

# Remote and Unsupervised Smartphone-Based Memory Assessments Detect Subtle Longitudinal Cognitive Change in Preclinical Alzheimer's Disease

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## Background

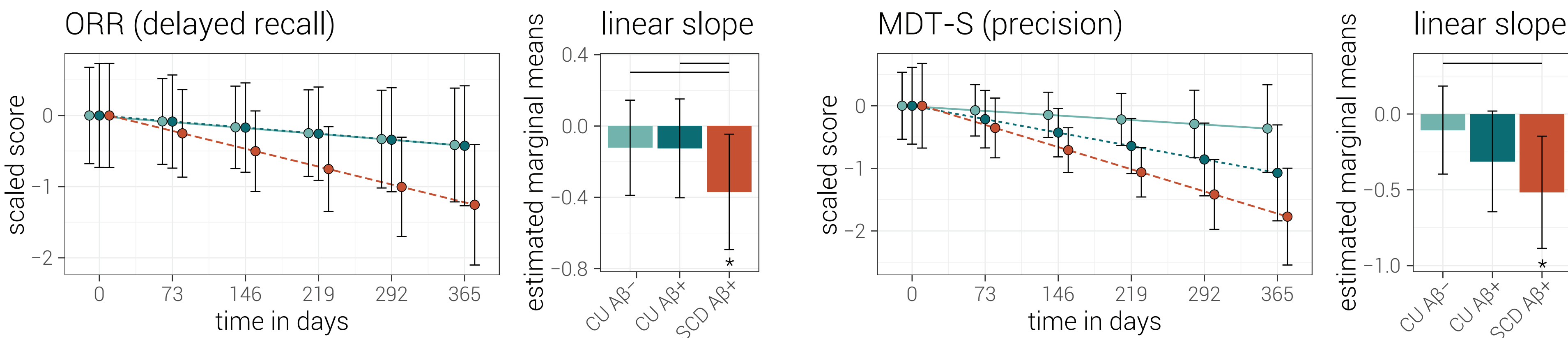
**Anti-amyloid therapies** will likely be more effective in early stages of AD and currently clinical trials investigate the treatment window in preclinical AD populations. If these trials succeed: **How do we identify and monitor individuals at this stage?**

**Requirements for sensitive measures in preclinical AD:**

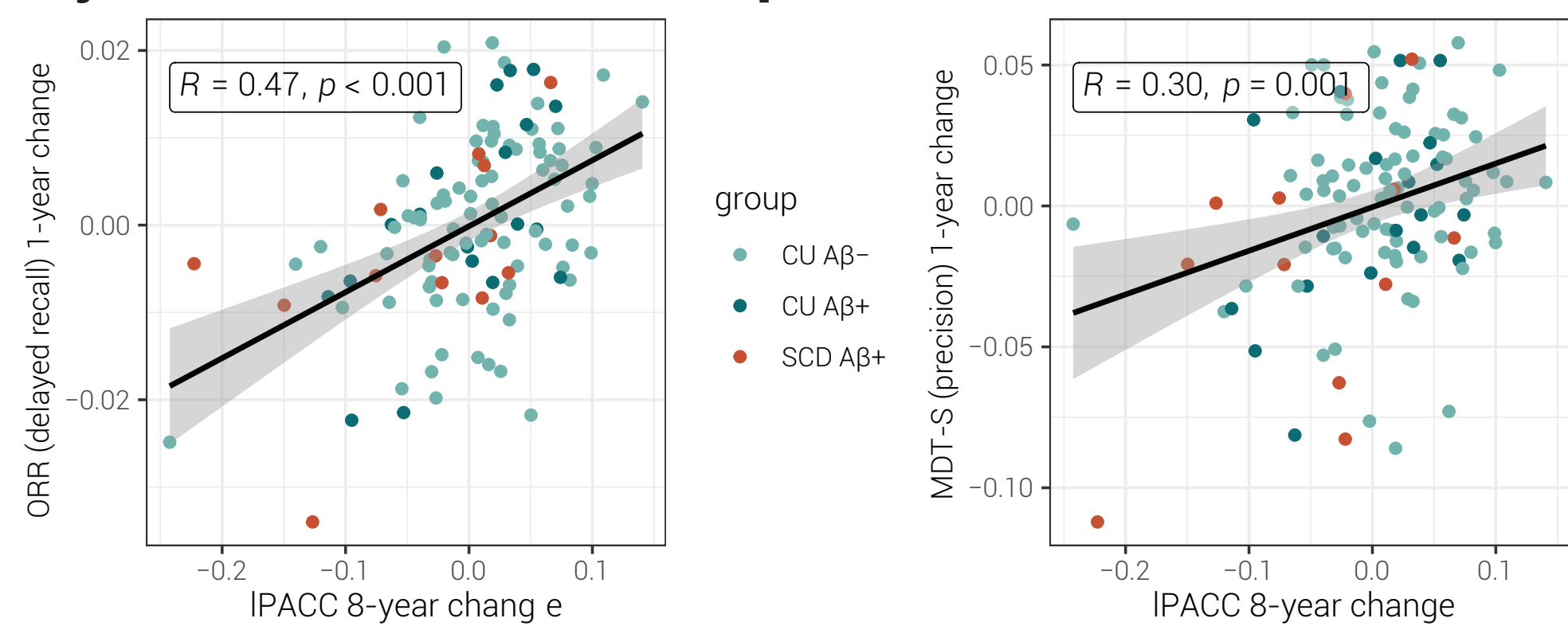
1. Target the **relevant cognitive function** and **brain network**<sup>1</sup>  
MTL-dependent memory functions are affected earliest by tau pathology
2. Administer tests at **high frequency**<sup>2</sup>  
Dense sampling reduces noise and allows to capture individual trajectories
3. Measure **precisely** and sensitively  
Continuous precision metrics can add to binary accuracy scoring

## ORR score and MDT-S precision decline in preclinical AD

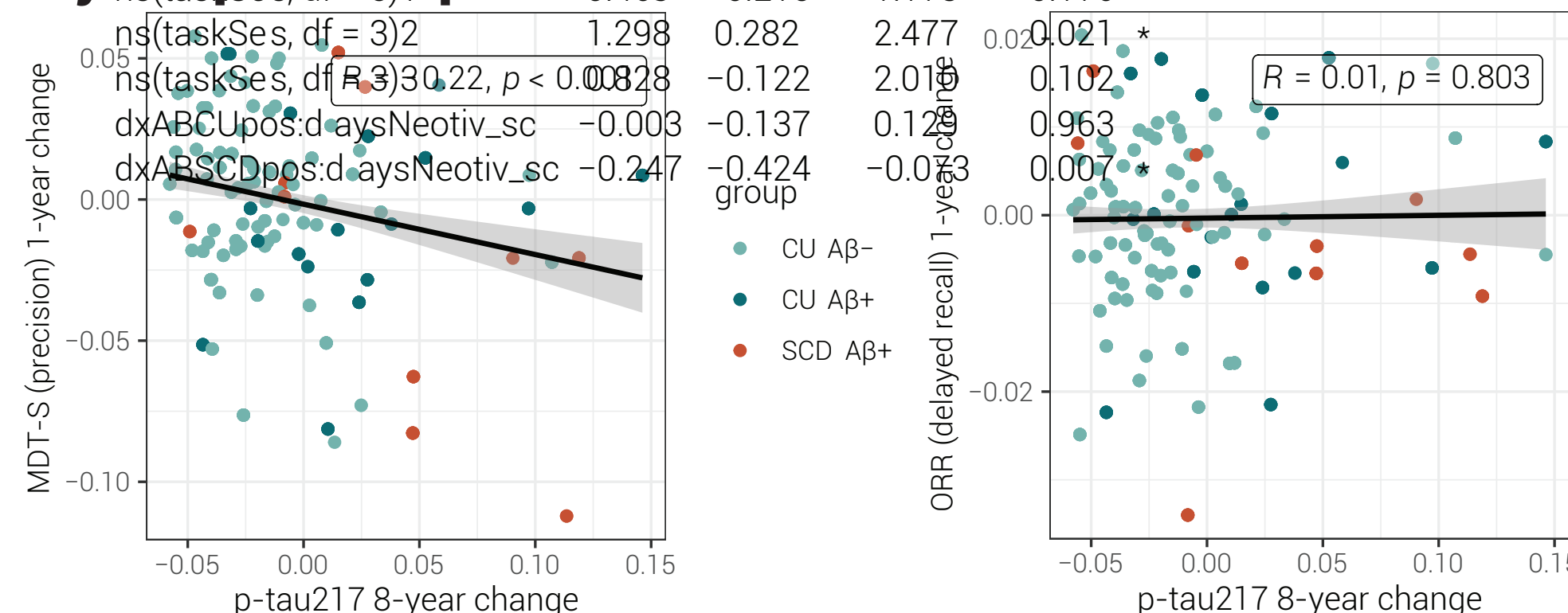
**Delayed Associative Memory and Scene Mnemonic Discrimination Precision decline in SCD Aβ+**



**Short-term smartphone-based 1-year slopes are correlated with 8-year in-clinic PACC5 slopes**



**Short-term smartphone-based 1-year slopes are correlated with 8-year plasma p-tau217 increase**



|                   | All            | CU Aβ-      | CU Aβ+ (Stage 1) | SCD Aβ+ (Stage 2) |
|-------------------|----------------|-------------|------------------|-------------------|
| N                 | 127            | 91          | 19               | 17                |
| Age (years)       | 70.0 ± 6.4     | 68.8 ± 6.0  | 72.4 ± 5.9       | 73.6 ± 7.6        |
| Sex (female)      | 0.386 (68%)    | 0.399 (64%) | 0.105 (53%)      | 0.016 *           |
| Education (years) | 15.9 ± 2.6     | 16.1 ± 2.6  | 16.2 ± 2.5       | 16.1 ± 2.9        |
| Study cohort      | -0.026         | -0.136      | 0.067            | 0.609             |
| DELCODE           | 0.083 (31%)    | 0.203 (29%) | 0.415 (21%)      | 0.268             |
| Memory clinic     | -0.431 (1%)    | 0.473       | 0.340            | 1 (6%)            |
| WRAP              | 0.079 ± 0.280  | 0.131       | 0.469            | 0.162             |
| MMSE              | -0.148 ± 0.358 | 0.054       | 0.182            | 0.162             |
| IPACC             | -0.158 ± 0.571 | 0.274       | 0.450            | 0.827             |
| IPACC             | 0.10 ± 0.59    | 0.19 ± 0.58 | -0.02 ± 0.44     | -0.19 ± 0.67      |

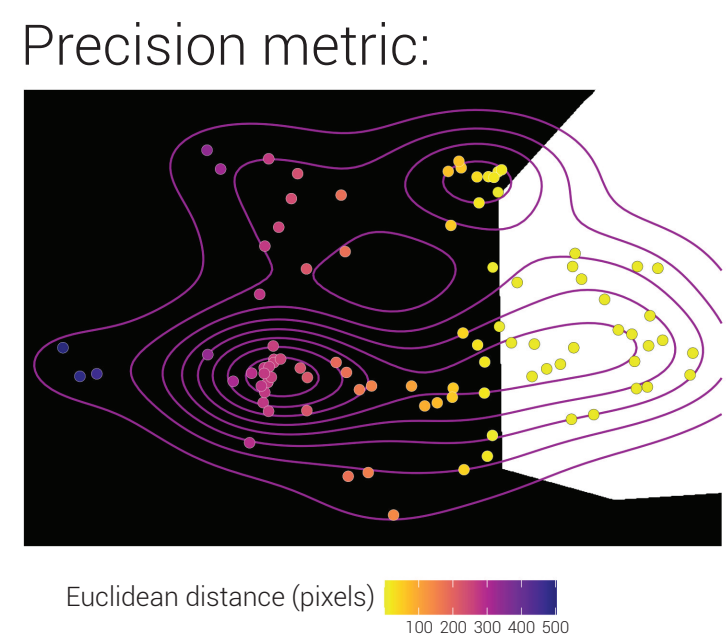
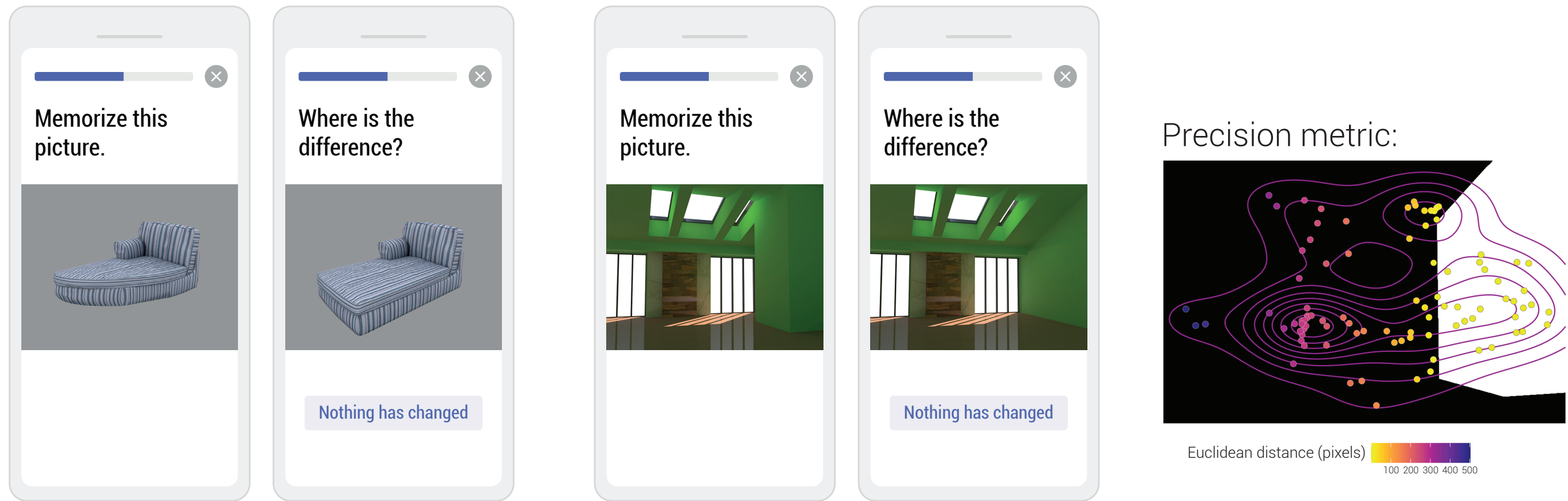
Ab positivity was defined using CSF Aβ42/40 or Aβ PET. When unavailable, CSF Aβ42/40 was predicted by a binomial logistic regression model including plasma p-tau181, plasma Aβ42/40, ApoE4 carrier status and age.

Plasma p-tau217 was defined using the Quanterix Simoa® ALZpath assay.

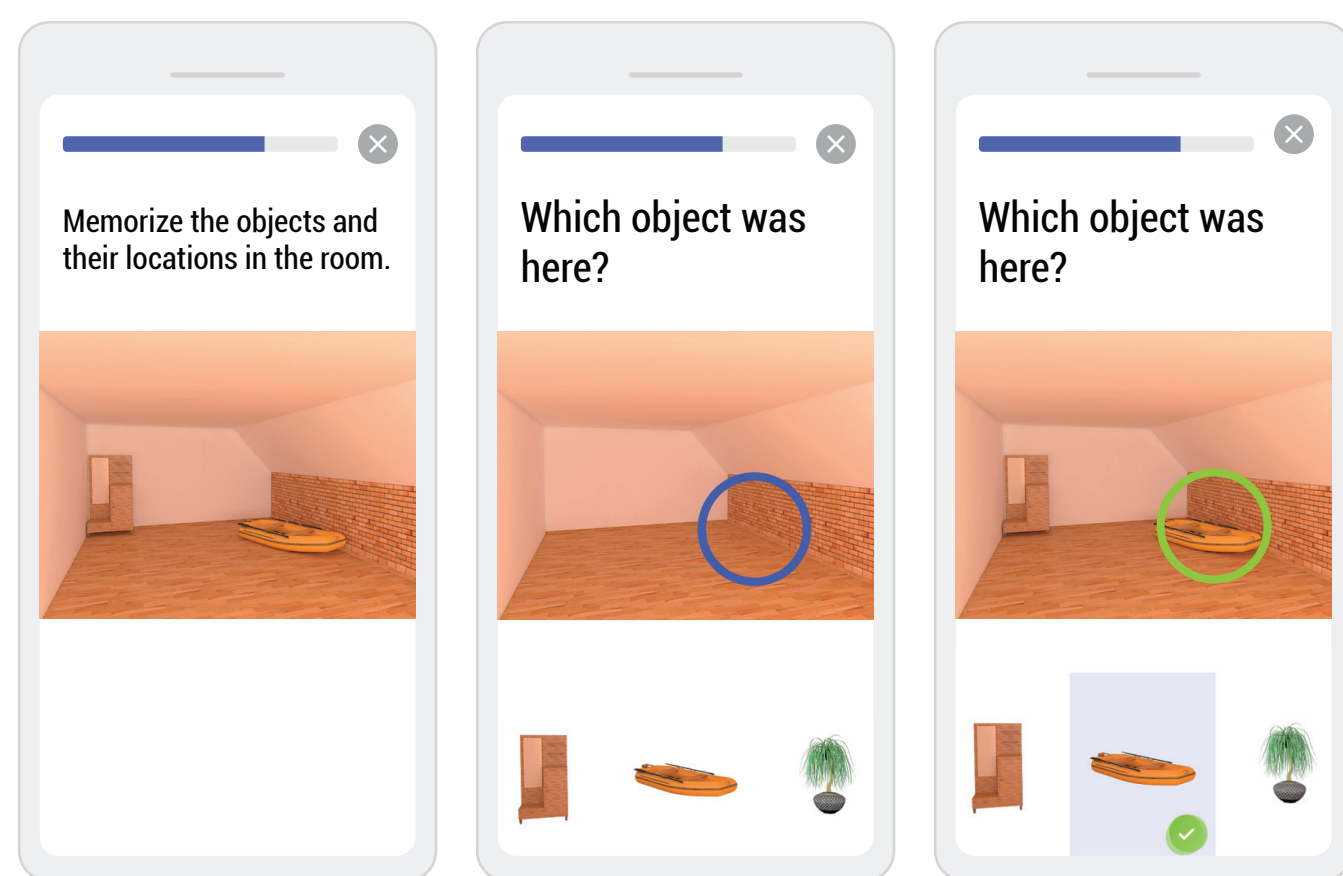
Polk et al., in preparation

## Methods

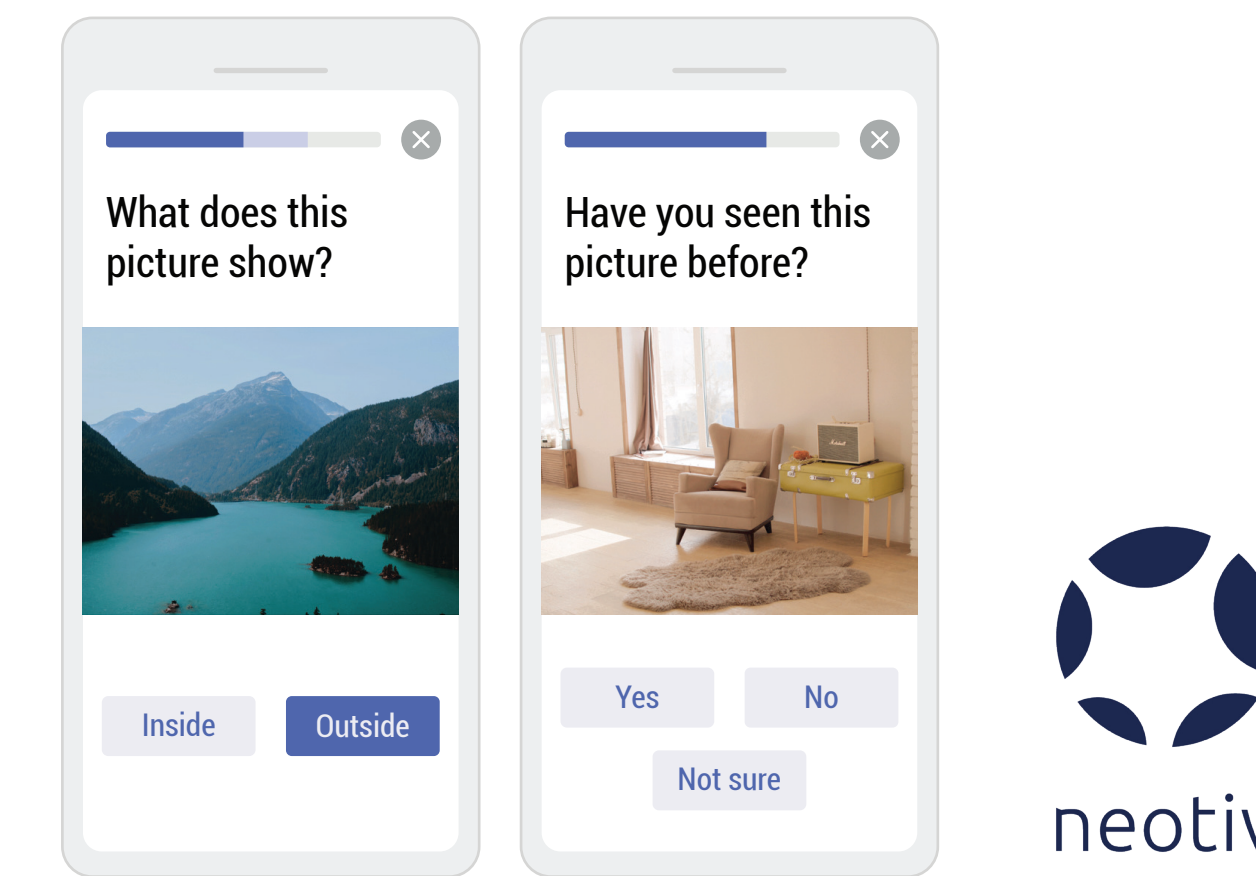
### Mnemonic Discrimination Task for Objects and Scenes



### Object-in-Room Recall



### Complex Scene Recognition



## Conclusion

- Digital cognitive assessments show **differential sensitivity** across disease stages
- **Preclinical cognitive phenotype** characterized by an early breakdown of **MTL-dependent mnemonic precision** and **associative memory**

