Patients with Mild Cognitive Impairment stratified by baseline blood plasma pTau217 show differences in CANTAB-assessed cognitive decline

CAMBRIDGE COGNITION

AI-Mind

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Introduction

- With currently available diagnostic technology, many patients with dementia receive a diagnosis only after symptoms emerge, when they are likely beyond the reach of potentially disease-modifying therapies.
- The AI-Mind project was a 5-year, multicentre, European study which aimed to develop AI-based tools to aid clinical assessment of dementia risk in patients with Mild Cognitive Impairment (MCI).
- A previous analysis found associations between blood plasma pTau217 levels and CANTAB measures at baseline, with CANTAB comparable to standard paper and pencil tasks.[1]
- In this analysis of data from the AI-Mind cohort, we used CANTAB to assess cognitive impairment in patients with MCI over 2 years, stratified by baseline pTau217 levels.

Methods

- Patients with MCI aged 60–80 years (N = 1022) were recruited between 2022 and 2024 from five clinical sites in four countries (Norway, Finland, Italy, and Spain).
- Digital cognitive assessments (CANTAB), blood sampling and collection of clinical and demographic metadata were performed at baseline and at 8, 16 and 24 months.[2]
  - The cognitive battery included DMS, PRM, PAL, SWM and RVP, with one clinically relevant outcome measure from each task selected for analysis, along with two novel reaction time measures from PAL.
- Participants with non-missing pTau217 data and CANTAB data from at least 3 time points (n = 713) were stratified by baseline plasma pTau217 levels into three groups: Low, ≤3 pg/mL; Intermediate, >3–<6 pg/mL; and High, ≥6 pg/mL.
- Cognitive scores were adjusted for age, sex and education, and group means were plotted across time points with 95% CIs using bootstrapping (sample = 1000).

See the **supplementary material** for further details on the study design and statistical methods.

E-poster **Supplementary material** **References**

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Results

Figure 1. AI-Mind study design

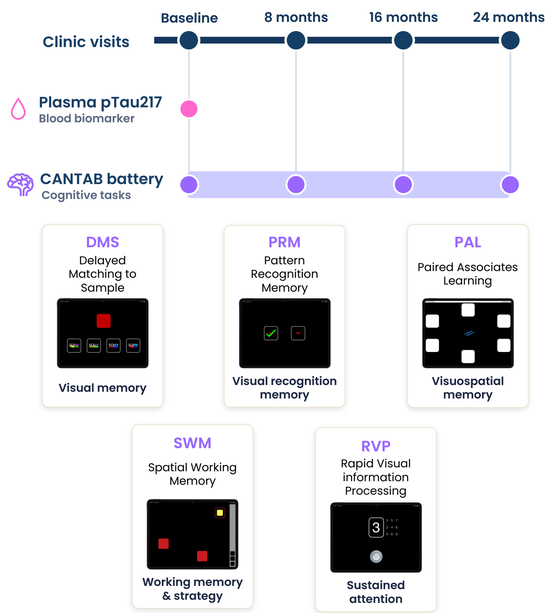
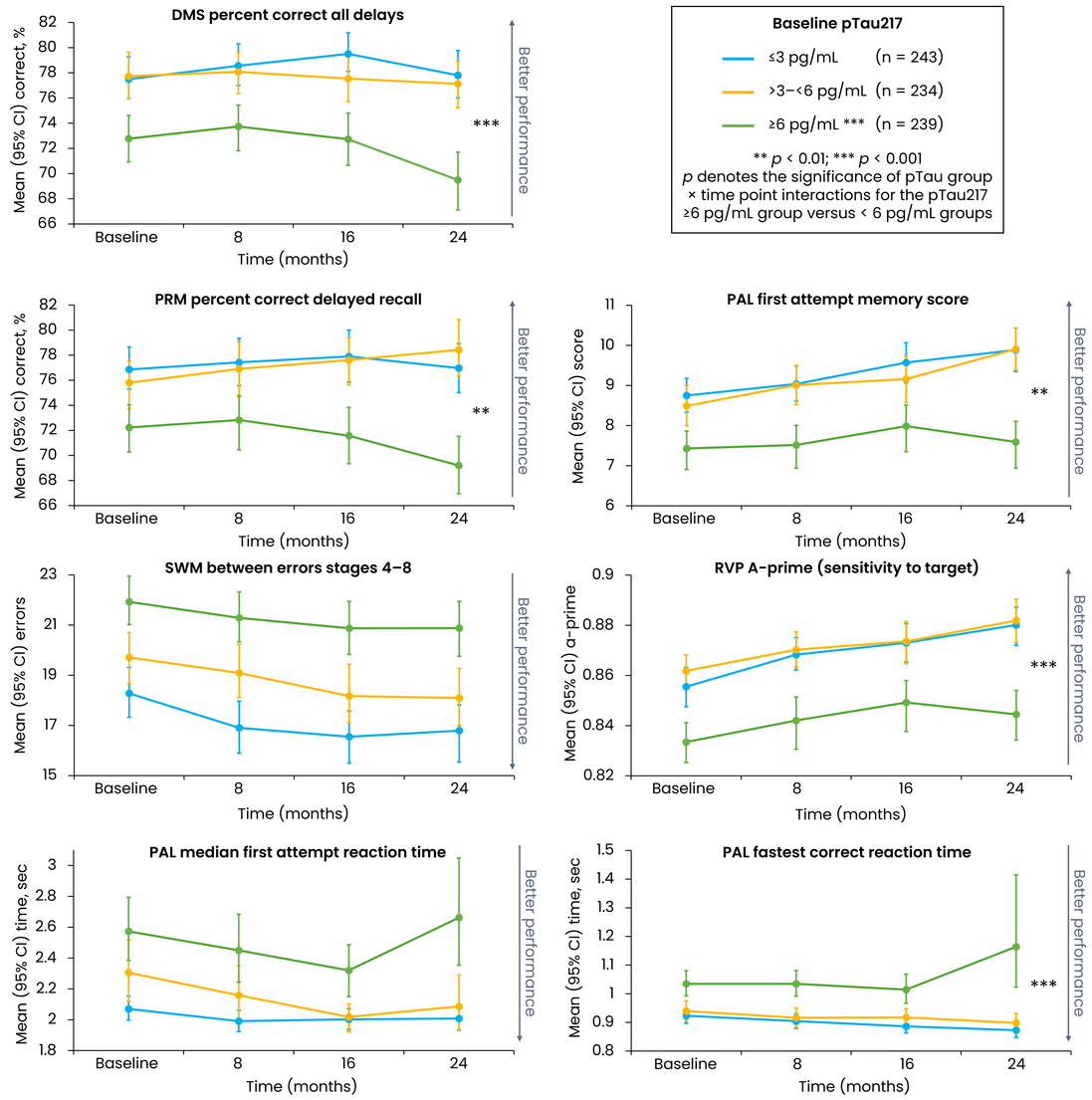


Table 1. Baseline demographics and clinical characteristics

Demographic/ characteristic	Overall (N = 713)	Low pTau217 ≤3 pg/mL (N = 243)	Intermediate pTau217 >3–<6 pg/mL (N = 232)	High pTau217 ≥6 pg/mL (N = 238)
Age	69.9 (5.5)	68.5 (5.3)	69.6 (5.3)	71.8 (5.3)
Sex, n (%)				
Female	412 (57.8)	137 (56.4)	136 (58.6)	140 (58.8)
Male	301 (42.2)	106 (43.6)	96 (41.4)	98 (41.2)
Education	3.6 (1.3)	3.8 (1.2)	3.5 (1.3)	3.5 (1.3)
DMS percent correct all delays	75.5 (14.7)	78.5 (13.6)	77.4 (14.3)	70.9 (15.0)
PRM percent correct delayed recall	74.4 (15.3)	77.6 (13.7)	75.3 (15.9)	70.5 (15.4)
PAL first attempt memory score	8.0 (4.0)	9.0 (3.7)	8.3 (4.0)	6.8 (4.0)
SWM between errors stages 4-8	20.1 (8.1)	17.6 (8.3)	19.7 (7.3)	23.0 (7.8)
RVP A-prime	0.8 (0.1)	0.9 (0.1)	0.9 (0.1)	0.8 (0.1)
PAL median first attempt reaction time	2336.7 (1432.1)	2005.5 (657.5)	2312.8 (1536.0)	2677.6 (1757.1)
PAL fastest correct reaction time	959.4 (300.2)	894.0 (198.9)	928.7 (253.7)	1051.8 (369.3)

All data are mean (SD) unless otherwise specified.

Figure 2. CANTAB measures were sensitive to differential cognitive decline by baseline pTau217 levels over 24 months in patients with MCI, with SWM also sensitive to an intermediate pTau217 effect



Conclusions

Brief in-clinic assessments, including novel speed-based PAL measures, were **sensitive to pTau-associated cognitive decline** over 24 months in an MCI cohort

Higher baseline **pTau217 concentration was associated with poorer SWM performance** in a concentration-dependent manner, sustained across 24 months

These findings support **CANTAB as a scalable tool for monitoring cognitive decline** in risk groups defined by baseline biomarker levels

This work anticipates future analyses to evaluate CANTAB alongside blood-based biomarkers for the prediction of progression to AD

Abbreviations

CANTAB, Cambridge Neuropsychological Test Automated Battery; **CI**, confidence interval; **DMS**, Delayed Matching to Sample; **MCI**, Mild Cognitive Impairment; **PAL**, Paired Associates Learning; **PRM**, Pattern Recognition Memory; **pTau217**, phosphorylated tau at threonine 217; **RVP**, Rapid Visual information Processing; **SD**, standard deviation; **SWM**, Spatial Working Memory.

Disclosures

AJK, **NT** and **FC** are employees of Cambridge Cognition and may own stock or stock options in Cambridge Cognition.

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