NEUROFILAMENT LIGHT CORRELATES WITH BRAIN ATROPHY, COGNITIVE AND MOTOR PERFORMANCE IN SUBJECTS WITH CEREBRAL WHITE MATTER HYPERINTENSITIES

Kartau M[1], Melkas S[1], Kartau J[2], Arola A[3,4], Laakso H[3,4], Pitkänen J[1], Lempiäinen J[1], Koikkalainen J[5,6], Lötjönen J[5,7], Korvenoja A[8], Ahlström M[1], Herukka S-K[9], Erkinjuntti T[1], Jokinen H[3,4]

[1] Department of Neurology, Helsinki University Hospital and University of Helsinki, Helsinki, Finland
[2] School of Mathematics and Statistics, University of Glasgow, University Place, Glasgow G12 8QQ, UK
[3] Division of Neuropsychology, HUS Neurocenter, Helsinki University Hospital and University of Helsinki, Helsinki, Finland
[4] Department of Psychology and Logopedics, Faculty of Medicine, University of Helsinki, Helsinki, Finland
[5] Combinostics Ltd, Tampere, Finland
[6] Faculty of Health Sciences, University of Eastern Finland, Kuopio, Finland
[7] Department of Neuroscience and Biomedical Engineering, School of Science, Aalto University, Espoo, Finland
[8] Medical Imaging Center, Radiology, University of Helsinki and Helsinki University Hospital
[9] University of Eastern Finland, Institute of Clinical Medicine / Neurology

BACKGROUND

The usefulness of **neurofilament light (NfL) as a biomarker** for small vessel disease (SVD) has not yet been established. We examined the relationship between NfL level, neuroimaging changes, and clinical findings in subjects with varying degrees of cerebral white matter hyperintensities (WMH).

METHODS

A subgroup of participants (n=35) in the **Helsinki SVD Study** underwent an analysis of NfL in cerebrospinal fluid (CSF) and plasma as well as a brain magnetic resonance imaging (MRI), and neuropsychological and motor performance assessments. Subjects were recruited from the imaging registry of the Helsinki University Hospital (HUS), Finland within the period of October 2016 and March 2020. Plasma and CSF samples were collected from January 2019 to March 2020. Because CSF NfL levels were higher compared to plasma NfL levels, we primarily used the former for statistical analysis.

WMH were first evaluated visually by a neuroradiologist using the modified Fazekas scale and further evaluated using an **automated multi-stage segmentation method** on FLAIR images.

In **neuropsychological assessment** we used global cognition score as the primary outcome and processing speed, executive functions and memory as the key domain-specific outcomes.

To evaluate **motor functions** we used Timed Up and Go (TUG) test as well as measurements of gait speed and balance.

RESULTS

CSF NfL did not correlate significantly with total WMH volume (r=0.278, p=0.105). However, strong correlations were observed between **CSF NfL level and volumes of cerebral grey matter** (r=-0.569, p<0.001), **cerebral cortex** (r=-0.563, p<0.001), and **hippocampi** (r=-0.492, p=0.003).

CSF NfL was also consistently associated with **performance in global cognition** (r=-0.403, p =0.016), **executive functions** (r=-0.402, p=0.017), **memory** (r=-0.463, p=0.005), and **processing speed** (r=-0.386, p=0.022).

In motor skills tests, **CSF NfL was correlated with Timed Up and Go test results** (r=0.531, p=0.001), and **gait speed** (r=-0.450, p=0.007), but not with results in single-leg stance test.

Plasma NfL level showed the same correlations but somewhat weaker. A full summary of the correlation tests of interest and their corresponding 95% confidence intervals (CIs) can be seen in figure 1.

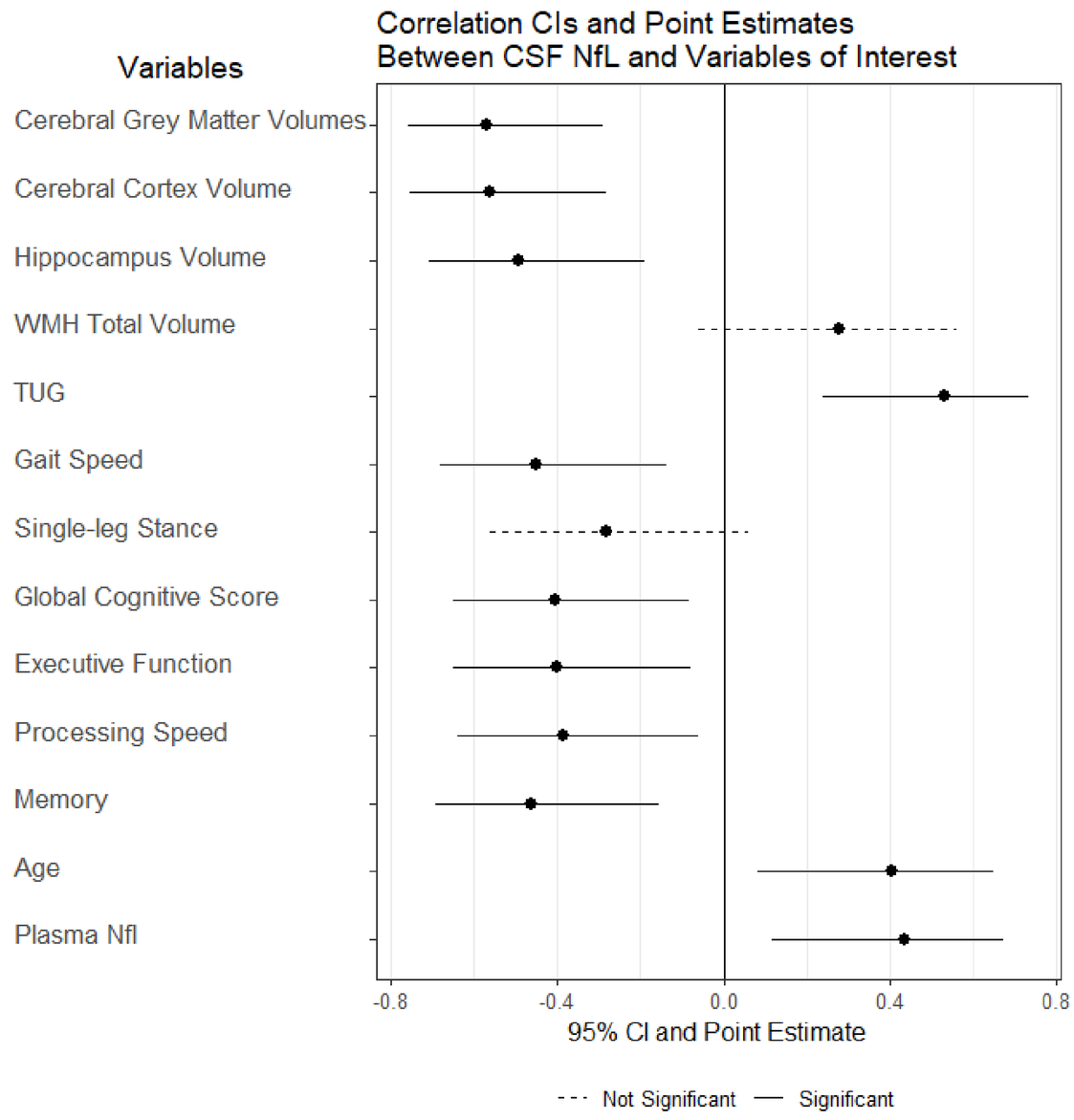

Figure 1 *Summary of correlation tests of interest.*

CONCLUSIONS

- NfL level was strongly related to global gray matter and hippocampal atrophy, but not with WMH severity.
- NfL was consistently associated with cognitive and motor performance.
- Our results suggest that NfL generally reflects frailty in the central nervous system.