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Thursday

Clinical value of multiplexed CSF neurodegeneration biomarkers in familial and sporadic frontotemporal dementia

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State of Art: The diagnostic performance of available neurodegeneration biomarkers has not been directly compared in frontotemporal dementia (FTD).

Methodology: CSF biomarkers associated with neurodegeneration (NfL, NfH, GFAP, NPTX-2, YKL-40, tau, 14-3-3, TDP-43, APP, progranulin, alpha-synuclein, BDNF, SNAP-25, and synaptotagmin-5) were quantified with the Somascan v3.0 proteomics platform in independent cohorts of familial (original ALLFTD: 49 *C9orf72*, 33 *GRN*, 37, *MAPT* mutation carriers, 60 age-matched controls) and sporadic pathologically-confirmed (validation UCSF: 34 FTLD-tau, 13 FTLD-TDP, 28 age-matched controls) FTD. Area under the receiver-operating characteristic curves (AUC) determined diagnostic value. Linear models determined relationships with disease severity (CDR+NACC/FTLDsb), and general linear models the effect of disease severity with genotype.

Results: Good discriminators (i.e., AUC>0.800) of symptomatic disease were GFAP, NfH, NfL and NPTX-2, in both cohorts. NPTX-2 (b=-0.710, 95% CI -0.776 – 0.629, p<0.001) had the strongest age- and sex-corrected relationship with disease severity in both cohorts. The neurofilaments and GFAP also correlated strongly with disease severity. Weak (b<0.4) relationships with disease severity were observed for alpha-synuclein in familial disease, and APP, TDP-43, BDNF and SNAP-25 in sporadic disease. YKL-40 and synaptotagmin-5 had weak relationships with disease severity in both cohorts. Asymptomatic and symptomatic *GRN* mutation carriers had lower progranulin levels compared to other groups.

Conclusion: The neurofilaments, GFAP and NPTX-2 have diagnostic value in familial and sporadic FTD. Somamer proteomics is a sensitive tool for multiplexed CSF phenotyping in FTD.

Conflicts of interest

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