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The stressed out brain

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Clinical studies of adolescents suffering from depression have shown an interesting connection between early life stress and the immune system. "Those who have experienced childhood trauma and adversity tend to have higher levels of inflammation biomarkers in their blood," explained Heather Brenhouse, an assistant professor of psychology at Northeastern University.

Many of the emotional and behavioral problems associated with early life stress don't appear until adolescence, she said, "so you've got this group of kids who will go on to be sick, but you can't identify them early." If, however, those inflammation biomarkers are present before clinical problems arise, then doctors could use them to predict future mental illness.

Backed by a new grant from the National Institutes of Health, Brenhouse is investigating whether such biomarkers are present in rat models that experience early life stress as well as how inflammation may be linked to neural circuitry problems that give rise to mental illness. Understanding that connection, she said, could reveal new treatment options in addition to early detection opportunities provided by biomarkers.

In previous research, Brenhouse found evidence of inflammation in the brains of adolescent animals that were separated from their mothers during their youth. When she looked for similar evidence in juvenile animals, however, she came up empty handed.

For her new study, Brenhouse will be taking small blood samples to test

for cytokines—molecules released during an immune response—at various points before adolescence. Over time, she will closely monitor for signs of cognitive disorders during adolescence.

At the same time, she will investigate how early life stress changes the brain's neural circuitry in these adolescents, particularly focusing on identifying how significant the role of the NR2A—of a particular type of neurotransmitter receptor in the prefrontal cortex—plays in mental illness caused by early life stress. These receptors, she said, bind a molecule called glutamate, which is implicated in diseases such as schizophrenia. In animals with early life stress, the concentration of NR2As is higher.

"We know that NR2A is upregulated," she said, we just don't know if it's important yet."

Brenhouse's work will also involve analyzing whether blocking inflammation changes how these NR2A receptors functions.

"Our nervous system and our immune system are constantly in communication, for good reason," Brenhouse said. "Think about it: when you're sick, you need to behave differently." So-called "sickness behavior," she said, is one of the easiest ways to think about the connection between the two systems.

When it comes to stress, however, the story is a little more complicated. In some cases, stress activates the immune system, while in others it deactivates it. "We're trying to figure out how early life stress, in particular, changes the development of the immune system and how that winds up leading to neuroinflammation later on."

Provided by Northeastern University