CSF B-AMYLOID AS A PUTATIVE BIOMARKER OF DISEASE PROGRESSION IN MULTIPLE SCLEROSIS

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Background

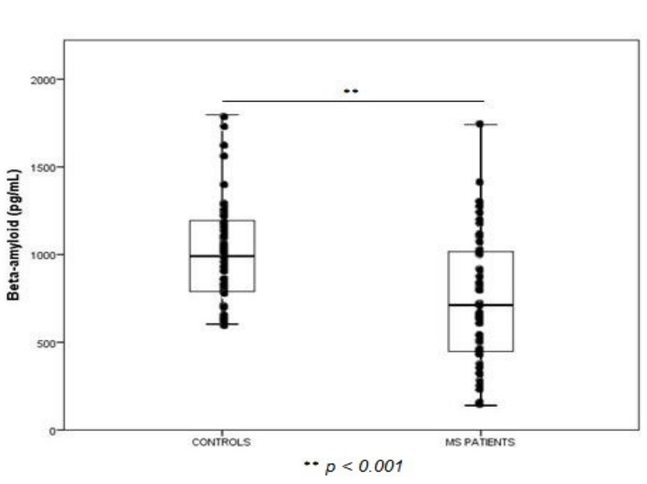
Multiple sclerosis (MS) is the most common chronic inflammatory disease of the central nervous system (CNS), characterised by demyelination, axonal degeneration and gliosis. The mechanisms underlying axonal damage still need to be fully clarified, and, currently, there are no reliable prognostic biomarkers of disease progression. Our objectives were to assess whether cerebrospinal fluid (CSF) tau and β-amyloid (Aβ) levels were altered in newly diagnosed MS patients and correlated with disability. Moreover, we investigated whether these CSF biomarkers associate with macroscopic brain tissue damage measures'.

Materials and Methods

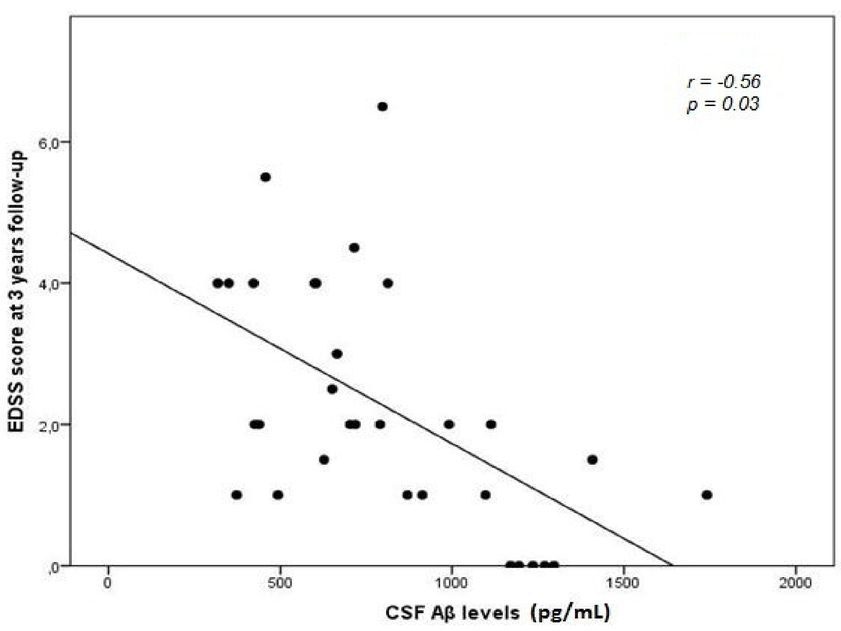
CSF Aβ and tau levels were determined by enzyme-linked immunosorbent assay in CSF samples from 48 newly diagnosed MS patients, followed-up clinically for three years by recording their Expanded Disability Status Scale score at 6 months intervals, and 45 controls. All patients underwent Magnetic Resonance Imaging at baseline and at the end of follow-up to quantify their lesion load (LL).

Principal demographic, laboratory and clinical characteristics of subjects at baseline

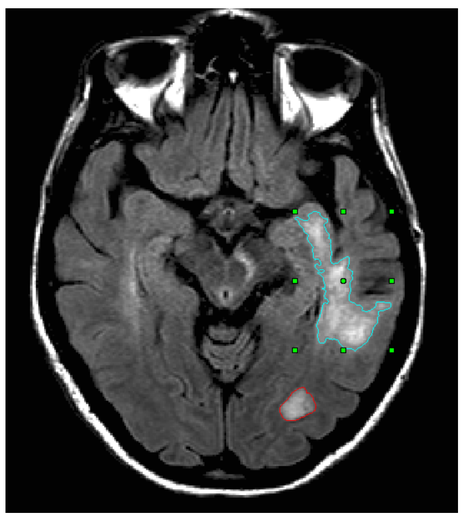
	MS PATIENTS	CONTROLS
Number of subjects	48	45
Gender (F:M)	34:14	23:22
Age (mean SD) [yrs]	35.5 ± 9.6	43 ± 10
Disease duration (mean ± SD) [mths]	8 ± 13	-
Intrathecal IgG synthesis n (%)	36 (75)	-
EDSS (median; IQ1-IQ3) score	2.0; 2.0-3.0	-
Aβ (mean ± SD) [pg/ml]	739.6 ± 367	1001.7 ± 283.6
TAU (mean ± SD) [pg/ml]	130.8 ± 136.9	174.7 ± 144.9



Scatter-plot of CSF Aβ levels in MS patients and controls at diagnosis

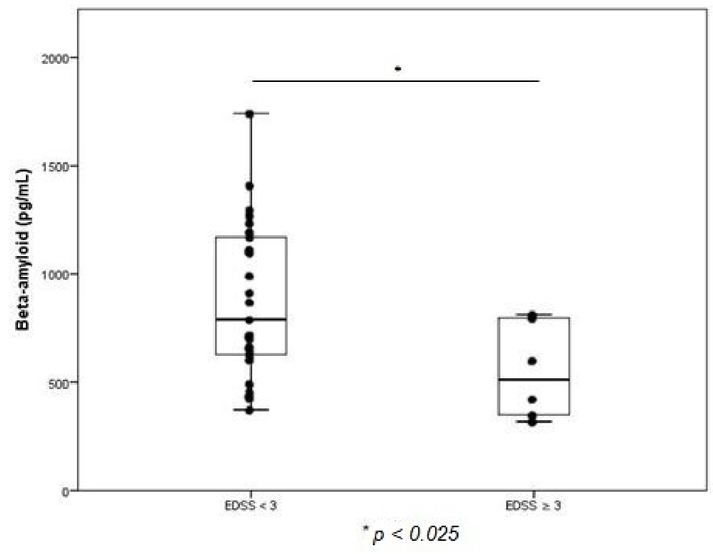


Scatter-plot of linear regression of EDSS score at 3 years follow-up in function of the CSF Aβ levels



Clinical characteristics and CSF profiles in MS patients reclassified by disease severity at follow-up

	MS PATIENTS - EDSS < 3	MS PATIENTS - EDSS ≥ 3
Number of subjects	25	6
EDSS score at baseline (median; IQ1-IQ3)	2.0; 2.0-2.5	2.5; 2.0-2.5
EDSS score at 3 years follow up (median; IQ1-IQ3)	1.5; 1.0-2.5	4.0; 4.0-4.0
Intrathecal IgG synthesis n (%)	22 (88)	4 (67)
Aβ (mean ± SD) [pg/ml]	884 ± 352.7	526 ± 221.6
TAU (mean ± SD) [pg/ml]	160.2 ± 143	94.7 ± 52



Scatter-plot of CSF Aβ levels stratified according to EDSS (< 3 or ≥ 3) at 3-year follow up

Results

- CSF Aβ levels were significantly reduced in patients compared to controls (p<0.001)
- Lower CSF Aβ levels at baseline were a disability predictor at 3 years follow-up (p=0.009)
- CSF tau levels correlated with T2- and T1-LL (p<0.001)

Conclusions

CSF Aβ reduction is a promising biomarker of neurodegeneration and may predict patients' clinical outcome.

Therefore, CSF Aβ should be considered as a potential biomarker of prognostic value.

References

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