

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

Physiology

- VGKC autoantibodies
 - Directed against a protein that is complexed with potassium channels in both peripheral nervous system and CNS

TESTS TO CONSIDER

[Voltage-Gated Potassium Channel \(VGKC\) Antibody with Reflex to LGI1 and CASPR2 Screen and Titer 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 \(VGKC\) 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 2009456](#)

Method: Semi-Quantitative Indirect Fluorescent Antibody

Aid in diagnosis of LGI1 disorders

[Contactin-Associated Protein-2 Antibody, IgG with Reflex to Titer 2009452](#)

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 2009460](#)

Method: Semi-Quantitative Indirect Fluorescent Antibody

Aid in diagnosis of LGI1 and CASPR2 disorders

- 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 – ≥1:10
 - Suggests LGI1 antibody-related disease
- Negative – <1:10
 - Does not rule out disorders associated with VGKC complex antibodies

CASPR2 Antibody, Serum

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

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

[Autoimmune Encephalitis Reflexive Panel 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 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

[Autoimmune Neuromuscular Junction Reflexive Panel 2005640](#)

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; VGKC antibody; VGCC antibody; titin antibody; striated muscle antibody; and LGI1 and CASPR2 antibodies

- Other unidentified targets

See [Related Tests](#)

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](#)

RELATED TESTS

[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

[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

[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

ARUP Laboratories is a nonprofit enterprise of the University of Utah and its Department of Pathology.
500 Chipeta Way, Salt Lake City, UT 84108 | (800) 522-2787 | (801) 583-2787 | aruplab.com | arupconsult.com
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