Naturally occurring brain signaling chemical may be useful in understanding Parkinson's

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Targeting the neuroinflammatory causes of Parkinson's disease with a naturally present brain chemical signal could offer a better understanding of the clinical mechanisms of the disease and open a future therapeutic window, reports a team of researchers from the University of South Florida Department Neurosurgery and Brain Repair and the James A. Haley Veterans' Administration Hospital, Tampa.

Their findings are published online in the *Journal of Neuroinflammation*.

Brain inflammation has been clearly shown in PD, and the brain's microglia - small cells that regulate the chemical environment of neural cells - play a role in the inflammatory process and disease progression, said study lead author Paula C. Bickford, PhD, professor of neurosurgery at USF and a senior research career scientist at the Haley VA Hospital.

"In the brain, one aspect of immune regulation occurs through neurons," said Dr. Bickford. "Immune cells called microglia can damage neurons by producing bioactive molecules. On the other hand, a neuron-generated signaling chemical, or fractalkine, also called CX3CL1, suppresses the activation of microglia. Our study examined whether adding CX3CL1 beyond normal levels could decrease microglial activation and, therefore, play a neuroprotective role by helping prevent the loss of important neural cells in an animal model of Parkinson's disease."

Using rat models of Parkinson's with known inflammatory components, the researchers added CX3CL1 in varying doses and found that, in all cases, CX3CL1 (which has a single receptor - CX3CR1 found on microglia) reduced the loss of dopamine cells. The loss of dopamine rich nerve fibers in the brain is a key aspect of Parkinson's, leading to movement-related symptoms such as tremors, muscle stiffness, balance problems and slowness.

"This was likely mediated by the accompanying change in microglial-induced inflammation," said USF doctoral student Mibel Pabon, a study co-author.

"This suggests that the communication between neurons and glial cells may play a role in Parkinson's disease neurodegeneration," said Carmelina Gemma, PhD, co-lead scientist for the study, assistant professor in USF's Department of Neurosurgery and Brain Repair, and a research biologist at the James A. Haley Veterans' Hospital. "We found that even small increases in CX3CL1 can be neuroprotective by suppressing microglia activation and, therefore, reducing inflammation."

The researchers concluded that the CX3CR1/CX3CL1 "axis" may be an important target for drug discovery efforts aimed at modulating microglia activation associated with Parkinson's disease."

More information: http://www.jneuroinflammation

Provided by University of South Florida