Genes and dementia

Alzheimer's Research UK

Make breakthroughs possible

Contents

This information is for anyone who wants to know more about the link between genes and dementia. This includes people living with dementia, their carers, friends and families.

The booklet gives an overview of what genes are and how they are involved in the different diseases that cause dementia, along with information on genetic testing and current research.

The information here does not replace any advice that doctors, pharmacists or nurses may give you but provides some background information that we hope you will find helpful.

This booklet was updated in November 2018 and is due to be reviewed in November 2020. Please contact us if you would like a version with references or in a different format.

What is dementia?

The word dementia describes a group of symptoms including memory loss, confusion, mood changes and difficulty with day-to-day tasks.

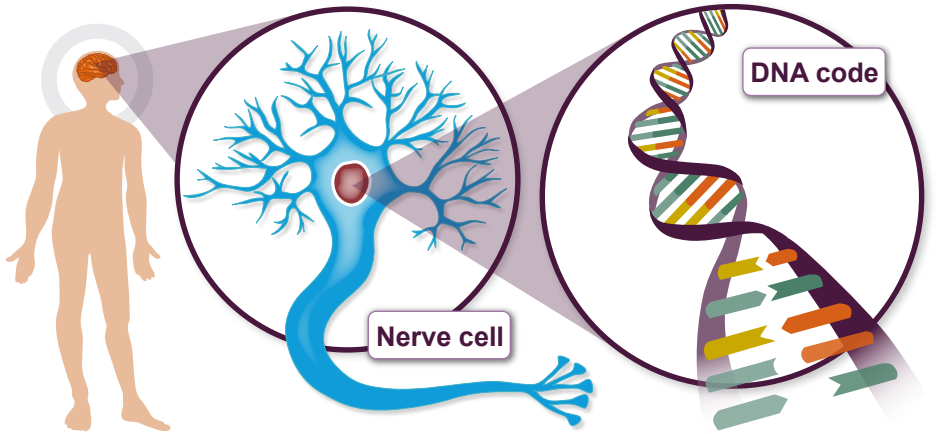
There are a number of different causes of dementia, including Alzheimer's disease, vascular dementia, dementia with Lewy bodies and frontotemporal dementia.

For more detailed information on dementia, ask for our leaflets '**All about dementia**' and '**Treatments for dementia**' or talk to your doctor.

What are genes?

Genes are the instructions for making living things and we inherit them from our parents.

Each gene is a portion of DNA 'code', which holds the information our cells need to make a specific protein. Proteins make up our tissues and organs, and many have specific functions, like carrying messages between nerve cells.



As dementia is so common, many of us will have a relative living with the condition – but this does not mean we will develop it too.

What role do our genes play in dementia?

Most cases of dementia are not caused by genes we inherit from our parents. Dementia is caused by diseases in the brain and the likelihood of developing dementia will usually depend on our age, medical history and lifestyle, as well as our genes.

Risk genes

The exact DNA code that makes up a particular gene varies naturally across the population, meaning that you might have a slightly different version of a gene to the person next to you. This is called genetic variation. Often these differences have no effect on us, but sometimes they may slightly alter our risk of diseases like cancer, diabetes and Alzheimer's. While having a risk gene may increase the likelihood of getting dementia, it doesn't mean a person will definitely develop it because there are many factors at play.

Faulty genes

In very rare cases, a person may inherit a gene that doesn't work properly from one of their parents. This faulty gene is called a genetic mutation and may affect how the body functions. Some mutations can have a very strong effect, and can cause a person to develop a disease no matter what other risk factors they have. Rare forms of Alzheimer's and some cases of frontotemporal dementia can be caused by faulty genes and passed down in families. Having one of these rare mutations makes someone almost certain to develop the disease during their lifetime.

Genes and Alzheimer's disease

Late-onset Alzheimer's

Late-onset Alzheimer's affects people over the age of 65. It is the most common form of Alzheimer's disease and is likely to be caused by a combination of risk factors including our age and lifestyle. Our genetic make-up may also play a part if we carry some risk genes.

To date, scientists have found versions of over twenty different genes that are associated with an altered risk of Alzheimer's. However, having one of these versions may only have a small effect on our risk, and there is still a lot to be understood about these genes and their importance.

The most well-known risk gene with the largest effect on risk is called APOE. This gene makes a protein that helps keep our brain cells healthy. There are three different versions of it – APOE2, APOE3 and APOE4 – and we inherit one APOE gene from each parent.

People who have one copy of APOE4 (roughly 1 person in every 4) are around three times more likely to be affected by Alzheimer's and to develop the disease at a younger age. A small number of people (about 1 person in 50) inherit two copies of APOE4 – one from each parent. They may be more than eight times more likely to develop Alzheimer's. However, due to other contributing factors, they still may never develop the disease.

Is genetic testing available?

Genetic tests can be used to tell us whether we have inherited a gene linked to a particular disease and to predict whether we will develop a disease later in life. For late-onset Alzheimer's, there is no genetic test available on the NHS. Most of the genes discovered so far only have a relatively small effect on risk and many people who have them still won't develop Alzheimer's. Equally, people without them can still develop the disease, so such a test would not be useful.

Early-onset Alzheimer's

Around 1 in 20 people with Alzheimer's develop the disease at a younger age, usually in their 50s or early 60s. For many cases of early-onset Alzheimer's, the cause is still unclear.

A very small number of early-onset Alzheimer's cases are caused by a faulty gene passed down in families. This can be called 'familial' or 'early-onset inherited' Alzheimer's. It usually affects many members of the same family, typically in their 30s, 40s or 50s, but occasionally symptoms can start at a later age. The faulty gene can only be passed down directly from an affected parent, it does not skip generations.

So far three faulty genes have been linked to early-onset inherited Alzheimer's. These genes are called:

amyloid precursor protein (APP)

presenilin 1 (PSEN1)

presenilin 2 (PSEN2)

These genes are involved in the production of a protein called amyloid. If the gene is faulty, there can be an abnormal build-up of amyloid in the brain that causes clumps or 'plaques', a characteristic feature of Alzheimer's.

People who carry one of these faulty genes will develop Alzheimer's and their children have a 50% (one in two) chance of inheriting the gene and developing the disease too. It is important to stress that faulty versions of these genes are very rare and only account for a small fraction of cases of the disease.

The Familial Alzheimer's Disease (FAD) Support Group helps families affected by mutations in the PSEN1, PSEN2 or APP genes. More information can be found at **www.raredementiasupport.org/fad** You can also email **contact@raredementiasupport.org** or call **07388 220323**.

Is genetic testing available?

If someone has a strong family history of Alzheimer's at a young age, genetic testing may be available on the NHS. A blood test is used to confirm a mutation in the PSEN1, PSEN2 or APP genes. This is known as diagnostic genetic testing and must be done at a specialist centre. A consent form must be completed before the test is carried out and it can take several months to get a result.

As these mutations are carried in families, a person's next of kin, and ideally the whole family, should be involved in the discussion about genetic testing. If the exact mutation affecting a person is known, their children and siblings can also be tested for it. This type of test is given to those without symptoms and is called predictive genetic testing. It is only performed after a period of genetic counselling, which helps people to understand the risks and benefits of being tested.

While tests are normally considered for those over the age of 18, younger family members can be involved in these discussions. You can read more about the decision to take a genetic test on page 16.

Genes and other dementias

Vascular dementia

Vascular dementia is caused when blood flow to the brain is reduced, damaging nerve cells. This can happen as a result of a stroke or damage to blood vessels deep in the brain. The majority of cases of vascular dementia are not caused by faulty genes. We may carry genes that affect our risk of stroke, heart disease or other diseases that may contribute to vascular dementia. However, lifestyle factors such as smoking, lack of exercise, obesity, alcohol and diet are also important.

There are rare genetic disorders that can cause vascular dementia by damaging blood vessels in the brain. One is called CADASIL (cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy) and can be passed down through families. CADASIL only affects around 1,000 people in the UK.

Lifestyle factors

such as smoking, lack of exercise, obesity, alcohol and diet may affect our risk of vascular dementia

Dementia with Lewy bodies

Dementia with Lewy bodies is caused by a build-up of abnormal proteins in the brain and may have symptoms similar to those seen in Parkinson's disease. Age is currently the biggest known risk factor for dementia with Lewy bodies, although research is underway to find out whether genes may also play a role.

Frontotemporal dementia

Frontotemporal dementia (FTD), originally called Pick's disease, is a rarer form of dementia mostly affecting people under the age of 65 years. The symptoms of FTD can be quite varied but include changes that mostly affect behaviour or language. There are different types of FTD, and these are likely to have different causes.

Some people with FTD have a family history of dementia and the condition may be inherited in some of these families. For behavioural variant FTD, a third to half of people could have a family history. This figure is thought to be much lower for other forms of FTD.

Overall, around one in ten cases of FTD are thought to be caused by a faulty gene passed down in families. Several genes have been found that can cause these inherited forms of FTD, including:

tau (MAPT)

progranulin (GRN)

C9ORF72

Mutations in the tau gene can cause the tau protein to behave abnormally, forming toxic clumps that can damage brain cells. We still need to understand more about how mutations in progranulin and C9ORF72 cause the disease. The C9ORF72 gene can cause people to develop motor neurone disease, FTD or both conditions and may affect members of the same family differently.

In cases of FTD that are not caused by faulty genes, the risk factors are not yet fully understood and research is ongoing.

Is genetic testing available?

Diagnostic and predictive testing is available on the NHS for the mutations known to cause frontotemporal dementia. If there is a strong history of frontotemporal dementia in your immediate family or your doctor suspects that you may have a genetic disorder that increases your risk of vascular dementia, they may offer to refer you for genetic testing.

For more detailed information about these causes of dementia, please see our leaflets '**What is frontotemporal dementia?**', '**What is vascular dementia?**' and '**What is dementia with Lewy bodies?**' or speak to your doctor.

Dementia and Down's syndrome

People with Down's syndrome are born with an extra piece of DNA. This means they also have an extra copy of the APP gene which leads to the amyloid build-up associated with Alzheimer's disease. While not everyone with Down's syndrome will go on to develop symptoms of Alzheimer's, the risk is much higher. Around 1 in 10 of those with Down's syndrome develop Alzheimer's between the ages of 40-49 years. This increases to over half of people aged 60-69 years.

Genetic tests for mutations that cause dementia are only appropriate for a very small number of people.

Should I ask about genetic testing?

It depends on the disease that caused the dementia in your family, how many family members were affected and at what age they developed the condition.

Deciding to take a genetic test for dementia is a big decision and needs very careful thought. Many people may not wish to know if they carry a faulty gene that causes dementia. Others may feel it would help them and their families to plan for the future. This is something you can discuss with your doctor.

Not all mutations that cause dementia have been identified, meaning that some families may have many affected members, but no mutation can be found. Therefore, a negative test result cannot always rule out a genetic cause of a disease.

If a test is appropriate, your doctor should be able to refer you to a genetic counsellor or geneticist. They will discuss with you the pros and cons of taking a test and any limitations the test may have. They will also tell you where the results will be kept, who they will be shared with and what the next steps would be. For people found to have a genetic mutation that causes dementia, these discussions can also cover the options available when considering starting a family.

Several months of genetic counselling are required before family members can undergo predictive genetic testing. This allows them to discuss what a potential test result may mean, considering a broad range of areas like finances, insurance and family planning. Predictive genetic testing is not the right decision for everyone and it is OK to decline testing after a period of genetic counselling.

How can I reduce my risk of dementia?

For the vast majority of dementias, our genes are only one factor affecting our risk. There are likely to be many other factors involved, such as age and lifestyle. While we can't change our age or genes, research has suggested that up to a third of all cases of dementia could be avoided through lifestyle changes. There are simple things we can do that may help lower our risk:

- **Keep mentally and physically active**
- **Exercise regularly**
- **Don't smoke**
- **Eat a healthy balanced diet**
- **Control high blood pressure**
- **Control your blood glucose if you have diabetes**
- **Keep cholesterol at a healthy level**
- **Control your weight**
- **Only drink alcohol within the recommended limits.**

For more detailed information about risk factors for dementia, contact us for our free booklet '**Reducing your risk of dementia**', or speak to your doctor.

Research into genetics

Alzheimer's Research UK has funded more than

£6.7 million

of pioneering research to understand the genetic basis of dementia.

Pinpointing new genes and understanding how they work provides vital clues about the cause of diseases like Alzheimer's, taking researchers closer to new treatments.

Our researchers have already discovered over 20 risk genes for diseases like Alzheimer's. We're helping them to build on this knowledge through cutting-edge drug discovery projects to develop effective new treatments for these diseases.

Through research we'll bring about breakthroughs that will change lives. Thanks to the generosity of our supporters, we plan to fund many more studies into the genetics of dementia.

Find out more

If you have questions about dementia research or want to find out more about how to get involved in research, contact our **Dementia Research Infoline** on **0300 111 5 111** or email **infoline@alzheimersresearchuk.org**

The Infoline operates 9.00-5.00pm Monday to Friday. Calls cost no more than national rate calls to 01 or 02 numbers and should be included in any free call packages.

We are the UK's leading dementia research charity dedicated to making life-changing breakthroughs in diagnosis, prevention, treatment and cure.

We welcome your comments to help us produce the best information for you. You can let us know what you think about this booklet by contacting us using the details below.

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