

Astrocyte-PET in Alzheimer's Disease Amyloid Cascade: Results from The ASTEROID Cohort

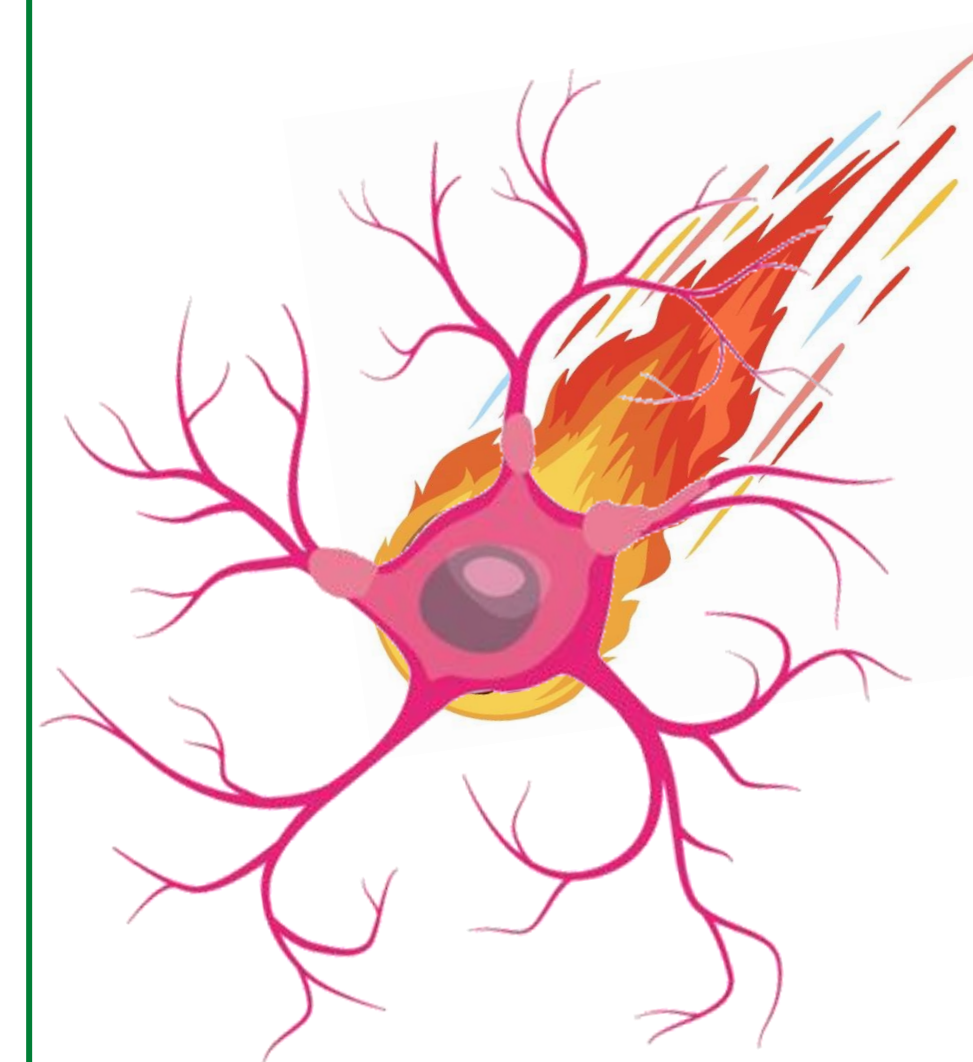
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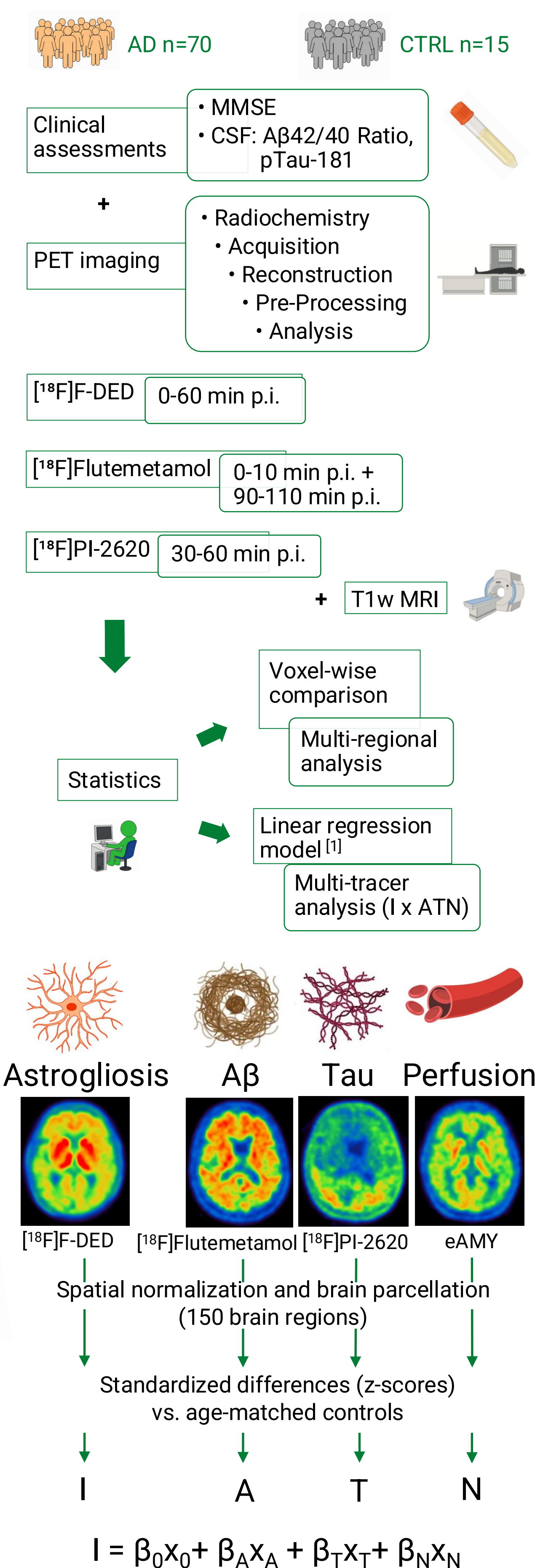
INTRODUCTION

■ Neuroinflammation is increasingly recognized as a hallmark in neurodegenerative diseases like Alzheimer's disease (AD), complementing the staging of cognitive decline, functional impairment and pathological aggregation of β -amyloid and tau

■ This study investigates the spatiotemporal dynamics of **reactive astrogliosis**, captured by the novel MAO-B specific radiotracer [¹⁸F]Fluorodeprenyl-D2 ([¹⁸F]F-DED), across clinical AD stages and in relation to β -amyloid and tau pathology

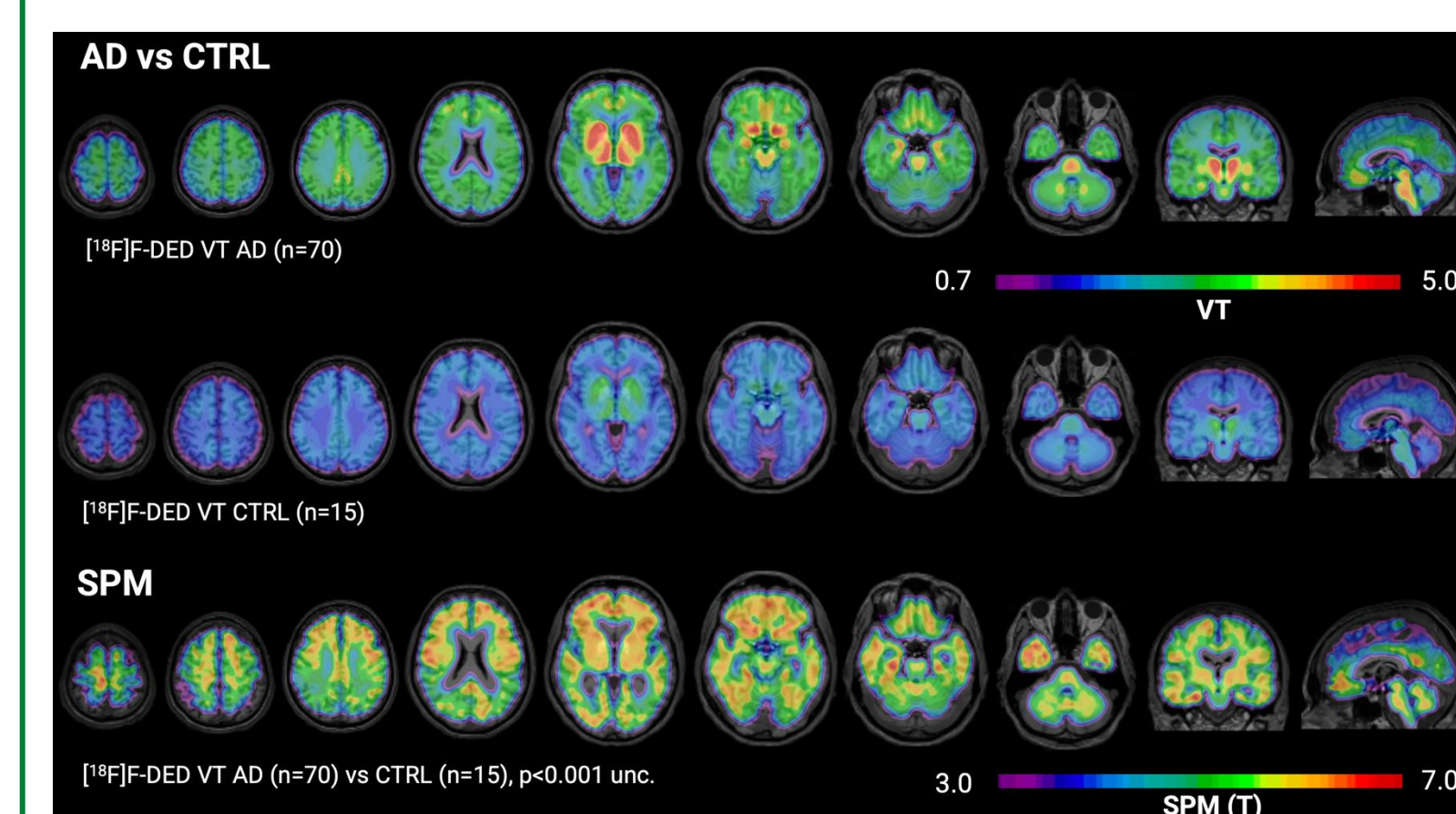


METHODS

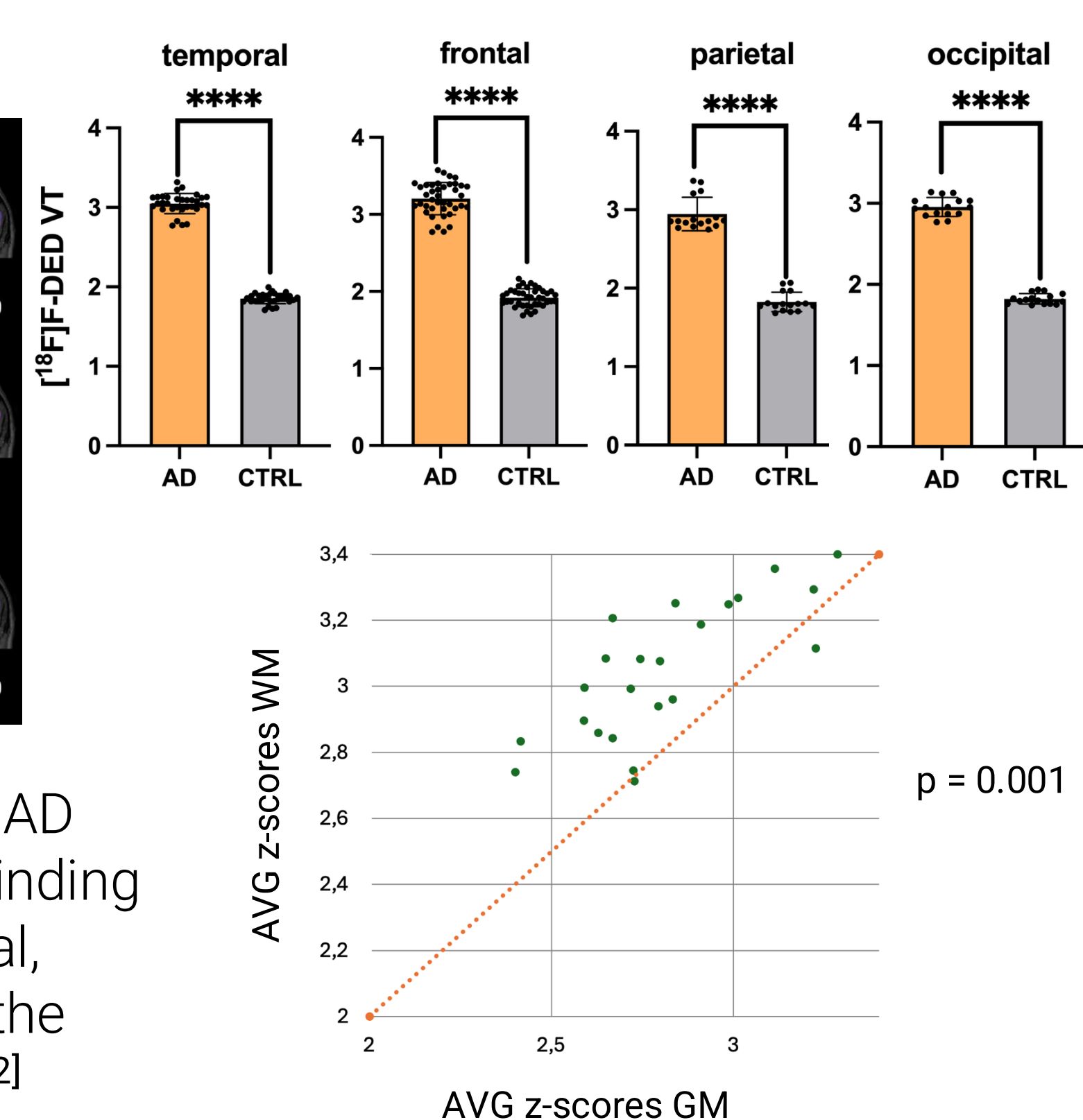


RESULTS

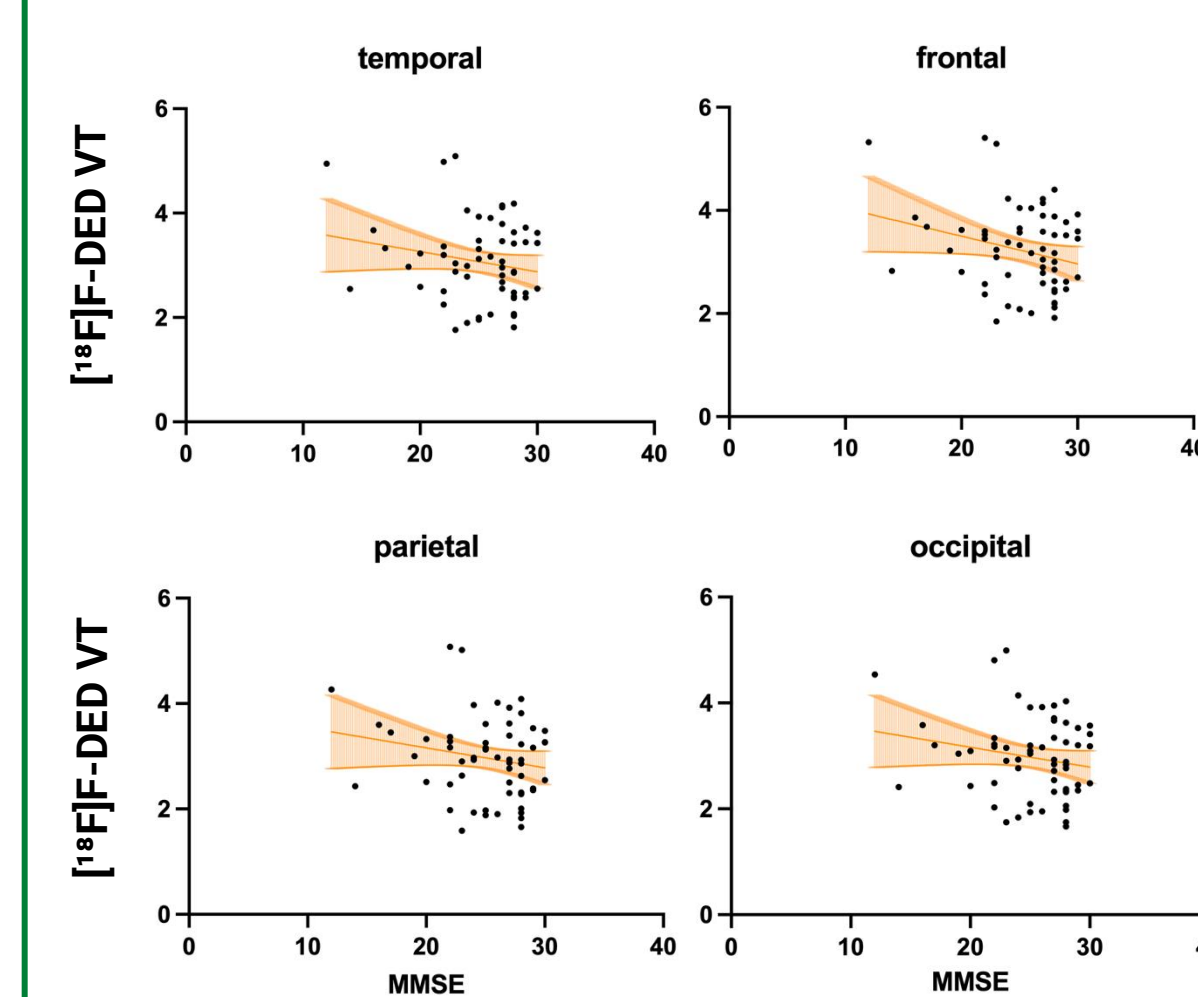
I) [¹⁸F]F-DED PET



■ Compared with controls, individuals of the AD continuum showed significant [¹⁸F]F-DED binding in cortical regions including frontal, temporal, parietal and occipital areas, pronounced in the **white matter** in contrast to the grey matter [2]

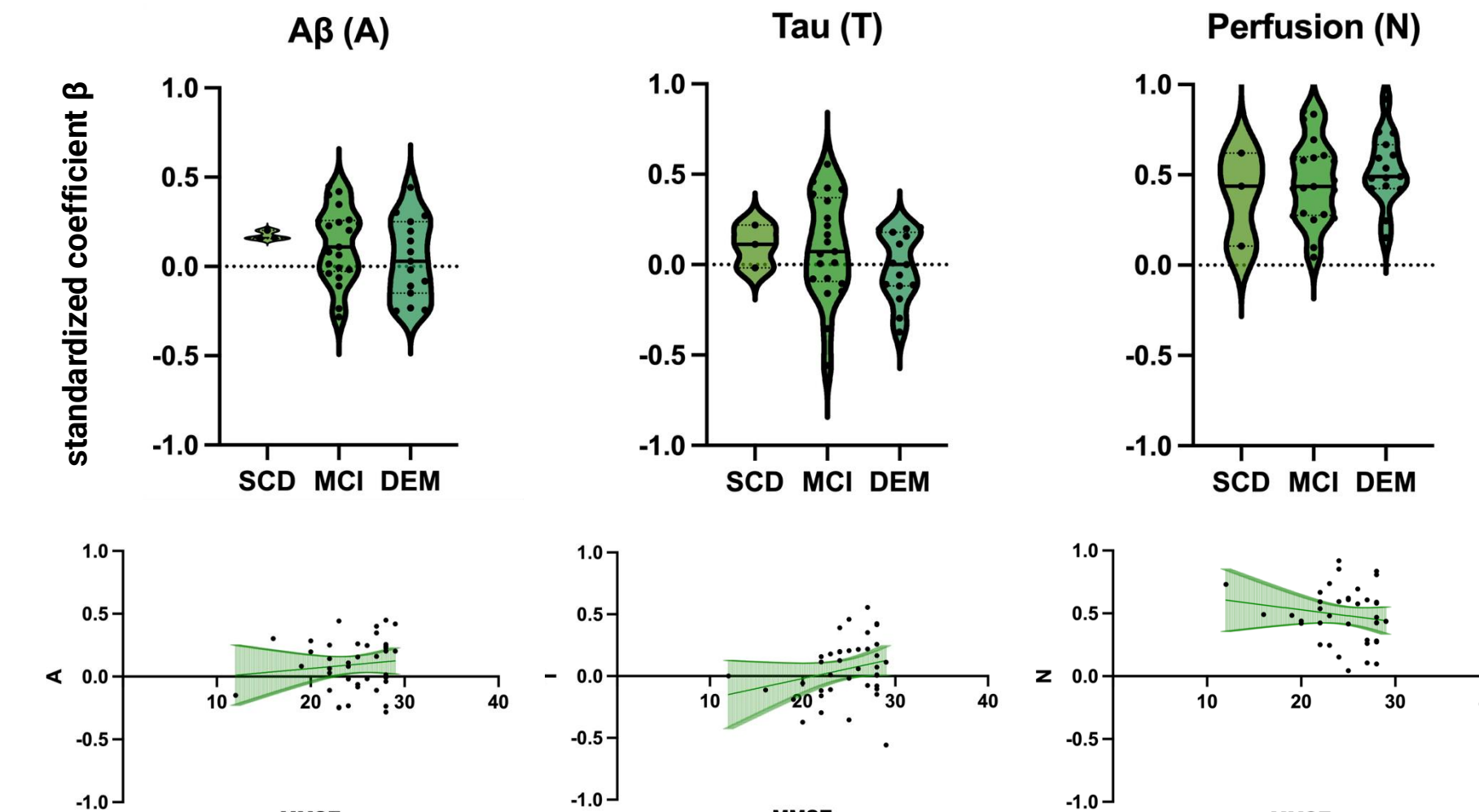


II) [¹⁸F]F-DED PET vs MMSE



■ No significant association was observed between regional [¹⁸F]F-DED binding and cognitive performance measured by the MMSE, although highest tracer uptake was frequently present in the **early-stage** individuals

III) ATNI Regression



■ Multivariable regression analyses revealed a **positive** association between astrocyte activation and regional **amyloid** burden, while **negative** associations with regional **tau** burden were more prominent in later disease stages

■ Astrocyte PET signals showed a consistent **positive** relationship with regional **perfusion**, suggesting a potential link between reactive astrogliosis and neuronal hyperactivity

CONCLUSIONS

- [¹⁸F]F-DED PET demonstrates:
 - significantly higher binding in patients of the AD continuum
 - increased VT values as early as initial stages
 - subcortical white matter prevalence in binding differences
- Astrocyte activation closely relates to regional perfusion and amyloid pathology, while its association with tau deposition appears stage-dependent
- These findings support [¹⁸F]F-DED PET as a promising biomarker of reactive astrogliosis and highlight a potential role of astrocytes in early pathophysiological mechanisms of AD

REFERENCES

- 1 Finze A, et al., *Individual regional associations between Aβ-, tau- and neurodegeneration (ATN) with microglial activation in patients with primary and secondary tauopathies.* Mol Psychiatry. 2023. **28**(10): 4438-4450.
- 2 Jaisa-Aad M, et al., *Characterization of monoamine oxidase-B (MAO-B) as a biomarker of reactive astrogliosis in Alzheimer's disease and related dementias.* Acta Neuropathol. 2024. **147**(1):66.