Structural CNS changes, neuropsychological impairment and sleep disorder in myotonic dystrophy type 1: a genotype-phenotype study
(The DM1-Neuro study)

A study to investigate the relationship between genetic factors and the effects of myotonic dystrophy type 1 on the brain.

Information Sheet

You are being invited to take part in a research study. Before you decide to participate, it is important for you to understand why the research is being done and what it would involve. Please take the time to read the following information carefully, and discuss it with friends or relatives if you wish. Please ask us if anything is not clear to you, or if you would like more information.

Why have I been chosen?
We are inviting you to participate as you have previously been diagnosed with myotonic dystrophy type 1. We hope to recruit 40 men and women affected by myotonic dystrophy to take part in this study.

What is the purpose of this study?
Myotonic dystrophy type 1 is one of the most common forms of inherited muscle weakness in adults. As well as muscle symptoms, some people with myotonic dystrophy experience poor quality of sleep and feel excessively sleepy during the day. Some also feel that their concentration is impaired, or that aspects of their thinking are affected.

Myotonic dystrophy type 1 is caused by a change affecting the body’s instructions, the DNA. Specifically, it results from the expansion in size of a particular sequence of the DNA code. This DNA expansion is often seen to become larger in successive generations of a family affected by myotonic dystrophy, with larger expansions associated with earlier onset and more severe symptoms. Changes also occur in the size of the DNA expansion over an affected person’s lifetime, although the traditional genetic test does not take account of these changes.

An existing study led by Professor Darren Monckton at the University of Glasgow, called the Genetic Variation in Myotonic Dystrophy study, has developed a more accurate method of measuring changes in the DNA expansion over time. You may have provided blood samples for...
this study in the past, although if not you will need to consent separately to join the Genetic Variation in Myotonic Dystrophy study if you wish to participate in the DM1-Neuro study.

The main aim of this research study is to build on the knowledge gained by the Genetic Variation in Myotonic Dystrophy study, seeking to understand how these changes in the DNA expansion over time relate to the severity of symptoms people experience. We will also look at relationships between changes seen on MRI scan of the brain and symptoms such as excessive sleepiness, sleep disturbance and impairment of thinking.

While this study is not testing any treatments for myotonic dystrophy, it will contribute to better understanding of how the disease affects aspects of brain structure and function, which is an important step towards identifying how new treatments might work. Furthermore, understanding the relationship between genetic factors and the impact of the disease will help to design better trials to test new therapies for myotonic dystrophy, hopefully shortening the time taken for treatments which prove effective to be made available to patients. Finally, improved understanding of the relationship between genetic factors and symptoms may also enable patients to be offered more specific information about how the condition is likely to affect them in the future based on their blood test results.

What does this study involve?
If you agree to participate, a member of the research team will contact you to arrange the following investigations. Some flexibility can be offered in terms of the timing and the order in which they are completed to accommodate your availability and preference.

· **MRI scan of the brain** - This will be done at the Institute of Neurological Sciences at the South Glasgow University Hospitals campus. You would be required to lie flat for around 60 minutes while a scan is taken of your head. Although the machine is open at both ends, it may make some people feel confined (claustrophobic), and can be noisy. We will provide you with earplugs or headphones to wear during the scan. Since the MRI machine uses a strong magnet that will attract other metals, some people may not be able to undergo a scan; for example, those with an electronic pacemaker or implanted defibrillator. A member of the research team will carry out a full safety checklist before beginning the scan. If you are not able to have an MRI scan, you may still be eligible to participate in other parts of this study.

· **Blood tests** – On the morning you attend for your MRI scan, a few drops of blood will be taken by making a small pinprick on your earlobe. You will also be asked to provide around 2 teaspoons (8-10ml) of blood from a vein, usually in your arm or hand, for the Genetic Variation in Myotonic Dystrophy study. This can usually be taken along with your routine blood samples at your clinic appointment. Blood taken for the Genetic Variation in Myotonic Dystrophy study will be analysed to look at changes in the size of the DNA expansion responsible for myotonic dystrophy, as well as looking at the sequence of the DNA code both within the expanded section and neighbouring portions of DNA.

· **Neuropsychological testing and quality of life questionnaires** - a member of the research team will first take you through a series of questions and simple tasks designed to assess how well some parts of the brain are working. These should take no longer than one hour, and you will be encouraged to take a short break once they are complete. The researcher will then help you to
answer a series of questionnaires, intended to assess how the symptoms of myotonic dystrophy impact your day-to-day life. This will take around one further hour.

We also ask that a close family member, friend or carer be present at this session. This person will be asked to answer some brief questions relating to you. Some of these questions are of a somewhat personal nature, for example asking how they feel you manage in social situations.

You may ask for a researcher to visit you at home to carry out these assessments, or they can be carried out in a clinic room at the South Glasgow University Hospitals campus.

· *Sleep study* – In order to assess the quality of your sleep and to screen for abnormal breathing patterns overnight, a member of the research team will visit you at home in the evening and help you to attach some lightweight equipment to your body. The equipment consists of elasticated bands which go around the chest, some lightweight tubing which sits under the nose, sensors attached to wires which stick to the scalp and a small plastic box. You will be asked to wear this equipment over a single night’s sleep, and to set an alarm to get up around 07:30 the next day.

· *Sleep resistance test* – On the morning after your sleep study, a member of the research team will return to your home before 9:30am. You will be asked to keep wearing the equipment used for your sleep study, and to sit on top of your bed propped up with pillows. You will then be asked to remain like this with the lights dimmed, and try not to fall asleep for 40 minutes. The test will be repeated for another 40 minutes on the same day at 11:30am and 1:30pm. The researcher will leave your home between these test sessions.

**Will I be told my results?**

At present it is not possible to make accurate predictions about how myotonic dystrophy will affect an individual based on the genetic measurements we obtain from blood samples. We therefore will not inform you of these results. However if the other investigations, such as MRI scans or sleep studies, give a result which suggests you might benefit from further investigation or treatment we will inform both you and your GP of this, and refer you to the relevant specialist. **If you are concerned about symptoms such as excessive sleepiness however, you should not rely on results from the research study to investigate these, and should instead discuss your symptoms with your usual doctors.**

If you wish to be informed of the outcome and conclusions of the study as a whole, please indicate this on your consent form and we will send you a summary when the study is completed.

**How do I participate?**

If you wish to participate, then we would be grateful if you might indicate this on the Expression of Interest Form enclosed, and return this in the Freepost envelope provided. This will inform us that you are interested in participating. You can keep this information sheet (that you are reading) for your records.
What happens next?
If you have an appointment with Clinical Genetics in the near future, you may sign the consent form to take part in the study at this appointment. Otherwise, a member of the research team will contact you once we have received your Expression of Interest form to explain the next steps.

Do I have to take part?
No. If you choose not to participate in the study, this will not influence your care or management of your myotonic dystrophy. We would still appreciate if you would let us know you do not wish to take part by returning the Expression of Interest Form.

What happens to my data obtained from this study?
Any data collected from you which includes identifiable details such as name, address or date of birth will only be accessible to the direct study team, and will be stored in locked filing cabinets or secure computers in accordance with the Data Protection Act 1998. Data which allows you to be identified will not be shared with third parties.

Data which are anonymised, which you therefore cannot be identified from, including MRI images may be shared with research collaborators or other relevant research groups based elsewhere in the UK or internationally, including countries outside of the European Union. By making this information available to other researchers we hope to maximise the potential benefit of information produced by the study.

Will my taking part be kept confidential?
Only your GP would usually be informed of your involvement with the study. However anonymised data relating to your participation may be shared with other researchers as outlined above.

Are there any risks to taking part?
This study is not testing a new drug or medical intervention, therefore the risk of harm to participants is very low. As with any blood test, obtaining the blood samples required may produce some local bruising or tenderness.

A full safety checklist will be completed before undertaking the MRI scan, and if there are any doubts regarding your suitability to undergo the scan, the team will not proceed with this. In undertaking an MRI scan of the brain, there is a small but significant chance of the scan showing something which was not expected. Examples might include changes consistent with a previous stroke or a small bleed. Very rarely, findings such as a tumour or a swollen blood vessel called an aneurysm may be made. The chance of an unexpected finding of any kind is low, perhaps around 2-3%. If we do make any findings which require further investigation or treatment, we will inform both you and your GP and refer you to the appropriate specialist without delay.

Who has reviewed the study?
The study has been reviewed by the West of Scotland Research Ethics Committee.
If you have a complaint about any aspect of the study

If you are unhappy about any aspect of the study, please contact the researcher in the first instance. However the normal NHS complaints mechanism is also open to you.

If you do not understand anything or would like more information, please ask the doctor who gave you this sheet or contact the research team on the details at the top of this letter.

If you wish to have advice from someone independent from the study team, you may contact Dr Esther Kinning, Consultant Clinical Geneticist on Tel. 0141 354 9300.

Thank-you for your time and co-operation.