

1 Introduction

- Probabilistic Model of Alzheimer's Disease (AD) (Frisoni et al., 2022): amyloid and tau can be modulated by stochastic and genetic factors, especially APOE ϵ 4.
- Soluble triggering receptor expressed on myeloid cells 2 (sTREM2) and glial fibrillary acidic protein (GFAP) are thought to play an important role in AD pathophysiology.

Neuroprotective?

Neurotoxic?

Research question

How are CSF TREM2 and GFAP associated with AD pathology, and are these association different across APOE ϵ 4 carriership?

2 Methods

Data from the Alzheimer's Disease Neuroimaging Initiative database (ADNI) database
Biomarkers measured in CSF (Roche ECLESYS and SomaScan Proteomics)

Sample n=728, Longitudinal subsample n=265

a

Pseudotime analysis to estimate sTREM2/GFAP levels across AD pathology course

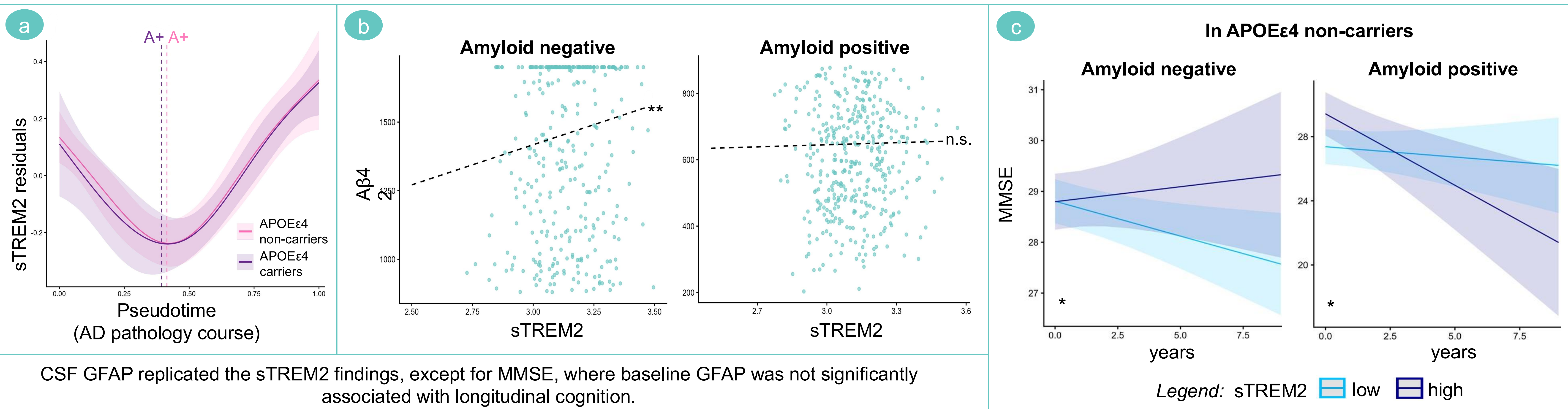
b

Cross-sectional sTREM2/GFAP associations with AD pathology and cognition

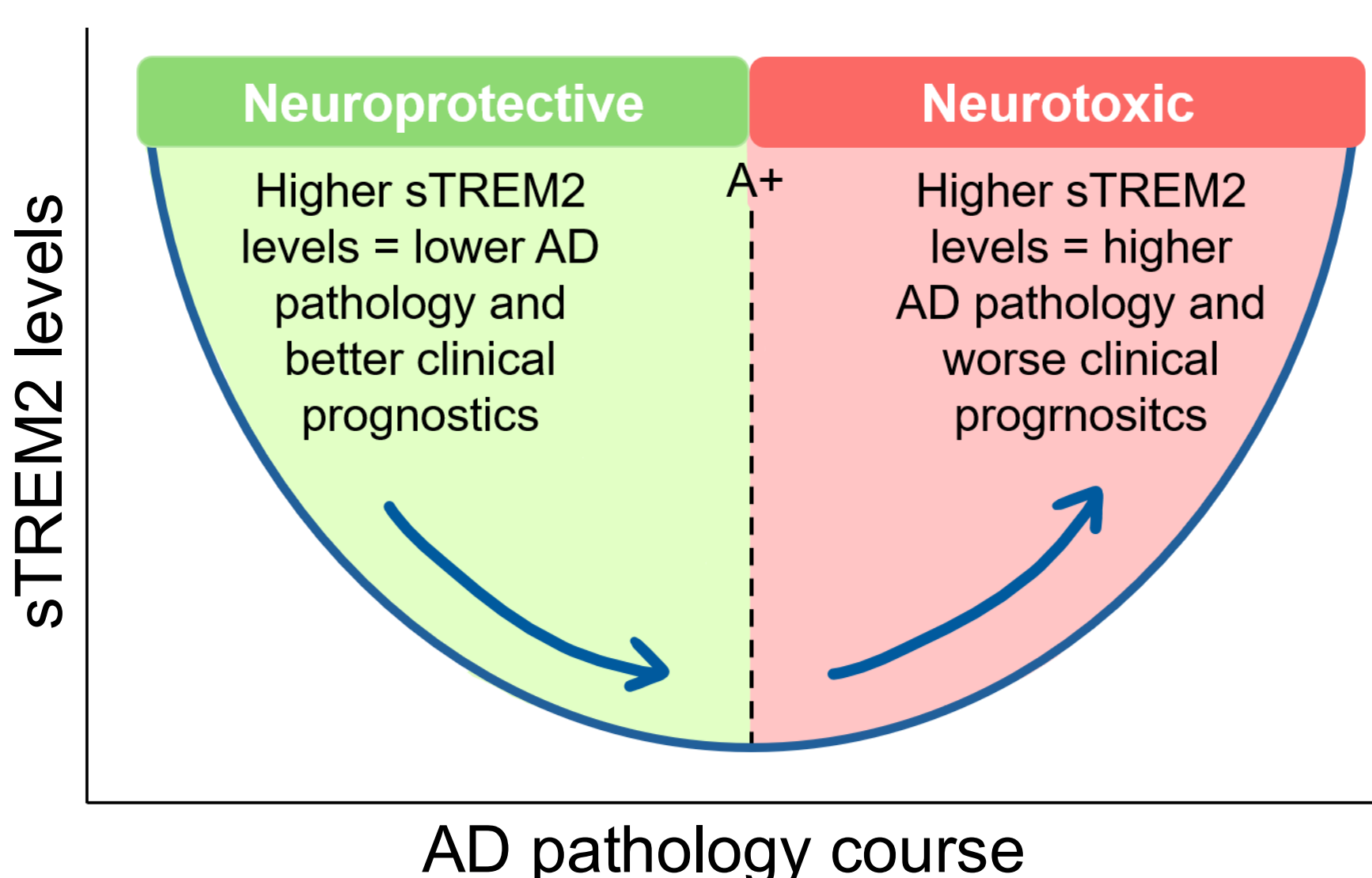
c

Baseline sTREM2/GFAP as a longitudinal predictor of AD pathology and cognition

3 Main Results



4 Conclusions



- sTREM2 and GFAP follow a dual-wave pattern, with elevated levels observed in both early and later disease stages.
- Early high concentrations appear neuroprotective, whereas later increases may become neurotoxic.
- Although APOE ϵ 4 does not influence sTREM2 trajectories, the stage-dependent predictive effects of sTREM2 on cognitive decline are evident only in APOE ϵ 4 non-carriers.

Take Home message

sTREM2 is predictive of cognitive decline in the absence of strong genetic risk. APOE ϵ 4 carriers present cognitive decline regardless of sTREM2, suggesting that they follow a more deterministic AD pathology course.

5 Reference and Affiliations

Frisoni, G. B., Altomare, D., Thal, D. R., Ribaldi, F., Van Der Kant, R., Ossenkoppele, R., Blennow, K., Cummings, J., Van Duijn, C., Nilsson, P. M., Dietrich, P.-Y., Scheltens, P., & Dubois, B. (2022). The probabilistic model of Alzheimer disease: The amyloid hypothesis revised. *Nature Reviews Neuroscience*, 23(1), 53-66. <https://doi.org/10.1038/s41583-021-00533-w>

¹ Laboratory of Neuroimaging of Aging (LANVIE), University of Geneva, Geneva, Switzerland.

² Geneva Memory Center, Department of Rehabilitation and Geriatrics, Geneva University Hospitals, Geneva, Switzerland.

Contact:

augusto.martinsmendes@unige.ch
kamila.kocher@etu.unige.ch