

Stiff-Person Spectrum Disorders including Progressive Encephalomyelitis with Rigidity and Myoclonus, Interpretation, Spinal Fluid

## Overview

### Useful For

Interpretation for the evaluation of stiff-person spectrum disorders, including the classical or focal forms, such as stiff-limb or stiff-trunk, and progressive encephalomyelitis with rigidity and myoclonus, using spinal fluid specimens

### Method Name

Only orderable as part of profile. For more information see SPPC / Stiff-Person Spectrum Disorders Evaluation, including Progressive Encephalomyelitis with Rigidity and Myoclonus, Spinal Fluid.

Medical Interpretation

### NY State Available

Yes

## Specimen

### Specimen Type

CSF

### Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
CSF	Refrigerated (preferred)	28 days	
	Frozen	28 days	
	Ambient	72 hours	

## Clinical & Interpretive

### Clinical Information

Stiff-person spectrum disorders include classical stiff-person syndrome, focal stiff-person forms (stiff-limb and stiff-trunk), and a severe encephalomyelitic form known as [progressive encephalomyelitis with rigidity and myoclonus](#) (PERM). Paraneoplastic and idiopathic autoimmune causes may be differentiated by a neuronal IgG antibody profile. The unifying clinical and electrophysiologic characteristic is central nervous system hyperexcitability. Clinical manifestations include stiffness, spasms, heightened startle responses, and falls. For the classical stiff-person form, the low back and lower extremities are principally affected. The stiff-limb phenotype may affect one or more limbs without truncal involvement. Truncal manifestations include low back spasms and deformity, with sudden chest wall spasms and

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breathing difficulties. In addition, patients with PERM have encephalopathy (often with seizures), myoclonus (muscle jerking), and dysautonomia. The most common IgG biomarker detected in stiff-person spectrum is glutamic acid decarboxylase 65 (GAD65) antibody. These patients generally have a classical or limited stiff-person form, almost always have antibody values above 20.0 nmol/L, have accompanying non-neurological autoimmune disease in 50% (type 1 diabetes and thyroid disease being most common), and almost always without accompanying cancer. Amphiphysin-IgG positivity is most frequently encountered in patients with occult breast adenocarcinoma presenting with limb stiffness and spasms; neurogenic changes are usually detectable on clinical exam and electromyography. Glycine receptor (GlyR [alpha1 1 subunit]) autoimmunity patients present more commonly with PERM or stiff-limb phenotype rather than the classical stiff-person form. Associated neoplasms in GlyR antibody positive patients include thymoma, but a general search for age- and sex-pertinent cancers should also be undertaken. Dipeptidyl-peptidase-like protein-6 (DPPX) antibody is associated with diverse central and autonomic presentations, including PERM. B-cell blood dyscrasias should be tested for in DPPX-IgG positive cases. All stiff-person spectrum patients, both seropositive and seronegative, may be immune therapy responsive. GlyR-IgG may be predictive of immune therapy response, including in patients with coexisting GAD65 antibody.

### Reference Values

Only orderable as part of profile. For more information see SPPC / Stiff-Person Spectrum Disorders Evaluation, including Progressive Encephalomyelitis with Rigidity and Myoclonus, Spinal Fluid.

### Interpretation

Spinal fluid antibody positivity supports the clinical diagnosis of stiff-person spectrum disorder (classical stiff-person, stiff-limb, stiff-trunk, or progressive encephalomyelitis with rigidity and myoclonus). A paraneoplastic basis should be considered.

### Cautions

Negative results do not exclude the diagnosis of stiff-person spectrum disorder or progressive encephalomyelitis with rigidity and myoclonus (PERM). Glutamic acid decarboxylase 65 (GAD65) antibody positive values below 20 nmol/L should be interpreted with caution. Lower values are encountered in 8% of the general population. However, GAD65 autoimmunity (any antibody value) is associated with other autoimmune diseases that can cause neurological symptoms, including type 1 diabetes, pernicious anemia, hypothyroidism, and adrenal insufficiency.

### Clinical Reference

1. Hinson SR, Lopez-Chiriboga AS, Bower JH, et al: Glycine receptor modulating antibody predicting treatable stiff-person spectrum disorders. *Neurol Neuroimmunol Neuroinflamm*. 2018 Jan;5:e438
2. Hutchinson M, Waters P, McHugh J, et al: Progressive encephalomyelitis, rigidity, and myoclonus: a novel glycine receptor antibody. *Neurology*. 2008 Oct;71(16):1291-1292
3. Martinez-Hernandez E, Arino H, McKeon A, et al: Clinical and immunologic investigations in patients with stiff-person spectrum disorder. *JAMA Neurol*. 2016 Jun;73(6):714-720
4. McKeon A, Martinez-Hernandez E, Lancaster E, et al: Glycine receptor autoimmune spectrum with stiff-man syndrome phenotype. *JAMA Neurol*. 2013 Jan;70(1):44-50
5. McKeon A, Robinson MT, McEvoy KM, et al: Stiff-man syndrome and variants: clinical course, treatments, and outcomes. *Arch Neurol*. 2012 Feb;69(2):230-238
6. Pittock SJ, Lucchinetti CF, Parisi JE, et al: Amphiphysin autoimmunity: paraneoplastic accompaniments. *Ann Neurol*. 2005 Jun;58(1):96-107

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- Pittock SJ, Yoshikawa H, Ahlskog JE, et al: Glutamic acid decarboxylase autoimmunity with brainstem, extrapyramidal, and spinal cord dysfunction. Mayo Clin Proc. 2006 Sep;81(9):1207-1214
  - Tobin WO, Lennon VA, Komorowski L, et al: DPPX potassium channel antibody: frequency, clinical accompaniments, and outcomes in 20 patients. Neurology. 2014 Nov;83(20):1797-1803
  - Walikonis JE, Lennon VA: Radioimmunoassay for glutamic acid decarboxylase (GAD65) autoantibodies as a diagnostic aid for stiff-man syndrome and a correlate of susceptibility to type 1 diabetes mellitus. Mayo Clin Proc. 1998 Dec;73(12):1161-1166

## Performance

### Method Description

A neuroimmunology expert reviews the laboratory data and an interpretive report is issued.

### PDF Report

No

### Day(s) Performed

Varies

### Report Available

5 to 10 days

### 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

Not Applicable

### LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
SPPCI	Stiff-Person/PERM Interp, CSF	69048-7

## Test Definition: SPPCI

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Result ID	Test Result Name	Result LOINC® Value
614602	Stiff-Person/PERM Interp, CSF	69048-7
618909	IFA Notes	48767-8