Scientists discover genetic mutation that causes Parkinson's disease

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A large team of international researchers have identified a new genetic cause of inherited Parkinson's disease that they say may be related to the inability of brain cells to handle biological stress. The study, published in the September issue of the *American Journal of Human Genetics*, continues to fill in the picture of Parkinson's disease as a complex disorder influenced by multiple genes, say neuroscientists at Mayo Clinic's campus in Florida who helped lead the investigation.

Although to date, only a small number of families have been identified with this form of Parkinson's disease, the scientists say the study offers a direct insight into how the gene, EIF4G1, can lead to death of brain cells , resulting in Parkinson's disease and related neurodegenerative disorders.

This gene is unlike others that have been found to cause Parkinson's disease in that it controls the levels of proteins that help a cell to cope with different forms of stress, such as those routinely found in aging cells, says Justus C. Daechsel, Ph.D., a Mayo neuroscientist who is the study's co-lead investigator.

Given the function of this gene, this discovery opens up a new area of research within Parkinson's disease and other neurodegenerative diseases , adds study co-author Owen Ross, Ph.D., a Mayo Clinic neuroscientist. The insights gained from how mutations in EIF4G1 lead to cell death might help us develop new therapies to treat or slow Parkinson's disease.

This study began with the identification by French researchers of a large family in northern France with inherited Parkinson's disease. Researchers discovered the EIF4G1 mutation in the French family and in other affected families in the U.S., Canada, Ireland, and Italy.

Much is already known about the protein, EIF4G1. For example, when a cell is undergoing stress the EIF4G1 protein helps initiate the production of other proteins to help the cell cope. Such stresses occur naturally as people age, and if a brain cell cannot adequately respond, it will die. That inability to adapt led to Parkinson's disease in the families studied, Dr. Daechsel says.

This is the third gene that Mayo researchers have found which causes Parkinson's disease, according to Dr. Ross. He adds that Mayo researchers have also identified a number of genetic variants that increase a person's risk of developing the more common sporadic late-onset form of the disease.

We believe that many of the genes implicated in familial Parkinson's disease may be playing a role in the sporadic form of the disease, because as many as 20 percent of individuals with Parkinson's report a first-degree relative with the disorder, Dr. Ross says. This latest finding adds another piece in the complex Parkinson's puzzle.

More information: www.cell.com/AJHG/

Provided by Mayo Clinic