Antibody-mediated encephalitis and psychosis

The four cases of N-methyl-d-aspartate (NMDA) receptor antibody encephalitis with associated psychosis reported in December¹ raise an important and emerging issue and highlight that psychiatrists should include the condition in the differential diagnosis for patients presenting with acute psychosis. But there are some aspects that need clarification. The authors state that ‘this case series demonstrates a new and treatable cause of psychosis’⁴, inferring that the association of psychosis with these antibodies was previously unknown. However, since the first 100 patients with NMDA receptor antibody encephalitis were reported in 2008,² this association has been well documented; psychosis is typically the first presentation and many cases were seen by psychiatrists before neurologists become involved.¹²³

The association of these antibodies with psychosis is highly relevant because they bind to key neuronal surface proteins and are therefore likely to be pathogenic. Indeed, NMDA receptor antibody encephalitis is a condition that responds to immunomodulation and, importantly, there is thought to be an initial ‘treatment window’ for optimal immunomodulation.⁴⁵ The authors¹ speculate that ‘there may be a pure psychiatric presentation associated with lower antibody titres’. Indeed, a recent study found that 3 out of 46 patients with first-episode psychosis had NMDA receptor antibodies.⁶ This extremely important finding has profound implications for psychiatrists before neurologists become involved.¹²³

As Barry et al² point out, the condition does indeed provide some support for the NMDA receptor hypofunction hypothesis for psychosis. Some proponents of this theory have linked NMDA receptor hyfopfunction to first-rank psychotic symptoms in particular.² It is important that future studies of auto-antibody-associated psychosis characterise symptomatology in full, as this could allow for a level of clinical–pathological correlation rarely attained in psychiatry.

Declarations of interest


have written an editorial on this topic published in the February issue of the Journal.