Medical Xpress

Immune molecule regulates brain connections

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The number of connections between nerve cells in the brain can be regulated by an immune system molecule, according to a new study from UC Davis. The research, published Feb. 27 in the journal *Nature Neuroscience*, reveals a potential link between immunity, infectious disease and conditions such as schizophrenia or autism.

Schizophrenia, autism and other disorders are associated with changes in connectivity in the brain, said Kimberley McAllister, associate professor in the Center for Neuroscience and Departments of Neurology and Neurobiology, Physiology and Behavior at UC Davis. Those changes affect the ability of the brain to process information correctly.

"Certain immune genes and immune dysregulation have also been associated with autism and schizophrenia, and the immune molecules that we study in brain development could be a pathway that contributes to that altered connectivity," McAllister said.

The study does not show a direct link between immune responses and autism, but rather reveals a molecular pathway through which a peripheral immune response or particular genetic profile could alter early brain development, McAllister said.

The researchers looked at a protein called Major Histocompatibility Complex type 1 (MHC type I). In both rodents and humans, these proteins vary between individuals, and allow the immune system to distinguish between 'self' and 'non-self.' They play a role, for example, in

rejecting transplanted organs and in defending against cancer and virus infections.

In this and another recently published study, McAllister's group found that MHC type I molecules are present on young brain cells during early postnatal development. To test their function, they studied mice lacking MHC type I on the surface of neurons, as well as isolated neurons from mice and rats with altered levels of MHC type I. They found that when the density of these molecules on the surface of a brain cell goes up, the number of connections, or synapses, it has with neighboring brain cells goes down. The reverse was also true: decreased MHC expression increased synaptic connections.

"The effect on synapse density was mediated through MHC type I proteins," McAllister said.

"But these immune proteins don't just regulate synapse density, they also determine the balance of excitation and inhibition on young neurons -- a property critical for information processing and plasticity in young brains."

Expression of MHCI on neurons was itself regulated by neural activity, the team found, and MHCI mediated the ability of neural activity to alter synaptic connections.

About 10 years ago, other researchers discovered that MHC type I is involved in elimination of connections during a critical period of late postnatal brain development.

"We have now found that there is another role for MHC type I in establishing connections during early postnatal development of the brain," McAllister said.