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Thursday

Distinct neuroinflammatory mechanisms in Frontotemporal Lobar Degeneration and Alzheimer's Disease

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State of the art: Neuroinflammation is considered a contributor of pathophysiology in neurodegenerative diseases, such as Frontotemporal Lobar Degeneration (FTLD) and Alzheimer's Disease (AD), and its modulation seems to have therapeutic efficacy in AD. Whether different proteinopathies (FTLD-Tau, FTLD-TDP-43 or AD pathology) display distinct neuroinflammatory profiles remains unclear.
Methodology: Using Olink Inflammation panels, we measured 737 inflammatory proteins in CSF from 45 FTLD (28 presumed/proven FTLD-Tau and 17 FTLD-TDP-43) and 22 AD patients. ANCOVA F-tests, adjusting for age and sex, was used to compare groups with correction for multiple testing by Benjamini-Hochberg FDR method.
Results: 15 neuroinflammatory proteins were significantly different between AD and FTLD ($p<0.05$); 14 were increased in AD compared to FTLD. Of them, 6 proteins (NRGN, SMOC2, ACHE, DNAJA2, FGF5, and SPON1) have been reported in AD and involved in cognitive functioning, protein folding, and other neuronal pathways. Only one protein, C3, a pro-inflammatory complement protein, was decreased in AD compared to FTLD. Interestingly, this protein was previously shown as upregulated in AD brains, compared to controls and correlated with neurodegeneration. Remarkably, 12 proteins were increased in AD compared to FTLD-Tau, suggesting distinct inflammatory mechanisms across different tau isoforms. No differences between AD and FTLD-TDP-43, possibly due to the frequent TDP-43 co-pathology in AD brains. No difference was seen between FTLD-Tau and FTLD-TDP-43.
Conclusion: FTLD and AD patients display distinct inflammatory profiles with FTLD-Tau but not FTLD- TDP-43 patients being significantly different from AD patients. Our results underscore that proteinopathy-specific neuroinflammation may play a role in neurodegeneration.

Conflicts of interest

N/A