輕度阿茲海默症之血漿p-tau181與認知退化、腦部變化之關係

The association among plasma p-tau181, cognitive progression and structural brain change in early Alzheimer's disease

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Background

Plasma levels of phosphorylated tau 181 (p-tau181) is one of the potential blood-based biomarkers for the diagnosis of Alzheimer's disease (AD). However, the association among plasma p-tau181 and cognitive progression and structural brain change still needs to be investigated.

Methods

AD and mild cognitive impairment (MCI) patients diagnosed with a multidisciplinary consensus meeting were recruited. Cognitive function was assessed at baseline and at annual follow-ups. Plasma p-tau181 levels at baseline were measured using Quanterix SIMOA kits and was natural logarithmic transformed for analysis. The regional cortical thickness and volumes of baseline brain MRI were measured using the FreeSurfer image analysis suite. T-tests and multiple regression were used for analyses.

Results

A total of 154 AD and 19 MCI patients were recruited (mean age = 77.6 ± 7.1 years, 42% male, 37% APOE ε4 carrier, and mean MMSE = 20.7 ± 4.3). There were 133 patients (76.9%) having at least two annual follow-up and the mean follow-up time was 2.1 ± 0.4 years. The baseline plasma p-tau181 levels were correlated with the rates of MMSE decline per year ($r = -0.303$, $p < 0.001$). After adjusting for age, gender, education, APOE ε4 carrier status and baseline MMSE, the baseline plasma p-tau181 levels were still associated with with the yearly MMSE decline ($\beta = -0.304$, $p < 0.001$) and was able to predict MMSE decline>3 per year (OR=4.27, 95% CI 1.56–11.70). With addition of plasma p-tau181, the AUROC of predicting faster MMSE decline was 0.736 (0.617–0.854) as compared with the AUROC of 0.625 (0.482–0.767) using demographics alone.
There were 146 patients (129 AD and 17 MCI) with valid brain MRI. The cross-sectional analyses with adjustments of age, gender, education and APOE ε4 carrier status showed significant association between plasma p-tau181 levels and right middle temporal thickness ($\beta = -0.47$, $p < 0.001$), left cuneus thickness ($\beta = -0.27$, $p = 0.004$), right accumbens area volume ($\beta = -0.27$, $p = 0.002$) and central cingulate cortex volume ($\beta = 0.230$, $p = 0.010$).

Conclusion

Higher plasma p-tau181 levels were associated with the faster rate of MMSE decline in AD and MCI patients. Plasma p-tau181 showed more consistent correlations in cortical thickness than regional brain volume. Our study suggested that the plasma p-tau181 could be a potential biomarker for tracking cognitive decline and reflecting structural brain changes in AD and MCI patients.

Figure. 1 Correlation of plasma p-tau181 level and yearly rate of MMSE decline over 2 years.

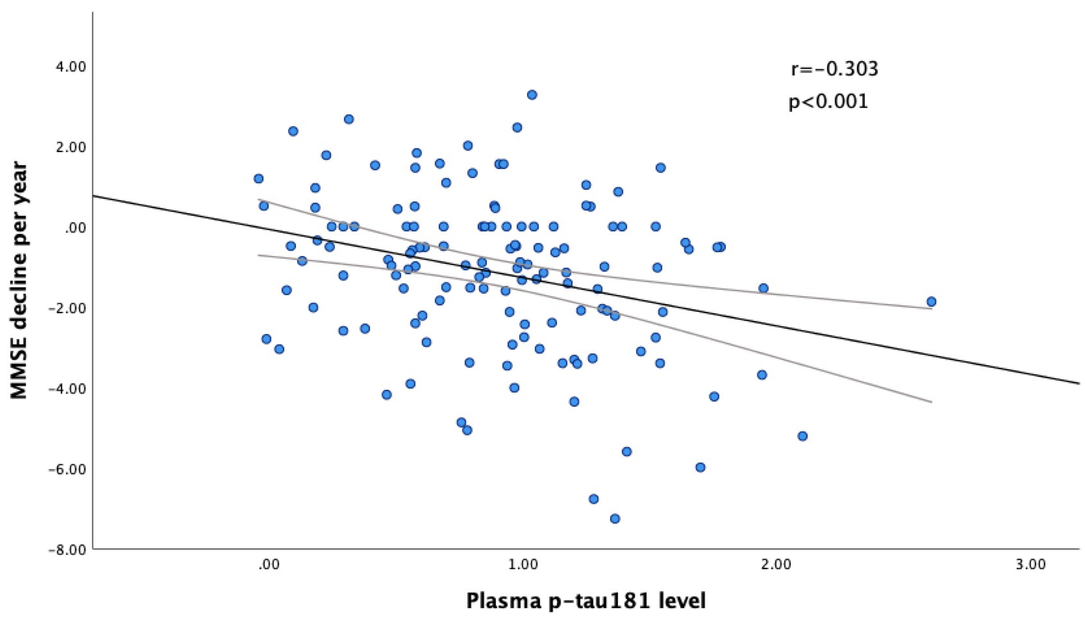
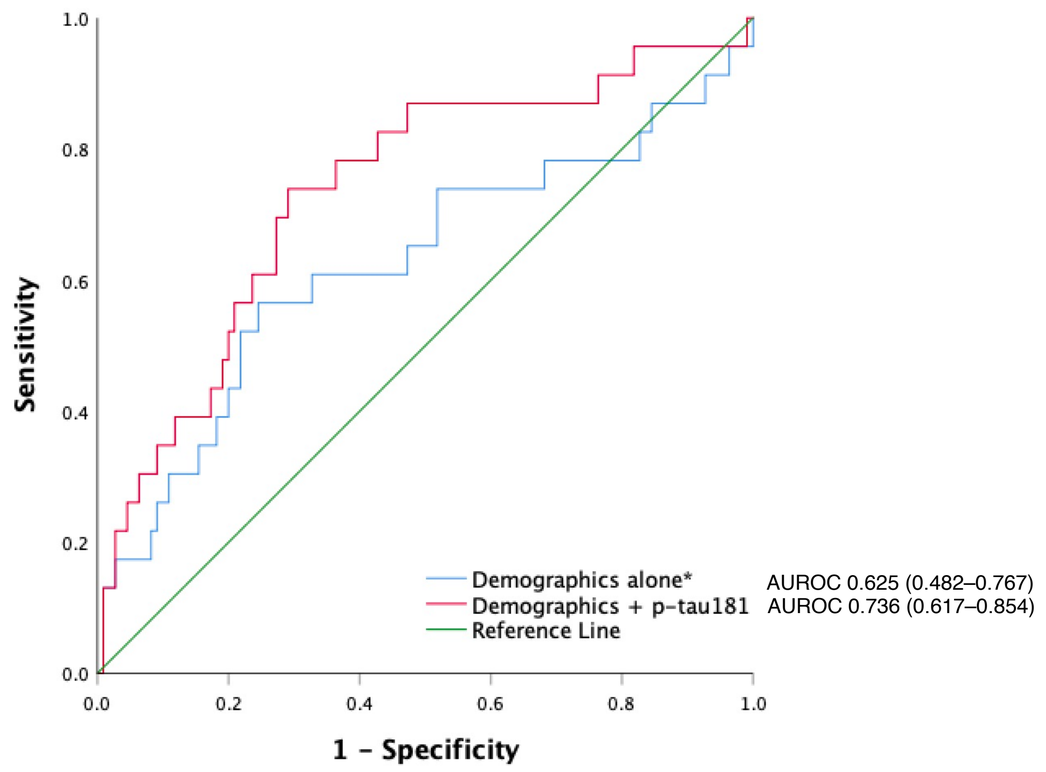


Table. 1 Group comparisons of yearly MMSE decline more than 3 points.

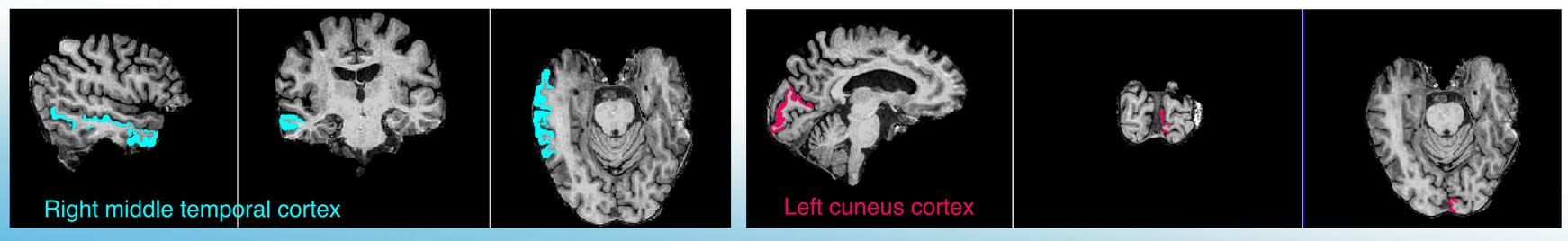
		No (N=110) n (%) or mean±SD	Yes (N=23) n (%) or mean±SD	p-value
Male		45 (40.9%)	8 (38.1%)	0.585
E4 carrier		44 (40.4%)	7 (30.4%)	0.391
Baseline Dx[a]	MCI	17 (15.5%)	2 (8.7%)	0.526
	AD	93 (84.5%)	21 (91.4%)	
Age (Year)		77.6 ± 6.7	76.5 ± 9.6	0.601
Education (Year)		10.2 ± 4.4	10.1 ± 5.0	0.916
Baseline MMSE		21.4 ± 4.0	20.2 ± 4.5	0.182
p-tau181		0.846 ± 0.473	1.173 ± 0.484	0.003**

a. Baseline diagnosis
** p<0.005

Figure. 2 ROC curve of predicting faster cognitive decline, defined as yearly MMSE decline >3.



*Demographics alone: age, gender, education years, E4 carrier status, baseline MMSE



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