NMDAR-antibody encephalitis

By Professor Sarosh Irani, Professor of Autoimmune Neurology and Honorary Consultant Neurologist, University of Oxford and Oxford University Hospitals, UK and reviewed by Dr Sophie Binks, Clinical Fellow, Oxford Autoimmune Neurology Group,

Contents

What is NMDAR-antibody encephalitis?

The major role of our immune system is to recognise and remove infection. However, sometimes components of the immune system, such as antibodies, may instead – in error - react with proteins in our own body. This causes an autoimmune disease, and when against proteins in the brain we call this 'autoimmune encephalitis'. If the brain protein is the N-methyl-D-aspartate receptor (NMDAR), the condition is termed NMDAR-antibody encephalitis, or anti-NMDAR encephalitis.

The NMDAR helps control thoughts, mood, and movements, and therefore antibodies against NMDA receptors are likely to alter these functions. This encephalitis affects the brain more widely than purely the limbic system, and therefore it is not typically classified as a limbic encephalitis (LE, see separate Factsheet on **Limbic encephalitis**).

Symptoms

The disease often comes on over 1-4 weeks and mainly affects young people, with around 40% of cases under 18 years of age. Females are affected more often than males. At onset, the most distinctive features include prominent and mixed psychiatric symptoms, seizures, confusion and memory loss. The psychiatric features often include bizarre and rather disturbing behaviours with mood changes, and patients are often initially looked after in mental health hospitals. They may see things which aren't there, develop strange beliefs or appear agitated. After this, often 10 to 20 days later, patients develop a movement disorder, variations in blood pressure, heart rate and temperature and lose awareness. The movement disorder often consists of continuous writhing and twitching of face and limbs but can also be a generalised slowing-down of movements. Most patients develop several of these features, but very rarely individual patients may experience only a few of these features.

Diagnosis

In light of these symptoms and signs, clinicians can request the NMDA receptor antibody test to diagnose this condition. This is best tested in both blood and spinal fluid.

Once a patient has been diagnosed with NMDAR-antibody encephalitis, an underlying tumour should be sought, typically with pelvic and/or body imaging. While older patients may have a variety of tumours detected, recent reports suggest that around ~30% of women, especially those between 20 and 35 years of age, have an underlying tumour, most commonly an ovarian teratoma. This is usually a non-cancerous tumour but is thought to stimulate the production of NMDA receptor antibodies.

In addition, some patients develop NMDAR-antibody encephalitis shortly after herpes simplex virus encephalitis, and this is therefore considered another trigger of the condition.

However, in most patients the cause remains unknown.

Treatment and prognosis

If these symptoms and signs are recognised, other causes excluded (particularly infections) and the antibody is found in the spinal fluid, treatments should be started. Treatment consists of immune therapies and removal of a tumour, if present.

The immune therapies used to dampen down the immune system include steroids (drugs to reduce inflammation), plasma exchange (when some of a person's blood is taken out from a vein, and the plasma part of the blood which contains antibodies is separated and replaced with new plasma and then put back into the vein in a drip), or, less frequently, immunoglobulins (a blood product given into the vein in a drip).

In addition, some patients are treated with other drugs which dampen down the immune system. These include rituximab, which is now recommended by NHS guidelines for patients who have not made adequate improvement with first line therapies, and was recently shown to reduce the risk of future relapses. Another drug called cyclophosphamide can sometimes be used either with or instead of rituximab.

All these drugs have, sometimes serious, known side-effects but their benefits are generally felt to outweigh possible side-effects. For more information on these drugs please see the **Immunotherapy in autoimmune encephalitis** factsheet.

Prompt therapies offer a good chance of substantial recovery in the majority of patients. As they improve, there may be a reduction in the amount of NMDA receptor antibody in the person's blood or spinal fluid when the test is repeated. Some patients are now being treated after recognition of the clinical symptoms and signs, while the antibody result is awaited, to try to further expedite recovery. However, recovery is usually slow and many patients spend a few months in hospital, including time on the intensive care unit undergoing ventilation. Early in the illness, it is important that doctors realise there may be few or no signs of recovery in patients who do eventually respond. Those who return to work typically only do so after a year or two but most patients have some problems with memory, mood or behaviour which can be significant or subtle.

In summary, NMDAR-antibody encephalitis is an autoimmune disease that causes psychiatric features, confusion, memory loss and seizures followed by a movement disorder and loss of consciousness. The disease can respond well to various therapies that dampen down the immune system and the removal of an underlying tumour if one is found, but improvement is often slow and persistence and patience are often required to achieve more impressive longer term improvements.

FS057V5 NMDAR antibody encephalitis

Date created: April 2010; Updated: December 2022; Review date: December 2025

Disclaimer: We try to ensure that the information is easy to understand, accurate and up-to-date as possible. If you would like more information on the source material and references the author used to write this document please contact Encephalitis International. None of the authors of the above document has declared any conflict of interest, which may arise from being named as an author of this document.

Support our information

With our support, no one has to face encephalitis alone. Our advice and information is available free of charge to everyone affected but we are truly grateful when supporters feel able to contribute a little to the cost of these resources. Please make a donation today by visiting www.encephalitis.info/donate or text the word DOCTOR to 70085 to donate £5.

Thank you!

Encephalitis International, 32 Castlegate, Malton, North Yorkshire, YO17 7DT, UK

Administration: +44 (0) 1653 692583 **Support**: +44 (0) 1653 699599

Email: mail@encephalitis.info **Website**: www.encephalitis.info

Encephalitis International is the operating name of the Encephalitis Support Group.

Registered Charity England and Wales No: 1087843; Registered Charity in Scotland No: SC048210

Charitable Company registered in England and Wales No: 04189027