Introduction

Over the last decade, researchers have been able to identify a number of instances where Parkinson disease appears to be caused by mutations (errors in the genetic code) in certain genes. In these cases, the mutated gene is passed from generation to generation, resulting in a greater number of Parkinson disease cases within an extended family.

There are several ways in which a trait or disorder can be passed down through a family. If a disease is autosomal dominant, it means you only need one abnormal copy of a gene from a parent in order for you to inherit the disease. In this circumstance, the parent who passed on the abnormal copy often has the disease as well.

In contrast, the term ‘autosomal recessive’ refers to a genetic condition that appears only in individuals who have received two abnormal copies of a gene, one copy from each parent. The parents are usually both carriers of a single mutation, and so usually do not exhibit the signs of the disease since the gene is ‘recessive’ to its normal counterpart gene. Each of their offspring has a 25% chance of getting both abnormal copies of the gene, in which case, they may be affected by the disease.

Forms of Parkinson disease due to mutations in a single gene (monogenic) are rare, accounting for about 10-15% of cases of Parkinson disease.\(^1\),\(^2\)

Autosomal dominant Parkinson disease

There are several autosomal dominant genes in Parkinson disease including \textit{LRRK2}, \textit{alpha-synuclein}, and \textit{VPS35}.\(^3\) Of these, the most frequent cause is mutations in \textit{LRRK2}. The most common mutation in \textit{LRRK2} (Gly2019Ser) is found in at about 4% of patients with hereditary Parkinson disease,\(^4\) but the frequency of this mutation is especially high in particular populations such as Ashkenazi Jews and North Africans. In general, Parkinson disease caused by \textit{LRRK2} mutations cannot be distinguished from typical (idiopathic) forms of Parkinson disease on clinical grounds alone. Similarly, patients with the \textit{VPS35} mutation have a clinical picture that is identical to typical Parkinson disease patients who do not have the mutation.\(^3\) On the other hand, patients with \textit{alpha-synuclein} mutations often have a type of Parkinson disease that is complicated by additional features such as dementia.\(^5\)
Autosomal recessive Parkinson disease

There are many different genes that are known to cause autosomal recessive forms of Parkinson disease include the Parkin, PINK1, DJ-1, and ATP13A2 genes.\(^6\) Patients with mutations in Parkin, PINK1 and DJ-1 often have a similar clinical picture which includes Parkinson disease symptoms starting early in life, slower progression of the disease, and a good response to treatment with levodopa. Your doctor may notice some other neurological signs (e.g. dystonia, increased reflexes). Patients with mutations in the ATP13A2 gene often present with a form of Parkinson disease (Kufor-Rakeb syndrome) which is complicated by other neurological features such as dementia.

A link between Parkinson disease and Gaucher disease

Gaucher disease is a condition that affects the blood, liver, spleen and bones. It has been known for quite a long time that Gaucher disease is caused by mutations in both copies of the glucocerebrosidase gene. Researchers noticed that family members of patients with Gaucher disease would frequently develop Parkinson disease. It is now apparent that a single abnormal copy of the glucocerebrosidase gene is sufficient to make you susceptible to developing Parkinson disease.\(^7\)\(^8\)

Which patients with Parkinson disease should undergo genetic testing?

It is up to your doctor whether they think genetic testing is worthwhile. Your doctor might think genetic testing is worthwhile if you have a positive family history of Parkinson disease or if your symptoms started at an early age (e.g. age < 40 years). Your doctor might decide to refer you to a Neurogenetics Clinic for genetic counselling.

Why is it important to know about genetic forms of Parkinson disease?

In most cases, knowing that you have a mutation in Parkinson disease gene is not going to make an immediate change to your management. However, it may be important for genetic counselling and family planning, and sometimes even for genetic diagnosis in at-risk pregnancies.

Furthermore, understanding genetic forms of Parkinson disease is very important for Parkinson disease research. Researcher can look at the proteins that are coded for by these genes, and this provides insights into the disease pathways. Hopefully, these discoveries will eventually lead to a treatment for Parkinson disease that targets the underlying disease mechanism.

References and Further Reading:

Support groups:

Parkinson's Australia
http://www.parkinsons.org.au/

Parkinson's ACT
Phone: 02 6290 1984
http://www.parkinsons.org.au/ACT/

Parkinson's NSW
Address: Building 21, Macquarie Hospital 120 Coxs Rd, North Ryde NSW 2113
Phone: (02) 8875 8900

Parkinson's Queensland
Address: 2/25 Watland St, Springwood QLD 4127
Phone: 1800 644 189

Parkinson's SA
Phone: 1800 644 189
http://parkinsonssa.wordpress.com/about-parkinsons-sa-new/
Parkinson’s Tasmania
Phone: (03) 6229 2509

Parkinson’s Victoria
Address: 8b Park Rd, Cheltenham VIC 3192
Phone: 1800 644 189

Parkinson’s Western Australia
Address: The Niche Suite B, 11 Aberdare Rd, NEDLANDS WA 6009
Phone: (08) 9346 7373
http://www.parkinsonswa.org.au/

Shake It Up Australia Foundation
https://shakeitup.org.au/

The Michael J. Fox Foundation for Parkinson’s Research
https://www.michaeljfox.org/