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Thursday

Alzheimer's Disease Biomarkers in 4-Repeat Tauopathy Syndromes: Results from the 4R-Tau Neuroimaging Initiative (4RTNI)

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State of the Art: Plasma P-tau217 is validated as specific marker of AD, but utility is uncertain in primary 4R-tauopathy (4RT) syndromes such as CBS, PSP, and nfvPPA. We therefore compared plasma P-Tau217 to Aβ and tau PET in 4RT, especially within CBS where up to 40% of cases are due to primary AD.

Methodology: 4RT were recruited from 4RTNI; biomarker-confirmed AD and cognitively normal (CN) controls were from UCSF. Plasma P-Tau217 was measured on the MSD platform, and compared to Aβ and flortaucipir (FTP) PET. Clinical-biomarker associations were explored using imaging analyses and longitudinal mixed effect modelling.

Results: Plasma P-Tau217, Aβ PET centiloids, and FTP temporal SUVR were elevated in AD (n=54) compared to CN (n=68), CBS (n=118), PSP (n=119), and nfvPPA (n=40). Within CBS, each AD biomarker was elevated in CBS-AD compared to CBS-4RT. In the entire cohort, strong correlations were seen between P-Tau217 and Aβ centiloids (ϱ=0.68) and FTP temporal SUVR (ϱ=0.74). ROC analyses of P-Tau217 had AUC 0.92 validated against Aβ PET visual read and AUC 0.94 for FTP temporal SUVR>1.27. CBS-AD (n=12) and CBS-4RT (n=39) differed in longitudinal atrophy, with CBS-4RT resembling PSP progression. CBS-4RT also showed faster rates of motor decline on a modified PSP Rating Scale than CBS-AD.

Conclusion: We validated plasma P-Tau217 against Aβ and FTP PET and found excellent diagnostic performance in differentiating AD from 4RT in the entire cohort, and in distinguishing CBS-AD from CBS-4RT. We also identified differences in progression between CBS-AD and CBS-4RT that may facilitate clinical trials.

Conflicts of interest

N/A