MedicalXpress

Molecule reduces accumulation of toxic protein in Parkinson's disease model

July 24 2019

Parkinson's disease often begins with small tremors. Over time symptoms worsen. Tremors become shakes and stiffness takes the body hostage. People with advanced stages of the neurodegenerative disease often have trouble with coordination, walking and maintaining their balance. Currently no cure exists for the condition and available treatments only address symptoms. No therapies are able to slow the progression of the disease yet.

Now an international team of researchers led by Jay Schneider, Ph.D., a professor in the department of pathology, anatomy and cell biology at Thomas Jefferson University, report new information that may in part explain how a molecule called GM1 ganglioside protects the brain against major features of Parkinson's disease. The discovery further points to GM1 as one of the first potential treatments to directly impact the degenerative processes that cause the disease.

Dr. Schneider has been investigating the therapeutic potential of GM1 in Parkinson's disease for nearly 30 years. In previous research, he and colleagues showed that Parkinson's patients have less GM1 than healthy patients in the part of the brain most affected by Parkinson's, called the substantia nigra. Other researchers followed this work to show in cell culture models that GM1 interacts with a protein called alpha-synuclein. In Parkinson's disease, alpha-synuclein can form clumps, which can become toxic to brain cells in the substantia nigra and lead to cell death. "The accumulation of alpha-synuclein aggregates has been proposed as one of the major pathological processes in Parkinson's disease," Dr.

Schneider says.

In the new work, Dr. Schneider and colleagues show that giving daily GM1 doses to animals that overproduce alpha-synuclein inhibits the toxic effects of the protein.

"When we looked in the brains of these animals, not only did we find we could partially protect their dopamine neurons from the toxic effects of alpha synuclein accumulation, we had some evidence that these animals had smaller and fewer aggregates of alpha-synuclein than animals that received saline injection instead of GM1," Dr. Schneider says.

In addition to protecting brain cells from death, the treatment also reversed some early motor symptoms, the team announced June 10th in the journal *Scientific Reports.*

The researchers suspect that less GM1 in the brains of Parkinson's disease patients may facilitate the aggregation of alpha-synuclein and increase its toxicity.

"By increasing GM1 levels in the brains of these patients, it would make sense that we could potentially provide a slowing of that pathological process and a slowing of the disease progression, which is what we found previously in a clinical trial of GM1 in Parkinson's disease patients," Dr. Schneider says.

The team is now following up on their results to find out what other effects GM1 might have on alpha-synuclein.

"It's important to understand how GM1 is working because there might be other ways we could manipulate GM1 levels in the brain to have a beneficial effect," Dr. Schneider says.

More information: Jay S. Schneider et al, GM1 Ganglioside Modifies α-Synuclein Toxicity and is Neuroprotective in a Rat α-Synuclein Model of Parkinson's Disease, *Scientific Reports* (2019). DOI: 10.1038/s41598-019-42847-x