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Immune activation in pregnant mice affects offspring, potential implications for neurodevelopmental disorders

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A brief kick to the immune system of a pregnant mouse can cause persistent changes in the brains of the offspring, according to new research from the University of California, Davis, Center for Neuroscience.

The findings may help researchers better understand the causes of such neurodevelopmental disorders as schizophrenia and autism, and could point to new ways of preventing the conditions. A paper on the work is published online in the journal *Brain, Behavior and Immunity*.

Kimberley McAllister, professor at the Center for Neuroscience and departments of Neurology, and Neurobiology, Physiology and Behavior, and her colleagues dosed pregnant mice with a chemical, poly (I:C), which mimics a viral infection. They then measured the levels of 23 different cytokines in the brains of the offspring after they were born.

Cytokines are immune-signaling molecules that come into play as the body mounts defenses against infections and other triggers. Cytokines also appear to play a role in normal brain development after birth.

Throughout postnatal development and into adulthood, the mice showed distinct patterns of cytokines in several brain regions. These patterns differed from the patterns seen in the offspring of untreated mice. (The researchers did not find evidence of inflammation in the animals'

brains.)

As seen in earlier experiments by others, the offspring of treated mice did show changes in behavior consistent with animal models of autism and schizophrenia.

It's known that when a mother's immune system responds to a virus or other trigger, cytokines cross the placenta into the offspring, McAllister said. Previously, this had been shown to happen only around the time of infection.

The researchers had expected to see high levels of cytokines in the brains of treated mice. They were surprised to find that, during the time of greatest brain growth after birth, the brains of treated mice had lower cytokine levels than those of untreated mice.

"We showed there are changes in immune-signaling molecules in the mother that are sustained in the offspring," McAllister said. "Remarkably, the direction of change in these proteins is opposite to what was expected."

Judy Van de Water, a professor at the UC Davis MIND Institute who studies the role of the immune system in neurodevelopmental disorders, said it was an interesting discovery that called for further investigation.

"It's clear that maternal immune responses can affect both the developing brain and immune system of offspring, but there are likely additional risk factors that predispose to such responses resulting in autism or schizophrenia," she said.

If cytokine changes are found to play a role in neurodevelopmental disorders, it might be possible to target these cytokines to restore typical brain development.

Provided by UC Davis