Anti-NMDA Receptor (NR1) IgG Antibodies

**Indications for Ordering**
- Confirm diagnosis of anti-N-methyl-D-aspartate receptor (NMDAR) encephalitis
- May be used in monitoring treatment response in individuals who are antibody positive

**Test Description**
- N-methyl-D-Aspartate Receptor Antibody, IgG, Serum with Reflex to Titer
- N-methyl-D-Aspartate Receptor Antibody, IgG, CSF with Reflex to Titer
  - Semiquantitative indirect fluorescence antibody assay (IFA) using a human cell line (HEK293) transfected with the NR1 receptor subunit
- Autoimmune Encephalitis Reflexive Panel
  - Semiquantitative IFA/semiquantitative enzyme-linked immunosorbent assay (ELISA)
- Autoimmune Neurologic Disease Reflexive Panel
  - Semiquantitative IFA/qualitative immunoblot/quantitative radioimmunoassay/ semiquantitative ELISA

**Tests to Consider**

**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 and CSF

**Primary tests**
- N-methyl-D-Aspartate Receptor Antibody, IgG, Serum with Reflex to Titer 2004221
  - 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
  - Confirm diagnosis of anti-NMDAR encephalitis
  - May be used in monitoring treatment response in individuals who are antibody positive
- Autoimmune Encephalitis Reflexive Panel 2013601
  - Differential evaluation of encephalitis of unknown origin with subacute onset of seizures, confusion, memory loss, and/or behavioral change
  - For adults and patients with suspicion of cancer, additional evaluation of paraneoplastic autoantibodies is recommended
    - Refer to Paraneoplastic Antibodies (PCCA/ANNA) by IFA with Reflex to Titer and Immunoblot 2007961
  - Individual tests in panel (may also be ordered separately)
    - N-methyl-D-Aspartate Receptor Antibody, IgG, Serum with Reflex to Titer 2004221
    - Glutamic Acid Decarboxylase Antibody 2001771
    - Voltage-Gated Potassium Channel (VGKC) Antibody 2004890
    - Aquaporin-4 Receptor Antibody 2003036
    - Aquaporin-4 Receptor Antibody, IgG by IFA with Reflex to Titer, Serum 2013320
    - Leucine-Rich, Glioma-Inactivated Protein 1 Antibody, IgG with Reflex to Tier 2009456
    - Contactin-Associated Protein-2 Antibody, IgG with Reflex to Tier 2009452

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Autoimmune Neurologic Disease Reflexive Panel 2013944
- 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)
  - Paraneoplastic Antibodies (PCCA/ANNA) by IFA with Reflex to Titer and Immunoblot 2007961
  - Amphiphysin Antibody, IgG 2008893
  - CV2.1 Screen by IFA with Reflex to Titer 2013956
  - N-methyl-D-Aspartate Receptor Antibody, IgG, Serum with Reflex to Titer 2004221
  - Glutamic Acid Decarboxylase Antibody 2004890
  - Aquaporin-4 Receptor Antibody 2003036
  - Aquaporin-4 Receptor Antibody, IgG by IFA with Reflex to Titer, Serum 2013320
  - Leucine-Rich, Glioma-Inactivated Protein 1 Antibody, IgG with Reflex to Tier 2009456
  - Contactin-Associated Protein-2 Antibody, IgG with Reflex to Titer 2009452
  - Voltage-Gated Potassium Channel (VGKC) Antibody 2004890
  - Acetylcholine Receptor Modulating Antibody 2005636
  - Striated Muscle Antibodies, IgG with Reflex to Titer 0050746
  - Serine Protease 3 Antibody 0050527
  - Myeloperoxidase Antibody 0050526
  - Voltage-Gated Calcium Channel (VGCC) Antibody 0099521
  - NMDA Receptor Antibody, IgG 0099521

Related tests
Paraneoplastic Reflexive Panel 2013955
- Aid in the diagnosis of paraneoplastic neurological syndromes associated with ANNA-1 (Hu), ANNA-2 (Ri), PCCA-1 (Yo), amphiphysin, and CV2.1 antibodies
Paraneoplastic Antibodies (PCCA/ANNA) by IFA with Reflex to Titer and Immunoblot 2007961
- Aid in the diagnosis of paraneoplastic neurological syndromes associated with malignancy
- Order based on clinical presentation
Antinuclear Antibody (ANA) with HEp-2 Substrate, IgG by IFA 3000082
- Preferred ANA screening test for connective tissue disease
ANCA-Associated Vasculitis Profile (ANCA/MPO/PR-3) with Reflex to ANCA Titer 2006480
- Preferred reflex panel for the workup of suspected vasculitis
- Panel detects ANCA, MPO, and PR-3 antibodies
- For patients with a history of vasculitis, refer to Anti-Neutrophil Cytoplasmic Antibody with Reflex to Titer and MPO/PR-3 Antibodies 2002068
- Individual antibody tests are available
  - Serine Protease 3 Antibody 0050527
  - Myeloperoxidase Antibody 0050526
Antiphospholipid Syndrome Reflexive Panel 2003222
- Preferred initial panel when APS is strongly suspected

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Test Interpretation

Sensitivity/specificity

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

Results

- Positive – NMDAR IgG antibody identified in serum
  - Strongly supportive of a diagnosis of anti-NMDAR encephalitis
- Negative – absence of NMDAR antibodies
  - Does not rule out a diagnosis of other forms of autoimmune encephalitis