

Brain chemical finding could open door to new schizophrenia drugs

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New research has linked psychosis with an abnormal relationship between two signalling chemicals in the brain. The findings, published in tomorrow's edition of the journal *Biological Psychiatry*, suggest a new approach to preventing psychotic symptoms, which could lead to better drugs for schizophrenia.

Schizophrenia is one of the most common severe mental health conditions. Sufferers experience symptoms of psychosis - an inability to distinguish between reality and imagination - such as [hallucinations](#) and delusions. The condition tends to begin in the late teens or twenties, and usually persists for the rest of the sufferer's life.

Brain chemicals called neurotransmitters carry signals from one nerve cell to another. Research has linked schizophrenia with abnormally high levels of a [neurotransmitter](#) called dopamine in a region of the brain called the striatum. Drugs currently used to treat schizophrenia block the effects of dopamine in the brain. These drugs are not effective for all patients, and can have serious side effects.

The new pilot research, funded by the Medical Research Council (MRC), provides evidence that high levels of dopamine in people with [psychotic symptoms](#) occur as a consequence of changes in another [brain chemical](#), glutamate. Glutamate-releasing cells in a brain region called the hippocampus connect to the striatum and influence the activity of dopamine-releasing cells. Drugs that interfere with glutamate signals in the brain might therefore be able to prevent psychotic symptoms in

people with schizophrenia.

"Schizophrenia is a devastating illness that destroys the lives of people who are afflicted and those around them," said Dr James Stone of the Department of Medicine at Imperial College London, first author of the study. "At the moment, the drugs we have just aren't adequate. They don't help everybody, and they don't stop some of the most debilitating symptoms."

The researchers carried out brain scans on 16 people with an at-risk mental state for psychosis and 12 healthy volunteers, to measure the levels of glutamate and dopamine. In people with early signs of psychotic symptoms, there was a negative correlation between glutamate levels in the hippocampus and dopamine levels in the striatum area. There was a particularly marked correlation in the subjects who went on to develop psychosis later. There was no correlation in the healthy subjects.

"In healthy volunteers, there's no clear relationship between glutamate and dopamine, but in people with early signs of psychosis, we see this abnormal relationship," Dr Stone said. "This suggests that the signalling pathway between the [hippocampus](#) and the striatum is dysfunctional, and we might be able to treat this by targeting the glutamate system. If drugs that act on glutamate signalling can prevent psychotic symptoms, it would mean a real shift in the way that people are treated for schizophrenia.

"The next step will be to see if these results are confirmed in a larger group of people. There are already a number of promising drug candidates that interfere with glutamate signalling, so hopefully in a few years we'll be able to start testing new treatments for people with schizophrenia."

Professor Chris Kennard, chair of the MRC Neuroscience and Mental Health Board, said:

"Studies like these are helping to unravel the complex mechanisms of psychiatric illness and bring us a step closer to more effective, targeted drugs for patients with schizophrenia. The MRC funds research like this in order to bring scientific findings from the lab bench to patient bedside, more quickly. If we can develop new drugs that prevent psychotic symptoms, it would mean a real benefit for patients with [schizophrenia](#)."

More information: J.M. Stone et al. "Altered relationship between hippocampal glutamate levels and striatal dopamine function in subjects at ultra high risk of psychosis." *Biological Psychiatry*, 1 October 2010.

Provided by Imperial College London

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