different from each other

RESULTS (cont.)

- **Qmci Positive Subgroup** (n = 23)
 - 65% (15) had CI on NTB
 - 22% (5) had elevated pTau217
 - 30% (7) had intermediate pTau217
- **pTau217 + Qmci Patterns**
 - Elevated pTau217 (n = 5):
 - 3 had CI on NTB (memory and EF)
 - Intermediate pTau217 (n = 7):
 - 6 CI on NTB: Memory (5) and EF (2)
- **NTB identified slightly more** patients with elevated and intermediate levels of pTau217 (7 and 10, respectively) than the Qmci (5 and 7, respectively).

Conclusions

- ❖ Combining cognitive screening with pTau217 levels shows potential for identifying individuals at higher risk of cognitive impairment in primary care settings.
- ❖ 75% of patients who screened positive on the Qmci and had intermediate to elevated levels of pTau217 were cognitively impaired on a neuropsychological test battery.
- ❖ This combined approach may improve early detection of Alzheimer’s disease in real-world primary care settings and inform allocation of limited resources.

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