

## Voltage-Gated Potassium Channel Antibody Disorders

Voltage-gated potassium channel antibody disorders include limbic encephalitis, faciobrachial dystonic seizures, and peripheral nerve hyperexcitability disorders that may occur following immunotherapy and/or plasmapheresis.

### Disease Overview

#### Incidence

Unknown

#### Symptoms

- Limbic encephalitis (mainly LGI1 antibodies)
  - Amnesia
  - Seizures
  - Disorientation
  - Psychiatric disturbance
  - Peripheral nerve hyperexcitability
  - Neuromyotonia
  - CSF usually normal
- Morvan syndrome (mainly CASPR2 antibodies)
  - Limbic encephalitis
  - Neuromyotonia
  - Confusion
  - Amnesia
  - Insomnia
  - Pain
  - Autonomic dysfunction: hyperhidrosis, constipation, urinary incontinence

#### Diagnostic Issues

Antibody testing may aid in diagnosis

- Should be performed only when neuromuscular and/or neurological symptoms are present
- Anti-VGKC disorders are rare and present with symptoms similar to those of other encephalitic disorders
- Antibody testing should not be used for screening
- Antibodies may be associated with paraneoplastic (autoimmune) or nonparaneoplastic neurological disorders
- Not all neurological disorders or antibodies are associated with tumors
  - In most antibody-mediated, non-neoplastic-associated diseases, individuals improve substantially with immunotherapy
  - Important to diagnose these illnesses due to therapeutic responsiveness

#### Tests to Consider

##### Voltage-Gated Potassium Channel (VGKC) Antibody with Reflex to LGI1 and CASPR2 Screen and Titer, Serum 2009463

**Method:** Quantitative Radioimmunoassay/Semi-Quantitative Indirect Fluorescent Antibody

- Screening test for VGKC antibody receptor complex-associated autoantibodies
- Reflexes to CASPR2 and LGI1 antibodies

##### Voltage-Gated Potassium Channel (VGKC) Complex Antibody Panel with Reflex to Titer, CSF 3001996

**Method:** Quantitative Radioimmunoassay/Semi-Quantitative Indirect Fluorescent Antibody

##### Voltage-Gated Potassium Channel (VGKC) Antibody, Serum 2004890

**Method:** Quantitative Radioimmunoassay

Screening test for VGKC antibody receptor complex-associated autoantibodies

##### Voltage-Gated Potassium Channel (VGKC) Antibody, CSF 3001387

**Method:** Quantitative Radioimmunoassay

Screening test for VGKC antibody receptor complex-associated autoantibodies

##### Leucine-Rich, Glioma-Inactivated Protein 1 Antibody, IgG with Reflex to Titer, Serum 2009456

**Method:** Semi-Quantitative Indirect Fluorescent Antibody

Aid in diagnosis of LGI1 disorders

##### Leucine-Rich, Glioma-Inactivated Protein 1 Antibody, IgG with Reflex to Titer, CSF 3001992

**Method:** Semi-Quantitative Indirect Fluorescent Antibody

Aid in diagnosis of LGI1 disorders

##### Contactin-Associated Protein-2 Antibody, IgG with Reflex to Titer, Serum 2009452

**Method:** Semi-Quantitative Indirect Fluorescent Antibody

Aid in diagnosis of CASPR2 disorders

## Physiology

- VGKC autoantibodies
  - Directed against a protein that is complexed with potassium channels in both peripheral nervous system and CNS
    - CASPR2
      - Present in ~50% of individuals with neuromyotonia
      - CASPR2 antibodies are common in individuals with thymic malignancies
    - LGI1
      - Not directed against the potassium channels
      - Associated with limbic encephalitis, faciobrachial dystonic seizures, hyponatremia, and myoclonic movements
      - Disorders are rarely associated with tumors
- VGKC RIA test can be used as a general screen for VGKC-complex antibodies directed against
  - LGI1
  - CASPR2
  - Other unidentified targets

## Test Interpretation

### Results

#### VGKC Antibody, Serum

- Positive: >88 pmol/L
  - Suggests VGKC antibody-related disease
- Indeterminant: 32-87 pmol/L
  - Retest in 2-4 weeks
- Negative: 0-31 pmol/L
  - Likelihood of VGKC antibody-related disease is reduced but not necessarily eliminated

#### VGKC Antibody, CSF

- Positive: >1.1 pmol/L
  - Suggests VGKC antibody-related disease
- Negative: 0.0-1.1 pmol/L
  - Likelihood of VGKC antibody-related disease is reduced but not necessarily eliminated

#### LGI1 Antibody, Serum

- Positive:  $\geq 1:10$ 
  - Suggests LGI1 antibody-related disease
- Negative: <1:10
  - Does not rule out disorders associated with VGKC complex antibodies

#### CASPR2 Antibody, Serum

- Positive:  $\geq 1:10$ 
  - Suggests CASPR2 antibody-related disease
- Negative: <1:10
  - Does not rule out disorders associated with VGKC complex antibodies

#### Contactin-Associated Protein-2 Antibody, IgG with Reflex to Titer, CSF 3001986

**Method:** Semi-Quantitative Indirect Fluorescent Antibody

Aid in diagnosis of CASPR2 disorders

#### Leucine-Rich, Glioma-Inactivated Protein 1 Antibody, IgG and Contactin-Associated Protein-2 Antibody, IgG with Reflex to Titers, Serum 2009460

**Method:** Semi-Quantitative Indirect Fluorescent Antibody

Aid in diagnosis of LGI1 and CASPR2 disorders

#### Autoimmune Encephalitis Reflexive Panel, Serum 2013601

**Method:** Semi-Quantitative Indirect Fluorescent Antibody/Semi-Quantitative Enzyme-Linked Immunosorbent Assay/Quantitative Radioimmunoassay

- Differential evaluation of encephalitis of unknown origin with subacute onset of seizures, confusion, memory loss, and/or behavioral change
- Panel includes NMDA receptor antibody, VGKC antibody, GAD65 antibody, AQP4 antibody, and LGI1 and CASPR2 antibodies.
- For adults and patients with suspicion of cancer, additional evaluation of paraneoplastic autoantibodies is recommended
- Individual tests in panel may also be ordered separately

#### Autoimmune Encephalitis Extended Panel, Serum 3001431

**Method:** Semi-Quantitative Indirect Fluorescent Antibody/Quantitative Radioimmunoassay/Semi-Quantitative Enzyme-Linked Immunosorbent Assay

- Differential evaluation of encephalitis of unknown origin with subacute onset of seizures, confusion, memory loss, and/or behavioral change
- Testing for LGI1 and CASPR2 antibodies always performed
- Panel includes NMDA receptor antibody, VGKC antibody, GAD65 antibody, AQP4 antibody
- For adults and patients with suspicion of cancer, additional evaluation of paraneoplastic autoantibodies is recommended
- Individual tests in panel may also be ordered separately

See [Anti-NMDA Receptor \(NR1\) IgG Antibodies](#) test fact sheet for more information on the evaluation of NMDA antibodies in autoimmune encephalitis.

## Limitations

### VGKC Antibody

- Presence of VGKC antibodies should be used in conjunction with clinical manifestations for
  - Neuromyotonia spectrum of disorders
  - VGKC antibody-associated limbic encephalitis
- Should not be used as the sole criterion for diagnosis
- VGKC receptor-complex proteins may be coprecipitated by anti-VGKC antibodies, including
  - LGI1
  - CASPR2
  - Other unidentified targets

## Related Information

[N-methyl-D-Aspartate \(NMDA\)-Type Glutamate Receptor Autoantibody Disorders - Anti-NMDA-Receptor Encephalitis](#)  
[Paraneoplastic Neurological Syndromes and Associated Disorders - PNS](#)  
[Paraneoplastic Neurological Syndromes Testing Algorithm - Serum](#)

## Related Tests

[Autoimmune Encephalitis Reflexive Panel, CSF 3002787](#)

**Method:** Semi-Quantitative Indirect Fluorescent Antibody/Quantitative Radioimmunoassay/Semi-Quantitative Enzyme-Linked Immunosorbent Assay

[N-methyl-D-Aspartate Receptor Antibody, IgG, Serum with Reflex to Titer 2004221](#)

**Method:** Semi-Quantitative Indirect Fluorescent Antibody

[N-methyl-D-Aspartate Receptor Antibody, IgG, CSF with Reflex to Titer 2005164](#)

**Method:** Semi-Quantitative Indirect Fluorescent Antibody

[Glutamic Acid Decarboxylase Antibody 2001771](#)

**Method:** Semi-quantitative Enzyme-Linked Immunosorbent Assay

[Glutamic Acid Decarboxylase Antibody, CSF 3002788](#)

**Method:** Semi-quantitative Enzyme-Linked Immunosorbent Assay

[Aquaporin-4 Receptor Antibody 2003036](#)

**Method:** Semi-Quantitative Enzyme-Linked Immunosorbent Assay

[Aquaporin-4 Receptor Antibody, IgG by IFA with Reflex to Titer, Serum 2013320](#)

**Method:** Semi-Quantitative Indirect Fluorescent Antibody

[Alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic Acid \(AMPA\) Receptor Antibody, IgG by IFA with Reflex to Titer, Serum 3001260](#)

**Method:** Semi-Quantitative Indirect Fluorescent Antibody

[Gamma Aminobutyric Acid Receptor, Type B \(GABA-BR\) Antibody, IgG by IFA with Reflex to Titer, Serum 3001270](#)

**Method:** Semi-Quantitative Indirect Fluorescent Antibody

[Myelin Oligodendrocyte Glycoprotein \(MOG\) Antibody, IgG by IFA with Reflex to Titer, Serum 3001277](#)

**Method:** Semi-Quantitative Indirect Fluorescent Antibody

### Autoimmune Neuromuscular Junction Reflexive Panel 3003017

**Method:** Quantitative Radioimmunoassay/Qualitative Radiobinding Assay/Semi-Quantitative Flow Cytometry/Semi-Quantitative Indirect Fluorescent Antibody

- Acceptable reflexive panel for the differential diagnosis of acquired neuromuscular junction disorders
- Panel includes acetylcholine receptor binding, blocking, and modulating antibodies; ganglionic acetylcholine receptor antibodies; P/Q-type and N-type voltage-gated calcium channels; voltage-gated potassium channels; titin antibody; striated muscle antibodies; leucine-rich glioma-inactivated protein 1 antibody; and contactin-associated protein-2 antibody IgG with reflex to titers

See [Related Tests](#)

[Paraneoplastic Antibodies \(PCCA/ANNA\) by IFA with Reflex to Titer and Immunoblot 2007961](#)

**Method:** Semi-Quantitative Indirect Fluorescent Antibody/Qualitative Immunoblot

[Antinuclear Antibody \(ANA\) with HEp-2 Substrate, IgG by IFA 3000082](#)

**Method:** Semi-Quantitative Indirect Fluorescent Antibody

[ANCA-Associated Vasculitis Profile \(ANCA/MPO/PR3\) with Reflex to ANCA Titer 2006480](#)

**Method:** Semi-Quantitative Indirect Fluorescent Antibody/Semi-Quantitative Multiplex Bead Assay

[Antiphospholipid Syndrome Reflexive Panel 2003222](#)

**Method:** Electromagnetic Mechanical Clot Detection/Semi-Quantitative Enzyme-Linked Immunosorbent Assay

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