Test Definition: PSYCF

Psychosine, Spinal Fluid

Overview

Useful For

Aiding in the biochemical diagnosis of Krabbe disease using cerebrospinal fluid specimens

Follow-up of individuals affected with Krabbe disease

Follow-up testing after an abnormal newborn screening result for Krabbe disease

Monitoring individuals at risk to develop late onset Krabbe disease

Monitoring individuals with Krabbe disease after hematopoietic stem cell transplantation

Genetics Test Information

Krabbe disease (globoid cell leukodystrophy) is an autosomal recessive lysosomal disorder caused by deficient activity of the enzyme galactocerebrosidase.

Krabbe disease is clinically variable and infantile-onset Krabbe disease is the most severe variant with rapid neurological regression resulting in early death.

Highlights

This test is used as a biomarker of Krabbe disease for individuals with reduced galactocerebrosidase (GALC) activity.

For cerebrospinal fluid (CSF) testing, psychosine is typically ordered when CSF is collected primarily to determine protein content in a patient at risk of or monitored for the development of signs of Krabbe disease.

Elevations in psychosine support a diagnosis of Krabbe disease; therefore, psychosine quantitation is a useful biomarker in determining if an individual has active disease. In addition, psychosine may be a valuable biomarker to monitor disease progression or treatment response.

Psychosine may also be elevated in saposin A cofactor deficiency, which results in a similar clinical phenotype to Krabbe disease, but patients typically have normal GALC activity in vitro.

Method Name

Liquid Chromatography Tandem Mass Spectrometry (LC-MS/MS)

NY State Available

Yes

Specimen

Specimen Type

CSF

Ordering Guidance

This test is recommended as a diagnostic or monitoring test when spinal fluid is collected primarily to determine protein content in a patient at risk of or monitored for the development of signs of Krabbe disease.

An additional and less invasive diagnostic or monitoring test is measurement of psychosine in red blood cells; see PSYR / Psychosine, Whole Blood.

Shipping Instructions

Send on dry ice. Avoid freeze thaw cycles.

Necessary Information

1. Patient's age is required.

2. Date of hematopoietic stem cell transplantation (HSCT), if performed.

Specimen Required

Container/Tube: Sterile vial.

Specimen Volume: 0.15 mL

Collection Instructions: Do not aliquot.

Forms

If not ordering electronically, complete, print, and send a Biochemical Genetics Test Request (T798) with the specimen.

Specimen Minimum Volume

0.1 mL

Reject Due To

Gross hemolysis	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
CSF	Frozen	7 days	

Clinical & Interpretive

Clinical Information

Krabbe disease (globoid cell leukodystrophy) is an autosomal recessive lysosomal disorder caused by deficient activity of the enzyme galactocerebrosidase (GALC). GALC facilitates the lysosomal degradation of psychosine (galactosylsphingosine) and 3 other substrates, galactosylceramide, lactosylceramide, and lactosylsphingosine. Krabbe disease is caused by variants in the *GALC* gene, and it has an estimated frequency of 1 in 100,000 births.

The clinical course of Krabbe disease can be variable, even within the same family. Eighty-five percent to 90% of patients present before the first year of life with central nervous system impairment, including increasing irritability, developmental delay, and sensitivity to stimuli. Rapid neurodegeneration, including white matter disease follows, with death usually occurring by 2 years of age. Late onset forms of the disease affect 10% to15% of individuals and are characterized by ataxia, vision loss, weakness, and psychomotor regression, typically presenting from age 6 months to the seventh decade of life.

Newborn screening for Krabbe disease has been implemented in some states. The early (presymptomatic) identification and subsequent testing of infants at risk for Krabbe disease may be helpful in reducing the morbidity and mortality associated with this disease. While treatment is mostly supportive, hematopoietic stem cell transplantation has shown some success if performed prior to onset of neurologic damage.

Psychosine is 1 of 4 substrates degraded by GALC and is a neurotoxin at elevated concentrations. It has been shown to be elevated in patients with active Krabbe disease or with saposin A cofactor deficiency and, therefore, may be a useful biomarker for the presence of disease or disease progression.

Reduced or absent GALC in leukocytes (CBGC / Galactocerebrosidase, Leukocytes) or dried blood spots (PLSD / Lysosomal and Peroxisomal Storage Disorders Screen, Blood Spot) along with elevated psychosine levels can indicate a diagnosis of Krabbe disease. Molecular sequencing of the *GALC* gene (KRABZ / Krabbe Disease, Full Gene Analysis and Large [30 kb] Deletion, Varies) allows for detection of the disease-causing variants in affected patients and carrier detection in family members.

Individuals with a disease phenotype similar to Krabbe disease may have saposin A cofactor deficiency. Saposin A cofactor deficiency also results in elevated psychosine levels. Testing for this condition via molecular analysis of *PSAP* is useful in those with elevated psychosine and normal to reduced GALC activity with normal molecular genetic *GALC* sequencing.

Reference Values

Normal < 0.04 nmol/L

Interpretation

An elevation of psychosine is indicative of Krabbe disease or saposin A cofactor deficiency.

Cautions

Asymptomatic patients with later onset Krabbe disease may have a normal psychosine concentration in cerebrospinal fluid.

Clinical Reference

1. Kwon JM, Matern D, Kurtzberg J, et al. Consensus guidelines for newborn screening, diagnosis and treatment of infantile Krabbe disease. Orphanet J Rare Dis. 2018;13(1):30. doi: 10.1186/s13023-018-0766-x

2. Orsini JJ, Escolar ML, Wasserstein MP, et al. Krabbe disease. In: Adam MP, Mirzaa GM, Pagon RA, eds. GeneReviews[Internet]. University of Washington, Seattle; 2000. Updated October 11, 2018. Accessed August 31, 2023. Available at: www.ncbi.nlm.nih.gov/books/NBK1238/

3. Turgeon CT, Orsini JJ, Sanders KA, et al. Measurement of psychosine in dried blood spots--a possible improvement to newborn screening programs for Krabbe disease. J Inherit Metab Dis. 2015;38(5):923-929

4. Wenger DA, Escolar ML, Luzi P, Rafi MA: Krabbe disease (globoid cell leukodystrophy). In: Valle D, Antonarakis S,

Ballabio A, Beaudet AL, Mitchell GA, eds. The Online Metabolic and Molecular Bases of Inherited Disease. McGraw-Hill; 2019. Accessed August 31, 2023. Available at https://ommbid.mhmedical.com/content.aspx?sectionid=225546481&bookid=2709

5. Guenzel AJ, Turgeon CT, Nickander KK, et al. The critical role of psychosine in screening, diagnosis, and monitoring of Krabbe disease. Genet Med. 2020;22(6):1108-1118

6. Thompson-Stone R, Ream MA, Gelb M, et al. Consensus recommendations for the classification and long-term follow up of infants who screen positive for Krabbe disease. Mol Genet Metab. 2021;134(1-2):53-59

Performance

Method Description

Psychosine is extracted from cerebrospinal fluid and quantified using an isotopically labeled internal standard by liquid chromatography tandem mass spectrometry.(Unpublished Mayo method)

PDF Report

No

Day(s) Performed

Tuesday, Thursday

Report Available

3 to 7 days

Specimen Retention Time

Indefinitely

Performing Laboratory Location

Mayo Clinic Laboratories - Rochester Main Campus

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. It has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information

82542

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
PSYCF	Psychosine, CSF	93686-4

Result ID	Test Result Name	Result LOINC® Value
606150	Interpretation (PSYCF)	59462-2
606146	Psychosine, CSF	93686-4
605158	Reviewed By	18771-6