NfL as a biomarker for neurodegeneration and survival in Parkinson disease

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Study objective
This study examined whether the levels of neurofilament light chain (NfL) in CSF reflect the severity of Parkinson disease (PD) or predict survival.

Classification of evidence
Class II.

What is known and what this paper adds
High CSF NfL (cNfL) levels in patients with early PD may predict progression to PD dementia. This investigation’s results suggest that high cNfL levels also reflect greater PD severity and predict shortened survival.

Participants and setting
The derivation cohort comprised 99 patients (mean age, 69.8 years; 61% male) with incident PD who participated in a population-based cohort study in northern Sweden. The validation cohort comprised 194 patients (mean age 68 years; 61% male) with new-onset, idiopathic PD recruited through the University Hospital of Umeå. 30 neurologically healthy controls were included in this study.

Design, size, and duration
Standardized clinical examinations, including the modified Hoehn and Yahr (HY) and Unified Parkinson’s disease Rating Scales (UPDRS), at least yearly. Medication was documented by Levodopa equivalent daily dose (LEDD). Some patients had diffusion tensor MRI and presynaptic imaging of dopamine transporter status with ¹²³I-FP-CIT single-photon emission computed tomography (SPECT). All participants in this analysis had a lumbar puncture and ELISA was used to measure NfL levels. Differences in cNfL concentrations between the PD cohorts, PD subtype groups, and between patients and controls were tested by one-way ANCOVA.

Primary outcome measures
The primary outcome was the association of cNfL levels with UPDRS scores, HY stages, and survival.

Main results and the role of chance
Higher cNfL in the early phase of PD was associated with greater severity of all cardinal motor symptoms except tremor, in both cohorts, as well as with shorter survival and impaired olfaction (higher UPDRS total scores (β, 2.8; p = 0.002), UPDRS part III scores (β, 2.7; p < 0.001), and HY stages (β, 0.1; p = 0.004) in both cohorts.) Baseline cNfL levels above the median value (903 ng/L) were associated with higher risk of death during follow-up (hazard ratio, 5.8; 95% confidence interval, 2.82–11.85; p < 0.001). After adjustment for age and sex, higher cNfL correlated with striatal dopamine transporter uptake deficits and lower fractional anisotropy in diffusion tensor imaging of several axonal tracts in the brain.

Bias, confounding, and other reasons for caution
The cohorts included patients without neuropathologically confirmed diagnoses.

Study funding/potential competing interests
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