MND Factsheet 2
The Genetics of MND

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What are genes?

Genes are the coded instructions we inherit from our parents, to tell our body how to work. They come in matching pairs. We inherit one of each pair from our mother and father. We have many thousands of genes, telling the body how to do different jobs. Our genes have a code (called the "genetic code") that is spelled out in letters. Changes in one or more letter of the code (called a "gene change" or more technically a "mutation") can make us more likely to develop some diseases, including motor neurone disease (MND).

How do genes cause MND?

There are lots of genes that tell our motor neurones (nerve cells) how to work. Gene changes in specific parts of our genetic code can influence our chance of developing a disease.

When reading or hearing about MND, you might hear about "genes associated with MND" and "MND genes". Those that are "associated" with MND are genes that seem to be linked to MND because changes in their genetic code are more common in people with MND than in other people. Most of these gene changes only slightly increase the chance of developing MND in an individual. Because of this uncertainty, testing for these gene changes could not be used in practice to find out the chance of someone developing MND. Instead, they are mainly important in helping scientists understand more about MND.

This leaflet will focus on a subset of genes that we shall call "MND genes". We all have these MND genes. However, people who have gene changes in these genes, changing the way they work, have a high chance of developing MND, and unlike those genes merely "associated" with MND, MND genes have a much clearer relationship with the development of MND. These gene changes can be inherited and explain why we sometimes find families where more than one person has MND (called "familial MND"). Common MND genes you might hear about are C9ORF72 and SOD1 but others have been discovered and the list continues to grow. C9ORF72 is topical because it was discovered recently, is the most common and also makes people more likely to develop a type of dementia called frontotemporal dementia.

How can people tell if a gene change has caused their MND?

Most people (9 in 10, 90%) with MND will be the only person in their family with it. This is termed "sporadic MND". This is not due to an MND gene change.

Only one in ten (10%) people with sporadic MND have an MND gene change. There are many reasons why such people do not have a relative with MND; for example, the gene change

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could have happened in them for the first time.
Some people with MND have a close relative with MND. Often this is familial MND, due to an inherited MND gene change. These people may be offered genetic testing by their Neurologist or Geneticist.
Some people with MND who have a close relative with dementia might also have familial MND. The chance of that depends on the type of dementia and how closely the person is related. These people should discuss their family history with their Neurologist or Geneticist.

How does genetic testing work for someone with MND?

It is possible to test a blood sample, looking for changes in many of the known MND genes. In Scotland, there are two types of genetic testing in people with MND – testing in a clinical (NHS) setting, and testing in a scientific (research) setting.
People whose MND is thought to be familial can have clinical genetic testing done through the NHS. This would happen after discussion with their Neurologist or Geneticist. There are three outcomes of such testing. The first is that a gene change is found that is the cause of the MND. If this happens, relatives could be seen at a Clinical Genetic clinic to discuss having a genetic test themselves. The second is that a gene change is found, but that it is not clear whether it is the cause of the MND or not. This would be discussed with their Doctor. The third and final possible outcome is that the altered gene is not found. In this case, it is important to remember that the person may still have familial MND, but that their specific gene change may not be detectable with current testing methods, or the gene that causes their MND may not even yet have been discovered. People with familial MND who do not wish to have a genetic test themselves can ask for their genetic sample to be stored with the NHS, so it could potentially be used for their relatives in the future.

Research genetic testing also happens as part of the CARE-MND project. The aim of this is to test lots of people with MND, so scientists can understand the genetics better. The hope is that this will improve our understanding of how and why MND comes about, enabling us to develop better treatments. Blood samples given for these projects are stored and tested in a research laboratory, outside the NHS. People giving samples will not receive their result and their sample cannot be used by their family in the future.

What is the chance of the relatives of someone with MND developing the condition?

The relatives of someone with sporadic MND are unlikely to develop MND. The chance of this is around 3 to 4 in 100 (3-4%).
In familial MND, the chance of close relatives developing the condition is increased. That chance depends upon what gene is altered and how closely the person is related. People with familial MND, and/or their relatives, can be seen at a Genetic clinic to discuss this.
Most known MND gene alterations are inherited in a pattern called autosomal dominant*. This means that the children of an affected person have a 1 in 2 (50%) chance of having inherited the gene change, and so being likely to develop MND themselves.
Some MND gene alterations are inherited in a pattern called autosomal recessive*. This means that the children of an affected person are unlikely to develop

MND, unless their parents were blood relatives of each other.

How does genetic testing work for the relatives of someone with MND?

Anyone in a family with possible familial MND can be seen at their local Clinical Genetic clinic to find out about their own risk. There are Regional Clinical Genetic Centres in Glasgow, Edinburgh, Dundee and Aberdeen and all run outreach clinics so people can be seen at a Hospital nearer to their home.
If there is someone in the family who has an MND gene change, then relatives can weigh up the advantages and disadvantages of having a genetic test in this specialist setting. If they choose, their blood sample can then be tested for the MND gene change found in their family to see if they have it or not.
If the person in the family with MND has not been found to have a gene change, then it is not possible to test relatives for the familial MND gene change.

Where can I find out more?

The Genetic Alliance has information on DNA, genes and mutations, patterns of inheritance, genetic testing and predictive genetic testing for relatives. (www.geneticalliance.org.uk/information)
There is also a good section on frequently asked questions about how genetic testing may affect insurance cover. (http://www.geneticalliance.org.uk/information/living-with-a-genetic-condition/insurance-and-genetic-conditions/)

The Scottish Genetics Education Network (ScotGEN) is a network for all individuals involved in teaching genetics for healthcare in Scotland. (https://www.scotgen.org.uk/)
They provide a range of leaflets on different genetic conditions. One leaflet is on Genetic testing and Consent, which is helpful for those considering genetic testing.
https://www.scotgen.org.uk/media/1161/006-genetic-testing-consent-2304951.pdf

If you wish to have genetic testing, you should speak to your MND care specialist or your GP in the first instance.