



Verbal recognition declines in later PET-Braak Stages as compared to verbal delayed recall



Translational Neuroimaging Laboratory

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1. Introduction

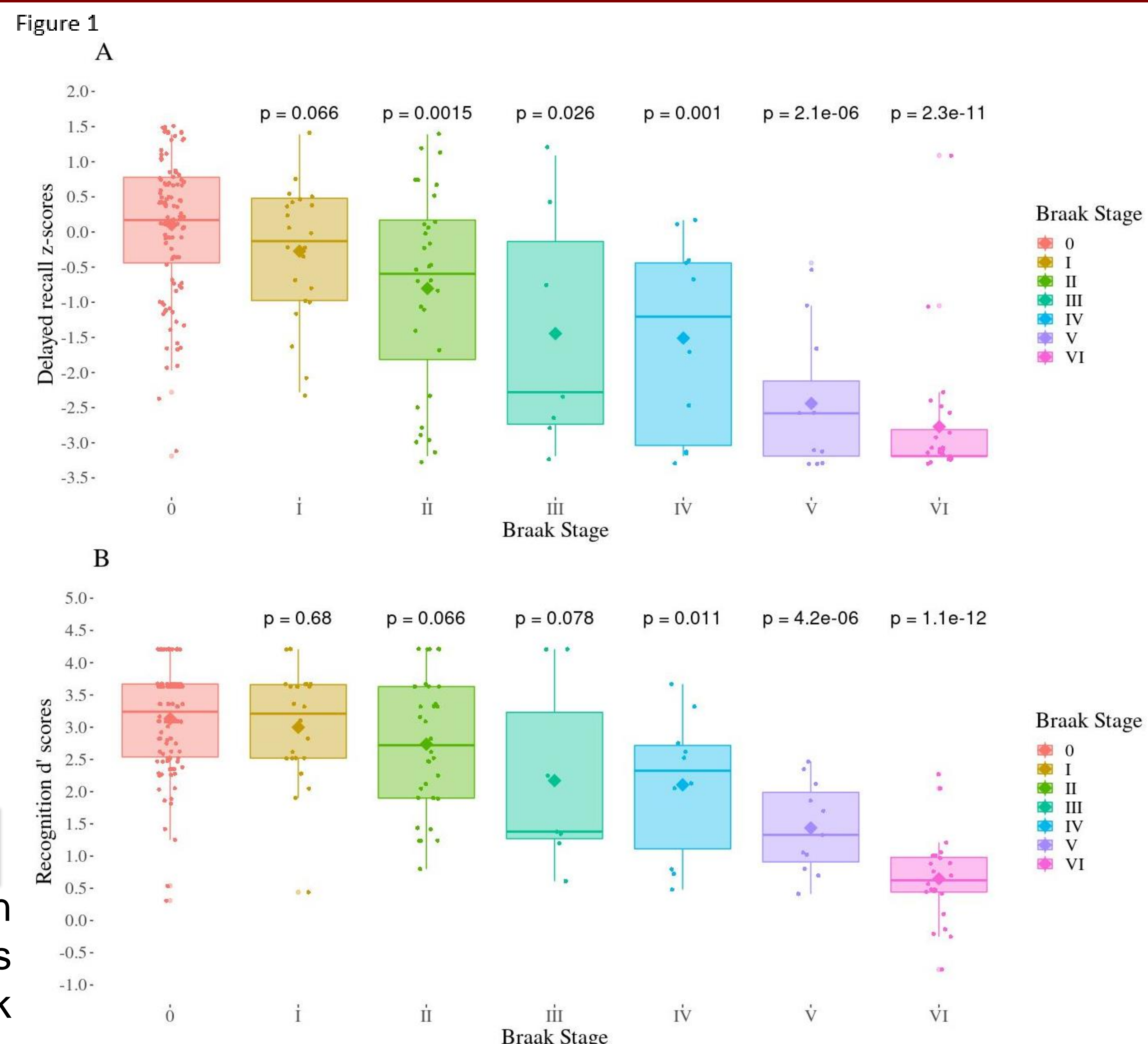
Cerebral amyloid- β plaques and neurofibrillary tangles are the neuropathological hallmarks of Alzheimer's disease, which accumulate decades prior to clinical dementia onset. Possibly the earliest cognitive sign of Alzheimer's disease is episodic memory decline, which has been linked to the aggregation of tau in the medial temporal lobe. Delayed free recall and recognition tests represent two ways to test episodic memory, and there is substantial debate on how performance in both types of tests is differentially affected through health and disease in older adults.

2. Objective

We investigated delayed recall and recognition memory dysfunction across the Alzheimer's disease spectrum using *in vivo* PET-Braak staging.

3. Methods

We included 144 cognitively unimpaired elderly, 39 amyloid- β + individuals with mild cognitive impairment and 29 amyloid- β + Alzheimer's disease patients from the TRIAD cohort (Table 1), who underwent [¹⁸F]MK6240 tau and [¹⁸F]AZD4694 amyloid PET imaging, structural T1-MRI and episodic memory assessments. We applied nonparametric comparisons and voxel-wise analyses.



Delayed recall decline at PET-Braak stage II and recognition decline at PET-Braak Stage IV. Mean and median memory scores as assessed by *in vivo* tau PET. (A) RAVLT delayed recall z-scores. (B) RAVLT-derived discriminability d' (recognition) scores. Adjusted p-values are displayed for the comparison between individuals in Braak 0 and individuals in more advanced Braak stages. FDR correction for multiple comparisons was applied.

Table 1. Demographics

	CU	MCI	P value	AD	P value
No.	144	39	—	29	—
Age, y, mean (SD)	71.7 (5.9)	72 (5)	0.69	66.9 (8)	0.005
Female, no. (%)	95 (66)	26 (67)	0.94	17 (59)	0.45
Education, y, mean (SD)	15.4 (3.7)	15.7 (3.7)	0.59	14.8 (3.1)	0.38
APOE $\epsilon 4$ carriers, %	36 (25)	22 (56)	<0.001	17 (59)	<0.001
[¹⁸ F]AZD4694 SUVR	1.45 (0.34)	2.35 (0.48)	<0.001	2.51 (0.45)	<0.001

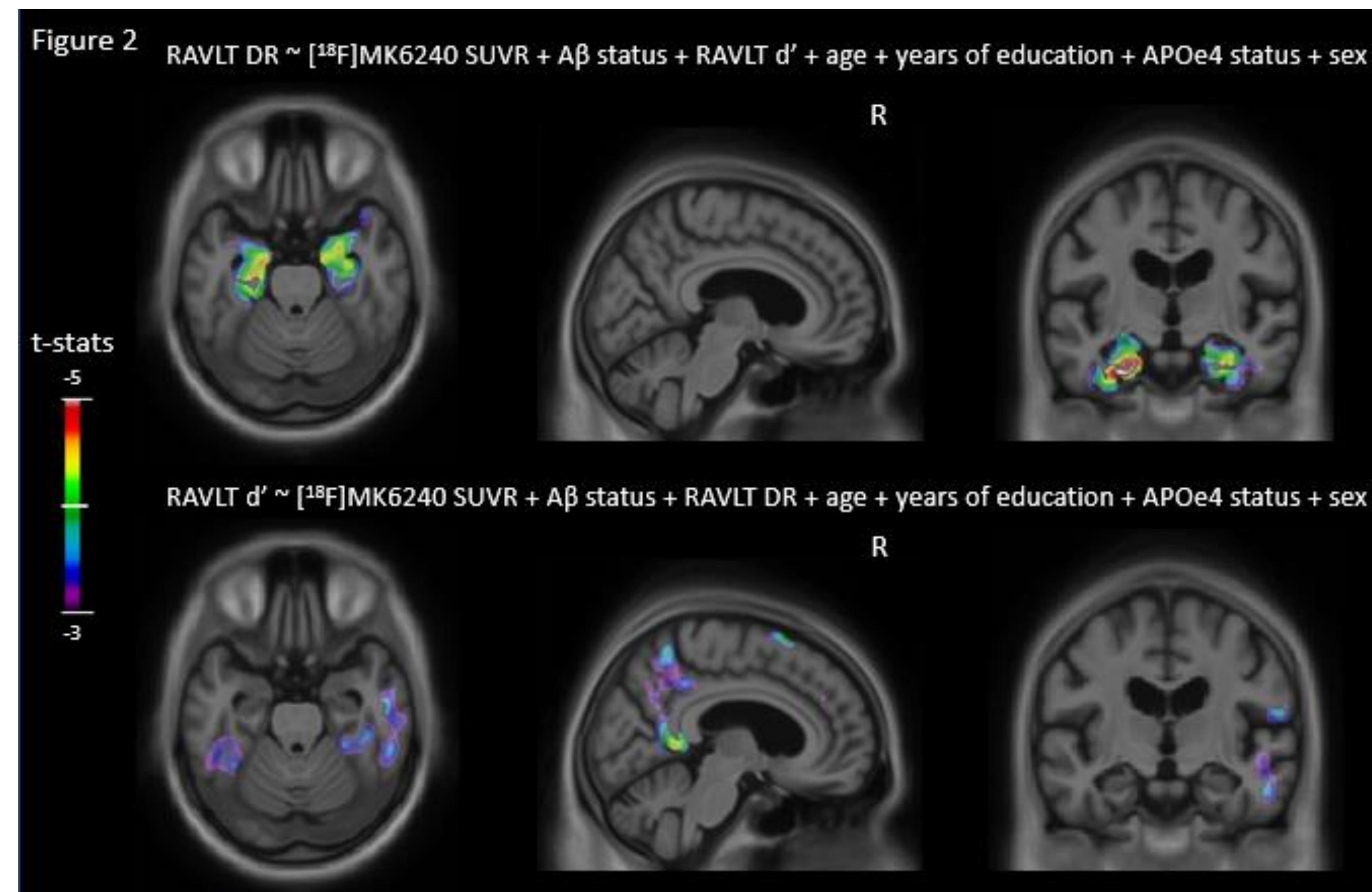
P values indicate values assessed with independent samples t tests for each variable except sex and APOE $\epsilon 4$ status, where contingency chi-square tests were performed (corrected with the Bonferroni procedure for multiple comparisons; significant if $p < 0.025$). P values reported are for comparisons with cognitively unimpaired subjects: the leftmost p values reflect comparisons between CU and MCI groups; the rightmost p values reflect comparisons between CU and AD groups. SUVR standardized uptake value ratio, CU cognitively unimpaired, MCI mild cognitive impairment, AD Alzheimer's disease.

4. Results

In comparison with PET-Braak stage 0, we found that reduced, but not clinically significant, delayed recall starts at PET-Braak stage II (Figure 1A), and that recognition displayed significant decline starting at PET-Braak stage IV (Figure 1B). Voxel-wise analyses revealed that delayed recall rendered stronger associations with tau PET in areas of early tau accumulation, whereas recognition displayed stronger correlations with tau PET in mostly posterior neocortical regions (Figure 2).

5. Conclusion

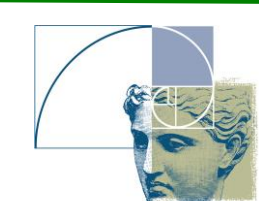
Our results support the notion that delayed recall and recognition deficits are predominantly associated with tau load in allocortical and neocortical areas, respectively. Overall, delayed recall seems to be more dependent on the integrity of anterior medial temporal lobe structures, while recognition appears to be more affected by tau accumulation in posterior neocortical regions.



Delayed recall scores are associated with tau deposition predominantly in the antero-mesial regions, while recognition predominates in posterior temporal and medial parietal cortices. T-statistical parametric maps were corrected for multiple comparisons using a random field theory cluster threshold of $p < 0.001$, overlaid on the Alzheimer's Disease Neuroimaging Initiative reference template. Two linear regression models were used, where either delayed recall z-scores or recognition d' scores were entered as outcome variables. Age, sex, years of education, APOE status, and amyloid- β standardized uptake value ratio were used as covariates.

References

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