

Disruption of Multivoxel Representations Underlying Mnemonic Discrimination in Preclinical Alzheimer's Disease

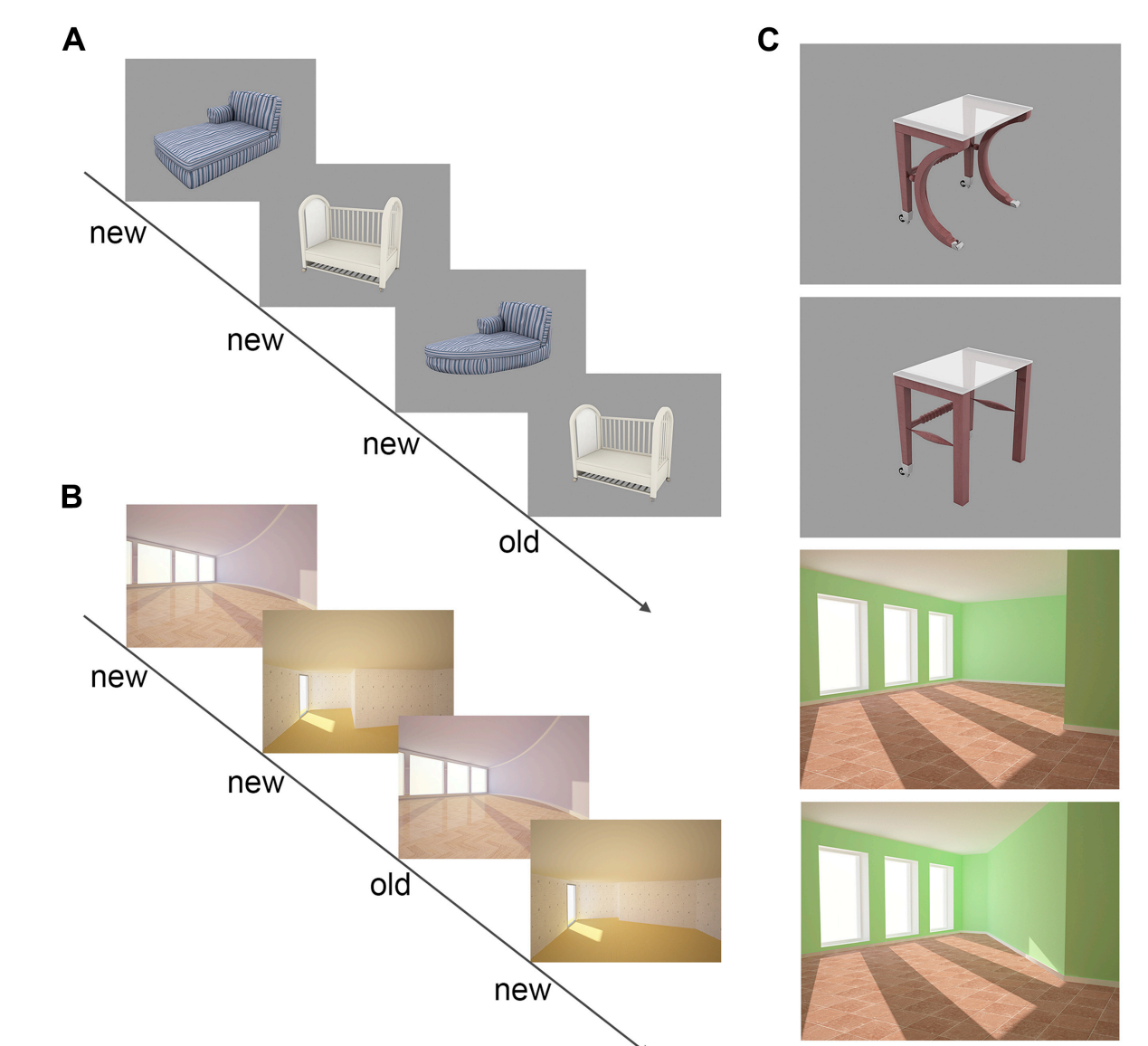
Loris Naspi¹, Helena M Gellersen¹, Anja Schneider^{2,5}, Annika Spottke^{7,8}, Frederic Brosse³, Stefan Teipel^{8,9}, Jens Wiltfang^{10,11,12}, Frank Jessen^{13,14,15}, Emrah Düzel^{1,16,17,18}, and David Berron¹

Background

- Alzheimer's disease pathology accumulates years before memory symptoms emerge.
- Early pathology affects medial temporal lobe regions that support episodic memory.
- Pattern separation** supports discrimination of highly similar memories¹.
- Multivariate fMRI can detect subtle changes in neural representations that may precede cognitive impairment.
- Aim:** Test whether amyloid-positivity alters neural representations supporting mnemonic discrimination in cognitively unimpaired individuals.

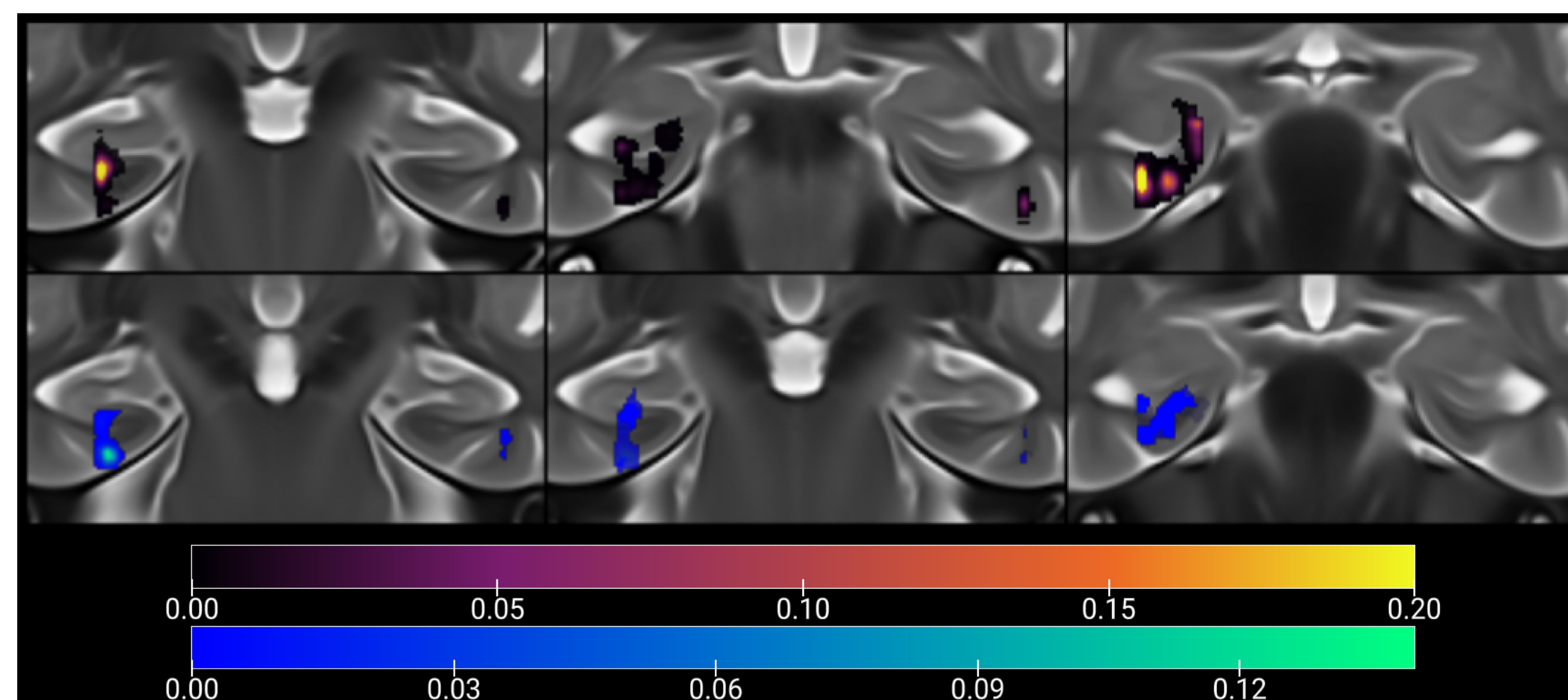
Methods

- 73 cognitively unimpaired older adults (DELCODE, 50 A β - and 23 A β +
- Amyloid status:** CSF A β 42/40 ratio.
- Plasma p-tau217** at baseline.
- 3T fMRI** during mnemonic discrimination task.
- Whole-MTL searchlight analysis



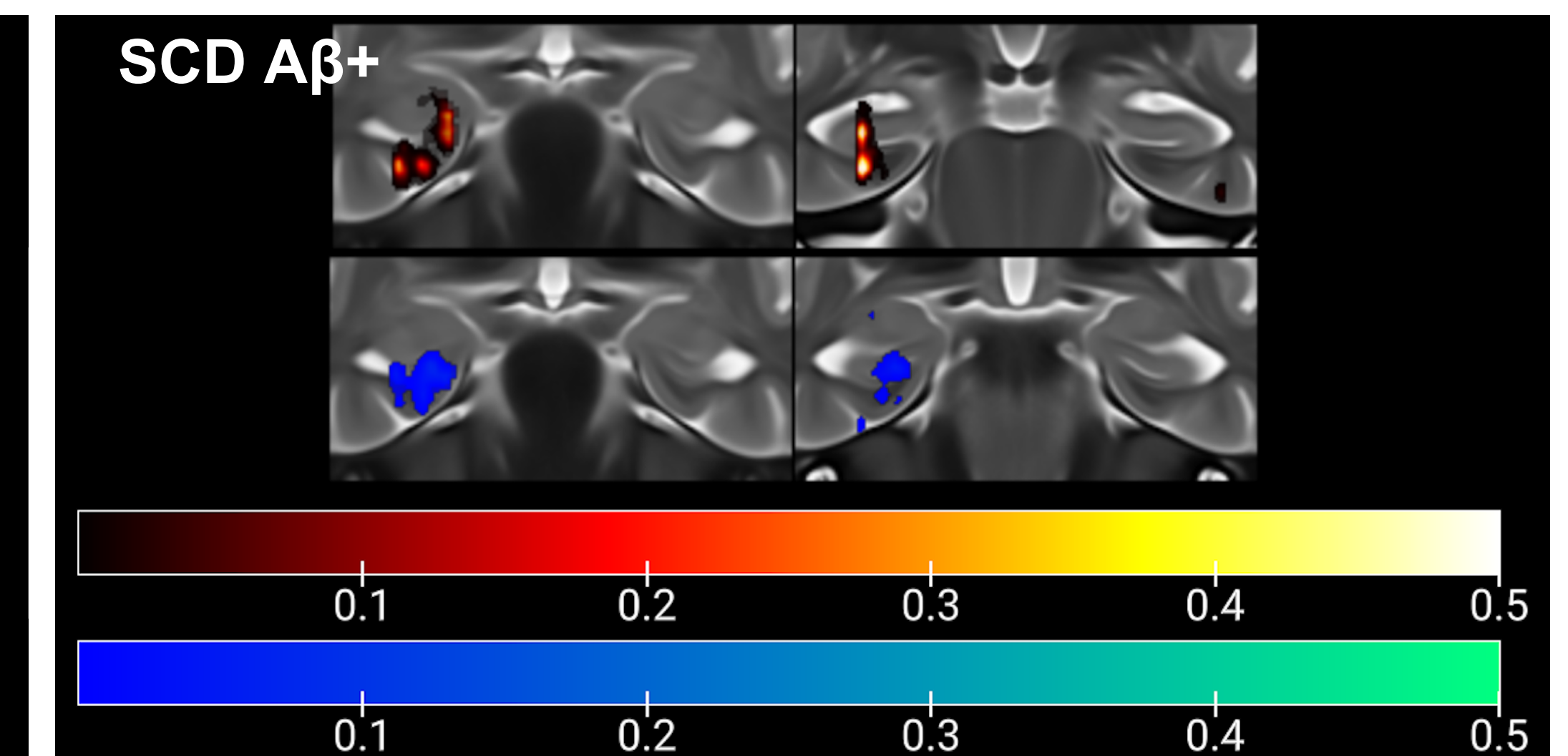
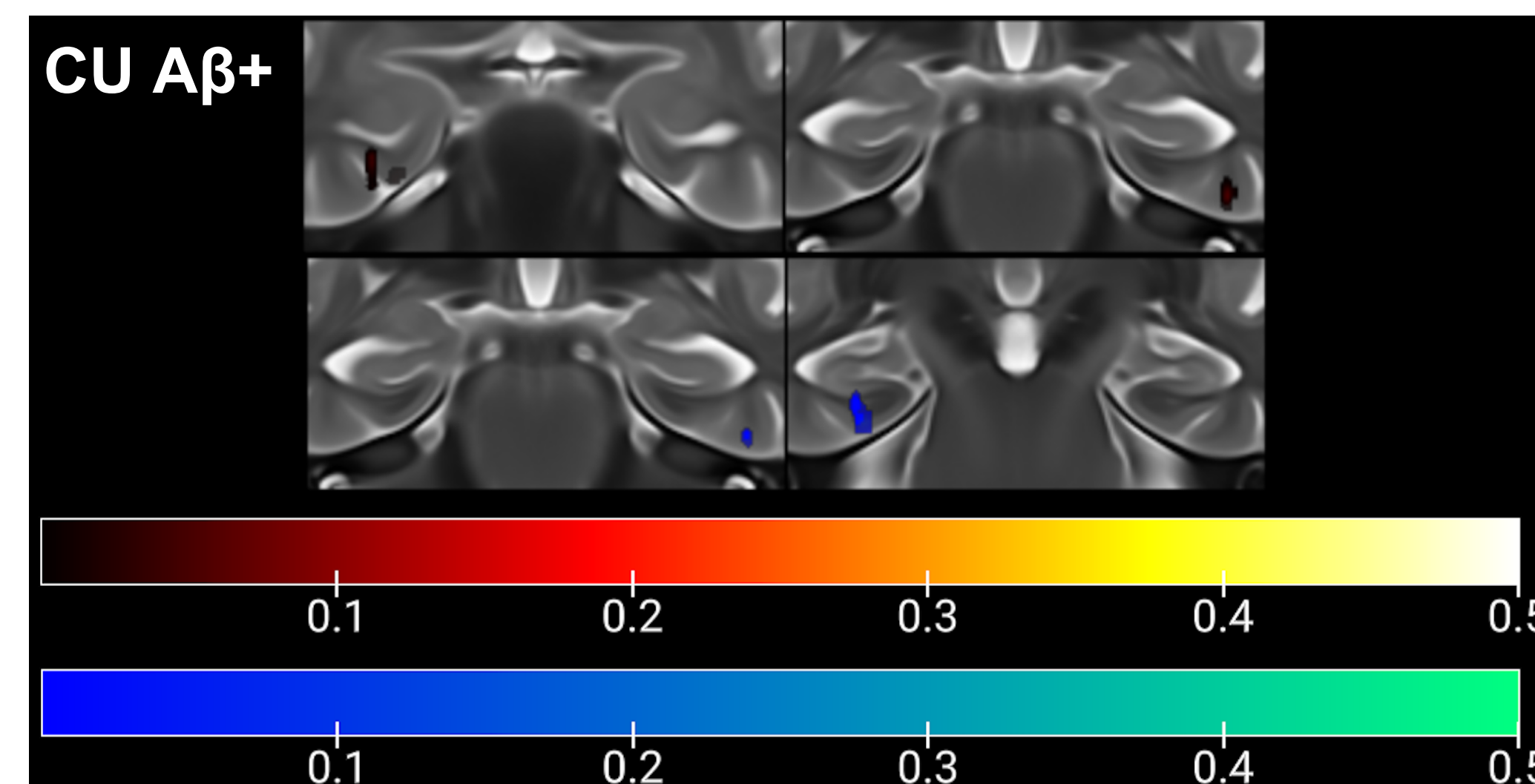
Preclinical AD is characterized by disrupted representations in the MTL

A β + show increased representational similarity compared to A β -



Bilateral ERC, BA35, BA36, and CA1-subiculum transition area

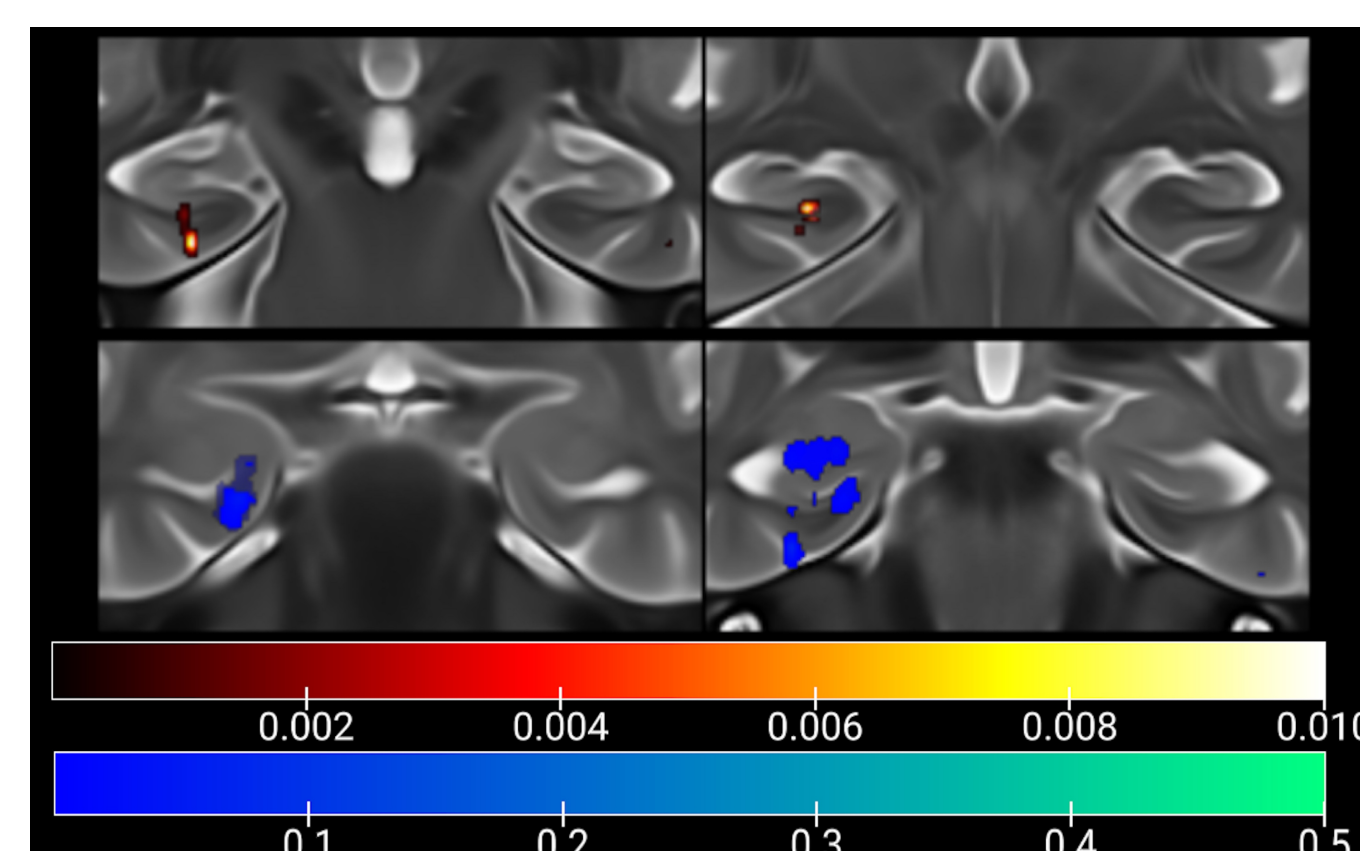
Impairment was confined to extrahippocampal regions in CU A β + with additional involvement of the hippocampus in SCD A β +



Across CU and SCD, higher baseline plasma p-tau217 was associated with disrupted memory representations in both extra-hippocampal and hippocampal regions.

Longitudinal representational decline

Individuals with higher baseline p-tau217 showed steeper decline in memory representations over 24-months in the same regions



Conclusion

- Amyloid positivity is associated with disrupted multivoxel memory representations in cognitively unimpaired individuals preceding cognitive impairment.
- Higher baseline p-tau217 predicts greater longitudinal decline of these representations.
- Multivariate fMRI may provide a sensitive marker of early AD-related neural dysfunction, even when overall memory performance is similar.