PD Nexus

Parkinson's Disease Genetics

Overview Fact Sheet

Parkinson's Disease

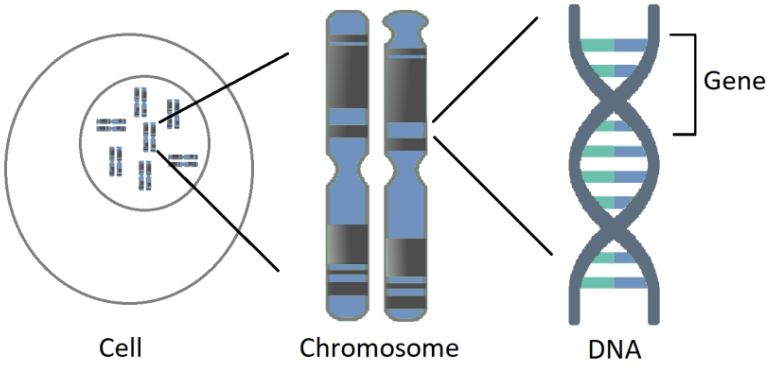
Parkinson's disease is the second most common movement disorder, occurring in 1-3% of the population. The age of onset is typically around age 60, though the disease can occur earlier or later. In Parkinson's disease, there is malfunction and loss of cells in the brain that produce dopamine as well as 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. A 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.

Genetics

DNA is the hereditary material located within our cells. Each cell in our body has an almost identical copy of our DNA in it. Genes are sections of our DNA that the body reads and interprets like instructions. Each gene has a specific function; some genes determine how we look, or regulate how our body digests food, while others protect our body from developing diseases like cancer or diabetes.



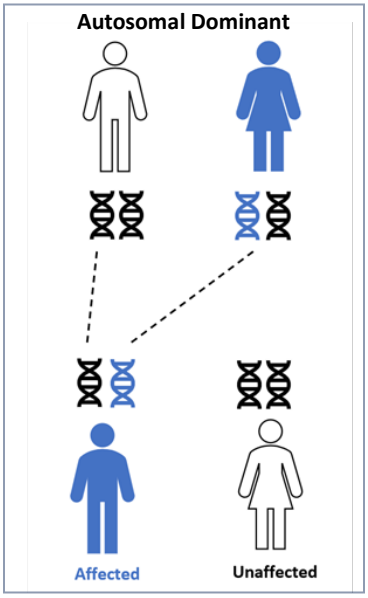
If there is a change in a gene, also called a mutation or variant, this can alter the function of the gene. We have two copies of every gene— one copy is inherited from our mother and the other is inherited from our father. If a person has a variant in a gene, then they have a chance to pass that change on to their children.

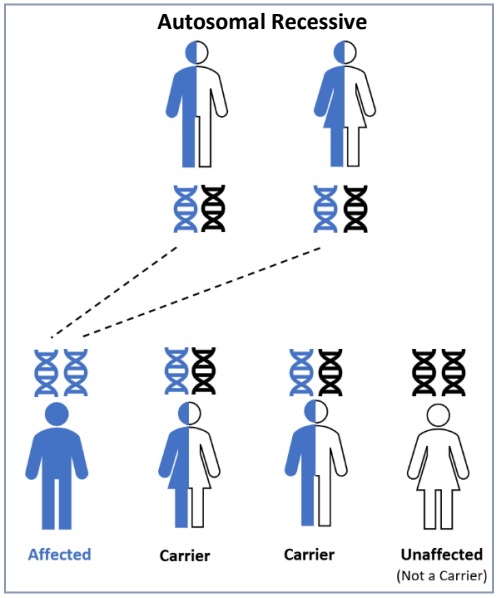
A change in the DNA sequence can occur anywhere within a gene, and there are many different variants that can be found within each gene. Some variants are clearly associated

with disease, while others are not. Variants known to be associated with disease are called pathogenic or likely pathogenic. Those that are not are called benign or likely benign. There are also variants of unknown significance, meaning we are not sure if they cause disease or not.

Inheritance

Some gene variants are inherited in an **autosomal dominant** fashion (see right). This means that it is only necessary to have one variant in a gene to have the associated disease or predisposition to disease. The disease-causing variant is often inherited through multiple generations with each parent having a 50% chance of passing the variant on to each child. Both males and females can pass on and inherit the variant. Some of the autosomal dominant genes have incomplete penetrance; this means that a gene variant may not cause Parkinson's disease in every person who inherits it.





Other gene variants are inherited in an **autosomal recessive** pattern (see left). This means that a person has to inherit two gene variants (one from each parent) to have the disease. Individuals with only one variant are sometimes called carriers and typically will not have the disease. If a person has two recessive variants, we can usually assume that one variant came from each of their parents. Individuals with two recessive variants will automatically pass one variant on to each child. Both males and females can pass on and inherit these variants.

In addition to the gene variants discussed above, there are other genetic factors being studied that may contribute to Parkinson's disease in small ways, and do not fit a dominant or recissive inheritance pattern.

Some individuals with Parkinson's disease are not found to carry a variant associated with the disease. This may be because a major genetic factor is not responsible for the condition, or because there is an unidentified variant not seen with the testing. A negative or normal genetic test result does not entirely reduce the risk to relatives, because other genetic and non-genetic risk factors may still be present and shared in a family. It can be frustrating to not have answers, but testing does help rule out some genetic causes of the disorder.

Some individuals with Parkinson's disease are found to carry a variant associated with the disease. This can help provide some answers as to why the disorder has occurred. In addition, family members may be at an increased risk to carry the variant. Individuals who carry a variant in a gene known to be associated with Parkinson's disease may be eligible to participate in certain research studies.

Resources

Genetics Home Reference-NIH: https://ghr.nlm.nih.gov/condition/parkinson-disease

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

American Parkinson Disease Association: https://www.apdaparkinson.org

Parkinson's Foundation: https://www.parkinson.org

For additional information about Parkinson's disease genetics and research visit PDNexus.org

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