

CAREGIVING BRIEF: GENETICS

My father had LBD and I'm worried about my children getting it. Should we pursue genetic testing?

Is there an increased risk of developing LBD if Alzheimer's disease runs in my family?

Genetic risk factors

There are two broad categories of changes in genes that are associated with the development of certain disorders. Genetic mutations are generally very rare. If a person inherits a disease-causing genetic mutation, they will likely develop that disease. At the other end of the spectrum are genetic changes called risk variants. These may increase or reduce a person's risk of developing a particular disorder, but do not directly cause it.

LBD is usually a sporadic disorder -- meaning ***it is not usually inherited*** directly from one generation to the next. Nonetheless, variations in certain genes can increase a person's risk of developing LBD. The genes most strongly implicated in LBD to date are:

- **SNCA**, the gene that "encodes" for the protein alpha-synuclein. (This means it includes the blueprint for where and how to produce alpha-synuclein.)
- **SCARB2**. This gene encodes lysosome membrane protein-2. (Lysosomes are bodies within cells that act as cellular waste disposals by digesting unwanted materials inside cells.)
- **GBA**: encodes another lysosomal protein, the enzyme β -glucocerebrosidase. (This enzyme processes certain fats, called glycolipids.)
- **APOE ϵ 4**. This variant of the gene for apolipoprotein E is the strongest known risk factor for AD. It is not yet clear if **APOE ϵ 4** increases LBD risk by the same mechanisms that it increases AD risk (for example, by promoting amyloid plaque buildup) or different ones.

What are DNA, Chromosomes and Genes?

Genetic mutations in a cell can lead to abnormal proteins and, in turn, disorders such as LBD

The nucleus of almost every human cell contains a "blueprint" that carries the instructions a cell needs to do its job. The blueprint is made up of DNA (deoxyribonucleic acid). The DNA is packed tightly together with proteins into compact structures called chromosomes. Normally, each cell has 46 chromosomes in 23 pairs, which are inherited equally from a person's biological parents. The DNA in nearly all cells of an individual is identical.

Each chromosome contains many thousands of segments, called genes. People inherit two copies of each gene from their parents, except for genes on the X and Y chromosomes, which, among other functions, determine a person's sex. The genes "instruct" the cell to make unique proteins that, in turn, dictate the types of cells made. Genes also direct almost every aspect of the cell's construction, operation, and repair.

Even slight changes in a gene can produce a protein that functions abnormally, which may lead to disease. Other changes in genes may increase or decrease a person's risk of developing a particular disease.

Source: National Institute on Aging

The gene variants associated with increased risk of LBD are relatively common: for example, about 14% of the general population carries the APOE ϵ 4 allele. However, possessing one of these gene variants does NOT indicate a person will develop LBD – only that one’s risk is increased.

Hereditary forms of LBD have been found only in rare circumstances, of patients with strong family histories of Lewy body disorders (i.e., multiple generations with multiple individuals with dementia with Lewy bodies or Parkinson’s disease). Therefore, genetic testing is not included in routine clinical diagnosis of LBD. Those interested in seeking genetic testing should first consult a genetic counselor.

Variations in the *SNCA* and *SCARB2* genes increase risk of Parkinson’s disease as well as LBD. However, the variations associated with LBD are found in different regions of the two genes than the ones associated with Parkinson’s disease.

Environmental/lifestyle risk factors

Unlike genetic risk factors, some environmental and lifestyle factors that increase disease risk can in theory be changed relatively quickly. Unfortunately, as of this writing, only a handful of studies have looked at preventable risk factors for LBD. Those studies suggest that LBD risk is increased in people with histories of depression, anxiety, or stroke, or a family history of Parkinson’s disease, and people who drink less caffeine than average.

LEARN MORE FROM LBDA:

- Genetic Mutation Increases Risk of Dementia in Lewy Body Diseases:
<http://www.lbda.org/content/genetic-mutation-increases-risk-dementia-lewy-body-diseases>
- Study Reveals Pathology and Genetic Associations with Dementia in Parkinson’s Disease:
<http://www.lbda.org/content/study-reveals-pathology-and-genetic-associations-with-dementia-in-pd>

National Institute on Aging

- Alzheimer’s Disease Genetics Facts Sheet:
<https://www.nia.nih.gov/alzheimers/publication/alzheimers-disease-genetics-fact-sheet>

National Human Genome Institute

- What Do We Know about Heredity and Parkinson's Disease?
<https://www.genome.gov/10001217/learning-about-parkinsons-disease/>

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