

Can Long-Term Accelerated Forgetting Improve Early Cognitive Screening for Alzheimer’s Disease?



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Key Findings

Aim: To investigate whether **7-day delayed recall** is a more sensitive cognitive marker of **Alzheimer’s disease pathology** than traditional 30-minute recall.

7-day recall retention was a significant predictor of biomarker status across both biomarker classifications, with **poorer long-term retention associated with Alzheimer’s disease pathology**.

An additional 7-day verbal memory task (accelerated long-term forgetting) does not clinically outperform existing 30-minute recall at predicting Alzheimer’s CSF biomarkers. When considering abnormality in both Amyloid and Tau, **7-day recall demonstrated higher sensitivity rates (80%)** when identifying **biomarker-positive individuals** compared to the **30-minute recall (60%)**. However, these differences were not significant in this small patient cohort.

The benefit of an added long-term recall may not outweigh the burden inflicted on patients and the NHS, but **further testing in real-world populations is warranted**.

Why do we need better memory tests?

The need for **earlier markers of Alzheimer’s disease** is increasing as disease-modifying therapies become available¹.

Evidence suggests that **accelerated long-term forgetting (ALF)**, where information is retained over standard testing intervals but forgotten more rapidly over days or weeks, may occur before cognitive impairment is detected on **conventional memory tests**². Longer recall intervals of 7–28 days have therefore been proposed as a **more sensitive measure of early memory dysfunction**³.

Existing baseline memory assessments provide valuable insight into a patient’s current cognitive state. However, commonly used delayed recall measures assess memory after only **20–30 minutes** and therefore principally evaluates **encoding and early memory consolidation** rather than **long-term memory storage**.



We **hypothesise** that **7-day recall** will demonstrate greater diagnostic accuracy for Alzheimer’s disease pathology than **30-minute delayed recall**.

Methods

Retrospective analysis of routine clinical data using data from the **PRECISE study** (HRA/Ethics permission) of people who had both neuropsychometric and cerebrospinal fluid biomarker testing.

- Participants completed a 12-word list memory task (**Hopkins Verbal Learning Test–Revised (HVLt-R)**)
- Recall tested at 30 minutes post learning with an additional 7-day post-learning trial.

Participants scoring **>2 SD** below the mean on HVLt-R 30-minute recall were not followed up for 7-day recall.

- This resulted in a selected subgroup with **ambiguous cognitive performance**.

Cohort Stratification
Subgroup selected based on completion of **HVLt-R with 7-day recall**.

Analysis 1: Dual-pathology positive (Amyloid/Tau) (n = 10) vs ≤1 abnormal biomarker (n = 47)

Analysis 2: Aβ42/40 positive (n=24) vs Aβ42/40 negative (n=23) (irrespective of pTau-181 status).

Lasso regression used to identify key predictors from HVLt-R
Best predictors:

- 30-minute raw score**
- 7-day retention (%)**

Logistic regression used to assess predictive value
Model performance assessed using **ROC curve analysis** and Sensitivity and specificity rates.

57 patients recruited from the Southmead Cognitive disorders Clinic.
Mean age 62.2 ± 9.6 years, 35% female, mean education 14.2 ± 2.8 years.

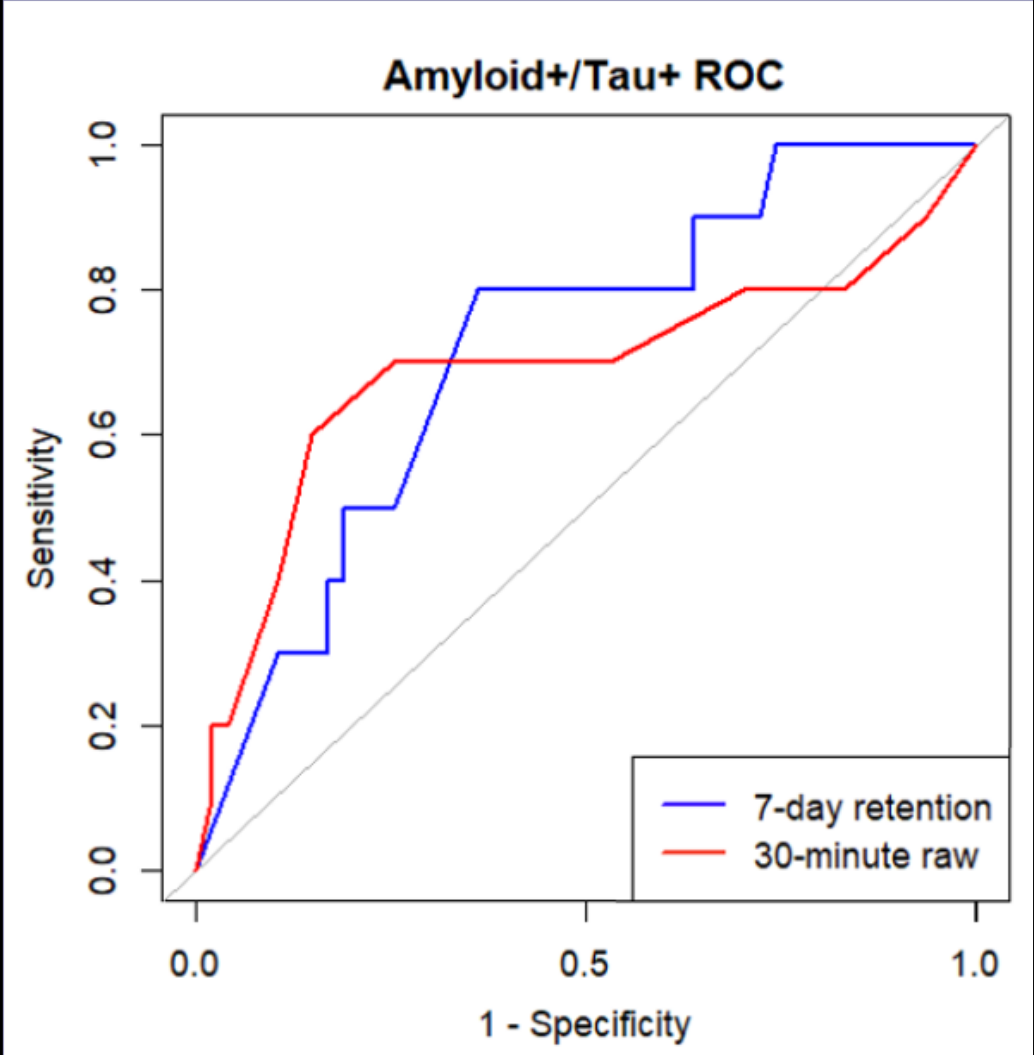
Results

Analysis 1) Amyloid+ & Tau+ versus ≤1 biomarker abnormality

30-minute raw score
AUC = **0.60**
Sensitivity = **60%**
Specificity = **85%**
TP = 6 | TN = 40 | FP = 7 | FN = 4

7-day retention
AUC = **0.72**
Sensitivity = **80%**
Specificity = **63%**
TP = 8 | TN = 30 | FP = 17 | FN = 2

No statistically significant difference between ROC curves (DeLong test): **p = 0.74**

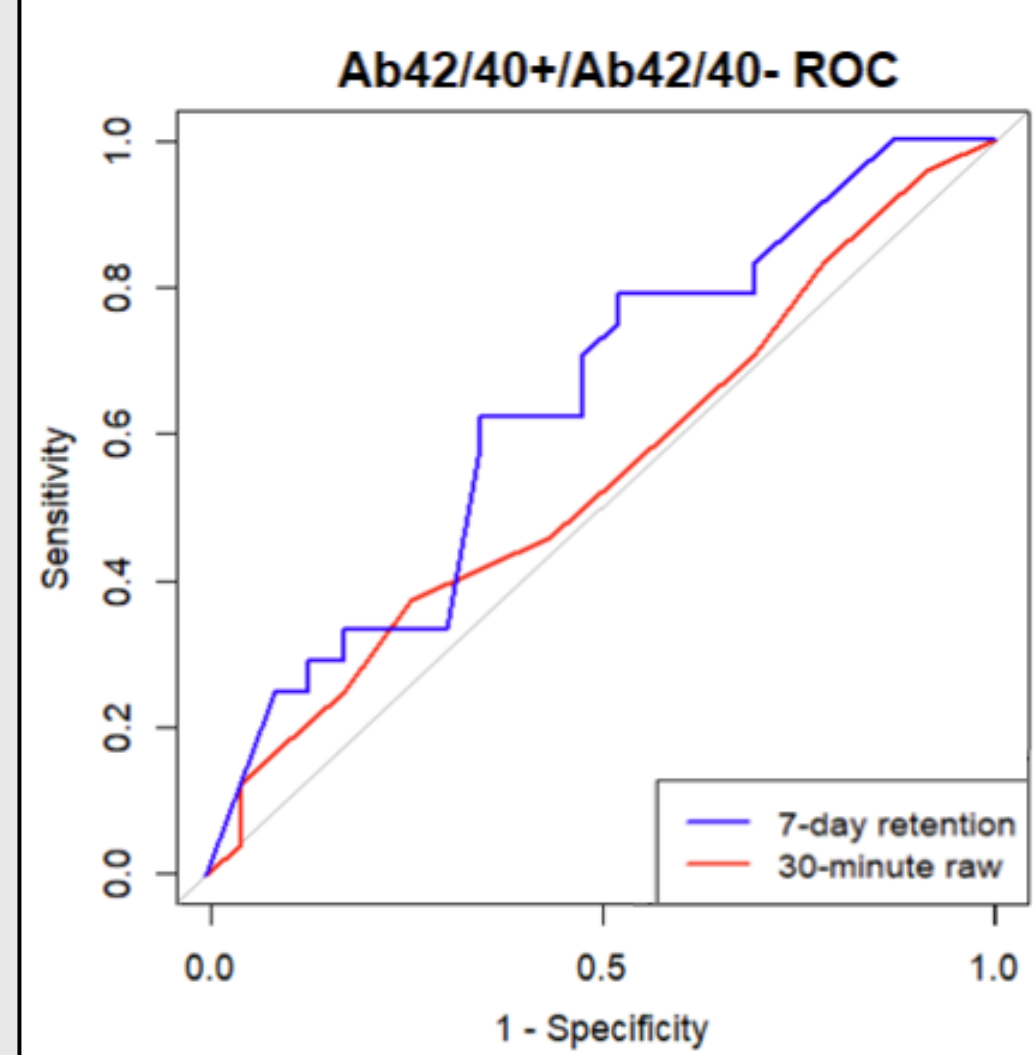


Analysis 2) Aβ42/40+ versus Aβ42/40- (Regardless of P-tau-181)

30-minute raw score
AUC = **0.55**
Sensitivity = **38%**
Specificity = **74%**
TP = 9 | TN = 17 | FP = 6 | FN = 15

7-day retention
AUC = **0.64**
Sensitivity = **63%**
Specificity = **65%**
TP = 15 | TN = 15 | FP = 8 | FN = 9

No statistically significant difference between ROC curves (DeLong test): **p = 0.243**



Conclusions

In both biomarker classifications, **7-day recall retention was a significant predictor of biomarker abnormality**, with **retention scores above 50% associated with a greater likelihood of biomarker normality**.

These findings suggest that **poorer long-term memory retention (7-day recall) is associated with molecular changes of Alzheimer’s disease**.

Larger samples sizes of real-world clinical populations are required to determine whether this is clinically useful as –

- In Analysis 1, **30-minute recall demonstrated comparable diagnostic performance to 7-days**.
- In Analysis 2, **30-minute recall test demonstrated poor sensitivity for identifying patients with abnormal biomarkers**.
- Age itself is also a strong predictor** of Alzheimer’s and therefore **age-bounded normative scores**, and biomarker levels should be determined for future use.
- the practical and logistical demands of implementing repeat testing in clinical practice mean **clinical utility should be clearly demonstrated** before wider roll-out.

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