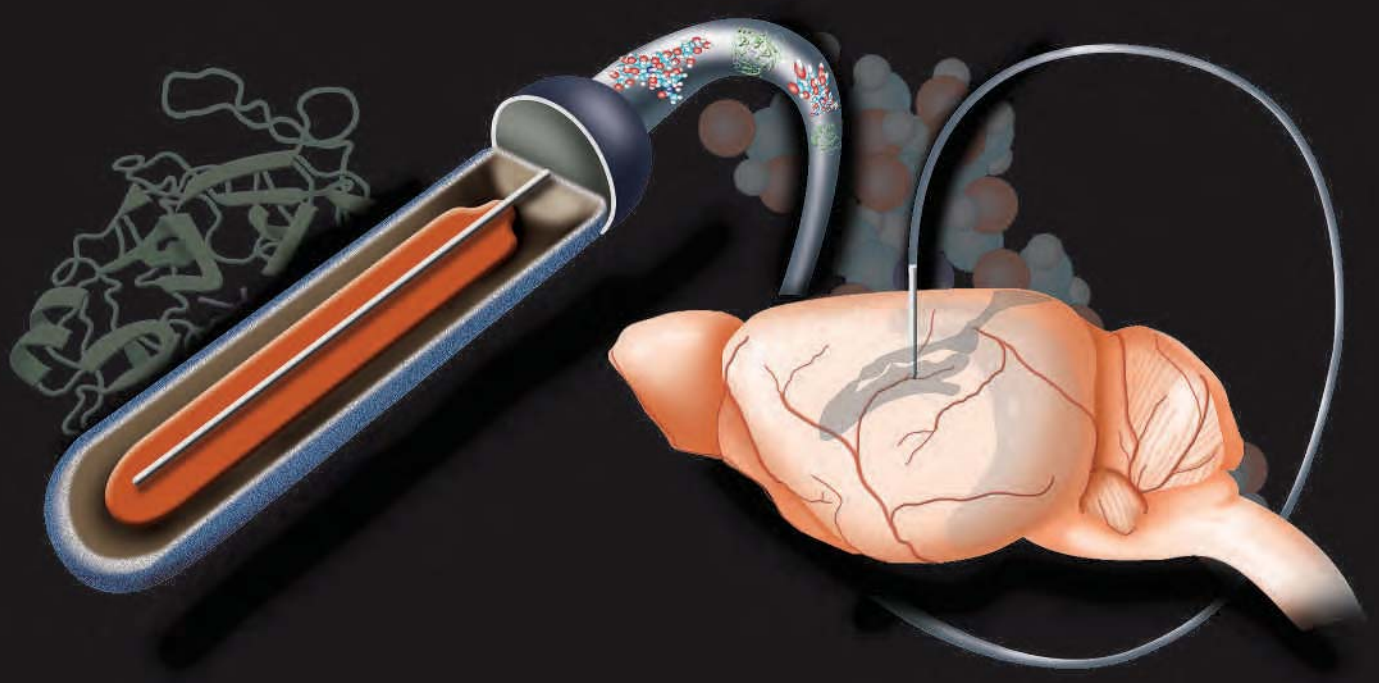
Study Shows Promise in Protecting the Brain Against Parkinson's Disease



A cannula is placed in the third ventricle in the brain and connected to a mini-pump filled with sialidase enzyme. The mini-pump continuously delivers the sialidase to the brain for four weeks.

Almost 200 years after London physician James Parkinson first wrote about "the shaking palsy"—now known as Parkinson's disease—there is still no known cure. A number of treatments exist to alleviate symptoms of the disease, but none slows or stops its progression. In 2013, a molecule called GM1 ganglioside showed potential, but it has proved difficult to make and deliver to patients. Now, Jefferson researchers have demonstrated a way to help the brains of mice produce more of their own GM1 ganglioside in a study published in the journal *PLOS ONE*.

"GM1 ganglioside has shown great promise in Parkinson's patients," says lead author Jay Schneider, PhD, professor in the Department of Pathology, Anatomy and Cell Biology. "However, considering the difficulties with the manufacturing 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 made by nerve cells in the brain but appears at much lower levels in people with Parkinson's and other neurodegenerative diseases. Although earlier work revealed that Parkinson's patients who were administered GM1 ganglioside displayed improvement, the current industry standard for obtaining GM1 ganglioside is to extract the substance from cow brains, which presents a number of manufacturing and safety concerns. The substance cannot be readily made synthetically.

"We were thinking, 'there's got to be a way around this,'" says 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, 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. Schneider and colleagues saw neuronal protection at similar levels to those seen in mice injected directly with GM1 ganglioside.

"We were excited to see that this could work in the mouse model," says 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."

Creating better ways of enhancing GM1 ganglioside levels could prove beneficial in a number of diseases, including Huntington's disease and Alzheimer's disease. 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.