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Antibodies to Brain Proteins May Trigger Psychosis

Reports new study in Biological Psychiatry

Philadelphia, PA, March 5, 2015 – Antibodies defend the body against bacterial, viral, and other invaders. But sometimes the body makes antibodies that attack healthy cells. In these cases, autoimmune disorders develop.

Immune abnormalities in patients with psychosis have been recognized for over a century, but it has been only relatively recently that scientists have identified specific immune mechanisms that seem to directly produce symptoms of psychosis, including hallucinations and delusions.

This ‘immune hypothesis’ is supported by new work published by Pathmanandavel and colleagues in the current issue of *Biological Psychiatry*. They detected antibodies to the dopamine D2 receptor or the *N*-methyl-D-aspartate (NMDA) glutamate receptor in a subgroup of children experiencing their first episode of psychosis, but no such antibodies in healthy children. Both are key neural signaling proteins that have previously been implicated in psychosis.

“The antibodies we have detected in children having a first episode of acute psychosis suggest there is a distinct subgroup for whom autoimmunity plays a role in their illness,” said Dr. Fabienne Brilot, senior author on the article and Head of the Neuroimmunology Group at The Children's Hospital at Westmead in Sydney.

It almost seems like a dirty trick. For decades psychiatrists have administered drugs that stimulate dopamine D2 receptors or block NMDA receptors. These drugs may briefly produce side effects that resemble symptoms of psychotic disorders, including changes in perception, delusions, and disorganization of thought processes. The current findings suggest that people may develop antibodies that affect the brain in ways that are similar to these psychosis-producing drugs.

“This study adds fuel to the growing discussions about the importance of antibodies targeting neural proteins and it raises many important questions for the field. Do these antibodies simply function like drugs in the brain or do they ‘attack’ and damage nerve cells in some ways?” questioned Dr. John Krystal, Editor of *Biological Psychiatry*. “Also, are these antibodies producing symptoms in everyone or do they function as a probe of an underlying, perhaps genetic, vulnerability for psychosis?”

Importantly, work is advancing rapidly in this area. Less than a decade ago, anti-NMDA receptor encephalitis was first identified, a disease characterized by inflammation of the brain that causes acute psychiatric symptoms including psychosis. It is commonly misdiagnosed as schizophrenia or bipolar disorder, but is a form of treatable brain inflammation caused by antibodies that attack the brain's NMDA receptors.

“The data from this study suggests that better interventions are possible, providing hope that major disability can be prevented for the subset of children experiencing acute psychosis with antibodies,” Brilot added. “These findings also contribute significantly to an emerging acceptance in the field of the involvement of autoimmune antibodies in neurological diseases. Combined, these investigations are providing a better understanding of the biology of psychiatric and neurological diseases, as well as pointing to novel treatment approaches for children with these debilitating illnesses.”

The article is “Antibodies to Surface Dopamine-2 Receptor and *N*-Methyl-D-Aspartate Receptor in the First Episode of Acute Psychosis in Children” by Karman Pathmanandavel, Jean Starling, Vera Merheb, Sudarshini Ramanathan, Nese Sinmaz, Russell C. Dale, and Fabienne Brilot (doi: 10.1016/j.biopsych.2014.07.014). The article appears in *Biological Psychiatry*, Volume 77, Issue 6 (March 15, 2015), published by Elsevier.

Notes for editors

Full text of the article is available to credentialed journalists upon request; contact Rhiannon Bugno at +1 214 648 0880 or Biol.Psych@utsouthwestern.edu. Journalists wishing to interview the authors may contact Fabienne Brilot at +1 02 9845 1456 or Fabienne.brilot@sydney.edu.au.

The authors' affiliations, and disclosures of financial and conflicts of interests are available in the article.

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