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Chemokine CSF concentrations are abnormal in genetic FTD within the GENFI cohort

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State of the art
Chronic neuroinflammation is a key underlying factor in frontotemporal dementia (FTD), the most common dementia among adults less than 60 years old. Chemokines are proteins involved in neuroinflammation that recruit and activate leukocytes to sites of injury and show dysregulated expression in biofluid levels during chronic neuroinflammation. The alterations in chemokine levels during neurodegenerative disease are poorly understood, and no large-scale study has previously investigated chemokine levels in a genetic FTD cohort.

Methodology
We measured concentrations of 18 chemokines in the CSF of 255 individuals from the GENFI cohort using the Olink Target-96 Inflammation panel. This included 79 *C9orf72* mutation carriers (56 presymptomatic, 23 symptomatic), 56 *GRN* mutation carriers (42 presymptomatic, 14 symptomatic), 36 *MAPT* mutation carriers (27 presymptomatic, 9 symptomatic), and 84 controls.

Results
CSF concentrations of several chemokines were significantly decreased in symptomatic compared to presymptomatic *GRN* mutation carriers: CCL13 (p=0.020), CXCL11 (p=0.012), CXCL10 (p=0.048), and MCP-2/CCL8 (p=0.047) and in symptomatic GRN mutation carriers compared to controls in CCL13 (p=0.019). However, over half of the chemokines measured (including CCL3, CCL2, CCL11, CCL23, CCL25, CXCL1, CXCL6, CXCL9, CX3CL1, and IL-8) did not show any significant differences between groups.

Conclusion
We find a significant decrease in concentration of a number of CSF chemokines in genetic FTD, particularly in those with *GRN* mutations. Whilst inflammation may be an important factor in genetic FTD, further work is needed to understand the role of chemokines as a biomarker of this process.

Conflicts of interest

N/A