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Cerebrospinal fluid neurofilament light chain differentiates behavioural variant frontotemporal dementia from 'phenocopy' non-progressors

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Background:
Neurofilament light (NfL) is a promising diagnostic and prognostic biomarker for frontotemporal dementia (FTD). This study explored the utility of using cerebrospinal fluid (CSF) NfL to differentiate neurodegenerative FTD from mimicking, 'phenocopy', non-progressive or potentially reversible 'pseudodementia' syndromes, an otherwise clinically challenging endeavour in complex patient cohorts with significant psychiatric and neurological comorbidities.

Methods:
This was a retrospective cohort study which involved analysis of CSF NfL, β-amyloid peptide 1-42 (Aβ1-42), phosphorylated tau (P-tau), and total tau (T-tau) levels in patients referred to a tertiary neuropsychiatry service, who received a lumbar puncture and for whom possible, probable or definite FTD was a differential diagnosis during their follow-up. Participants were classified as having a progressive FTD, static non-progressive, or phenocopy non-progressive diagnosis based on expert consensus from independent file reviews of each patient's longitudinal multidisciplinary assessment. Data from healthy controls were available for comparison. Data extraction was blinded to NfL levels.

Results:
A total of 63 participants were included: 20 FTD progressors, 8 static non-progressors, 15 'rescinded FTD diagnosis' or reversible 'FTD phenocopy' non-progressors, and 20 healthy controls. NfL distinguished neurodegenerative FTD from non-progressive phenocopy syndromes with an area under the curve (AUC) of 0.92 (95% CI=[0.888, 1.023]). An optimal cut-off of 726pg/mL yielded a sensitivity of 90% and specificity of 87%.

Conclusion:
CSF NfL has robust diagnostic utility in distinguishing FTD from non-progressive variants and mimics with high sensitivity and specificity. Further studies examining the role of plasma NfL in distinguishing progressive FTD from non-progressive syndromes, are warranted and underway.

Conflicts of interest

N/A