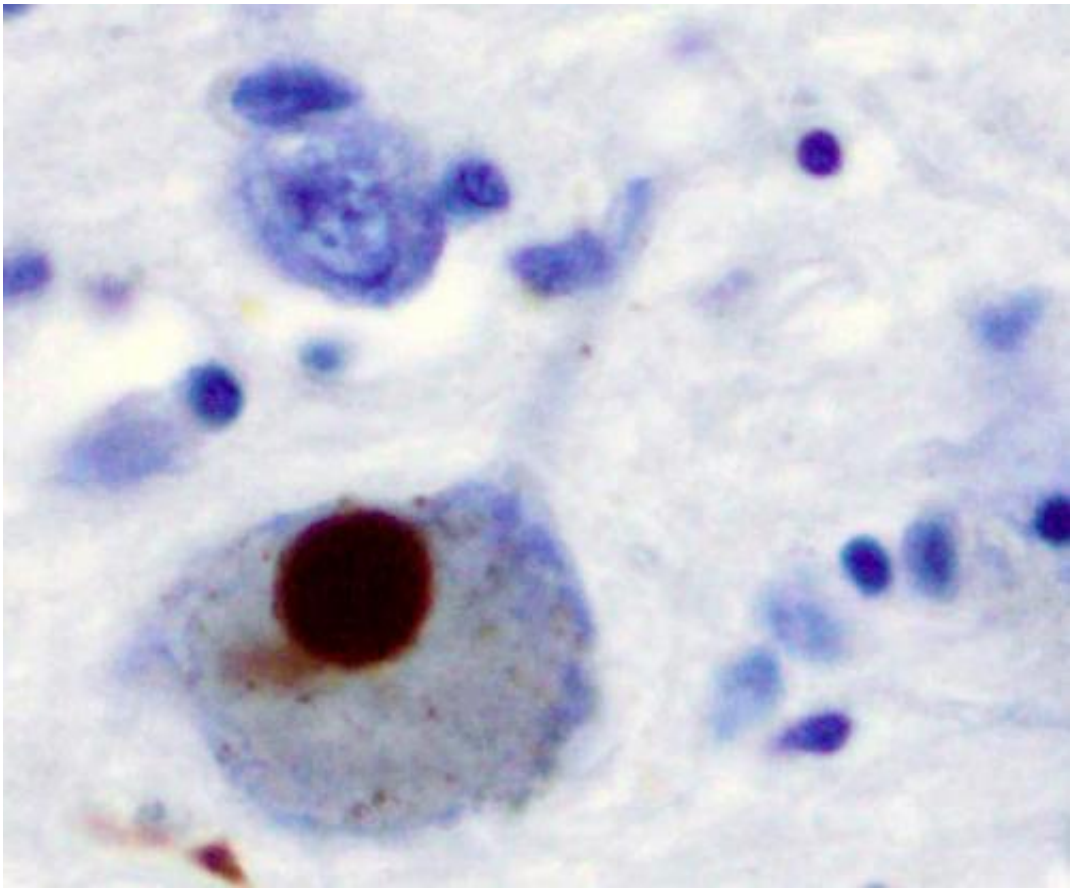
Protecting the brain from Parkinson's disease

December 2 2015



Immunohistochemistry for alpha-synuclein showing positive staining (brown) of an intraneural Lewy-body in the Substantia nigra in Parkinson's disease. Credit: Wikipedia

Although a number of treatments exist to alleviate the symptoms of

Parkinson's disease, to date, none reliably slow the progression of the disease. In 2013, a molecule called GM1 ganglioside showed promise in patients for not only relieving symptoms but also slowing disease progression. However, GM1 ganglioside has been difficult to make and to deliver to patients for regular use. Now, researchers at Thomas Jefferson University have demonstrated a way to help the brain of mice produce more of its own GM1 ganglioside in a study published December 2nd in the open access journal *PLOS ONE*.

"GM1 ganglioside has shown great promise in Parkinson's patients," says lead author Jay Schneider, Ph.D., Professor in the Department of Pathology, Anatomy and Cell Biology at the Sidney Kimmel Medical College at Thomas Jefferson University. "However, considering the difficulties with the manufacture of GM1 and its delivery to the brain, we wanted to see if we could coax the brain to make more of its own GM1."

GM1 ganglioside is normally made by nerve cells in the brain, but the substance is made at much lower levels in patients with Parkinson's and other neurodegenerative diseases. Although earlier work showed that patients who were administered GM1 ganglioside showed improvement in symptoms and progression, the current industry standard for obtaining GM1 ganglioside is to extract the substance from cow brains, which presents a number of manufacturing and potential safety concerns. Also, the substance cannot be readily made synthetically. "We were thinking, 'there's got to be a way around this,'" says Dr. Schneider, "instead of putting more GM1 into the brain, why not try to get the brain to make more of it."

Through a search of existing literature, Dr. Schneider and colleagues found that an enzyme called sialidase was capable of converting other naturally occurring ganglioside molecules in the brain into GM1 ganglioside. They tested their idea in a mouse model of Parkinson's

disease. After the researchers inserted a pump that continually injected the sialidase into the mouse brain, the researchers then simulated the onset of Parkinson's. In this mouse Parkinson's model, Dr. Schneider and colleagues saw neuronal protection at similar levels to those seen in mice injected directly with GM1 ganglioside.

"We were very excited to see that this could work in the mouse model," says Dr. Schneider. "As long-term delivery of sialidase enzymes to the brain would require implantation of a pump system, which might not be optimal, we are currently working on alternative gene therapy approaches to enhance GM1 levels in the brain," he added.

Creating better ways of enhancing GM1 ganglioside levels in the brain could prove beneficial in a number of diseases in addition to Parkinson's disease, such as in Huntington's disease and Alzheimer's disease. Dr. Schneider is currently investigating novel gene-therapy approaches that could enhance the GM1 ganglioside content of neurons and plans to investigate the neuroprotective potential of these approaches. Provisional patents on these technologies have been filed.

More information: J.S. Schneider et al., "Intraventricular Sialidase Administration Enhances GM1 Ganglioside Expression and is Partially Neuroprotective in a Mouse Model of Parkinson's Disease," *PLOS ONE*, DOI: 10.1371/journal.pone.0143351, 2015.

Provided by Thomas Jefferson University