

Anti-NMDA Receptor (NR1) IgG Antibodies

Anti-N-methyl-D-aspartate receptor (NMDAR) encephalitis is an autoimmune disease caused by antibodies against the brain protein, NMDA. Affected individuals display distinctive symptoms, including significant psychiatric disturbances, seizures, confusion, memory loss, and agitation. Women are affected more often than men. Testing is used to confirm a diagnosis of NMDAR encephalitis and to monitor disease progression and treatment response.

Disease Overview

Incidence

Unknown

Age of Onset

Affects all age groups, with a low prevalence in individuals >50 years

Symptoms

- Prodromal symptoms similar to a nonspecific viral-like illness
 - Low-grade fever
 - Headache
- Rapid progression to other neurological symptoms (psychotic and catatonic phases)
 - Autonomic dysfunction (hypoventilation, tachycardia, hypertension, hyperthermia)
 - Cardiac dysrhythmias
 - Delusions, psychoses
 - Dyskinesia, movement disorders
 - Hallucinations
 - Memory loss
 - Paranoia
 - Seizures
 - Unresponsiveness
- Significant portion of patients are nonparaneoplastic
 - Ovarian teratoma is the most common tumor-related cause
 - Men, women, and children without tumors have also been diagnosed with anti-NMDAR encephalitis

Diagnostic Issues

- Neurological symptoms of anti-NMDAR encephalitis are clinically indistinguishable from encephalitis associated with etiologies of
 - Infection
 - Toxin/metabolic
 - Autoimmune
- Diagnosis is based on the exclusion of other causes

Tests to Consider

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

Method: Semi-Quantitative Indirect Fluorescent Antibody

- Confirm diagnosis of anti-NMDAR encephalitis
- May be used in monitoring treatment response in individuals who are antibody positive

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

Method: Semi-Quantitative Indirect Fluorescent Antibody

- Confirm a diagnosis of anti-NMDAR encephalitis
- May be used in monitoring treatment response in individuals who are antibody positive

[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
- 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 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

- Anti-NMDAR IgG antibody detected in serum confirms the diagnosis of anti-NMDAR encephalitis
 - Abdominal imaging (ultrasound or MRI) should also be performed due to strong association with ovarian neoplasms
 - Testicular ultrasound should replace abdominal ultrasound in men

Physiology

- NMDA receptors are ligand-gated cation channels necessary for synaptic transmission
 - Highly expressed in the forebrain, limbic system, and hypothalamus
- NMDA receptors are composed of two subunits – NR1 and NR2
- Anti-NMDA IgG binds to NMDA receptors (usually NR1)
 - Decreases the number of receptors on postsynaptic neuronal dendrites, causing synaptic dysfunction
 - Presumed cause of psychotic symptoms characteristic of anti-NMDAR encephalitis

Typical Testing Strategy

Initial testing to rule out infectious process may include

- Complete blood count with platelet count and differential
- Electrolyte panel
- Cerebrospinal fluid (CSF) testing
 - Protein, glucose, cell count with differential
 - Viral polymerase chain reaction testing
 - Herpes simplex virus
 - Human herpes virus-6
 - Varicella-zoster virus
 - Enterovirus
 - Oligoclonal band profile
 - Bacterial culture and Gram stain
 - Fungal culture
 - CSF antigen testing
- Computerized tomography/magnetic resonance imaging
- Other testing based on symptoms/history (eg, metabolic disorders, multiple sclerosis)

Consider the following tests based on clinical presentation, age, sex, and/or risk for cancer:

- Autoimmune serologies for
 - Antinuclear antibodies (ANA)
 - Antineutrophil cytoplasmic antibodies (ANCA)
 - Antiphospholipid syndrome (APS)
 - Thyroiditis
- Autoimmune encephalitis evaluation
- Paraneoplastic antibody evaluation
- N-methyl-D-aspartate receptor antibody, serum or CSF

Test Interpretation

Sensitivity/Specificity

- Analytical sensitivity: unknown
- Analytical specificity: ~100%

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 [Voltage-Gated Potassium Channel Antibody Disorders](#) test fact sheet for more information on the evaluation of VGKC antibody in autoimmune encephalitis.

[Autoimmune Neurologic Disease Reflexive Panel, Serum 3003058](#)

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

- Comprehensive panel for evaluation of paraneoplastic and neuromuscular junction disorders, and/or encephalitis, in the presence or absence of malignancy
- Individual tests in panel may also be ordered separately

See [Related Tests](#)

Results

- Positive: NMDAR IgG antibody identified in serum strongly supports a diagnosis of anti-NMDAR encephalitis
- Negative: absence of NMDAR IgG antibody does not rule out a diagnosis of other forms of autoimmune encephalitis

Related Information

[N-methyl-D-Aspartate \(NMDA\)-Type Glutamate Receptor Autoantibody Disorders - Anti-NMDA-Receptor Encephalitis](#)

Related Tests

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

Method: Semi-Quantitative Indirect Fluorescent Antibody

[Paraneoplastic Reflexive Panel 3002929](#)

Method: Semi-Quantitative Indirect Fluorescent Antibody/Qualitative Immunoblot

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

Method: Semi-Quantitative Indirect Fluorescent Antibody/Qualitative Immunoblot

[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

[Autoimmune Neurologic Disease Reflexive Panel, CSF 3002887](#)

Method: Semi-Quantitative Indirect Fluorescent Antibody/Qualitative Immunoblot/Quantitative Radioimmunoassay/Semi-quantitative Enzyme-Linked Immunosorbent Assay

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

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

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