Detecting amyloid and tau pathology in Parkinson disease, 4R-tauopathies and control subjects with plasma pTau217

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Background and Aims

Plasma phospho-tau 217 (pTau217) is a biomarker for Alzheimer's disease (AD) pathology, reflecting amyloid (Aβ) and tau burden, but its role in Parkinson disease (PD) and 4-repeat(4R)-tauopathies remains incompletely understood. We measured plasma pTau217 across the cognitive spectrum of Lewy body diseases (PD, Dementia with Lewy bodies [DLB]) and in 4R-tauopathies, comparing these groups to cognitively unimpaired (CU) and mild cognitive impairment (MCI) individuals.

Methods

Participants included 18 cognitively normal PD (PD-NC), 32 PD with MCI, and 7 PD with dementia (PDD), alongside 4 DLB patients, grouped as PDD/DLB. The 4R-tauopathy group included 28 Progressive Supranuclear Palsy (PSP) and 4 corticobasal syndrome (CBS) patients, compared to 51 CU and 26 MCI individuals. Ptau217 was measured using the fully automated Lumipulse platform, with values adjusted for creatinine levels. Further, the presence of AD-pathology was defined using a validated cut-off based on Aβ-PET. See **Table 1**.

Results

PTau217 levels were significantly lower in PD-NC and CU individuals compared to those with greater cognitive impairment (PD-MCI, PDD/DLB, and PSP/CBS), and MCI individuals (**Fig. 1**). AD co-pathology was identified in 28% of PDD/DLB and PSP/CBS patients, 16% of PD-MCI, and none of PD-NC. MCI showed the highest pTau217 positivity (35%), while 8% of CU were positive despite normal cognition (**Fig. 2**). In PD, pTau217 negatively correlated with cognitive performance, as assessed by Montreal Cognitive Assessment (MoCA) (**Fig. 3A**) and Mini-Mental State Examination (MMSE) (**Fig. 3B**).

Table 1. Demographic, clinical, and cognitive characteristics of clinical groups

Variables		CU (n = 51)		MCI (n = 26)		PD-NC (n = 18)		PD-MCI (n = 32)		PDD/ DLB (n = 11)		PSP/ CBS (n = 32)		Total sample (n =170)		
		Mean (SD)	min-max	Mean (SD)	min-max	Mean (SD)	min-max	Mean (SD)	min-max	Mean (SD)	min-max	Mean (SD)	min-max	F (df1, df2)/ χ^2 (df)	p-value	Post-hoc
Age		70.8 (3.71)	64-80	74.31 (5.68)	65-84	71.11 (5.83)	63-87	73.72 (5.88)	63-82	71.73 (6.34)	58-80	73.06 (6.22)	56-85	2.27 (5, 164)	**0.05**	
Sex, f/m		26/25		13/13		8/10		14/18		2/9		13/19		4.47 (5)	0.485	
Disease duration, yrs						8.44 (5.88)	1-19	9.16 (6)	1-23	5.91 (4.5)	1-14	3.88 (2)	1-9	7.41 (3, 88)	**<0.001**	j, l
pTau217, ng/L	§	0.12 (0.15)	0.03-1.05	0.22 (0.24)	0.04-0.91	0.08 (0.03)	0.04-0.18	0.15 (0.12)	0.03-0.57	0.16 (0.1)	0.05-0.39	0.17 (0.11)	0.03-0.55	21.38 (6)	**<0.001**	
Creatinine, mmol/L		76.98 (14.42)	53-115	75.08 (15.04)	51-112	67.17 (16.67)	37-106	66.13 (20.51)	31-114	71.09 (10.72)	53-85	69.19 (15.44)	35-101	2.55 (5,164)	**0.030**	b
pTau217, pos/ neg (% positivity)		4/47 (7.84%)		9/17 (34.62%)		0/18 (0%)		5/27 (15.63%)		3/8 (27.27%)		9/23 (28.13%)		15.59 (5)	**0.008**	a, d, e, i, j
pTau217, ng/L **(of positive cases)**	§	0.53 (0.36)	0.22-1.05	0.47 (0.26)	0.22-0.91	-	-	0.38 (0.13)	0.24-0.57	0.29 (0.08)	0.24-0.39	0.30 (0.11)	0.22-0.55	5.23 (4)	0.264	
MoCA	§	25.9 (2.71)	18-30	22.08 (3.47)	14-28	26 (2.3)	23-30	22.06 (3.16)	15-27	16.67 (3.84)	13-22	18.66 (4.25)	9-26	79.74 (5)	**<0.001**	a, b, c, d, f, g, h, i, j, k, l
MMSE	§	28.96 (1.17)	25-30	28.19 (1.5)	24-30	29.17 (0.99)	27-30	27.34 (1.64)	22-30	24.33 (3.08)	20-29	26.03 (2.82)	18-30	57.01 (5)	**<0.001**	b, c, d, f, g, h, i, j
H&Y	§					1.92 (0.81)	1-4	2.39 (0.83)	1-5	2.5 (1.14)	1-5	3.52 (1.12)	1-5	28.57 (3)	**<0.001**	j, l, m
LEDD	§					594.91 (472.2)	0-1720	448.54 (245.05)	56-1010	543.57 (486.7)	0-1150			0.42 (2)	0.811	
DAED	§					92.06 (105.45)	0-320	47.1 (74.23)	0-320	15 (39.69)	0-105			4.67 (2)	0.097	

Significant p-values are shown in bold. §, not normally distributed variables; (a) CU vs. MCI; (b) CU vs. PD-MCI; (c) CU vs. PDD/DLB; (d) CU vs. PSP/CBS; (e) MCI vs. PD-NC; (f) MCI vs. PDD/DLB; (g) MCI vs. PSP/CBS; (h) PD-NC vs. PD-MCI; (i) PD-NC vs. PDD/DLB; (j) PD-NC vs. PSP/CBS; (k) PD-MCI vs. PDD/DLB; (l) PD-MCI vs. PSP/CBS; (m) PDD/DLB vs. PSP/CBS.

Conclusions

Plasma pTau217 levels serve as a **scalable**, **non-invasive** marker of AD-pathology across Lewy body diseases, PSP/CBS, and MCI/CU populations. **AD co-pathology independently contributes** to cognitive deficits in PD, but not in PSP/CBS.

Fig 1. Plasma pTau217 levels across clinical groups. * < 0.05; ** < 0.01.

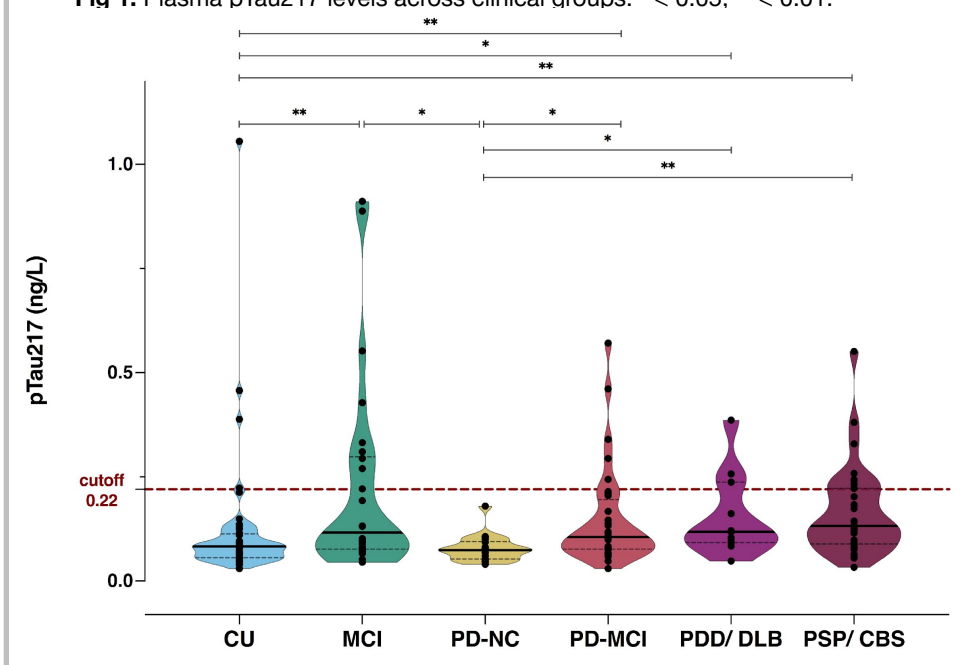


Fig 2. Prevalence of plasma pTau217-positive cases across groups. * < 0.05; ** < 0.01.

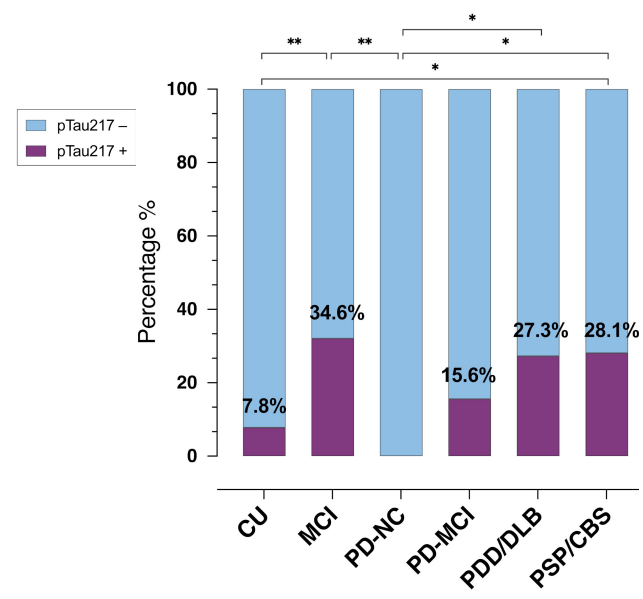
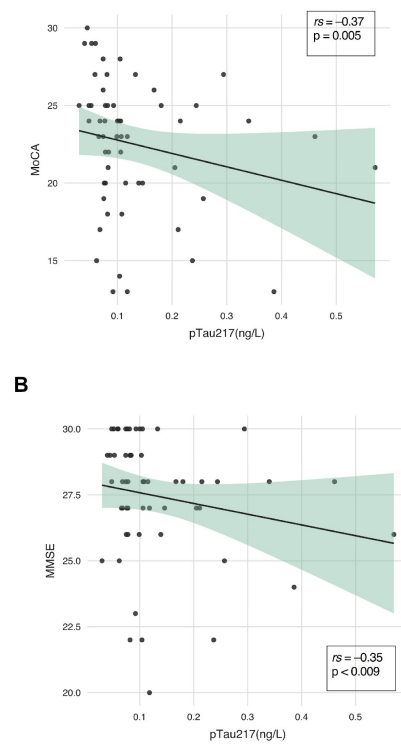


Fig 3. Correlation between plasma pTau217 levels and cognitive performance within the PD group (*n* = 57). Plasma pTau217 correlation with (A) MoCA, and (B) MMSE.



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