Overview

Useful For
Assessing neuronal damage related to various neurodegenerative diseases

Method Name
Digital Immunoassay

NY State Available
Yes

Specimen

Specimen Type
Plasma EDTA

Specimen Required
Collection Container/Tube: Lavender top (EDTA)
Submission Container/Tube: Plastic screw-top vial
Specimen Volume: 1.5 mL
Collection Information: Centrifuge and aliquot plasma into plastic vial. Do not submit specimen in original tube.

Specimen Minimum Volume
0.75 mL

Reject Due To

<p>| | |</p>
<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Gross hemolysis</td>
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<tr>
<td>Gross lipemia</td>
<td>OK</td>
</tr>
<tr>
<td>Gross icterus</td>
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Specimen Stability Information

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<tr>
<th>Specimen Type</th>
<th>Temperature</th>
<th>Time</th>
<th>Special Container</th>
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<tr>
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<tr>
<td></td>
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Clinical & Interpretive
Clinical Information

Neurofilaments (NF) are exclusively located in the neuronal cytoskeleton and are released to the interstitial fluid upon axonal injury or neurodegeneration. NF concentrations in cerebrospinal fluid (CSF) and blood have been shown to correlate with the extent of axonal damage or neurodegeneration in various diseases. Of the family of NF proteins, neurofilament light chain (NfL) has gained the most interest as a candidate marker of neurodegeneration. During axonal damage, NfL is released into the CSF, and eventually into the blood where concentrations are 40-fold lower than in the CSF. NfL concentrations increase with age with a reported increase in healthy control of 2.2% per year. While the specific cause of this increase has not been elucidated, it is believed to be related to aging itself as well as the development of subclinical ischemic events. NfL concentrations in blood reflect the extent of axonal damage, making them a generic marker of disease activity. Increases in NfL concentrations have been reported in individuals with traumatic brain injury, amyotrophic lateral sclerosis, multiple sclerosis, frontotemporal dementia, Alzheimer disease, and other neurodegenerative diseases.

Reference Values

<20 years: Not established
20 to 29 years: < or =8.4 pg/mL
30 to 39 years: < or =11.4 pg/mL
40 to 49 years: < or =15.4 pg/mL
50 to 59 years: < or =20.8 pg/mL
60 to 69 years: < or =28.0 pg/mL
70 to 79 years: < or =37.9 pg/mL
> or =80 years: < or =51.2 pg/mL

Interpretation

Blood neurofilament light chain (NfL) is a marker of neuro-axonal injury showing promising associations with outcomes in several neurological conditions. In neurodegenerative diseases, NfL could serve as a prognostic marker of decline and an efficacy biomarker of experimental therapies. In a meta-analysis of Alzheimer disease (AD), frontotemporal dementia, and amyotrophic lateral sclerosis (ALS), plasma NfL levels were elevated in patients compared to controls with utility in differentiating neurodegenerative conditions from non-neurodegenerative mimics. However, due to a lack of specificity to a particular neurodegenerative disease, its role as a diagnostic marker is limited.

In multiple sclerosis (MS), NfL is elevated in the blood of newly diagnosed patients and concentrations correlate with disease severity and prognosis. Early measures of blood NfL in newly diagnosed MS patients can predict brain atrophy and lesion load on magnetic resonance imaging. The use of blood NfL in serial disease monitoring and treatment response has been evaluated in various prospective clinical trials. Reductions in NfL concentrations after different treatments tend to follow the hierarchy of treatment efficacy, with greatest reductions observed with the most intensive treatments. A study that included over 1000 MS patients receiving various treatments, reported the largest reductions in plasma NfL concentrations following alemtuzumab treatment (54% reduction), and the smallest reduction with teriflunomide treatment (7%).

In AD, blood NfL concentrations have been shown to correlate with cortical thinning and cognitive decline in both sporadic and familial AD. However, at this point the clinical utility of blood NfL in AD is not fully understood.

In ALS, NfL concentrations have been suggested to be able to discriminate ALS from ALS-mimics. NfL levels at symptom onset may be prognostic of disease progression rate and may be used to stratify patients into groups with a similar
prognosis in clinical trials. Blood NFL concentrations remain relatively stable throughout the disease.

Parkinson disease (PD) patients with elevated NFL concentrations have been reported to have worse cognitive decline, brain cortical atrophy, and motor scores. Blood NFL concentrations in atypical forms of Parkinson disease are higher than in PD and may be used to help differentiate PD from atypical parkinsonian disorders.

In frontotemporal dementia (FTD), blood NFL was able to discriminate patients with the behavioral form of FTD from patients with primary psychiatric disorders. It has been suggested that blood NFL could be used to support the diagnosis of the behavioral form of FTD, monitor disease progression, and prognosis of FTD.

A study that evaluated blood NFL concentrations in 13 neurodegenerative disorders, Down syndrome, depression, and cognitive normal controls showed that plasma NFL concentrations were elevated in all cortical neurodegenerative disorders, ALS, and atypical parkinsonian disorders. Plasma NFL was clinically useful in differentiating atypical parkinsonian disorders from PD, in identifying dementia in Down syndrome, distinguishing neurodegenerative disorders from depression in older adults, and potentially identifying frontotemporal dementia in patients with cognitive impairment. Individuals with ALS, FTD, and Down syndrome with AD presented with the highest concentrations of plasma NFL.

Cautions
Increases in neurofilament light chain (NFL) are not disease specific. Results should only be used in conjunction with other clinical information when evaluating patients with neurodegeneration.

Higher concentrations of NFL may be found in persons with history of stroke, atrial fibrillation, myocardial infarction, chronic kidney disease, pregnancy, and diabetes.

Lower concentrations of NFL may be found in individuals who are obese (BMI ≥ 30).

All immunometric assays can, on rare occasions, be subject to a hooking effect at extremely high analyte concentrations (false-low results), heterophilic antibody interference (false-high results), or autoantibody interference (unpredictable effects). If the laboratory result does not fit the clinical picture, these possibilities should be considered.

Clinical Reference

Performance

Method Description

Neurofilament light (NFL) is measured on the Quanterix Simoa HD-X analyzer using the Simoa NF-Light advantage kit. The assay uses two NFL specific monoclonal antibodies. Sample, paramagnetic capture beads coated with anti-NFL antibody, and a biotinylated detector antibody are combined. Anti-NFL antibody coated paramagnetic capture beads and labeled biotinylated detector antibody will bind to NFL molecules present in the sample. Following a washing step, a conjugate of streptavidin-beta-galactosidase (SBG) is mixed with the capture beads. The captured NFL becomes enzymatically labeled when the SBG binds to the biotinylated detector antibodies. A second wash is performed, and the capture beads are resuspended in a resorufin beta-D-galactopyranoside (RGP) substrate solution.

This suspension is transferred to the Simoa Disc. Individual paramagnetic capture beads settle into 216,000 femtoliter-sized microwells designed to hold no more than one bead per well. The beads are sealed into the microwells while excess beads are washed away with a synthetic fluorinated polymer sealing oil. If NFL is present in the sample and subsequently captured and labeled, the beta-galactosidase hydrolyzes the RGP substrate and produces a fluorescent signal. This signal is detected and counted by the Simoa optical system. The concentration of NFL is interpolated from a standard curve.(Package insert: Simoa NF-Light Advantage Kit. Quanterix Corporation; 2019)

PDF Report

No

Day(s) Performed

Wednesday

Report Available

1 to 7 days

Specimen Retention Time

3 months

Performing Laboratory Location

Rochester

Fees & Codes

Fees

- Authorized users can sign in to Test Prices for detailed fee information.
Test Classification
This test was developed, and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information
83520

LOINC® Information

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