Low levels of pro-inflammatory agent help cognition in rats

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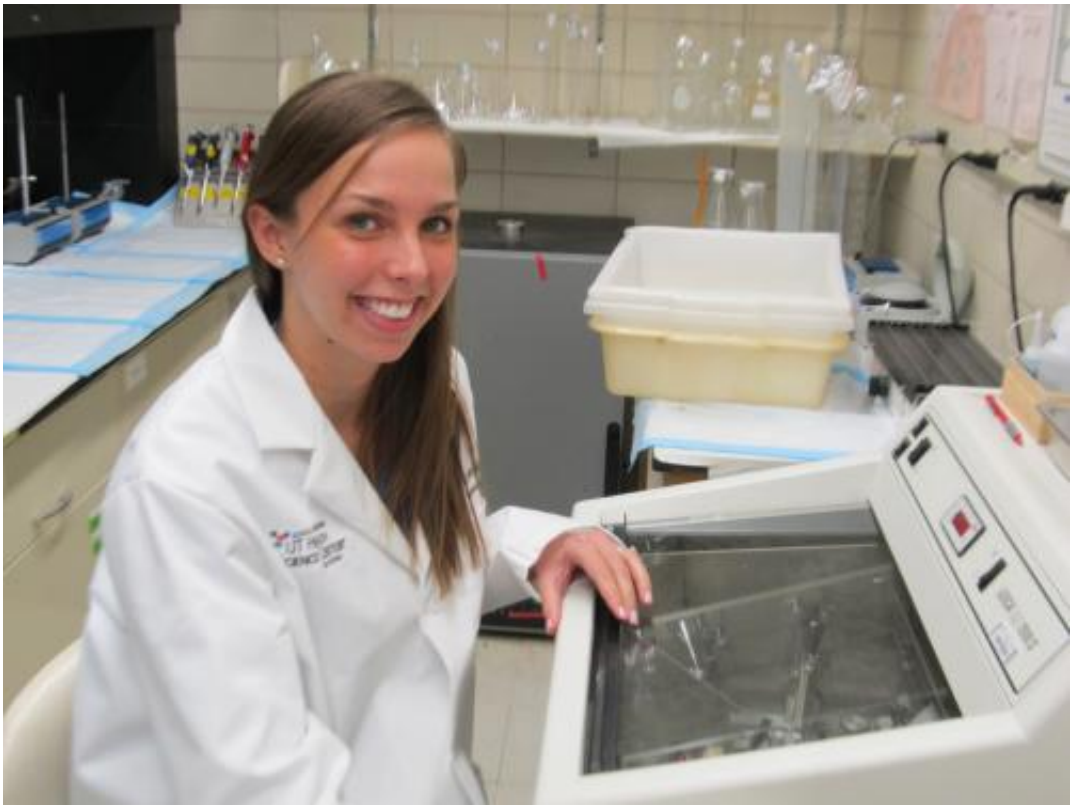

Jennifer Donegan, graduate student at The University of Texas Health Science Center at San Antonio, is lead author of a January 2014 report in the Journal of Neuroscience. The research found that neutralizing the cytokine interleukin-6 in the brain impaired reversal learning in both stressed and nonstressed rats. Reversal learning is a form of cognitive flexibility that is diminished in psychiatric diseases such as depression, schizophrenia and post-traumatic stress disorder. Cognitive flexibility is the ability to change previously learned thoughts and behaviors in response to changes in the environment. Cytokines are proteins produced by the immune system. Credit: UT Health Science Center at San Antonio

Although inflammation is frequently a cause of disease in the body, research from The University of Texas Health Science Center at San Antonio indicates that low levels of a pro-inflammatory cytokine in the brain are important for cognition. Cytokines are proteins produced by the immune system.

Jennifer Donegan, graduate student, and David Morilak, Ph.D., professor of pharmacology in the School of Medicine, found that neutralizing the cytokine interleukin-6 in the brain impaired reversal learning in both stressed and nonstressed rats. Reversal learning is a form of cognitive flexibility that is diminished in psychiatric diseases such as depression, schizophrenia and post-traumatic stress disorder. Cognitive flexibility is the ability to change previously learned thoughts and behaviors in response to changes in the environment.

"When we started the project, we thought cognitive flexibility would be impaired by stress-induced inflammation in a region of the brain called the prefrontal cortex," Donegan said. "We decided to block interleukin-6 during stress to prevent the cognitive deficit, and to our surprise this made things worse. This suggested that it may actually be beneficial to maintain a low level of this pro-inflammatory cytokine in the brain."

Low level corrected deficit

As a key next step, the scientists were then able to fix the cognitive deficit caused by stress by restoring a low level of the cytokine specifically in the prefrontal cortex. Both scientists caution, however, that there is still much to learn about interleukin-6's role in cognition and in diseases like depression. "We've replicated just one piece of a very complex disease so we can understand the biology," Dr. Morilak said. "We found that, in one brain region, one cytokine facilitates cognitive

flexibility and is beneficial after chronic stress. But we delivered the cytokine specifically into that brain region using a virus, which we cannot do in people. And its role in inflammation may be very different than in normal conditions. There's still a lot of work to do."

Donegan is on track to receive her Ph.D. later this year. She is lead author and Dr. Morilak is senior author of the study, published this month in the *Journal of Neuroscience.* The research is funded by the National Institute of Mental Health and the Brain & Behavior Research Foundation.

Provided by University of Texas Health Science Center at San Antonio