55° CONGRESSO SOCIETÀ ITALIANA DI NEUROLOGIA
24-28 Ottobre 2025
Padova Congress

Neurofilament light chains in cerebrospinal fluid reflect grey matter pathology and intrathecal inflammation in early multiple sclerosis

Francesca Gabriele[1], Matteo Foschi[1,2], Lorenzo Barba[3], Agnese Tamanti[4], Ermanna Turano[4], Federica De Santis[5], Bruno Bonetti[6], Simona Sacco[1], Roberta Magliozzi[4], Damiano Marastoni[4], Massimiliano Calabrese[4]

[1] *Department of Biotechnological and Applied Clinical Sciences, University of L'Aquila, L'Aquila, Italy*
[2] *Department of Neuroscience, Multiple Sclerosis Center - Neurology Unit, S.Maria delle Croci Hospital, AUSL Romagna, Ravenna, Italy*
[3] *Department of Neurology, Martin-Luther-University, Halle (Saale), Germany*
[4] *Neurology B, Department of Neurosciences, University of Verona, Italy*
[5] *Department of Neurology and Stroke Unit, S.S. Filippo and Nicola Hospital of Avezzano, Italy*
[6] *Neurology A, Azienda Ospedaliera Universitaria Integrata di Verona, Italy*

BACKGROUND

Focal and diffuse grey matter (GM) damage is a hallmark of Multiple Sclerosis (MS) pathology, associated with meningeal inflammation and a severe disease course. Neurofilament light chain (NfL) levels are considered potential markers of neuro-axonal damage, reflecting early pathological changes and disability accumulation in MS.[1,2] However, their relationship with GM pathology remains poorly explored.

AIMS

We aimed to i) evaluate the association of cerebrospinal fluid (CSF) NfL at diagnosis with cortical lesions (CLs) and cortical and deep GM atrophy; ii) assess their predictive value for GM damage progression; iii) examine their correlation with CSF inflammatory markers involved in cortical pathology, as reported in previous studies.[3]

METHODS

Seventy treatment-naïve patients with relapsing-remitting MS, diagnosed according to McDonald's revised 2017 diagnostic criteria, were enrolled at diagnosis. All patients underwent routine clinical assessments, including the Expanded Disability Status Scale (EDSS), and annual 3T brain and spinal cord MRI scans over 2 years. White matter lesion number (WMLN) and volume (WMLV), CLs number (CLN) and volume (CLV), global cortical thickness (CTh) and deep GM volumes were measured. CSF levels of 18 inflammatory markers associated with GM damage were assessed with multiplex immunoassay. CSF NfL levels were measured at diagnosis using the Human NF-light ELISA kit (MyBioSource, San Diego, CA, USA).

RESULTS

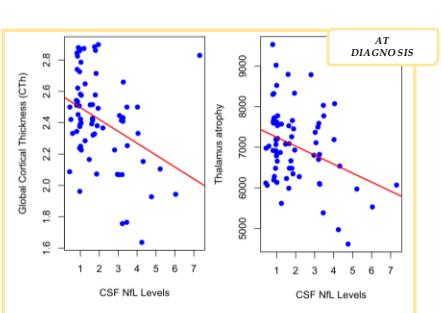
At diagnosis, higher NfL levels correlated with EDSS (β=0.149;p=0.034), increased CLN (β=0.076;p<0.001) and CLV (β=0.001;p<0.001), but not with WMLN and WMLV. Higher NfL levels were significantly correlated with reduced global CTh (β=-0.754;p=0.008) and volumes of deep GM structures, in particular thalamic atrophy (β=0.076;p=<0.001). At two-year follow-up, univariate analysis detected higher NfL levels in patients with reduced global CTh (β=-0.076;p=0.002), atrophy of the thalamus (β=-221.616;p=0.004), hippocampus (β=-0.069;p=0.028), insula (β=-0.158;p=0.003) and cuneus (β=-0.067;p=0.016). At two-year follow-up, multivariate analysis included age, sex, baseline EDSS, WMLV, revealing that higher NfL levels correlated with reduced global CTh (β=-0.055;p=0.024). Higher NfL levels and increased WMLV significantly correlated with thalamic atrophy (β=-171.169;p=0.026;β=-0.403;p=0.007, respectively). Finally, CSF NfL correlated with intrathecal inflammatory markers of cortical damage, including sCD163 (p=0.022), Pentraxin-3 (p=0.007), CX3CL1 (p=0.011), and CXCL13 (p=0.015).

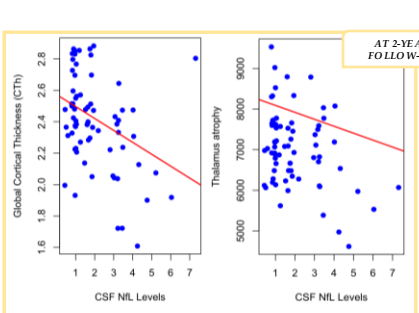
DISCUSSION

CSF NfL levels at diagnosis strongly reflect existing cortical pathology and predict GM atrophy progression over 2 years. Higher CSF NfL correlated with neuroaxonal damage, intrathecal inflammatory markers and reduced global CTh, particularly affecting deep GM structures like the thalamus.

CONCLUSIONS

Our findings suggest NfL as a reliable biomarker reflecting ongoing neurodegeneration associated with inflammatory processes and cortical damage in early MS.





REFERENCES

1. Bittner S, Oh J, Havrdová EK, Tintoré M, Zipp F. The potential of serum neurofilament as biomarker for multiple sclerosis. Brain. 2021 Nov 29;144(10):2954-2963.
2. Khalil M, Teunissen CE, Lehmann S, et al. Neurofilaments as biomarkers in neurological disorders - towards clinical application. Nat Rev Neurol. 2024 May;20(5):269-287.
3. Magliozzi R, Scalfari A, Pisani AI, et al. The CSF Profile Linked to Cortical Damage Predicts Multiple Sclerosis Activity. Ann Neurol. 2020 Sep;88(3):562-573.