Medical Xpress

Protein linked to Parkinson's disease may regulate fat metabolism

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National Institutes of Health researchers have found that Parkin, an important protein linked with some cases of early-onset Parkinson's disease, regulates how cells in our bodies take up and process dietary fats.

Parkinson's disease is a complex, progressive, and currently incurable neurological disorder characterized by shaking, stiffness, slowed movement, and impaired balance. Parkinson's primarily affects people over 50, but in about 5 to10 percent of cases it occurs in people as young as their 20s. This form of the disease, which affects actor, author, and Parkinson's activist Michael J. Fox, is known as early-onset Parkinson's.

Parkin mutations are present in as many as 37 percent of early-onset Parkinson's cases. However, laboratory mice with defective Parkin do not display obvious signs of the disease.

This preliminary study, which will appear online in the Journal of Clinical Investigation on Aug. 25, suggests defective Parkin may indirectly contribute to the development of some early-onset Parkinson's by changing the amount and types of fat in people's bodies.

"This discovery shows that the clues to understand Parkinson's disease may not necessarily be in the brain," said study leader Michael Sack, M.D., chief of the Laboratory of Mitochondrial Biology in Cardiometabolic Syndromes at the NIH's National Heart, Lung, and Blood Institute.

The research team, composed of scientists from the NHLBI and the NIH's National Institute of Neurological Disorders and Stroke, observed that mice with defective Parkin did not gain weight in response to a high-fat laboratory diet, as regular mice typically do.

When the researchers examined several organs of the Parkin-defective mice, they noticed that the cells contained low levels of certain proteins that transport fat in the body. In contrast, normal mice that were fed the same high-fat diet had high levels of these fat-carrying proteins, as well as high levels of Parkin, suggesting that Parkin is involved in fat transportation.

The researchers saw a similar pattern when they analyzed blood cells from patients enrolled at the NIH Parkinson's Clinic. In lab tests, cells from people with Parkin mutations had less ability to absorb fat. These results provide evidence that the findings could be relevant in humans.

As to how fat may be important in Parkinson's, Dr. Sack notes that the brain cells destroyed during the course of the disease are found in a region called the substantia nigra, which controls movement, among other roles. "The neurons in this part of the brain are extremely active. Each one has over 300,000 connections and is continuously transmitting information," he said. "These neurons require good support in the form of their fat and cholesterol membrane. If the right types of fat aren't available, then cell integrity will be sub-par and they could be prone to damage."

Dr. Sack and his colleagues plan some early-stage clinical studies on the connection between fat metabolism and Parkinson's. They will continue working with the NIH Parkinson's Clinic and encourage patients to participate in the research as it moves forward.

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