

# Early Parallel Increases But Spatial Uncoupling Of Cortical Iron And Amyloid- $\beta$ Burden Across The Alzheimer's Disease Continuum

Yiren Fan, Xiaodi Xie, Yingzhe Wang, Rui Li, Tongyao You, Shufen Chen, Jintai Yu, Mei Cui

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- Cortical QSM elevations emerge with amyloid positivity, supporting an A $\beta$ -positive disease-context signal.
- Regional QSM is more restricted and does not mirror A $\beta$  deposition, arguing against QSM as a local amyloid readout.

## INTRODUCTION

A $\beta$  defines the biological context of AD, but it does not fully explain regional vulnerability. QSM offers an MRI marker of iron-sensitive susceptibility.

### Study question

Does cortical QSM simply track A $\beta$ , or mark a spatially distinct susceptibility axis?

## METHODS

- **n = 697** memory-clinic participants
- **A/T groups:** Normal CU, Preclinical AD, MCI due to AD, AD dementia
- **A $\beta$  burden:** global Centiloids and ROI-level cortical maps
- **QSM:** voxel-weighted mean in 68 DK cortical ROIs
- **Spatial test:** ROI-level QSM-A $\beta$  vectors with ROI-wise FDR correction
- **Models:** adjusted for age and sex; amyloid PET also adjusted for tracer

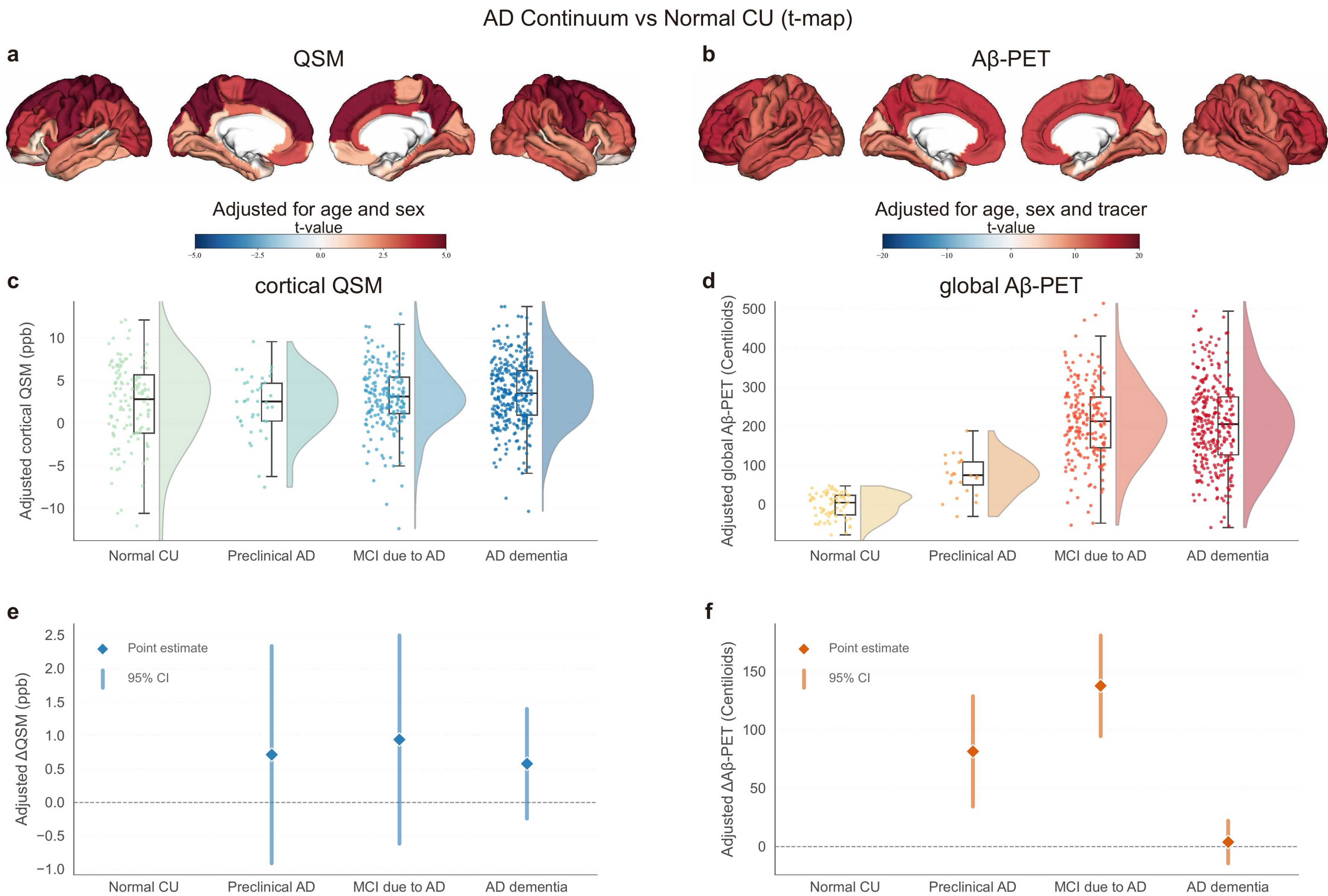
### Stage definitions

A-T- CU: 134  
A+T- Preclinical AD: 40  
A+T+ MCI due to AD: 200  
A+T+ AD dementia: 323

Interpretive guardrail  
the test is not whether QSM replaces A $\beta$ -PET. The question is whether QSM behaves as a local A $\beta$  surrogate or a distinct susceptibility signal.

## RESULTS

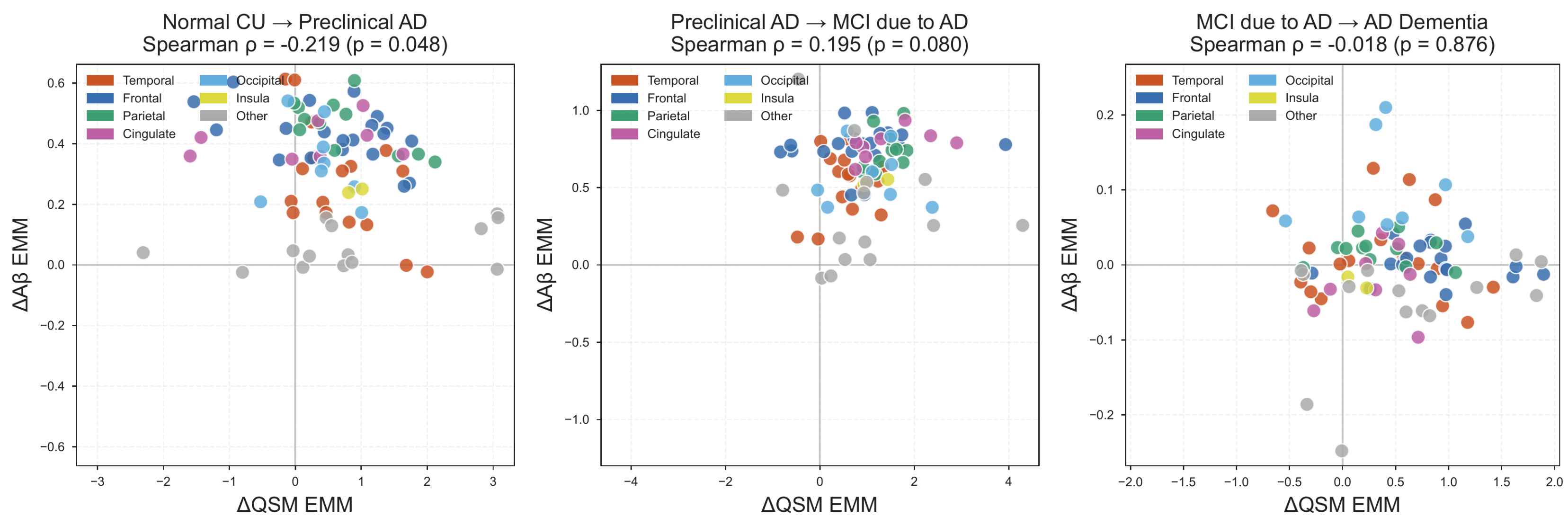
Fig. 1 | A $\beta$  rises broadly, whereas cortical QSM elevations are more regionally restricted



Surface maps compare each AD-continuum group with Normal CU; raincloud and estimation plots show adjusted distributions and adjacent-stage contrasts.

Reading of Fig. 1: A $\beta$  burden increases sharply and broadly; mean cortical QSM also rises with A $\beta$  positivity, but the cortical map is more restricted.

Fig. 2 | Adjacent-stage  $\Delta$ QSM shows weak and inconsistent spatial concordance with  $\Delta$ A $\beta$



QSM emerges with A $\beta$  positivity, but is not a local A $\beta$  readout.

## CONCLUSIONS

- **Amyloid-stage relevance:** cortical QSM elevations are detectable in an amyloid-positive disease context.
- **Topographic independence:** QSM elevations do not spatially mirror regional A $\beta$  deposition.
- **Biomarker implication:** QSM should not be interpreted as a direct spatial surrogate of amyloid PET.

### Cautious hypothesis

QSM may mark a spatially constrained susceptibility state beyond A $\beta$  topography.

Poster-level message  
Same amyloid disease context.  
Different cortical geography.

## REFERENCES

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## CONTACT



Scan QR for poster details  
Presenter: Yiren Fan  
Huashan Hospital, Fudan University  
Poster code:  
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