

## 1. Background

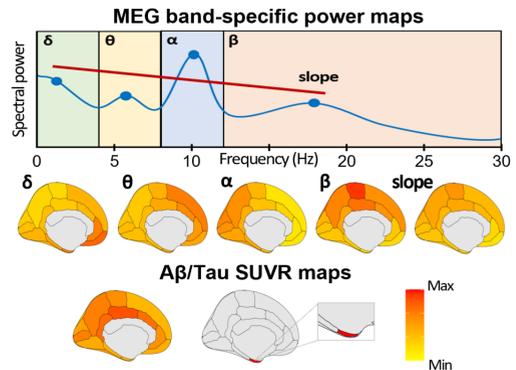
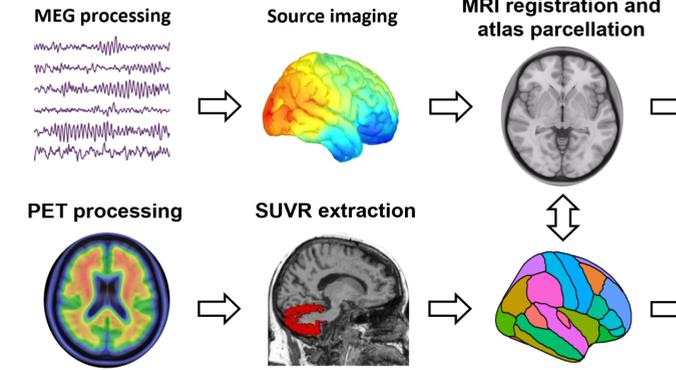
- Animal studies have shown that amyloid-beta (Aβ) is associated with neuronal hyperexcitability, while tau leads to neuronal hypoactivity (Busche et al, 2020).
- It remains unknown whether analogous changes can be detected non-invasively in the human brain during the preclinical phase of Alzheimer's disease (AD) (Maestú et al, 2020).

## 2. Study aim

- We studied the neurophysiological (MEG) changes associated with the early deposition of Aβ and tau (PET) in asymptomatic older adults with familial history of AD and addressed its implications for longitudinal cognitive performance.

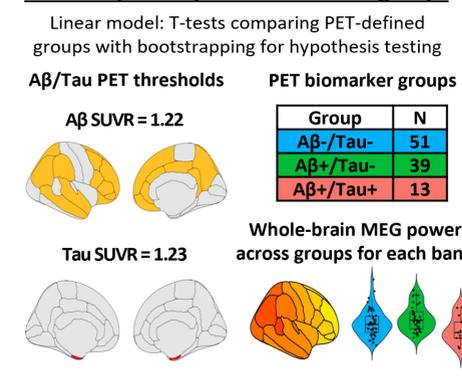
## 3. Methods

### Neuroimage data processing

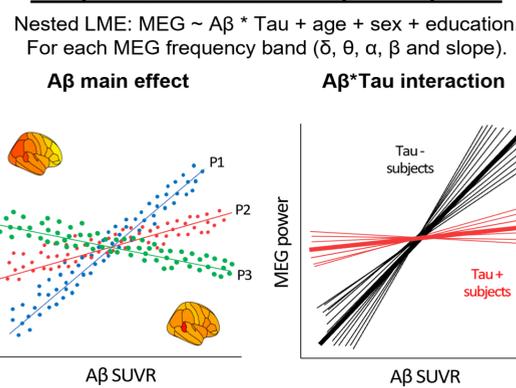


PREVENT-AD characteristics (N = 104)	
Age in years	67.4 (4.9)
Female % (n)	71.1 (74)
Years of education	15 (3.1)
Whole-brain Aβ SUVR	1.35 (0.35)
Entorhinal cortex tau SUVR	1.07 (0.14)
MMSE baseline score	28.8 (1.2)
RBANS Global cognition (slope)	-0.17 (2.43)
RBANS Immediate mem (slope)	-0.10 (3.15)
RBANS Delayed mem (slope)	0.89 (2.51)
RBANS Attention (slope)	-0.10 (2.85)

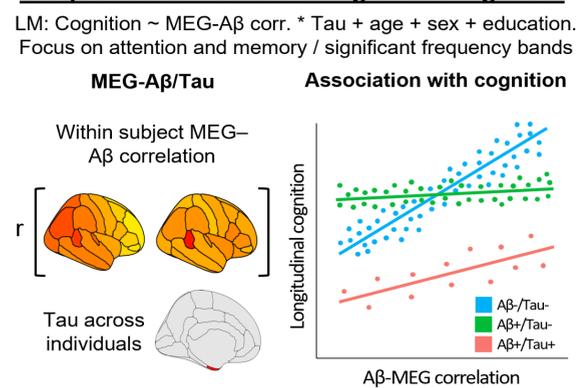
### A. MEG spectral power across PET groups



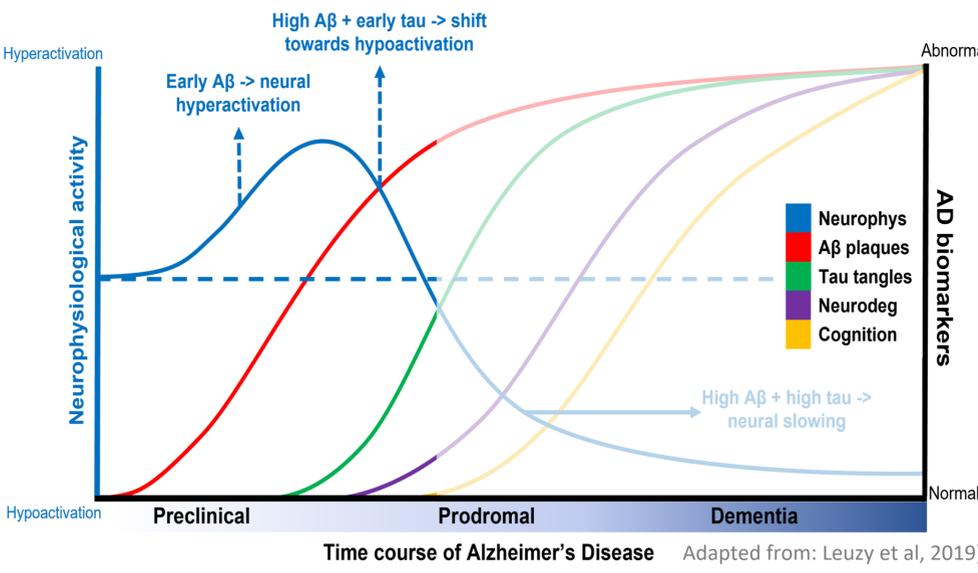
### B. Aβ/Tau effect on MEG spectral power



### C. Aβ/Tau related MEG changes and cognition

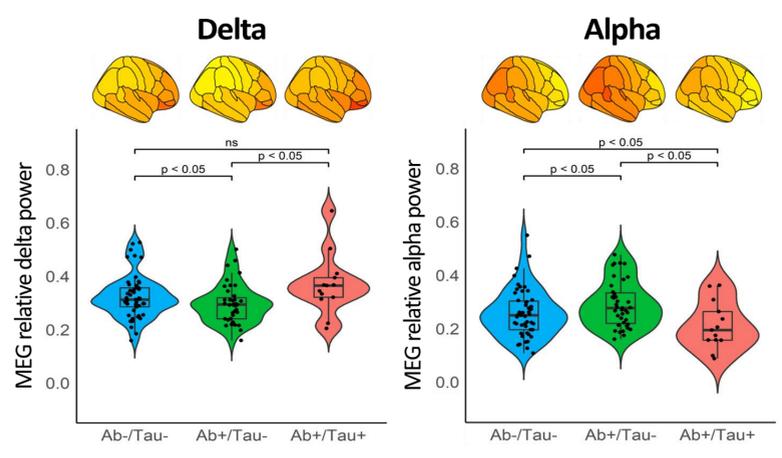


## Expected neurophysiological changes across the AD continuum

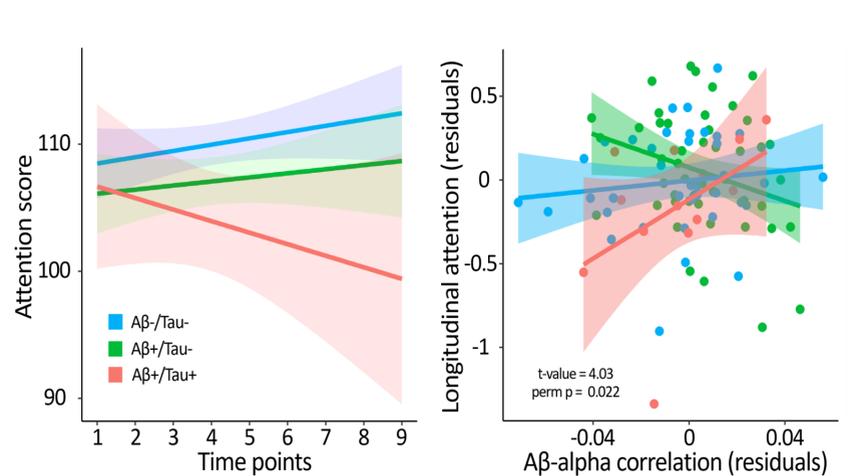


## 4. Results

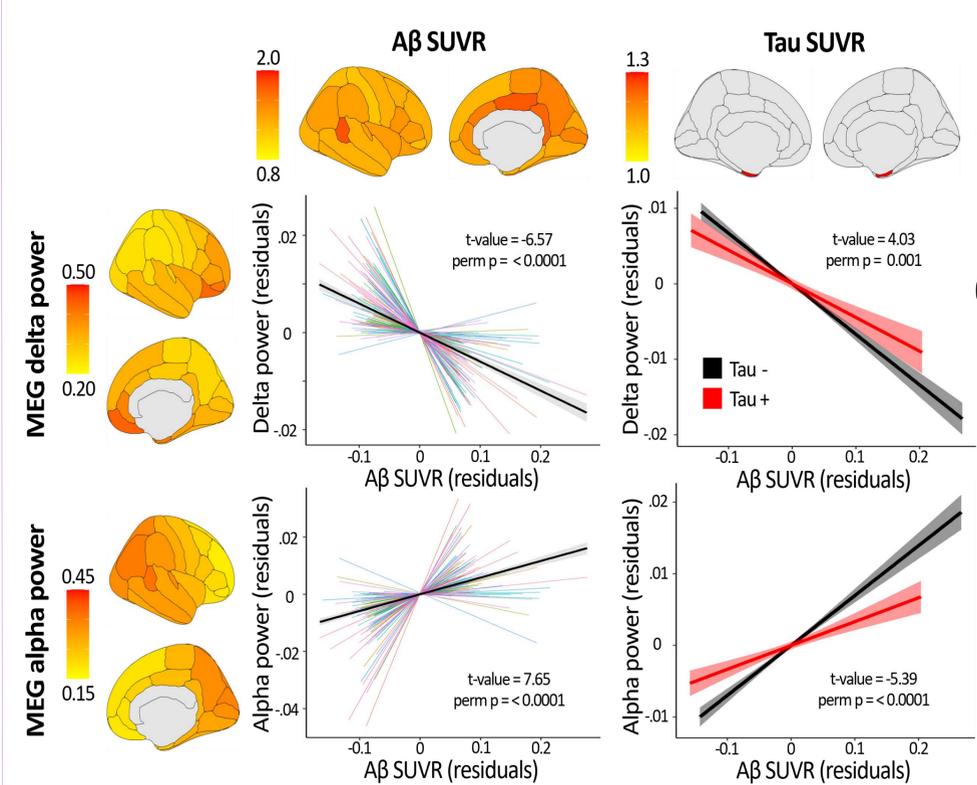
### A. Aβ+/Tau- group showed neural hyperactivity, while Aβ+/Tau+ displayed a shift towards hypoactivity



### C. The shift in the Aβ-MEG relation in high tau individuals was associated with longitudinal attentional decline



### B. LME models corroborated the Aβ induced hyperactivity, and the tau-related shift towards hypoactivity



## 5. Conclusion

- Aβ was associated with neural hyperactivity, while tau led to a shift towards neural hypoactivity that related to longitudinal decline in attentional scores.
- These early detectable neurophysiological changes may represent non-invasive biomarkers of the preclinical stages of AD (Maestú et al, 2020).

## 6. Acknowledgements



### References

Busche, M. A., & Hyman, B. T. (2020). Synergy between amyloid-β and tau in Alzheimer's disease. *Nature Neuroscience*, 23(10), 1183–1193.

Leuzy, A., Chiotis, K., Lemoine, L., Gillberg, P. G., Almkvist, O., Rodriguez-Vieitez, E., & Nordberg, A. (2019). Tau PET imaging in neurodegenerative tauopathies—still a challenge. *Molecular Psychiatry*, 24(8), 1112–1134.

Maestú, F., Cuesta, P., Hasan, O., Fernández, A., Funke, M., & Schulz, P. E. (2019). The importance of the validation of M/EEG with current biomarkers in Alzheimer's disease. *Frontiers in Human Neuroscience*, 13(17), 1–10.