Cerebrospinal fluid amyloid beta and glial fibrillary acidic protein concentrations in Huntington's disease

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Background

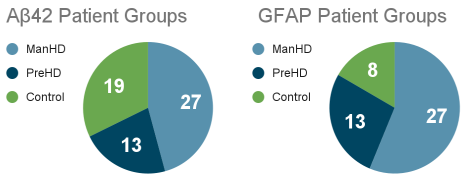
Huntington's disease (HD) is a monogenic disease without a proven cure so far. Biomarkers are needed for objective assessment of disease progression.There is evidence supporting both complex protein aggregation and astrocyte activation in HD.

Aim: In this study we assess the role of the 42 amino acid long amyloid beta (Aβ42) and glial fibrillary acidic protein (GFAP) as potential biomarkers in cerebrospinal fluid (CSF) of HD mutation carriers.

Methods

CSF was obtained from manifest HD patients (ManHD), premanifest HD-gene-expansion carriers (PreHD) and gene-negative controls (controls). Disease Burden Score (DBS) and Total Functional Capacity (TFC) were calculated. Protein concentrations were measured by enzyme-linked immunosorbent assays (ELISA) and intergroup differences were analysed using Mann-Whitney U test. Spearman correlations were calculated to assess association with disease stage. Age-adjustment was included in the statistical tests.

Results



	ManHD		PreHD		Control	
	mean (ng/l)	SD (ng/l)	mean(ng/l)	SD (ng/l)	mean (ng/l)	SD (ng/l)
AB42	741	361	468	183	535	238
GFAP	435	255	266	92.4	208	83.7

The Aβ42 levels were higher in the ManHD group compared with the PreHD (p=0.025). The GFAP levels were significantly higher in ManHD compared with both the PreHD and gene-negative controls (p=0.040, p=0.011, respectively).

GFAP correlated with DBS (r = 0.361, p = 0.028), TFC (r = −0.463, p = 0.005), and with 5-year risk of onset in PreHD (r = 0.694, p = 0.008). There was no correlation between Aβ42 concentration and DBS, TFC or 5-year risk of onset.

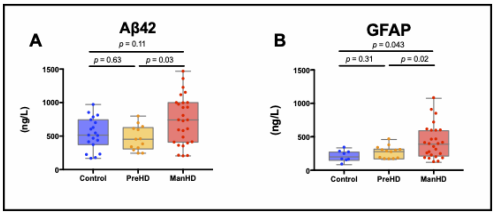


Fig 1. Concentrations of Aβ42 and GFAP by group. P-values are age adjusted

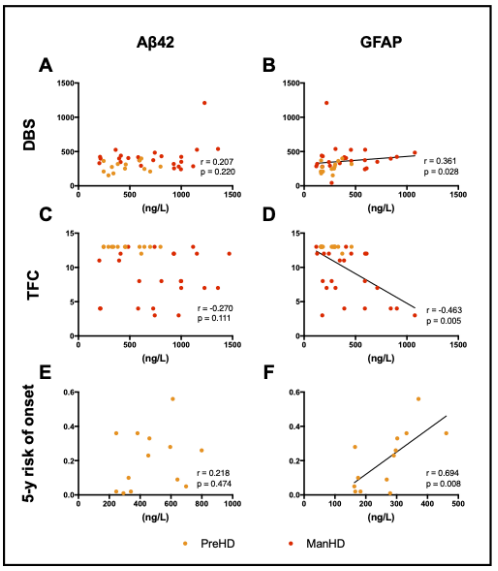


Fig 2. Correlations between protein levels and disease progression in Huntington's disease.

Conclusions

CSF Aβ42 levels did not correlate with disease stage suggesting no Aβ aggregation in HD. GFAP is a potential biomarker in HD with association to disease stage. Validation in a larger HD cohort and correlation with clinical phenotype would be of interest.

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