Cerebrospinal fluid biomarker

Tau cerebrospinal fluid biomarkers are reliable diagnostic markers for Alzheimer's disease (AD). However, their strong association with amyloid pathology may limit their reliability as specific markers of tau neurofibrillary tangles. A recent study showed evidence that a ratio of CSF C-terminally truncated tau (tau368, a tangle-enriched tau species), especially in ratio with total tau (t-tau), correlates strongly with tau PET tracer uptake. In this study, we set to evaluate the performance of the tau368/t-tau ratio in capturing tangle pathology, as indexed by a high-affinity tau PET tracer, as well as its association with severity of clinical symptoms.

Methods: In total, 125 participants were evaluated cross-sectionally from the Translational Biomarkers of Aging and Dementia (TRIAD) cohort (21 young, 60 cognitively unimpaired [CU] elderly [15 Aβ+], 10 Aβ+ with mild cognitive impairment [MCI], 14 AD dementia patients, and 20 Aβ- individuals with non-AD cognitive disorders). All participants underwent amyloid and tau PET scanning, with [18F]-AZD4694 and [18F]-MK6240, respectively, and had CSF measurements of p-tau181, p-tau217, and t-tau. CSF concentrations of tau368 were quantified in all individuals with an in-house single molecule array assay.

Results: CSF tau368 concentration was not significantly different across the diagnostic groups, although a modest increase was observed in all groups as compared with healthy young individuals (all $P < 0.01$). In contrast, the CSF tau368/t-tau ratio was the lowest in AD dementia, being significantly lower than in CU individuals (Aβ-, $P < 0.001$; Aβ+, $P < 0.01$), as well as compared to those with non-AD cognitive disorders ($P < 0.001$). Notably, in individuals with symptomatic AD, tau368/t-tau correlated more strongly with [18F]-MK6240 PET SUVR as compared to the other CSF tau biomarkers, with increasing associations being seen in brain regions associated with more advanced disease (isocortical regions > limbic regions > transentorhinal regions). Importantly, linear regression models indicated that these associations were not confounded by Aβ PET SUVr. CSF tau368/t-tau also tended to continue to become more abnormal with higher tau burden, whereas the other biomarkers plateaued after the limbic stage. Finally, the tau368/t-tau ratio correlated more strongly with cognitive performance in individuals with symptomatic AD as compared to t-tau, p-tau217 and p-tau181.

Conclusion: The tau368/t-tau ratio captures novel aspects of AD pathophysiology and disease severity in comparison to established CSF tau biomarkers, as it is more closely related to tau PET SUVR and cognitive performance in the symptomatic phase of the disease [1)]

Plasma phosphorylated Tau (P-Tau) levels and P-tau-T-tau ratio outperformed total Tau (T-tau) level as diagnostic and prognostic biomarkers for acute TBI. Compared with T-tau levels alone, P-tau levels and P-tau-T-tau ratios show more robust and sustained elevations among patients with chronic TBI [2)].

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2)
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