



# PLAIN LANGUAGE SUMMARY

## An overview of N-methyl D-aspartate receptor (NMDAR) antibody-associated encephalitis

Source - Seery N, Butzkueven H, O'Brien TJ, Monif M. Contemporary advances in anti-NMDAR antibody (Ab)-mediated encephalitis, *Autoimmunity Reviews*, April 2022, Volume 21, Issue 4, <https://doi.org/10.1016/j.autrev.2022.103057>

### WHY WE DID THIS WORK

- N-methyl D-aspartate receptor (NMDAR) antibody-associated encephalitis, or **anti-NMDAR encephalitis** is a type of autoimmune encephalitis. **Autoimmune encephalitis** occurs when parts of the body's immune system inappropriately attack certain components of nerve cells in the brain. Anti-NMDAR encephalitis is one of the most common defined types of autoimmune encephalitis. Young people who are on average 21 years of age, and females, experience the illness most commonly. But it can occur in older adults (over 45 years) and in young children (less than 12 years), where a relatively higher number of patients are males.
- To make a diagnosis, doctors record key symptoms (e.g. memory issues, personality change, changes to behavior alteration, or seizures) and clinical features from tests. The detection of antibodies that bind the receptor (NMDAR) from a patient's blood or cerebrospinal fluid (fluid that cushions the brain and spinal cord) are also used to confirm the diagnosis of anti-NMDAR encephalitis. **Antibodies** are proteins produced by the immune system that in normal circumstances have a role in fighting infections. In certain autoimmune diseases, antibodies, along with other parts of the immune system, target normal components of a healthy individual.
- Anti-NMDAR encephalitis can be treated using medications that selectively reduce components of the immune system, but as the illness is different from person to person, it is challenging to both diagnose and manage. The use of biological markers, or **biomarkers** (proteins, cells or other characteristics that can generally be detected via a certain test and are association with a particular disease), may be particularly useful for the diagnosis and assessment of how

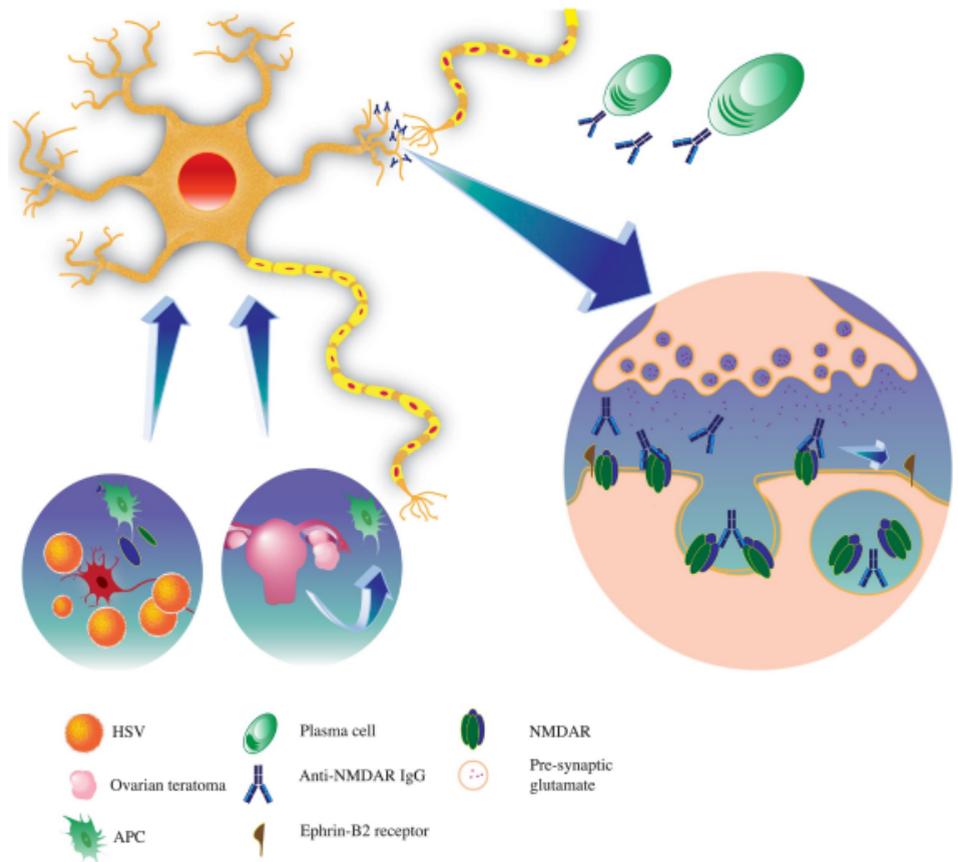


Figure 1 - Schematic showing a summary of the triggers and mechanisms involved in NMDAR encephalitis.

effective treatment is to manage a patient's illness. Accurate and specific biomarkers for anti-NMDAR encephalitis still do not exist.

- We did this update to collect the latest research findings from the field to inform researchers and clinicians who manage this condition and have a keen interest.

### WHAT WERE THE THINGS WE DISCOVERED

- The N-methyl D-aspartate receptor (NMDAR) belongs to a group called glutamate-gated ionotropic receptors. These receptors are mostly located in a region of the brain called the hippocampus (involved in learning and

memory) more so than other regions, and assist in excitatory transmission of nerve cells. In anti-NMDAR encephalitis, antibodies target a part of the receptor called GluN1. Anti-NMDAR antibodies exist in the serum part of blood and the cerebrospinal fluid.

- Biomarkers in cerebrospinal fluid that have been identified include B-cell and T-cell chemokines, which are molecules that serve to attract particular white cells to a given part of the body (in particular, CXCL13 and CXCL10), interferon gamma, tumor necrosis factor alpha and interleukins (in particular 6, 7, 10 and 17-A). The levels of certain of these biomarkers were found to also coincide with poor long-term outcomes in patients.

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## TRIGGERS OF ANTI-NMDAR ENCEPHALITIS

- Two known triggers for anti-NMDAR encephalitis are the presence of an **ovarian teratoma** (an unusual type of tumour that can express nervous tissue) and less commonly, a viral infection of the brain called HSV-encephalitis.
- Other than these two triggers, it is less understood what causes the illness. At a molecular level, patient antibodies induce complex changes to the nerves by disrupting the functioning of the receptor. These findings may explain the variety of symptoms that patients experience, and varying and often impressive degrees of recovery.

## CLINICAL FEATURES

- The diagnosis of the disease is not always straightforward. Symptoms and other clinical features may overlap with other diseases, and sometimes, at least in the blood, antibodies to the receptor may be seen without the disease itself. A broad range of clinical features exists in anti-NMDAR encephalitis. Patients can experience the following, which may change over time:
  - changes in behaviour and hallucinations (psychiatric symptoms)
  - difficulties in mental function (cognitive impairment)
  - seizures
  - abnormal movements
  - irregularities of the function of the autonomic nervous system (e.g. temperature, heart rate and breathing).
- Therefore, detection of certain proteins and molecules in the blood or spinal fluid may assist in the diagnosis of the disease and its management. A variety of candidates have been explored, but generally remain limited in their use in clinical practice.

## TREATMENT

- The cornerstone of treatment is suppression of the immune system. Research has shown that earlier treatment results in a better long-term outcome.
- Exciting new treatment options are emerging, but research studies for these treatments are limited to relatively small numbers of patients and their approval for use by government therapeutic agencies is still being considered. Therefore, we advise clinicians making the decision to use new therapies be made on based on each individual patient's situation.

## WHAT DO THE FINDINGS MEAN?

- This research can help clinicians understand how the illness progresses at the cellular and molecular level, its symptoms, the results of supportive tests (e.g. spinal fluid and MRI) and treatment options, and highlight areas of progress and needs in the current research.

- Most patients will have some degree of recovery in their illness following appropriate treatment, but some symptoms can persist, particularly issues in mental function. Cognitive rehabilitation and follow up with psychiatry and psychology. In some cases anti-psychotic medication, anti-depressants and mood stabilizers may also be warranted.

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We are also a member of the Monash Central Clinical School [Community and Research Engagement \(CaRE\) Program](#).



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### References

Research group - [monash.edu/medicine/ccs/neuroscience/research/monif-group](https://monash.edu/medicine/ccs/neuroscience/research/monif-group)

Australian Autoimmune Encephalitis Consortium project website - [monash.edu/medicine/autoimmune-encephalitis](https://monash.edu/medicine/autoimmune-encephalitis)

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