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Study suggests a new way to think about the brain's link to postpartum depression

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Chronic stress during pregnancy triggers an immune response in the brain that has potential to alter brain functions in ways that could contribute to postpartum depression, new research in animals suggests.

The study is the first to show evidence of this gestational stress response in the brain, which is unexpected because the immune system in both the body and the brain is suppressed during a normal pregnancy.

The Ohio State University researchers who made the discovery have been studying the brain biology behind postpartum depression for several years, creating depressive symptoms in pregnant rats by exposing them to chronic stress. Chronic stress during pregnancy is a common predictor of postpartum depression, which is characterized by extreme sadness, anxiety and exhaustion that can interfere with a mother's ability to care for herself or her baby.

Stress is known to lead to inflammation, which prompts an immune response to protect against inflammation's harmful effects. Based on what they already know about compromised brain signaling in rats stressed during pregnancy, the scientists suspect the immune cells in the brain responding to stress may be involved. If that's the case, the immune changes may create circumstances in the brain that increase susceptibility to depression.

In unstressed pregnant rats, the normal suppression of the immune system in the body and the brain remained intact throughout pregnancy.

In contrast, stressed rats showed evidence of neuroinflammation. The study also showed that the stressed rats' immune response in the rest of their bodies was not active.

"That suggests there's this disconnect between what's happening in the body and what's happening in the brain," said Benedetta Leuner, associate professor of psychology at Ohio State and lead author of the study. She speculated that the signaling changes her lab has seen before in the brain and this immune response are happening in parallel, and may be directly related.

Leuner presented the findings Saturday (Oct. 19, 2019) at the Society for Neuroscience meeting in Chicago.

In this work, rats are exposed to unpredictable and varied stressful events throughout their pregnancies, a practice that adds a component of psychological stress but does not harm the health of the mother or her offspring.

In the stressed animals, the researchers found numerous pro-inflammatory compounds that indicated there was an increase in the number and activity levels of the primary immune cells in the brain called microglia. Their findings also suggested the microglia were affecting brain cells in the process.

Leuner's lab previously determined in rats that chronic stress during pregnancy prevented motherhood-related increases in dendritic spines, which are hair-like growths on brain cells that are used to exchange information with other neurons. These same rats behaved in ways similar to what is seen in human moms with postpartum depression: They had less physical interaction with their babies and showed depressive-like symptoms.

Leuner and colleagues now plan to see whether the brain immune cells activated during gestational stress are responsible for the dendritic spine elimination. They suspect that microglia might be clearing away synaptic material on dendrites.

Leuner has partnered on this research with Kathryn Lenz, assistant professor of psychology at Ohio State, whose work explores the role of the immune system in brain development.

Though pregnancy was known to suppress the body's immune system, Lenz and Leuner showed in a previous study that the same suppression of the immune system happens in the brain during pregnancy—the number of microglia in the brain decreases.

"By layering gestational stress onto a normal pregnancy, we're finding this normal immunosuppression that should happen during pregnancy doesn't occur, and in fact there's evidence of inflammatory signaling in the brain that could be bad for dendritic spines and synapses," Lenz said. "But we've also found changes in the microglia's appetite. Every characteristic we've looked at in these cells has changed as a result of this stress."

The researchers are now trying to visualize microglia while they're performing their cleanup to see if they are eating synaptic material. They are also manipulating inflammatory changes in the brain to see if that reverses postpartum depression-like behavior in rats.

"We've seen the depressive-like symptoms and neural changes in terms of dendritic spines and synapses, and now we have neuroimmune changes suggesting that those microglia could be contributing to the neural changes—which we think ultimately underlie the behaviors," Leuner said.

More information: www.sfn.org/meetings/neuroscience-2019

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