MAYO CLINIC LABORATORIES

Test Definition: NSESF

Neuron-Specific Enolase (NSE), Spinal Fluid

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

Gross hemolysis	Reject
Gross lipemia	OK
Gross icterus	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
CSF	Refrigerated (preferred)	15 days	
	Ambient	72 hours	

Clinical & 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 kDa 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: < or =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 neuron-specific enolase-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 kidney 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.

In rare cases, some individuals can develop antibodies to mouse or other animal antibodies (often referred to as human anti-mouse antibodies [HAMA] or heterophile antibodies), which may cause interference in some immunoassays. Caution should be used in interpretation of results, and the laboratory should be alerted if the result does not correlate with the clinical presentation.

Clinical Reference

1. Burghuber OC, Worofka B, Schernthaner G, et al: Serum neuron-specific enolase is a useful tumor marker for small cell lung cancer. Cancer. 1990 Mar 15;65:1386-1390
2. Lamberts SW, Hofland LJ, Nobels FR: Neuroendocrine tumor markers. Front Neuroendocrinol. 2001 Oct;22(4):309-339
3. Aksamit AJ, Jr, Preissner CM, Homburger HA: Quantitation of 14-3-3 and neuron-specific enolase proteins in CSF in Creutzfeldt-Jacob disease. Neurology. 2001 Aug 28;57(4):728-730
4. Riley RD, Heney D, Jones DR, et al: A systematic review of molecular and biological tumor markers in neuroblastoma. Clin Cancer Res. 2004 Jan 1;10(1 Pt 1):4-12

5. Portela-Gomes GM, Hacker GW, Weitgasser R: Neuroendocrine cell markers for pancreatic islets and tumors. Appl Immunohistochem Mol Morphol. 2004 Sep;12(3):183-192
6. Wijdicks EF, Hijdra A, Young GB, Bassetti CL, Wiebe S, Quality Standards Subcommittee of the American Academy of Neurology: Practice parameter: prediction of outcome in comatose survivors after cardiopulmonary resuscitation (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology. 2006 Jul;67(2):203-210
7. Huang L, Zhou JG, Yao WX, et al: Systematic review and meta-analysis of the efficacy of serum neuron-specific enolase for early small cell lung cancer screening. Oncotarget. 2017 May 11;8(38):64358–64372
8. Cheng F, Yuan Q, Yang J, Wang W, Liu H: The prognostic value of serum neuron-specific enolase in traumatic brain injury: systematic review and meta-analysis. PLoS One. 2014 Sep 4;9(9):e106680

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.(Unpublished Mayo method)

PDF Report

No

Day(s) Performed

Monday through Saturday

Report Available

1 to 3 days

Specimen Retention Time

2 weeks

Performing Laboratory Location

Rochester

Fees & 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 account representative. 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 US Food and Drug Administration.

CPT Code Information

83520

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
NSESF	Neuron Specific Enolase, CSF	44802-7

Result ID	Test Result Name	Result LOINC® Value
NSESF	Neuron Specific Enolase, CSF	44802-7