

Comprehensive cross-sectional and longitudinal analyses of plasma neurofilament light across FTD spectrum disorders

Tania Gendron, Michael Heckman, Launia White, Austin Veire, Otto Pedraza, Alexander Burch, Leah Forsberg, Hilary Heuer, Daniel Geschwind, Rosa Rademakers, Eliana Marisa Ramos, Howard Rosen, Bradley Boeve, Adam Boxer, Leonard Petrucelli, On behalf of the ALLFTD Consortium .

State of the art

Frontotemporal dementia (FTD) treatment development is hamstrung by a lack of susceptibility/risk and prognostic biomarkers. We thus availed ALLFTD resources and undertook a comprehensive cross-sectional and longitudinal study to evaluate the staging and prognostic utility of plasma NfL.

Methodology

Using a digital immunoassay, we measured plasma NfL in clinically normal, mutation-negative individuals in kindreds with an FTD-causing mutation (controls, N=144), presymptomatic individuals with a C9orf72, GRN or MAPT mutation (N=85), and patients with behavioral variant FTD (bvFTD, N=289), nonfluent variant primary progressive aphasia (nfvPPA, N=72), semantic variant PPA (svPPA, N=84), corticobasal syndrome (CBS, N=89) or progressive supranuclear palsy-Richardson syndrome (PSP-RS; N=124).

Results

Baseline plasma NfL and rates of NfL change were higher in presymptomatic mutation carriers who phenoconverted compared to non-converters and controls. Plasma NfL was elevated in all FTD syndromes, and distinguished patients with only mild symptoms from controls, indicating it may allow a more rapid diagnosis of questionable cases. In addition, higher NfL associated with worse baseline performance and faster longitudinal decline on tests of global cognitive function, social change, language deficits and executive dysfunction in patients with FTD syndromes.

Conclusion

By facilitating the identification of individuals at risk of phenoconversion, and the early diagnosis of FTD, plasma NfL may inform participant selection for prevention and early treatment trials. Moreover, its prognostic utility may improve clinical trial efficiency and treatment outcome estimations. The extensive database created through this effort and ALLFTD is sure to ignite new lines of study on FTD spectrum disorders.

Conflicts of interest

no disclosures