

# Plasma and CSF neurofilament light

## Relation to longitudinal neuroimaging and cognitive measures

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### Study objective and summary result

The present study compared plasma and CSF neurofilament light chain (NfL) measurements in terms of cross-sectional and longitudinal associations with cognition and neuroimaging findings. It found that the prognostic utility of plasma NfL measurements is similar to that of CSF NfL measurements.

### What is known and what this paper adds

Most investigations of NfL as a putative prognostic marker for neurodegeneration have studied plasma or CSF measurements in isolation. This investigation elucidates the comparative prognostic utilities of plasma and CSF measurements.

### Participants and setting

The investigators analyzed data and samples collected from 79 individuals (81% cognitively unimpaired; 19% with mild cognitive impairment; 66% male; median baseline age, 76.4 years; interquartile range, 71.7–80.7 years) who participated in the Mayo Clinic Study of Aging (MCSA), a population-based study of Olmsted County, Minnesota residents. These individuals were selected based on the availability of necessary data.

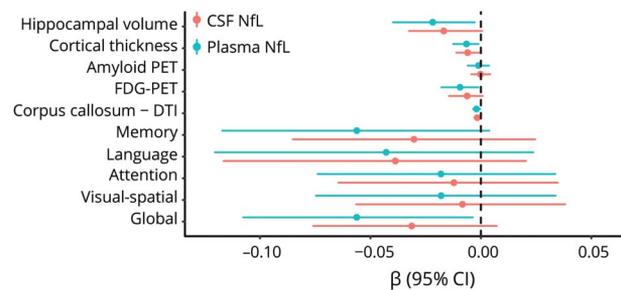
### Design, size, and duration

At baseline, the selected MCSA participants underwent measurements of plasma and CSF NfL levels, neuropsychological testing, and a battery of neuroimaging tests that included MRI, amyloid PET, and [<sup>18</sup>F]-fluorodeoxyglucose PET. They also underwent plasma NfL measurements and neuroimaging at 15–30-month follow-up visits. Plasma NfL was quantified with a Simoa assay, and CSF NfL was quantified with an ELISA. Linear mixed-effects models were used to determine whether baseline plasma and CSF NfL levels were associated with cognitive and neuroimaging outcomes.

### Main results and the role of chance

No cross-sectional associations were found. Higher baseline plasma NfL levels were longitudinally associated with worsened outcomes for global cognition and most neuroimaging

**Figure** Longitudinal associations between baseline plasma (blue) and CSF (red) NfL measurements and various outcomes



CI = confidence interval; FDG = [<sup>18</sup>F]-fluorodeoxyglucose; DTI = diffusion tensor imaging.

measures of neurodegeneration. Higher baseline CSF NfL levels were longitudinally associated with worsened outcomes for some neuroimaging measures of neurodegeneration. The  $\beta$  estimates for plasma and CSF NfL measurements were similar.

### Bias, confounding, and other reasons for caution

The sample size was small. The follow-up duration was short.

### Generalizability to other populations

The MCSA's geographically restricted recruitment may limit the generalizability of the results.

### Study funding/potential competing interests

This study was funded by various foundations and the US, EU, and Swedish governments. Some authors report receiving funding, personal fees, and committee appointments from healthcare companies; cofounding Brain Biomarker Solutions; serving as investigators on industry-sponsored clinical trials; and holding an endowed professorship. Go to [Neurology.org/N](http://Neurology.org/N) for full disclosures.

*A draft of the short-form article was written by M. Dalefield, a writer with Editage, a division of Cactus Communications. The authors of the full-length article and the journal editors edited and approved the final version.*

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