International Parkinson and Movement Disorder Society

Genetic Testing in Parkinson Disease (PD): Essential Facts for Patients

The field of genetics in Parkinson's disease (PD) has expanded tremendously in the past two decades. More recently, commercial and research testing have become available for people with PD. In two large studies in the USA and Europe (PD GENEration and ROPAD), about 10-15% of people with PD who get tested receive a positive report, (i.e., that a genetic risk factor has been identified.)

Each person carries two copies of their genes. One inherited from their father and one from their mother. The genes associated with PD can be divided crudely into three groups. The first group are dominant genes. In these cases, it is enough to inherit one "bad" (mutated) copy to develop PD. An example of it would be the alpha synuclein (SNCA) gene. The second type of genes are those in which two mutations are required to develop PD. Examples for these include Parkin (PRKN) and PINK-1. Mutations in these genes are often found in people who developed PD at a younger age, often in their 20s and 30s. The third group of genes includes those that are considered "risk factors". In these cases, most of those who carry the "bad" (pathogenic) copy will not develop PD, but the risk for PD is much increased. For example, carriers of bad copies (pathogenic) in GBA can have up to 10% risk for PD.

In addition, genetic testing can be used to identify if you have a medical condition that imitates PD but is not PD. For example, genetic testing panels for PD can include genes that cause dystonia or Wilson's disease or spinocerebellar ataxia (SCA 2,3).

The availability of genetic counseling and testing varies considerably across centers and countries. The type of testing can also vary. Most often, people with PD who get tested are offered a genetic panel that includes 5-62 genes. Genetic testing coverage by insurance may also vary significantly across different locations.

Of all the genes tested for PD, most commonly we identify mutations in the genes GBA and LRRK2.

GBA

Pathogenic variants in GBA are the most common genetic risk factors for PD. Between 5 to 10% of people with PD have a change in this gene. Most carriers of a GBA variant will never develop PD. Those who carry a GBA variant may experience PD symptoms at an earlier age compared to patients who don't have a genetic form of PD, and their disease may progress faster.

Inheriting a single GBA variant (from either parent) increases the risk for PD. Inheriting two variants in the gene (from both parents) further increases the risk for developing PD but can also cause a rare genetic disorder called Gaucher disease.

LRRK2

Pathogenic variants in the LRRK2 gene are present in about 1% of all patients with PD and 5% of those with a family history. These variants are more common in certain ethnic groups, including Ashkenazi Jews (about 15%) and North African Berbers (about 40%). While carrying a variant in LRRK2 increases the risk for PD, we estimate that most people with a pathogenic variant in LRRK2 will not develop PD. Those who carry a LRRK2 variant may experience PD symptoms at an earlier age compared to patients who don't have a genetic form of PD, but their disease may progress slower.

We recommend that if you are interested, you should talk to your doctor about genetic testing in PD. If genetic counselors are available in your location, speaking to a genetic counselor before and after taking the test can be extremely useful. Identifying whether you carry a genetic mutation can help you determine if you are eligible to be enrolled in certain clinical trials. Several ongoing clinical trials are already testing treatments for people who carry certain PD gene mutations in GBA and LRRK2. Knowing your genetic status may also provide a sense of empowerment and control but currently, there are no clear guidelines to how genetic information should direct the clinical care.

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