

GUIDELINES FOR PREDICTIVE TESTING FOR MOTOR NEURONE DISEASE . Origin Australia

Introduction

A significant amount of research has been conducted into the genetics of Motor Neurone Disease. The information below discusses some issues you may wish to consider in relation to genetic testing or the donation of blood to further research into Motor Neurone Disease.

GENETIC TESTING IN MOTOR NEURONE DISEASE (MND)

1. Background

'Motor Neurone Disease' is a general term used to describe a progressive degenerative disorder of a particular group of nerve cells in the spinal cord and brain called 'motor neurones'. Loss of these cells results in weakness and wasting of the muscles.

The disorder usually starts in middle life and once symptoms appear, life expectancy is generally 2-6 years, although it can occasionally be longer. Most people with MND are the only known person in their family with the disorder. They are said to have 'sporadic' MND. MND is sometimes inherited, with more than one affected person in a family. This is known as 'familial' MND.

Research has shown that about 20% of people with *familial* MND have the disorder because of a 'mutation' in the superoxide dismutase (SOD₁) gene on chromosome 21. A mutation is an error in the genetic code that causes the gene to work abnormally.

Some people with *sporadic* MND, (about 1%), may also have mutations on the SOD₁ gene. The proportion is not precisely known at present.

Other genes, as yet unidentified, can cause familial MND. Environmental factors may also influence whether someone develops MND.

If an individual has MND as a result of a mutation in SOD₁, each of their children has a 50/50 chance of inheriting the faulty gene. People who inherit a faulty SOD₁ gene have a high, but as yet uncertain chance of developing MND in later life. Some people with a mutation in their SOD₁ gene may never develop MND.

The age at which symptoms of MND appear in people with faulty SOD₁ genes varies greatly. They can start as early as the 20's and as late as the 80's. The age of onset can vary considerable in a family.

2. What is happening now?

Researchers are carrying out further studies -

- to develop laboratory testing for the SOD₁ gene to a point at which it is readily available to those who want it

- to monitor how many familial and sporadic cases of MND result from mutations in SOD₁
- to identify mutations in other genes which may cause familial MND
- to work out how many people with a faulty SOD₁ gene might be expected to actually go on to develop MND later in life
- to understand how MND is caused by faults in SOD₁
- to discover ways of preventing and treating MND.

3. **What does identification of mutations in the SOD₁ gene as a cause of familial MND mean for people with MND and their families?**

It is technically possible to test for mutations in the SOD₁ gene. This is true for both familial and sporadic MND.

If the disorder is caused by a SOD₁ mutation:

- it is possible to test other family members to determine if they also have a SOD₁ mutation, for example, the adult children or brothers and sisters of an affected person
- it is possible to test an unborn child to determine if it has inherited the SOD₁ mutation
- It is not possible to predict the age at which symptoms may appear in those shown to have a SOD₁ mutation, and some may never develop symptoms.

Research can now begin to increase our understanding of the mechanism by which SOD₁ mutations cause MND. Research may lead to treatments that can prevent or delay the onset of MND in someone with a defective SOD₁ gene.

It is possible that research on MND caused by SOD₁ mutations will speed up discovery of causes of other types of MND.

4. **Testing for SOD₁ mutations - some of the issues**

Why might I want to know if I have the SOD₁ mutations?

- to enable me to plan my life
- to help with decisions about marriage and having a family
- if I do not have the gene, the information may help when I apply for jobs, life insurance, superannuation or when taking on long-term financial commitments
- to provide information of importance to my children
- if I have the gene, and it becomes possible to prevent MND, I can make use of the preventative measures
- I am the sort of person who wants to know as much as possible about myself and my future and find it hard to live with uncertainty.

Why might I not want to know if I have the SOD₁ mutations?

- I would not change my plans regarding marriage and having a family, whatever the test result
- I can accept living with uncertainty and will be able to plan my life without knowledge of my genetic status

- if I have the gene, the information may limit my life opportunities for example, in relation to career choices, life insurance, superannuation and financial matters
- I do not think that I would cope with knowing that I have the gene and will have a high risk of developing MND
- I am always free to change my mind and can take the test in the future if, for example, a treatment becomes available that can prevent MND
- Relationships with my family, friends and workmates may change if I am shown to have the mutated gene.

Can children be tested?

- In general, children under 18 years of age should not be tested. People having this test must be able to give consent. They need to understand and accept the testing process and the implications of the test result.

Remember that this is a test that gives an indication of a person's future and can have tremendous effects on various aspects of life. The right of a parent to have information about their child does not outweigh the child's right to make a personal choice about whether or not to be tested.

Testing must be voluntary

- While each person will consider the views of family and friends, the person must take the final decision.

It would be quite wrong for someone to take the test because of pressure to do so.

How is the test performed?

- No testing is carried out until the person concerned has undertaken a process of counselling with a specialist genetic counsellor.
- The test is done on genetic material taken from a blood sample, and involves a substantial cost to the person undergoing testing. The fee is currently not refundable from Medicare.

Can DNA be stored?

- DNA can be stored frozen, so blood from people with the disorder can be collected now and used in the future to help other family members.

Who owns the test result?

- The result cannot be released to others without the formal consent of the person tested.

Who can provide support for those taking the test?

- family, close friends or other trusted people
- health professionals such as doctors, (geneticists, neurologists, psychiatrists, general practitioners), MND Associations, counsellors (including genetic

counsellors), and social workers. Testing needs to be offered as part of a formal program providing the information, counselling and support an individual needs when trying to decide whether to have the test, and after the result has been given.

Can I give a blood specimen for research, but without getting the result?

- Researchers are keen to receive blood samples from people with a family history, particularly if testing for the SOD1 mutation has proved to be negative in that family. (The SOD1 mutation is only responsible for about 20% of cases of familial MND, and other mutations that can cause familial MND are yet to be identified).

However, no standard procedure is presently in place for obtaining blood samples and transporting them to research laboratories without cost to the person donating the sample.

If you would like to support research in this way, please contact your local MND Association to check if arrangements are in place for you to donate a blood sample for this purpose.

If a person who has donated blood for research purposes wishes to find out at a later date whether they have a genetic mutation for familial MND, it would be necessary to follow the standard procedure of counselling and genetic testing as detailed above.

5. Whom can I contact if I want to learn more about testing?

- your regional clinical genetics unit. Addresses are provided on the back of this leaflet, via which you can be referred to your nearest genetic counselling clinic
- the neurologist who is treating/treated the person in your family with MND
- the local MND Association.

6. The Australian MND Associations

What role should the Associations play?

- prompting consensus between professionals and families about the design of protocols for testing
- producing and disseminating information
- advocating for the development of clinical programs which have a written protocol and provide full counselling and support for those taking the test
- promoting the sharing of knowledge and experience as research proceeds and clinical testing programs begin
- supporting clinical programs which provide diagnostic testing
- providing guidance and advice for patients/relatives and professionals
- promoting research - knowing that SOD₁ mutations can cause MND, work needs to be done to:
 1. understand the mechanism by which the faulty gene leads to the disease
 2. develop methods for prevention and treatment
 3. identify the other gene(s) which can cause MND when mutated.

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