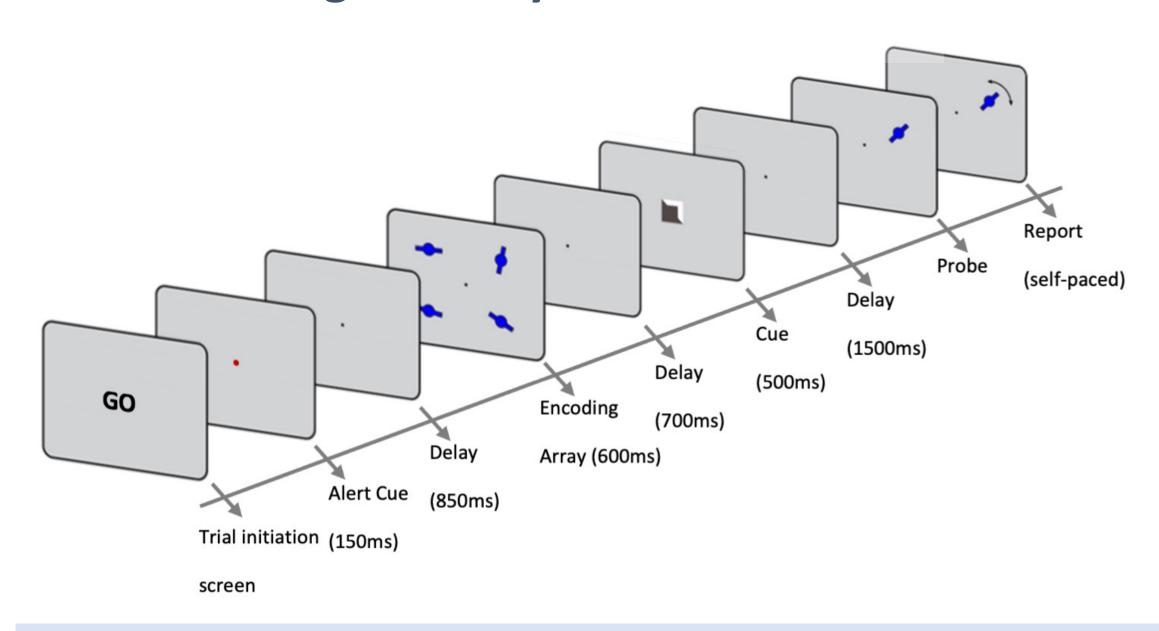
Internal Selective Attention Benefits in Cognitively Healthy APOE £4 Carriers

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Background

- The Apolipoprotein-E (APOE) ε4 allele is the highest known risk factor for developing Alzheimer's Disease (AD)¹, with a prevalence in $\varepsilon 3/\varepsilon 4$ carriers of 47%.
- APOE ε4 carriers have recently been shown to confer advantages in working memory, specifically when items were to be held in memory for short (1s) durations².
- One reason for this may be that APOE £4 carriers differentially use attention to aid working memory performance
- Here we explored whether cognitively healthy older heterozygote APOE4 (ε 3/ ε 4) carriers differed from APOE3 (ε 3/ ε 3) carriers in their ability to selectively attend to items held within working memory.

Retro-Cue Working Memory Precision Task^{3,4}



Task-Derived Measures

1. Neutral Cue Accuracy

Working memory precision, i.e., the level of precision with which the participants recalled the items from the encoding array accuracy following the spatially uninformative (neutral) cue⁴

2. Retro-Cue Benefit

The ability to selectively attend to items held within working memory, i.e., the extent to which performance benefited from the spatially-informative (retro) cue (Retro-Cue Accuracy – Neutral Cue Accuracy)

MEG Preprocessing Parcel Selection Left occipital α power as a marker of attentional engagement^{6,7}

MEG data (Elekta Neuromag) preprocessed with OSL⁵, epoched to the Cue

Preliminary Results: Behaviour

Participants were matched on age and years of education, and performed similarly on Montreal Cognitive Assessment (MoCA).

(A, B)

No effect of APOE,

Age, or APOE x Age

interaction

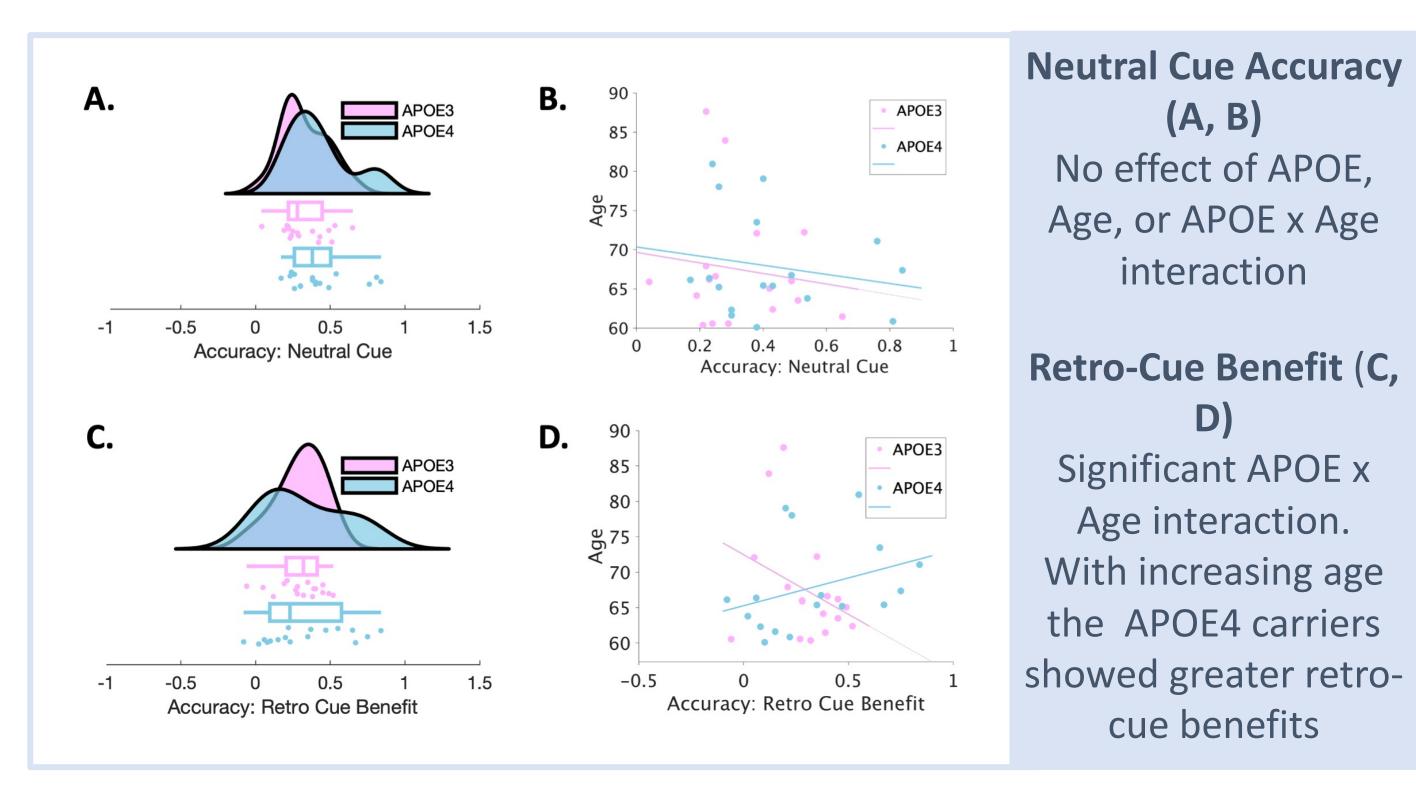
Significant APOE x

Age interaction.

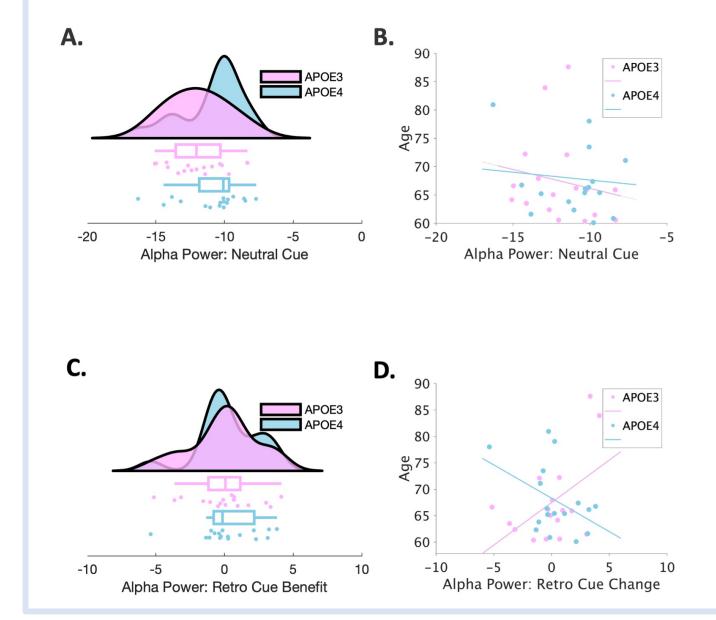
With increasing age

the APOE4 carriers

cue benefits



Preliminary Results: Alpha (α)



Neutral Cue α Power (A, B) No effect of APOE, Age, or APOE x Age interaction

Retro-Cue Benefit α power (A, B)

Significant APOE x Age interaction. With increasing age, APO3 carriers showed greater relative α power during the retro-cue 'benefit'

Interpretation & Future Directions

- Previously reported APOE4 advantages in working memory² may be attributed, at least in part, to differences in internal attention mechanisms.
- We observed that cognitively healthy older APOE4 carriers were increasingly better at focusing their attention within memory to improve performance. Critically, the two groups did not differ in working memory performance during the neutral cue.
- Our preliminary MEG analyses suggest that APOE3 and APOE4 groups additionally differ in occipital alpha power as they age. While APOE3 carriers showed increases in relative alpha during the retro-cue with age, possibly indicative of decreased attentional engagement (e.g.^{6,7}), these age-related alpha increases were absent in the APOE4 group.
- This raises the possibility that APOE4 carriers may offset age-related difficulties with attentional engagement, possibly as an adaptive compensatory mechanism (e.g.,³), to facilitate better working memory in later years.
- Future work should investigate the association between internal selective attention and resilience to Alzheimer's Disease in heterozygote £4 carriers who do not develop the disease

Brosnan MB, Sabaroedin K, Silk T, et al. Evidence accumulation during perceptual decisions in humans varies as a function of dorsal frontoparietal organization. Nat Hum Behav, 4(8), 844-855 (2020). doi:10.1038/s41562-020-0863-4