

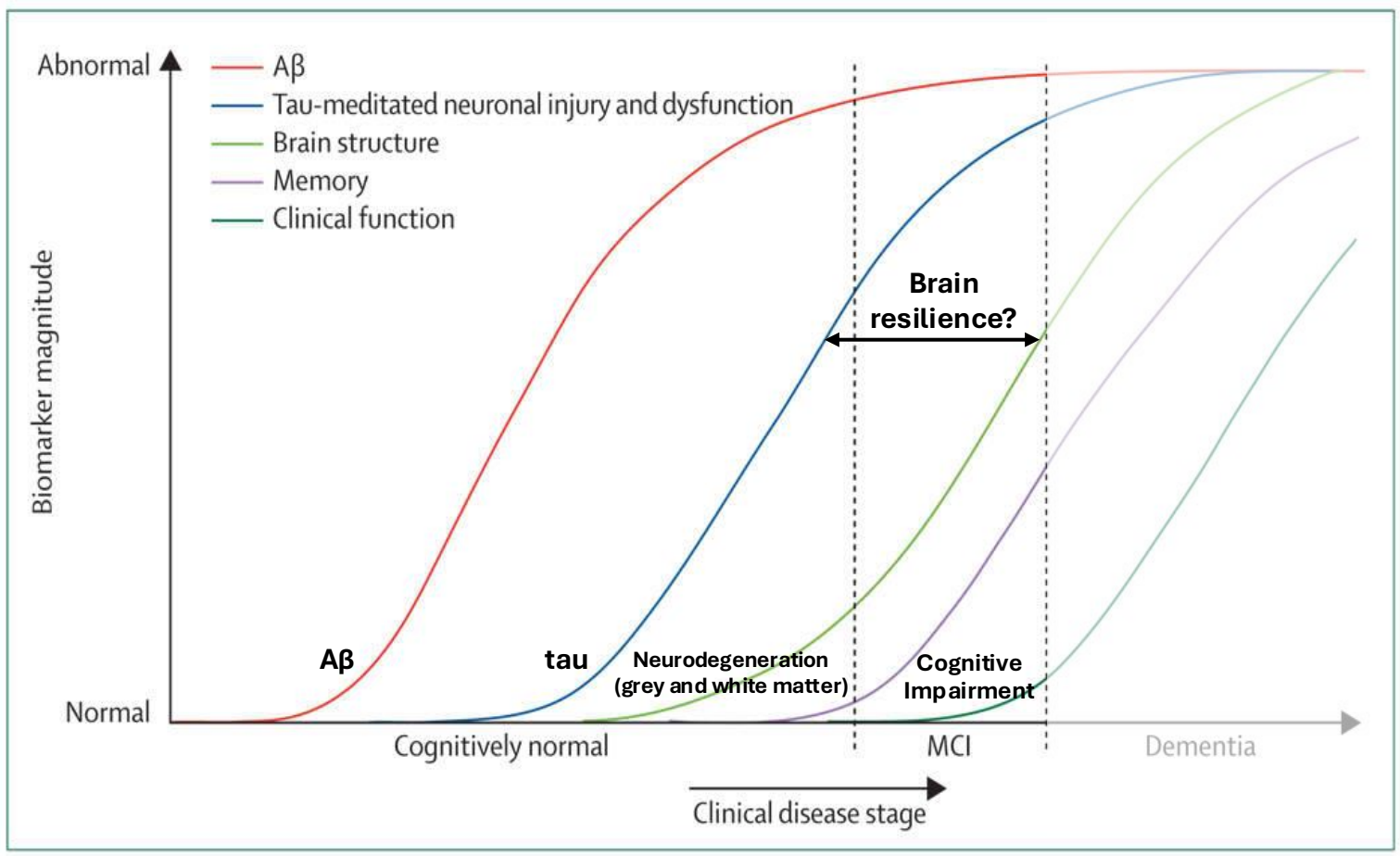
Grey- and White-matter Resilience to Tau in Relation to Cognition and the Effect of Sex in Alzheimer's Disease

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BACKGROUND

- Medial temporal regions** affected early by tau accumulation and grey-matter degeneration (Braak & Braak, 1991). **White-matter** changes have been less studied (Jacobs et al., 2018).
- Interindividual **heterogeneity** in the timing of pathological changes (tau and neurodegeneration) and cognitive outcomes = **brain resilience** and **sex**? (Bocancea et al., 2023; Ossenkoppele et al., 2020)



(adapted from Jack et al., 2010)

Objectives:

- Examine the link between **grey- and white-matter resilience to tau** and
 - Cognitive performance**
 - Cognitive decline over time**
- Investigate the effect of **sex** on these associations

METHODS

In **CU** and **MCI Aβ+** individuals;
Tau PET (mean SUVR entorhinal cortex and amygdala)

Grey matter (MRI)
entorhinal cortical
thickness



White matter (DTI)
MD of cingulum-hippocampal
connections

Brain resilience to tau = greater-than-expected brain integrity given tau burden

1. a) **Cognitive performance**
(general linear models)

1. b) **Cognitive decline**
(linear mixed-effects models)

Memory, Language, Executive Function, Visuospatial
* Controlling for age, education and cognitive status

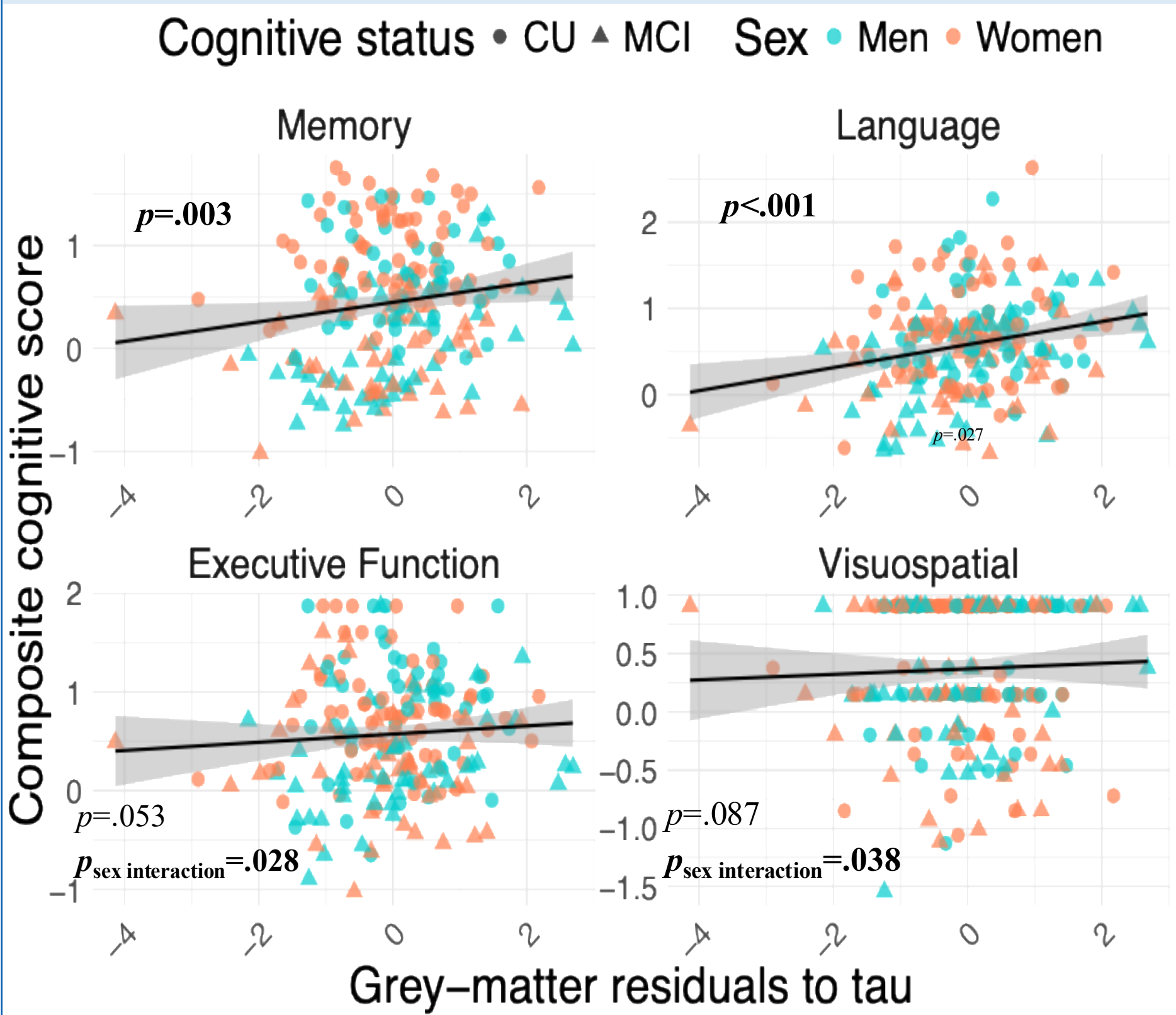
2. **Sex differences**
(interaction and sex-stratified models)

Cross-sectional analyses (n=205)		
	93 men	112 women
Cognitive status, n CU/MCI	43/50	70/42
Longitudinal analyses (at baseline) (n=151)		
	68 men	83 women
Follow-up duration, years	2.7 ± 1.3	2.6 ± 1.2
Cognitive status, n CU/MCI	30/38	52/31

RESULTS

1. a) Cognitive performance

- Grey-matter resilience** to tau was associated with better **memory** and **language** performance

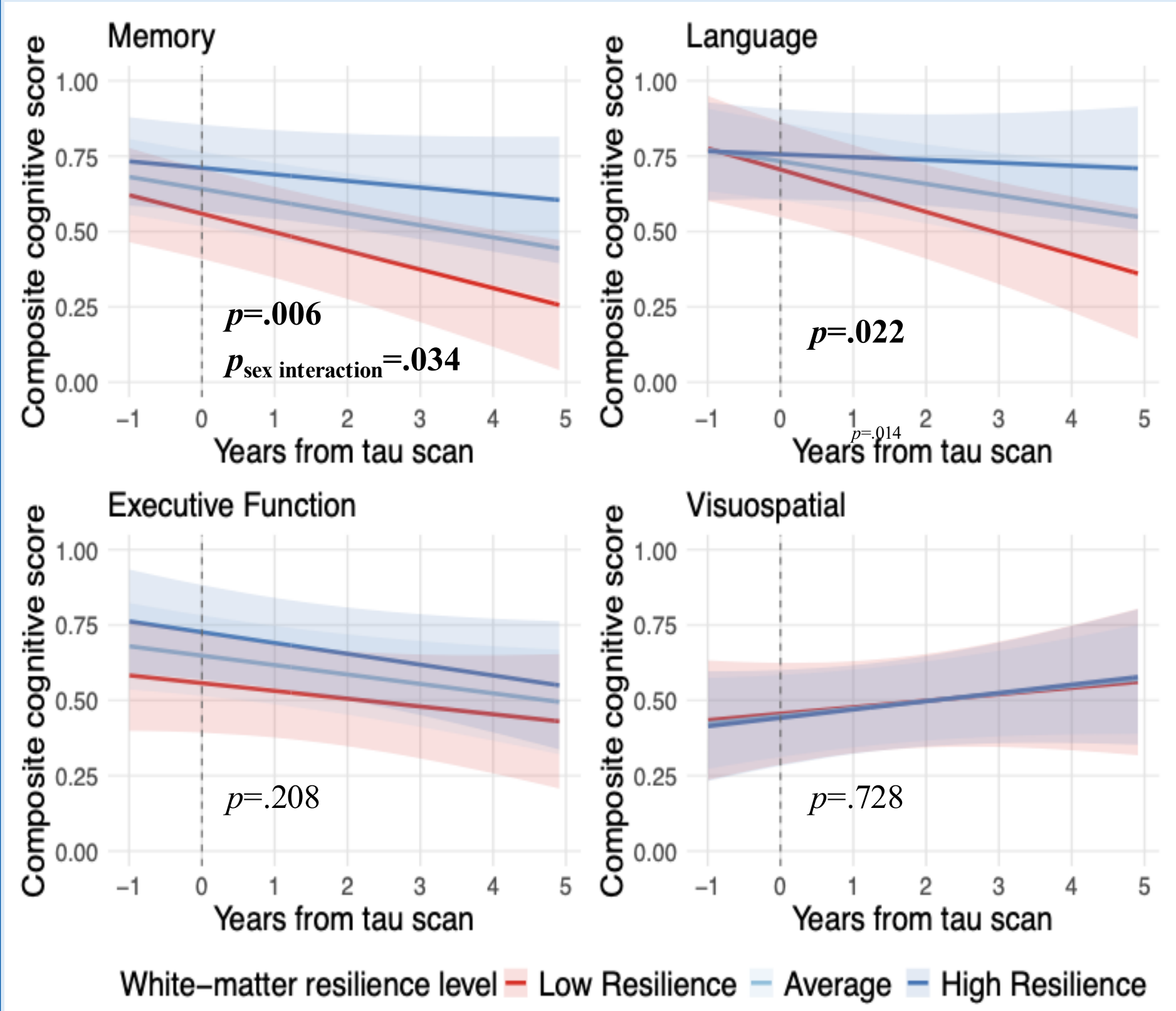


Grey-matter residuals to tau

- No association with white-matter resilience

1. b) Cognitive decline over time

- White-matter resilience** to tau was associated with slower **memory** and **language** decline

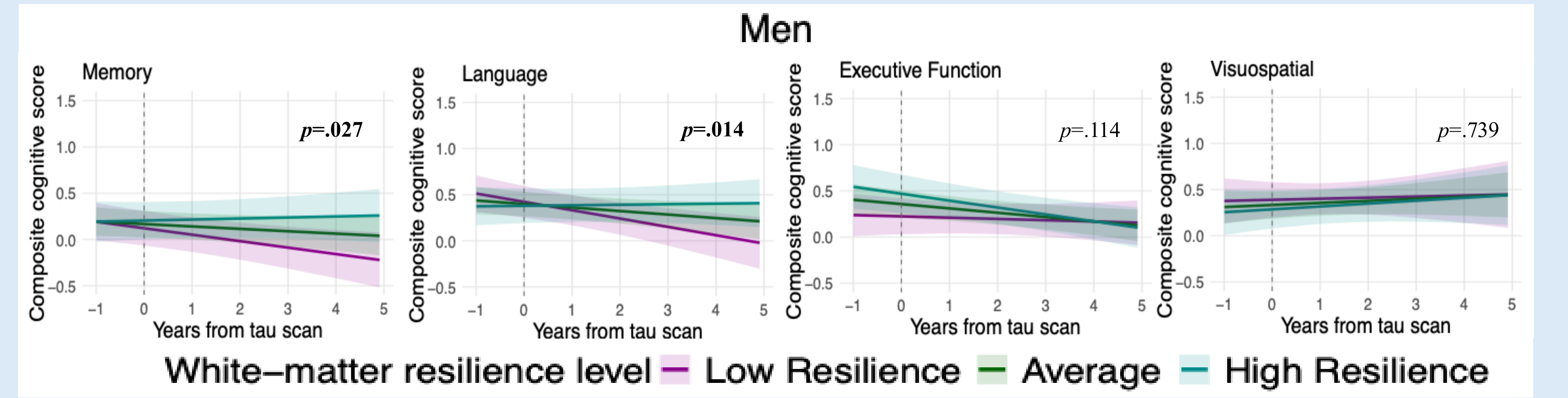


White-matter resilience level — Low Resilience — Average — High Resilience

- No association with grey-matter resilience

2. Sex differences

Men



White-matter resilience level — Low Resilience — Average — High Resilience

- Both **grey- and white-matter resilience to tau** were more strongly associated with **better cognitive performance** (sex interaction in executive function and visuospatial domains) and **slower decline** (memory and language in sex-stratified models) in **men**.

CONCLUSIONS

- Important to include measures of white-matter resilience, as it appears more sensitive to early cognitive changes in AD
- The effect of sex on the link between brain resilience and cognitive outcomes might help to understand sex differences in AD clinical progression

CONTACT AND REFERENCES

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