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Thursday

Imaging and CSF markers contributing to clinical heterogeneity in frontotemporal dementias

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State of the art

Frontotemporal lobar degeneration (FTLD) encompasses a group of syndromes including primary progressive aphasias (PPA), behavioral variant (bvFTD), corticobasal syndrome (CBS) and progressive supranuclear palsy (PSP). They display significant overlap in pathology and symptomatology yet remarkable heterogeneity even within each syndrome. This is especially true of sporadic cases, whose clinical presentation is complicated by age-related co-pathologies/co-morbidities, and increased prognostic uncertainty. We characterize MRI and CSF biomarkers of underlying vascular, inflammatory, AD-related, and misfolded α-synuclein-related pathology.

Methodology

Longitudinal scans from FTLDNI, 4RTNI, and a local dataset were segmented to examine white matter hyperintensities (WMH), regional brain volumes and their relationships to vascular risk factors and CSF biomarkers. The dataset included 136 controls, 42 bvFTD, 50 semantic and 45 nonfluent variant PPA, 90 CBS, and 85 PSP. CSF assays were performed on a local dataset of 110 patients. We examined AD biomarkers and YKL-40 levels, misfolded α-synuclein seeding activity (RT-QuIC), and neurofilament light-chain levels (SIMOA).

Results Linear mixed effect models on preliminary data showed a significant interaction between age, sex, and vascular history ($X^2(3)=7.9$, $p=0.05$) on total WMH volume (logged and normalized by brain volume). Incorporating diagnosis significantly improved fit ($X^2(3)=7.9$, $p=4.5e-8$), even after excluding controls, with differences driven by male bvFTD. No significant relationship was observed between WMH burden and either CSF biomarkers under study.

Conclusion WMH burden in FTLD is significant, varies between subtypes, and cannot be imputed to age-related and vascular factors. Additional inflammatory markers and clinical outcomes are being investigated.

Conflicts of interest

N/A