Anti-NMDAR encephalitis
By Sarosh Irani, Associate Professor and Consultant Neurologist, University of Oxford and John Radcliffe Hospital, Oxford, UK

What is anti-NMDAR encephalitis?
The major role of our immune system is to recognise and get rid of infection. But sometimes some components of the immune system, called antibodies, may instead react with proteins in our own body causing an autoimmune disease. When this reaction is against proteins in the brain it is called autoimmune encephalitis. If the brain protein is the N-methyl-D-aspartate (NMDA) receptor, the condition is termed NMDA-receptor antibody encephalitis, or anti-NMDAR encephalitis.

The NMDA receptor is a protein in the brain that helps control thoughts, mood and movements, and therefore antibodies against NMDA receptors are likely to have an important role in altering these functions. This encephalitis affects the brain more diffusely than purely the limbic system, and therefore it is not classified as a limbic encephalitis (LE, see separate Factsheet on LE).

Symptoms
At onset, the most distinctive features include prominent psychiatric symptoms, seizures, confusion and memory loss. Patients will sometimes show bizarre and often rather disturbing behaviours. They may see things which aren’t there, develop strange beliefs or appear agitated. Typically 10 to 20 days later, patients develop a movement disorder, variations in blood pressure, heart rate and temperature and may become less conscious. The movement disorder often consists of continuous writhing and twitching of face and limbs but can also be a generalised slowing-down of movement. Most patients develop several of these features, but very rarely individual patients may experience only a few of these features.
**Diagnosis**

The symptoms and signs seen in patients with anti-NMDAR encephalitis can be distinctive and are prompting many clinicians to request the NMDA receptor antibody test to diagnose this condition. The disease mainly affects young people, with around 30% of cases under 18 years of age. Women are affected more often than men.

Once a patient has been diagnosed with anti-NMDAR encephalitis, an underlying tumour should be looked for. While very few men have tumours detected (typically <5%), recent reports suggest that around 20-30% of women have an underlying tumour. The most common tumour found in women is called an ovarian teratoma. This is usually a non-cancerous tumour but is thought to stimulate the production of the NMDA receptor antibody.

**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), immunoglobulins (a blood product given into the vein in a drip) and 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).

In addition, some patients are treated with other drugs which dampen down the immune system, such as cyclophosphamide and rituximab. All drugs have known side-effects but their benefits are generally felt to outweigh possible side-effects.

Prompt therapies offer a good chance of substantial recovery in the majority of patients. As they improve, there is often 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 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 despite
treatment. 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,** anti-NMDAR encephalitis is a recently identified autoimmune disease that causes psychiatric features, confusion, memory loss and seizures followed by a movement disorder, loss of consciousness and changes in blood pressure, heart rate and temperature. 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.

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**Encephalitis Society, 32 Castlegate, Malton, North Yorkshire, YO17 7DT, UK**

**Administration:** +44 (0) 1653 692 583 **Support:** +44 (0) 1653 699599

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

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