GBA-ASSOCIATED PARKINSON'S DISEASE
INFORMATION FOR PATIENTS

Every person has a 1% to 3% chance of developing Parkinson's disease in his or her lifetime. Scientists now know that individuals with *GBA* gene changes (mutations) have a slightly higher risk of developing Parkinson's disease than the general population. However, the majority of people with *GBA* mutations will never develop Parkinson's disease.

If you have a *GBA* mutation and/or are concerned about your risk, speaking with a genetic counselor can be helpful. This fact sheet outlines basic information about Gaucher disease, Parkinson's disease, and the link between the two, as well as provides information regarding risks to individuals and their relatives.

Gaucher Disease

Gaucher disease is an inherited metabolic disorder caused by reduced amounts of an important enzyme called beta-glucocerebrosidase. The *GBA* gene provides instructions for making this enzyme, and having a change or mutation in this gene causes Gaucher disease. Mutations in the *GBA* gene either reduce or eliminate the amount of beta-glucocerebrosidase enzyme available, leading to the buildup of fatty substances called glycolipids. Symptoms of Gaucher disease include enlarged spleen/liver, abnormal blood cell counts, bone pain, fractures and, in some cases, neurologic problems. There are three recognized types of Gaucher disease. Type 1 is the most mild and common type, and can be either childhood or adult onset. There is treatment available for type 1 Gaucher disease called enzyme replacement therapy, which may help reduce many of the symptoms of the condition.

Gaucher disease is a recessive disorder. This means a person with a mutation in both copies of the *GBA* gene will usually have Gaucher disease. A person with a mutation in one copy of the *GBA* gene is called a carrier and not affected with Gaucher disease. A person with Gaucher disease typically inherits one *GBA* mutation from the mother and one from the father. Parents and children of a person with Gaucher disease are all carriers of a *GBA* mutation. Other relatives may be carriers, too. It is estimated that about 1 in 100 individuals in the general population and 1 in 18 individuals with Ashkenazi Jewish ancestry carry a *GBA* gene mutation. *GBA* mutation carriers often have no family history of Gaucher disease. Carrier screening is a genetic test that some people choose to have as part of the family planning process. A person who has carrier screening is sometimes screened for Gaucher disease and may learn *GBA* carrier status as part of this process.

Parkinson's Disease

Parkinson's disease is the second most common movement disorder. The age of onset is typically around age 60, though the disease can occur earlier or later. In Parkinson's disease, there is malfunction and loss of cells in the brain that produce dopamine as well as changes in other brain regions.

It is important to remember that symptoms, age of onset, and rate of progression can vary greatly from person to person. Diagnosis of Parkinson's disease is made based on the presence of clinical features, such as tremors, bradykinesia (slowness), and rigidity (stiff movements). People with Parkinson's disease can also experience non-motor symptoms such as sleep disorders, mood problems, and cognitive changes. Although there is not yet a cure or way to slow the progression of Parkinson's disease, there are medications and surgical options that can improve the symptoms. Lifestyle behaviors such as engaging in exercise may help delay onset and progression.

Parkinson's disease is a complex disorder, thought to be multifactorial in most families. It is likely caused by an interplay of both genetic and environmental factors. Some people may be the first to be diagnosed with Parkinson's disease in their family, others may have many family members with the disease. A number of genes have been identified as risk factors for Parkinson's disease, with many others likely unknown. The *GBA* gene connection to Parkinson's disease was discovered several years ago, and *GBA* is the most common of the currently known major gene mutations associated with Parkinson's disease.

GBA and Parkinson's Disease

Studies have shown that people with one or two *GBA* mutations are at an increased risk for developing Parkinson's disease. In general, *GBA* mutations are associated with an 8% to 12% risk of Parkinson's disease by age 80. In other words, approximately 1 in 10 people with a *GBA* mutation will develop Parkinson's disease, whereas 9 out of 10 will not. Thus, the majority of people with *GBA* mutations will never develop Parkinson's disease in their lifetime, which is why most individuals with *GBA* mutations may not have Parkinson's disease or any family history of Parkinson's disease.

Over 300 different *GBA* mutations have been identified; these mutations can be characterized as mild or severe as they relate to Gaucher disease. There is a very common *GBA* mutation called N370S that makes up 70% of all reported *GBA* mutations in the Ashkenazi Jewish population. It is thought that a lower risk to develop Parkinson's disease is associated with milder *GBA* mutations (such as the common N370S mutation), and that there is likely a higher risk for those who have severe mutation(s). It is also thought that a slightly higher risk may be associated with having a mutation in both *GBA* genes.

Having a discussion with a genetic counselor or other genetic health provider may be helpful in discussing these potential risks further and addressing concerns you may have for you and/or your family. This is especially true prior to undergoing genetic testing. If you are experiencing symptoms that you are concerned may be related to Parkinson's disease, a discussion with your physician and/or referral to a neurology specialist may be indicated.

Research Opportunities

There is increasing interest in identifying people who have inherited mutations in these genes, and connecting them with research initiatives for Parkinson's disease. Many research studies are interested in enrolling people with *GBA* mutations, regardless of personal or family histories of Parkinson's disease. The goals of these studies may be to better understand what contributes to Parkinson's disease and to develop new treatments. Trials of new therapies for people with Parkinson's disease and *GBA* mutations are ongoing.

Researchers at Indiana University School of Medicine have developed a registry called the Widespread Recruitment Database (WRD) to identify and educate people who have undergone or are interested in future genetic testing for mutations that increase their risk of Parkinson's disease, as well as volunteers interested in contributing to new or future Parkinson's disease research initiatives. Genetic counseling may be available to those who enroll in the project. To see if you qualify, you may start the survey at wrd.iu.edu/pd/. To learn more, you may email us at wrd@iu.edu or call 888-830-6299 with questions about the project.

Resources

- Genetics Home Reference – National Institutes of Health
- Michael J. Fox Foundation for Parkinson's Research
- American Parkinson Disease Association
- Parkinson's Foundation
- National Gaucher Foundation
- NSGC Find a Genetic Counselor