Neurofilament Light Chain and Clinical Progression in Early Multiple System Atrophy

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OBJECTIVE

- To assess one-year progression of biofluid markers and clinical symptoms in Multiple System Atrophy (MSA)

INTRODUCTION

- The advancement of MSA is profoundly aggressive, highlighting the critical need for biomarkers to delineate its progression over time.
- Emerging interest surrounds novel fluid biomarkers, notably neurofilament light chain (NfL), found in both cerebrospinal fluid (CSF) and plasma, as indicators of axonal damage in MSA.
- These fluid biomarkers hold promise for measuring the extent of disease, tracking its progression, and forecasting the onset of clinical manifestations associated with MSA.
- Our study involved monitoring changes in clinical severity alongside variations in NfL levels across a span of 12 months, aiming to establish a correlation between these biomarkers and the progression of the disease.

METHODS

- Fifteen participants who met the criteria for clinically possible or probable Multiple System Atrophy (MSA) were enrolled in our study.
- Neurological examinations and clinical assessments, including the Unified Multiple System Atrophy Rating Scale (UMSARS Parts 1 and 2) and the Natural History and Neuroprotection in Parkinson Plus Syndromes (PPS) scale for assessing motor severity, were conducted.
- Plasma neurofilament light chain (NfL) samples were collected every three months, and cerebrospinal fluid (CSF) samples were obtained every six months.
- Longitudinal changes were assessed using a random effects model with a random intercept.
- Clinical associations were explored using linear regression analysis.

RESULTS :PARTICIPANTS

N	15
Sex (M/F)	7/8
Age (years), mean	62.2
UMSARS Part 1, mean	16.9
UMSARS Part 2, mean	13.9
PPS Total score, mean	52.8

Table 1. Demographic and Clinical Data at baseline

RESULTS :PLASMA AND CSF NFL

- Across all participants, plasma NfL increased at an average rate of 0.56 pg/mL/month (p<0.001) (**Fig. 1**).
- The rate of CSF NfL increase over time was not statistically significant.
- There was a significant correlation between the changes in CSF NfL levels and the changes in plasma NfL levels from baseline to 12 months (r= 0.63, p=0.04).
- Over time one standard deviation increase in CSF NfL correlated with a 0.7304 standard deviation increase in Plasma NfL (r= 0.7304 p<0.001) (**Fig. 2**)

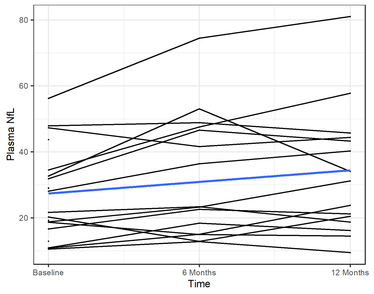

Fig. 1. Changes in plasma NfL. Spaghetti plots showing the NfL values for baseline, 6- and 12-months for all patients (black), and regression line (blue) illustrating the average trend in NfL values over time across the cohort.

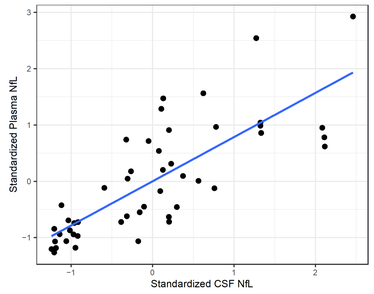

Fig. 2. Correlation between plasma and CSF NFL. Scatter plot and linear regression showing the relationship between plasma and CSF NfL.

RESULTS: CLINICAL CORRELATIONS

- To evaluate the associations between baseline NfL and clinical symptoms over time, we applied a simple linear regression, using baseline plasma or CSF NfL as a predictor of clinical change at 6 and 12 months.
- Baseline plasma and CSF NfL were independently associated with 6 and 12-month change in PPS and UMSARS part 2 (p<0.05) (**Fig. 3**).
- Plasma NfL was additionally associated with 6 and 12-month progression of UMSARS part 1 (p<0.05).

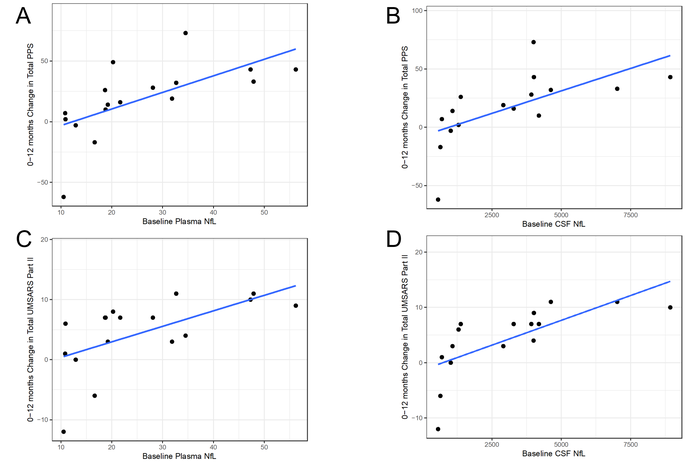

Fig. 3. Correlations with clinical scores. Scatter plot and linear regression showing the relationship between baseline NfL in plasma (A, C) and CSF (B, D) and changes in clinical symptoms over 12 months.

CONCLUSIONS

- Plasma and CSF NfL are associated with clinical worsening in MSA.
- Plasma NfL significantly increased over 12 months.
- These data suggest that NfL may be a marker of disease modification in studies of MSA.

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