Excitatory neurotransmitter glutamate is implicated in schizophrenia

Excerpt - Using human subjects with schizophrenia and a transgenic mouse model, a role for the glutamatergic system in the hippocampus has been elucidated.

Schizophrenia is a neurological disorder that typically has an onset in young adulthood, and is characterized by memory deficits, psychotic episodes and abnormal social behavior. In order to develop effective therapies, it is important to understand the changes that take place in the brain in schizophrenia.

Neurons or nerve cells in the brain do not physically touch each other. Communication between them takes place *via* molecules known as 'neurotransmitters'. The two important neurotransmitters in the brain are glutamate (which causes stimulation of neurons), and GABA (which causes inhibition of neurons). Adequate balance between excitation and inhibition is crucial for maintaining proper functioning of the nervous system. Once released, the neurotransmitter acts on specific receptors to carry on stimulation or inhibition. Glutamate, when released, acts on specific receptors known as NMDA receptors (among others). In schizophrenia, it is thought that the glutamatergic system, and in particular, the NMDA receptor function goes awry.

In the recent paper, the scientists wanted to see if this was the case in human subjects with schizophrenia, and they studied a part of the brain called the hippocampus. The hippocampus is situated in the temporal lobe and is thought to contribute to psychoses and memory deficits in schizophrenia. The results of this study are in the journal Molecular Psychiatry. The study has three parts.

First, the scientists recruited people with schizophrenia and controls, and performed a technique known as proton magnetic resonance spectroscopy. This technique tells us about metabolic changes that take place in the brain. Using this, the scientists found a reduction in glutamate (the excitatory neurotransmitter), without any changes in GABA in the hippocampus.

Second, the scientists collected postmortem samples from patients with schizophrenia and control subjects. They found a reduction in a particular subunit of the NMDA receptor called GluN1 subunit, but interestingly in only one part of the hippocampus called the dentate gyrus. This is important because different parts of the hippocampus have different functions. Similar to results of the first experiment, there were no changes in GABA neurotransmission.

Next, to see whether the reduction in GluN1 can cause a decrease in glutamate, the scientists used a transgenic mouse that was deficient in GluN1, but only in the dentate gyrus. These mice had deceased glutamate in the hippocampus, suggesting that a reduction of GluN1 in the dentate gyrus is sufficient to cause a decrease in glutamate.

In conclusion, using human subjects with schizophrenia and a transgenic mouse model, this study tells us that the excitatory i.e. glutamate system is involved in schizophrenia. One can envision that in the future, a drug that selectively targets GluN1 receptors can be developed, which could normalize levels of glutamate in the hippocampus, providing a novel therapy for schizophrenia.