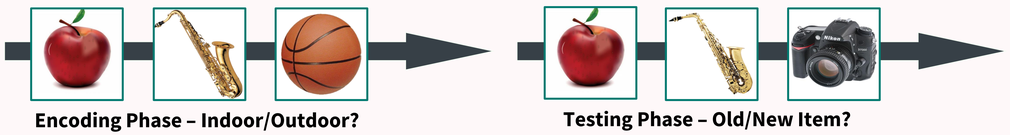
Effect of APOE4 genotype and AD-related CSF markers on cognitive decline in non-demented elderly

Faissal Sharif[1,2,3], Harry W M Steinbusch[3]

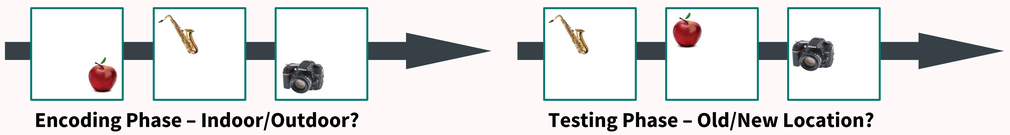
[1] Department of Neurobiology and Behavior, University of California, Irvine
[2] Department of Brain Sciences, Imperial College London
[3] The Faculty of Health, Medicine and Life Sciences (FHML), Maastricht University

Correspondence: fs419@ic.ac.uk

A – Object Memory



B – Spatial Memory



C – Temporal Memory

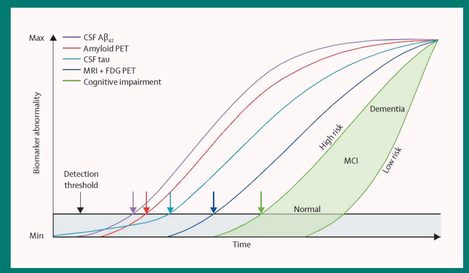
Mnenomic Similarity Task (MST). A testing paradigm for hippocampal memory function, as described by Stark, Yassa et al (2013) was used to assess discrimination ability on object (A), spatial (B) and temporal (C) domains. Alternating images were presented on a screen (2 s, 0.5 ISI) with each test consisting of an incidental encoding phase and a subsequent testing phase with repeat (target), similar (lure) or new (foil) images.

Background

152 Million Expected number of people with dementia in 2050

99.6 % Failure rate of drug research for Alzheimer's disease (AD)

- Levels of β-amyloid plaques (Aβ) and tau tangles change **decades before symptoms** arise
- Detecting these changes early opens a window of opportunity for **prevention** of the disease
- Effective **biomarkers** are therefore needed



Adopted from "Tracking pathophysiological processes in Alzheimer's disease: an updated hypothetical model of dynamic biomarkers." by Jack et al. 2013. *Lancet Neurol.*

Methods

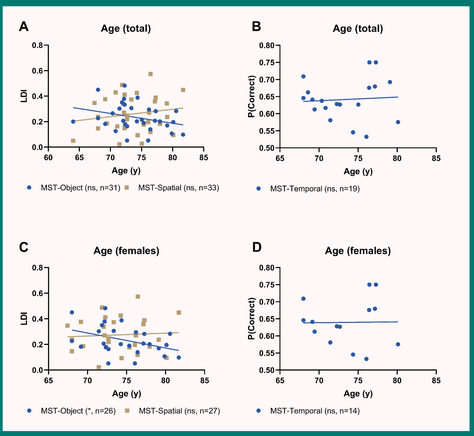
37 older older adults (64-81 years, M = 73.71) who were **free of dementia** (CDR = 0; MMSE ≥ 27) and any other major neurological and medical disorders were recruited. 29 subjects were female and most were highly educated (M = 16 years).

- **APOE4 genotyping** was performed through salivary samples and PCR to identify ε4 carriers vs noncarriers
- **Lumbar punctures** (spinal tap) were used to obtain CSF which was sampled for Aβ38, Aβ40, Abβ42, t-tau and p-tau levels

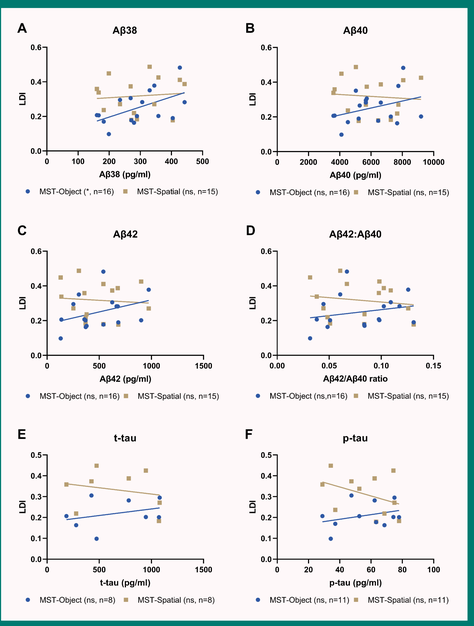
Conclusion

- APOE4 genotype and CSF Aβ and tau levels **alone cannot predict** mnemonic discrimination ability
- AD pathology is complex and **requires longitudinal studies** with **multivariate analyses**
- Effects on object discrimination are likely caused by selective disruption of the **perirhinal cortex (PrC) - lateral entorhinal cortex (LEC)** object processing pathway in earlier stages of the disease

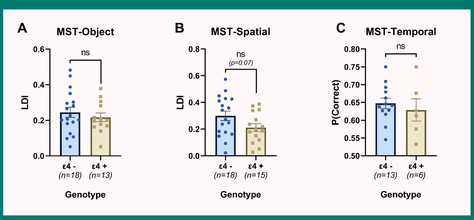
Results



MST task performance and age. In females, age predicted performance on the MST Object task .



MST task performance and Aβ and tau levels. In females, age predicted performance on the MST Object task.



APOE4 genotype and MST task performance. Overall, APOE4 genotype had no significant effect on MST task performance.