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Study links immune protein to abnormal brain development

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UCLA scientists have discovered that exposing fetal neurons to higher than normal levels of a common immune protein leads to abnormal brain development in mice.

Published Oct. 14 in the online Journal of Neuroimmunology, the finding may provide new insights into factors contributing to human neurological disorders like schizophrenia and autism.

The researchers studied a protein called major histocompatibility complex, or MHC. The protein plays a dual role in the body: It helps the immune system to identify infected cells, and it enables neurons to make the right connections with each other in the brain.

"When neurons sense infection or damage to the brain, they produce more MHC," said Daniel Kaufman, professor of molecular and medical pharmacology at the David Geffen School of Medicine at UCLA. "We wanted to explore whether higher levels of MHC affect how the brain develops."

Kaufman and his colleagues studied the development of mice whose neurons were genetically engineered to produce more MHC than normal.

Focusing on two key regions of the brain, the researchers looked at neurons that process vision and neurons involved in learning and memory. Next, the team compared these cells with their counterparts in normal mice.

What the scientists saw confirmed their hunch.

"The mice whose neurons produced extra MHC showed subtle changes in the connections between those neurons and other neurons in both brain regions," Kaufman said.

The UCLA finding could be of relevance in unraveling the origins of schizophrenia and autism, he noted.

"Infections in pregnant women have been associated with slightly higher risks for schizophrenia and autism in their children," he said. "Subtle changes in brain development due to excess MHC may explain this relationship."

Kaufman noted that female mice that contract infections during pregnancy also often give birth to offspring with behavioral abnormalities similar to autism and schizophrenia.

"We suspect that infection stimulates the mother's immune system to produce molecules that act like distress signals — they circulate through her blood and then enter the developing brain of the fetus," he said. "There, they alert neurons to make more MHC, which our study shows can lead to altered neuronal circuitry."

"This finding gives us greater insight into the role that MHC plays in the nervous system and may enhance our understanding of the factors that can contribute to neuropsychiatric disorders like autism and schizophrenia," Kaufman said.

Provided by University of California Los Angeles