

Parkinson's

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LRRK2 and sporadic PD

Parkinson's disease (PD) is the second most common cause of dementia. There are six known genes that cause familial PD, but only one - the LRRK2 (leucine-rich repeat kinase 2) gene has been associated with sporadic PD. The G2019S mutation in this gene is the most common of the 20 identified LRRK2 disease-causing mutations. In a meta-analysis researchers found 26 people homozygous for the G2019S mutation.¹ The study concluded there were no differences in the clinical features of patients having two copies of the most common mutation of LRRK2 gene and those who have only one copy.¹ Interestingly, three patients homozygous for the mutation exhibited no clinical signs of PD, an indication that the gene has incomplete penetrance. These findings support the theory that the majority of PD cases may only be explained by the interaction of a number of genes or genetic and environmental factors.

1. Ishihara L; Warren L; Gibson R; et al. Clinical Features of Parkinson Disease Patients With Homozygous Leucine-Rich Repeat Kinase 2 G2019S Mutations. *Arch Neurol.* 2006;63:1250-54.

Synuclein variations predispose to sporadic PD

An international research collaborative group consisting of researchers from 11 countries provided strong evidence that a genetic risk factor may account for 3 percent of PD. The study analyzed clinical and genetic data from ~2,700 PD patients and an equal number of age and gender matched healthy subjects. Results showed that individuals with longer lengths of a DNA segment that promotes the activity of the gene alpha-synuclein had a 1.5 times greater risk for PD.¹ Earlier, small studies showed that mutations in

the alpha-synuclein gene caused familial PD. Furthermore; small studies had suggested that mutations in the gene, while not sufficient to cause PD make people susceptible to the disease.

1. Demetrius M. Maraganore; Mariza de Andrade; et al. for the Genetic Epidemiology of Parkinson's Disease (GEO-PD) Consortium. Collaborative Analysis of α -Synuclein Gene Promoter Variability and Parkinson Disease. *JAMA.* 2006; 296:661-70.

Allergies linked to PD

It was recently discovered that allergic rhinitis is associated with the development of Parkinson's disease later in life.¹ Previous studies had shown that people who regularly take nonsteroidal anti-inflammatory drugs, such as ibuprofen, are less likely to develop PD.² These results prompted the investigators to look further into the links between diseases characterized by inflammation and Parkinson's. They studied 196 PD patients and age and gender matched healthy control subjects for the development of inflammatory disorders. The study found that those with allergic rhinitis were ~3 times more likely to develop Parkinson's. They did not find a similar association between inflammatory diseases such as lupus, rheumatoid arthritis, pernicious anemia, asthma or vitiligo and PD. Small sample size was a limitation to finding association with other inflammatory disorders.

1. Bower JH, Maraganore DM, Peterson BJ, Ahlskog JE, Rocca WA. Immunologic diseases, anti-inflammatory drugs, and Parkinson disease: A case-control study. *Neurology.* 2006; 67:494-96.
2. Chen H, Jacobs E, Schwarzschild MA, et al. Nonsteroidal antiinflammatory drug use and the risk for Parkinson's disease. *Ann Neurol.* 2005;58:963-67.