Test Definition: ASYNC

Alpha-Synuclein Protein Aggregates, Spinal Fluid

Overview

Useful For

Detection of pathogenic alpha-synuclein (alpha-synuclein aggregates) in adult patients being assessed for clinically uncertain cognitive decline or clinically uncertain parkinsonian syndromes

Special Instructions

- Spinal Fluid Specimen Collection Instructions for Alpha-Synuclein Protein Aggregates

Highlights

The SAAmplify-aSYN test is a cerebrospinal fluid biomarker test that benefits adult patients exhibiting signs and symptoms of clinically uncertain cognitive decline or clinically uncertain parkinsonian syndromes, such as Parkinson disease, atypical parkinsonism, dementia with Lewy bodies, Alzheimer disease, mild cognitive impairment, and multiple system atrophy.

Method Name

Seed Amplification Assay (SAA)

NY State Available

No

Specimen

Specimen Type

CSF

Specimen Required

Supplies: Sterile Specimen Tube, 6 mL (T485)
Container/Tube: Sterile tube
Specimen Volume: 1 mL
Collection Instructions:
1. Perform lumbar puncture and discard the first 1 to 2 mL of cerebrospinal fluid (CSF).
2. Collect CSF directly into a sterile tube.
3. Inspect specimen for visible discoloration. Specimen must be clear and colorless to perform testing. **Do not centrifuge**.
4. Freeze sample upright prior to placing in transport container.
5. Collection instructions can also be found on Spinal Fluid Specimen Collection Instructions for Alpha-Synuclein Protein Aggregates.
Note: Polypropylene tubes are recommended for transport.

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

Hemolysis	Reject
Icterus	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
CSF	Frozen (preferred)	60 days	
	Refrigerated	14 days	

Clinical & Interpretive

Clinical Information

Synucleinopathies are a family of neurodegenerative disorders diagnosed pathologically based on the presence of inclusions composed of aggregates of misfolded alpha-synuclein protein in the brain. Synucleinopathies are divided into two major subgroups: Lewy body disease (LBD) and multiple system atrophy (MSA). LBD is characterized by deposits of aggregated alpha-synuclein that develop in neurons (Lewy bodies or Lewy neurites); LBDs include Parkinson disease, dementia with Lewy bodies, and Parkinson disease dementia. MSA is characterized by deposits of aggregated alpha-synuclein that develop in oligodendrocytes (called glial cytoplasmic inclusions). Synuclein pathology is often also present as a co-pathology in other neurodegenerative disorders, including Alzheimer disease and mixed dementias. Therefore, the presence or absence of synuclein pathology is an important factor influencing diagnosis and disease course across a spectrum of motor and cognitive neurodegenerative disorders.

Historically, synucleinopathies have been diagnosed during life based on clinical symptoms, sometimes augmented by dopamine transporter single-photon emission computed tomography imaging, with definitive diagnosis only possible through identification of synuclein aggregates in the brain at autopsy. The alpha-synuclein seed amplification assay (SAA) detects aggregates of alpha-synuclein in cerebrospinal fluid (CSF). Studies have shown that detection of alpha-synuclein aggregates in CSF during life by SAA correlates with high sensitivity and specificity to the presence of synuclein pathology identified in the brain at autopsy.

Reference Values

An interpretive report will be provided

Interpretation

Detection of alpha-synuclein aggregates in cerebrospinal fluid is consistent with the presence of a synucleinopathy (eg,

Parkinson disease, dementia with Lewy bodies, Alzheimer disease with Lewy body pathology, and multiple system atrophy).

Cautions

Results must be interpreted in conjunction with other patient clinical information.

The alpha-synuclein (aSyn) protein test utilizes fluorescence to detect increases in aSyn aggregate formation. Validation studies have determined that certain substances such as blood, hemoglobin, and conjugated bilirubin may affect results at concentrations where visible discoloration is evident in the cerebrospinal fluid. The laboratory will evaluate all specimens submitted for suitability for testing. Sensitivity for detection of alpha-synuclein aggregates with a Detected-2 profile is low; therefore, results should be interpreted with caution for the purposes of rule in/rule out multiple system atrophy.

This test is for professional use only.

Supportive Data

Table: Update to Clinical Performance Assessment: SAAmplify-aSYN (CSF)
Performance (n/n) (95% CI)

Metric	Accuracy	Sensitivity	Specificity
Synucleinopathy(a)	84.4% (351/416) (95% CI: 80.5, 87.7)	79.3% (230/290) (95% CI: 74.2, 83.8)	96.0% (121/126) (95% CI: 91.0 96.7)
NSD(b)	91.3% (368/403 (95% CI: 88.1, 93.9)	86.1% (99/115) (95% CI: 78.4, 91.8)	93.4% (269/288) (95% CI: 89.9, 96.0)
MSA (c)	83.9% (338/403) 95% CI: 79.9, 87.3)	65.4% (106/162) (95% CI: 57.6, 72.7)	96.3% (232/241) (95% CI: 93.0, 98.3)

a. Performance assessment of results based on confusion-matrix outcomes for total synucleinopathy with a diagnosis of neuronal alpha-synuclein disease (NSD), multiple system atrophy (MSA), and pure autonomic failure (PAF).
b. Performance assessment of results based on confusion-matrix outcomes for a diagnosis of NSD.
c. Performance assessment of results based on confusion-matrix outcomes for a diagnosis of MSA.

Clinical Reference

1. Rizzo G, Copetti M, Arcuti S, Martino D, Fontana A, Logroscino G. Accuracy of clinical diagnosis of Parkinson disease: A systematic review and meta-analysis. Neurology. 2016;86(6):566-576. doi:10.1212/WNL.0000000000002350
2. Rizzo G, Arcuti S, Copetti M, et al. Accuracy of clinical diagnosis of dementia with Lewy bodies: a systematic review and meta-analysis. J Neurol Neurosurg Psychiatry. 2018;89(4):358-366. doi:10.1136/jnnp-2017-316844
3. Wenning GK, Stankovic I, Vignatelli L, et al. The Movement Disorder Society Criteria for the Diagnosis of Multiple System Atrophy. Mov Disord. 2022;37(6):1131-1148. doi:10.1002/mds.29005
4. Plastini MJ, Abdelnour C, Young CB, et al. Multiple biomarkers improve diagnostic accuracy across Lewy body and Alzheimer's disease spectra. Ann Clin Transl Neurol. 2024;11(5):1197-1210. doi:10.1002/acn3.52034
5. Tosun D, Hausle Z, Iwaki H, et al. A cross-sectional study of alpha-synuclein seed amplification assay in Alzheimer's disease neuroimaging initiative: Prevalence and associations with Alzheimer's disease biomarkers and cognitive function. Alzheimers Dement. 2024;20(8):5114-5131. doi:10.1002/alz.13858

Performance

Method Description

This test is a seed amplification assay (SAA). The novel SAA strategy essentially mimics the biological process in which in vivo protein misfolding and aggregation follows a seeding/nucleation mechanism. Briefly, cerebrospinal fluid samples are incubated with an excess of monomeric human recombinant (rec) alpha Syn (aSyn) and subjected to intermittent shaking/incubation cycles. If soluble misfolded aSyn aggregates are present in the sample, these aggregates are amplified using rec-aSyn as substrate. aSyn aggregates formed in the reaction are detected as an increase in fluorescence due to the presence of the amyloid-specific binding dye, thioflavin T. In the absence of aSyn seeds, fluorescence remains below the validated assay cutoff.

PDF Report

Referral

Day(s) Performed

Varies

Report Available

15 to 18 days

Performing Laboratory Location

Amprion Inc.

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 Amprion, Inc. This test is used for clinical purposes. It should not be regarded as investigational or for research. It has not been cleared or approved by the FDA. The laboratory is regulated under CLIA as qualified to perform high-complexity testing.

CPT Code Information

0393U

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
ASYNC	Alpha-Synuclein Aggregates, CSF	Not Provided

MAYO CLINIC LABORATORIES

Test Definition: ASYNC

Alpha-Synuclein Protein Aggregates, Spinal Fluid

Result ID	Test Result Name	Result LOINC® Value
ASYNC	Alpha-Synuclein Aggregates, CSF	Not Provided