

Impaired Path Integration represents an initial cognitive change in Autosomal Dominant Alzheimer's Disease

Andrea Castegnaro¹, Ana Baena², Juan Pablo Sánchez Escudero², Sofia Pepe³, Giedre Cepukaityte¹, Katarzyna Rudzka¹, David Aguillón², Neil Burgess¹, Francisco Lopera², Dennis Chan¹

¹ Institute of Cognitive Neuroscience, University College London, London, UK; ² Grupo de Neurociencias de Antioquia, Facultad de Medicina, Universidad de Antioquia, Medellín, Colombia; ³ Department of Psychology, Sapienza University of Rome, Rome, Italy

Path integration is impaired in cognitively unimpaired PSEN1 carriers before global cognition declines, one of the earliest cognitive changes in familial AD.

INTRODUCTION

METHODS (II)

METHODS (III)

DISCUSSIONS

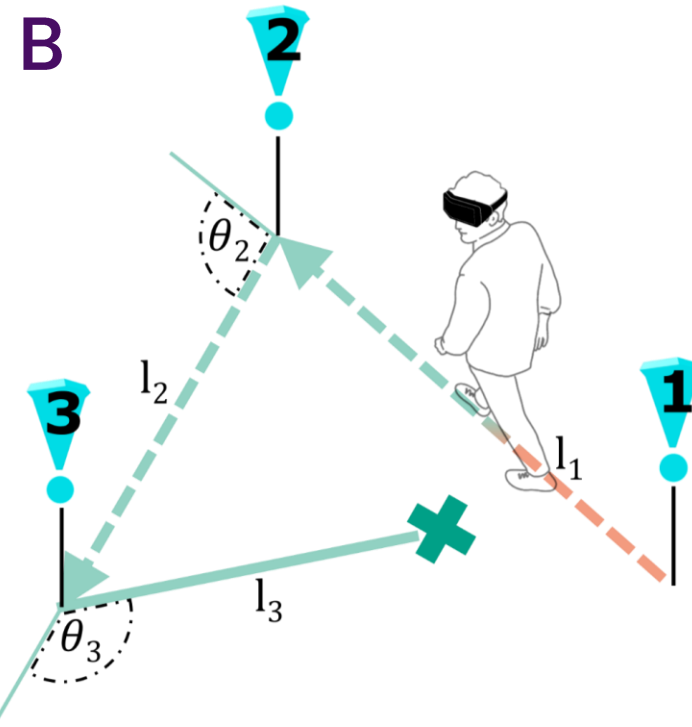
• **Path integration** is impaired in prodromal¹ and preclinical² sporadic Alzheimer's disease (AD)

• To determine the timing of PI deficits in AD relative to other cognitive impairments (e.g. episodic memory) we tested the Colombian PSEN1 E280A kindred with autosomal dominant AD.³

• We hypothesized that PI would be impaired in gene carriers prior to symptom onset and before, or at similar time, to deficits in other cognitive tests.

Each participant completed:

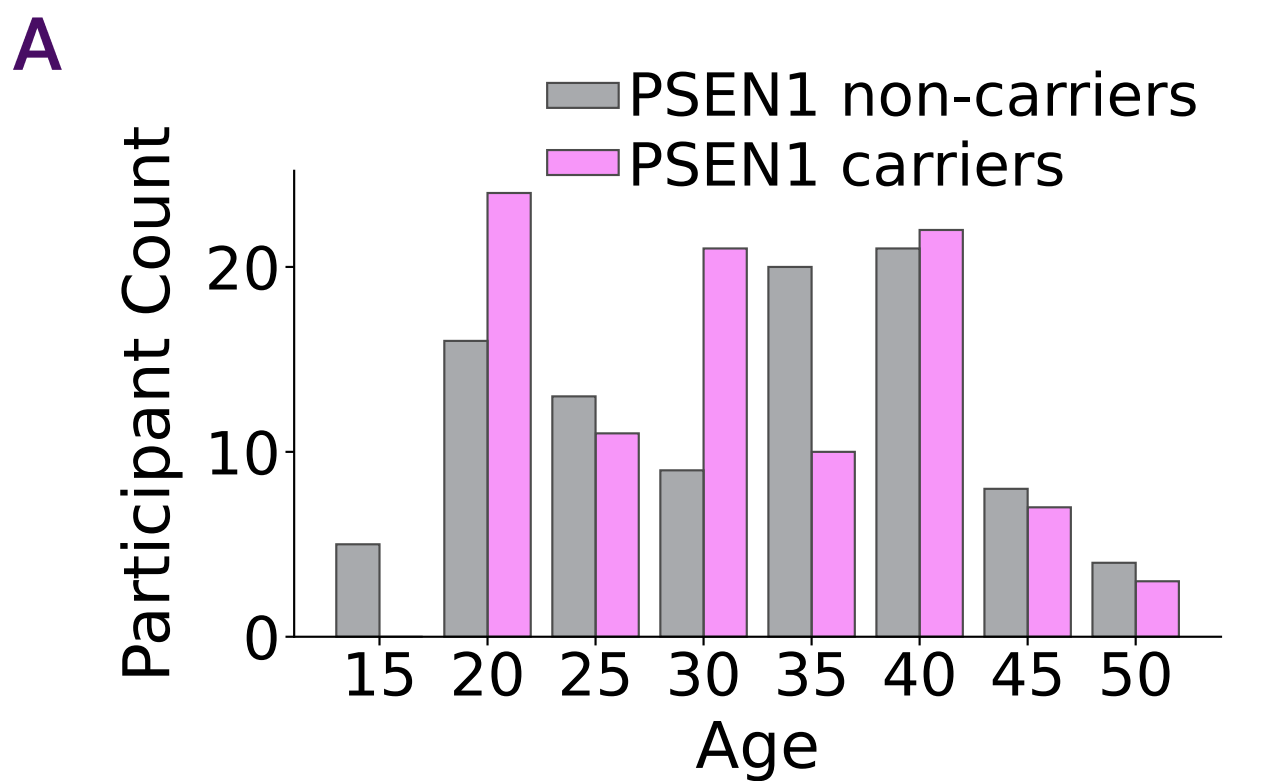
- an immersive virtual reality *triangle completion task* (TCT) to assess path integration¹ (fig. B)
- a comprehensive neuropsychological battery⁴ (fig. C)



Navigation	Path Integration		TCT
	Verbal		Word List
	Episodic		MBT
Memory	Semantic		Boston Naming
	Allocentric		4 Mountains test
Visuo-spatial	Ability		CP (copy)
			Rey (copy)
	Visual memory		CP (recall)
Executive Function			Rey (recall)
	Fluency		Animal Fluency
			Phonemic Fluency
General	Set Shifting		WCST
			TMT-B
	Attention		Digit Symbol (WAIS-III)
Fluid Intelligence			TMT-A
			IFS
			Raven Matrix

METHODS (I)

188 cognitively unimpaired (MMSE > 24 and FAST < 3) participants, 18–53 years. 92 PSEN1 E280A carriers, 96 non-carriers (Fig. A).

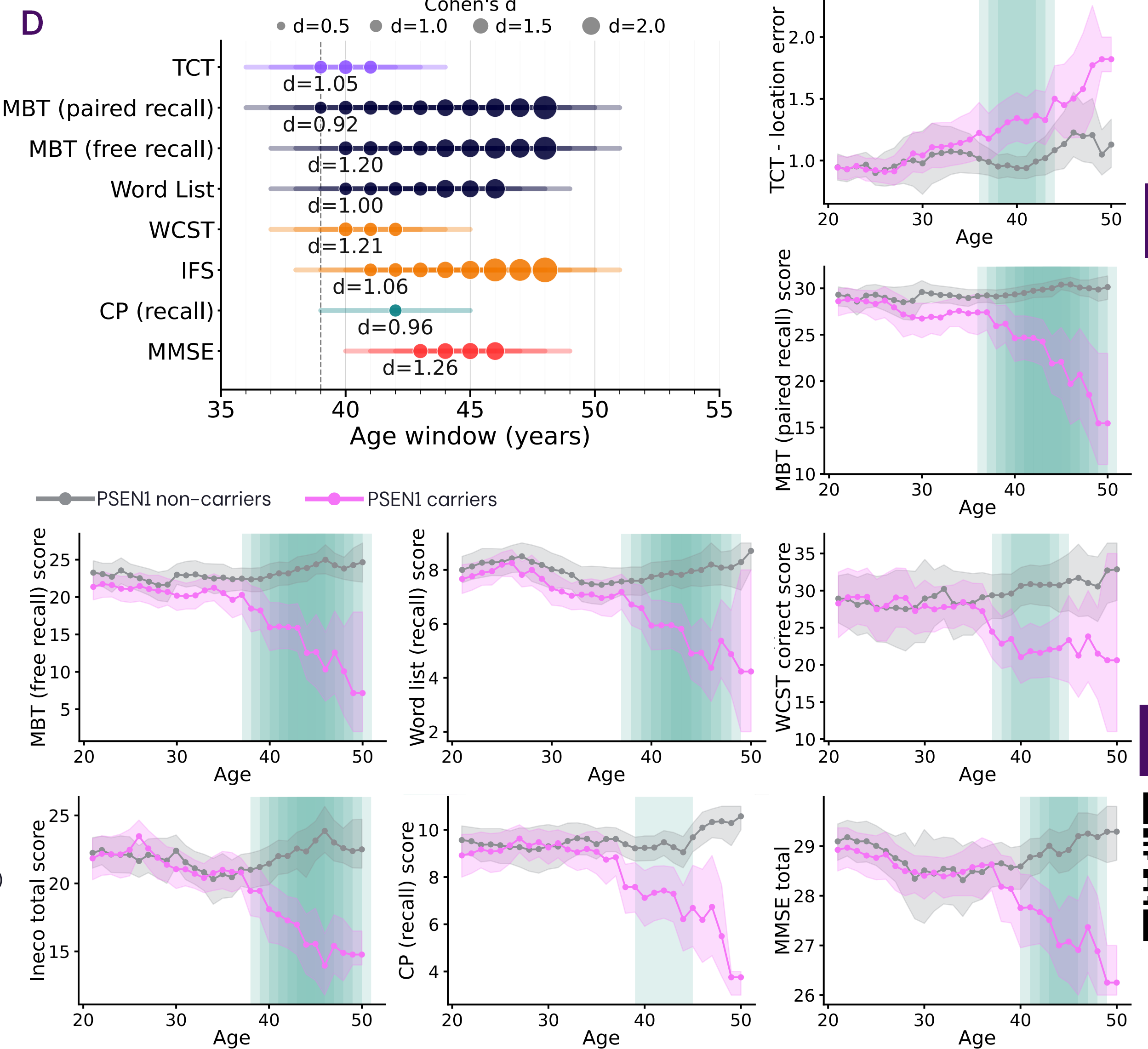


MBT=memory binding test; CP=Constructional Praxis; WCST=Wisconsin Card Sorting Test; TMT=Trail Making Test; IFS=INECO Frontal Screening

Bootstrapped 6-Year Age-windows

- Identified the earliest overlapping 6-year window showing a carrier – non-carrier difference
- Used 1,000 bootstrap resamples within each group
- Retained only windows FDR-significant in ≥80% of resamples

RESULTS



- Path integration diverges in unimpaired carriers by age ~39, before MCI onset (~44 yrs).
- It separates as early as episodic memory (MBT) and earlier than executive, visuospatial, and global (MMSE) measures.
- Effects at separation are large ($d > 1$).
- This work in a cohort with presymptomatic genetically confirmed AD builds on past work indicating that impaired path integration represents one of the initial cognitive deficits denoting the clinical onset of AD.

REFERENCES

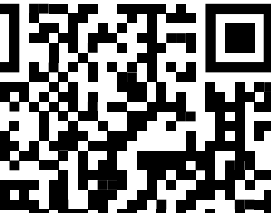
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CONTACT

 andrea.castegnaro.15@ucl.ac.uk
dennis.chan@ucl.ac.uk