Overview

Useful For
An auxiliary test in the diagnosis of Creutzfeldt-Jakob disease
An auxiliary test in the diagnosis of small cell lung carcinoma metastasis to central nervous system or leptomeninges

Method Name
Homogeneous Time-Resolved Fluorescence

NY State Available
Yes

Specimen

Specimen Type
CSF

Specimen Required
Container/Tube: Sterile vial

Specimen Volume: 0.5 mL

Forms
If not ordering electronically, complete, print, and send a Neurology Specialty Testing Client Test Request (T732) with the specimen.

Specimen Minimum Volume
0.3 mL

Reject Due To
<table>
<thead>
<tr>
<th>Gross hemolysis</th>
<th>Reject</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gross lipemia</td>
<td>OK</td>
</tr>
<tr>
<td>Gross icterus</td>
<td>Reject</td>
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</tbody>
</table>

Specimen Stability Information

<table>
<thead>
<tr>
<th>Specimen Type</th>
<th>Temperature</th>
<th>Time</th>
<th>Special Container</th>
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</thead>
<tbody>
<tr>
<td>CSF</td>
<td>Refrigerated (preferred)</td>
<td>15 days</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ambient</td>
<td>72 hours</td>
<td></td>
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</table>

Clinical and Interpretive

Clinical Information
Enolase is a glycolytic enzyme that catalyzes the conversion of 2-phosphoglycerate to phosphoenolpyruvate. Enolase exists in the form of several tissue-specific isoenzymes, consisting of homo or heterodimers of 3 different monomer-isoforms (alpha, beta, and gamma). Neuron-specific enolase (NSE) is a 78 kD gamma-homodimer and represents the dominant enolase-isoenzyme found in neuronal and neuroendocrine tissues. Its levels in other tissues, except erythrocytes, are negligible. The biological half-life of NSE in body fluids is approximately 24 hours.

Due to this organ specificity, concentrations of NSE in serum or, more commonly, cerebrospinal fluid (CSF) are often elevated in diseases that result in relative rapid (hours/days to weeks, rather than months to years) neuronal destruction. Measurement of NSE in serum or CSF can therefore assist in the differential diagnosis of a variety of neuron-destructive and neurodegenerative disorders. The most common application is in the differential diagnosis of dementias, where elevated CSF concentrations support the diagnosis of rapidly progressive dementias, such as Creutzfeldt-Jakob disease (CJD). NSE might also have utility as a prognostic marker in neuronal injury. For example, there is increasing evidence that elevated serum NSE levels correlate with a poor outcome in coma, in particular when caused by hypoxic insult.

**Reference Values**

Normal: ≤15 ng/mL

Indeterminate: 15-30 ng/mL

Elevated: >30 ng/mL

Elevated results may indicate the need for additional workup. Possible causes may be NSE-secreting central nervous system/leptomeningeal tumor or rapid neuronal destruction from a variety of causes. In the context of dementia, elevated results may be suggestive of Creutzfeldt-Jakob disease.

**Interpretation**

The diagnosis of Creutzfeldt-Jakob disease (CJD) is highly complex and involves clinical history and neurologic examination, detection of characteristic periodic sharp and slow wave complexes on electroencephalographs, magnetic resonance imaging (hyperintense basal ganglia), and exclusion of other possible causes of dementia, in addition to cerebrospinal fluid (CSF) examination. Consequently, patients are often diagnosed as having possible, probable, or definite CJD based upon the constellation of clinical findings. Detection of elevated CSF levels of NSE protein in these patients assists in the final diagnosis.

A CSF neuron-specific enolase (NSE) within the normal reference range makes sporadic CJD very unlikely, but can be observed in less rapidly progressive forms of CJD, such as variant CJD related to infection with prions that cause bovine spongiform encephalopathy. With the previous Mayo Clinic-developed assay, in a group of carefully pre-selected patients with a probable diagnosis of CJD and an indeterminate or elevated NSE concentration in CSF, the respective diagnostic sensitivities of approximately 87% and approximately 80%, and diagnostic specificities of approximately 66% and approximately 83% were observed.

Small cell lung carcinoma central nervous system metastases, particularly if they involve the leptomeninges, will lead to, usually substantial, elevations in CSF NSE concentrations.

**Cautions**

Do not interpret neuron-specific enolase (NSE) levels in spinal fluid as absolute evidence for the presence or absence of malignant disease. Results must be used in conjunction with information from the clinical evaluation of the patient and other diagnostic procedures.

Interferences or artefactual elevations should be suspected if the clinical NSE test results are at odds with the clinical picture of other tests. The laboratory should be contacted for assistance in these situations.
Hemolysis can lead to significant artefactual NSE elevations, since erythrocytes contain NSE. Hemoglobin concentrations as low as 20 mg/dL were shown to cause invalid NSE concentrations.

Proton pump inhibitor treatment, hemolytic anemia, hepatic failure, and end-stage renal failure can also result in artefactual NSE elevations.

Other false-positive results depend on the testing context. When performing NSE testing for tumor diagnosis or follow-up, recent epileptic seizures, brain injury, encephalitis, stroke, and rapidly progressive dementia might result in false-positive results.

When NSE testing is performed to assist in the diagnosis of Creutzfeldt-Jakob disease (CJD), recent epileptic seizures, brain injury, encephalitis, stroke, and NSE-secreting tumors can cause false-positive NSE elevations in cerebrospinal fluid (CSF).

There is insufficient evidence to support CSF NSE measurements in the prognostic evaluation of coma patients. Serum NSE should be used for this application, in conjunction with clinical predictors (pupillary light responses, corneal reflexes, motor responses to pain, myoclonus, status epilepticus), electroencephalogram, sensory-evoked potentials, and imaging.

NSE values can vary significantly between methods and assays. Serial follow-up should be performed with the same assay. If assays are changed, patients should have their baseline level reestablished.

This assay is an immunometric assay, and can, in rare situations, be affected by false-low results in the presence of extremely high NSE concentrations ("hooking") or autoantibodies to NSE, as well as by false-high results in the presence of heterophile antibodies.

**Clinical Reference**


**Performance**
Method Description
Neuron specific enolase (NSE) is measured in this homogeneous automated immunofluorescent assay on the BRAHMS Kryptor. The Kryptor uses TRACE (time resolved amplified cryptate emission) technology based on a non-radioactive transfer of energy. This transfer occurs between 2 fluorescent tracers: the donor (europium cryptate) and the acceptor (XL665). In the NSE assay, 2 monoclonal antibodies are labeled, 1 with europium cryptate and 1 with XL665. NSE is sandwiched between the 2 antibodies, bringing them into close proximity. When the antigen-antibody complex is excited with a nitrogen laser at 337 nm, some fluorescent energy is emitted at 620 nm and the rest is transferred to XL665. This energy is then emitted as fluorescence at 665 nm. A ratio of the energy emitted at 665 nm to that emitted at 620 nm (internal reference) is calculated for each sample. Signal intensity is proportional to the number of antigen-antibody complexes formed, and therefore to antigen concentration. (Package insert: BRAHMS NSE Kryptor. Thermo Fisher Scientific BRAHMS LLC, Version 20.04.2012)

PDF Report
No

Day(s) and Time(s) Test Performed
Monday through Friday; 8 a.m.-2 p.m.
Saturday; 8 a.m.-1 p.m.

Analytic Time
1 day

Maximum Laboratory Time
4 days

Specimen Retention Time
2 weeks

Performing Laboratory Location
Rochester

Fees and Codes

Fees
- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their Regional Manager. For assistance, contact Customer Service.

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 U.S. Food and Drug Administration.

CPT Code Information
83520

LOINC® Information
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<tbody>
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<td>NSESF</td>
<td>Neuron Specific Enolase, CSF</td>
<td>44802-7</td>
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<table>
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<tr>
<th>Result ID</th>
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