NUFFIELD DEPARTMENT OF CLINICAL NEUROSCIENCES

(Division of Clinical Neurology)

West Wing, Level 6
John Radcliffe Hospital, Oxford, OX3 9DU
www.ndcn.ox.ac.uk
Tel: +44(0)1865 231893
Email: enquiries@ndcn.ox.ac.uk

Oxford University Hospitals NHS
NHS Foundation Trust

'ACORN' Study

Study ethics reference: 23/LO/0507
Version 2.1 14 January 2025
Chief Investigator: Dr Alexander G. Thompson

Participant Information Sheet – Family Members

You are being invited to take part in a research study. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully. Talk to others about the study if you wish.

This document tells you the purpose of this study and what will happen to you if you take part as well as more detailed information about the conduct of the study.

Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part. We are planning to recruit participants into this study for five years, so you can decide to participate later on if this is more convenient.

What is the purpose of the study?

The purpose of this study is to investigate possible causes of nerve damage in patients with a fault in a gene known as C9orf72. This faulty gene is known to cause Amyotrophic Lateral Sclerosis (ALS; also known as motor neuron disease or MND) and a linked condition called Frontotemporal Dementia (FTD). To carry out the study, we need to obtain blood and other tissue samples from carriers of the faulty version of the C9orf72 gene who have ALS or FTD, as well as their family members who do not have ALS or FTD symptoms. We also need to study a group of people with ALS or FTD who do not have this faulty gene, in order to compare results. Finding out why patients carrying the faulty C9orf72 gene develop ALS and FTD may help us in the future to find treatments to help prevent these conditions.

The C9orf72 fault (also known as a mutation) is the most common genetic cause of ALS and FTD and is present from birth in patients who carry it. By studying samples such as blood, skin, and spinal fluid from patients and relatives, we can gain an understanding of the processes that are at work in this inherited form of ALS and FTD. Samples from blood and the fluid that surrounds the brain as well as brain imaging and electrical nerve tests, can help us study the disease at a molecular level. This will help us to increase our understanding of the underlying biology that is relevant to the faulty gene and eventually help us to better monitor responses to treatments during future research studies. Eventually, all of this knowledge may contribute towards the development of new treatments for patients with ALS and FTD who have the faulty C9orf72 gene and ALS and FTD in general.

The study will also lead to the curation of a national register of C9orf72 patients, and their asymptomatic family members, for possible inclusion in future clinical trials or other academic studies (subject to your consent).

Why have I been invited to participate?

You may have been approached by the neurology team looking after the member of your family. You may have also heard about this study from your family member, or may have contacted us directly. Donating biological samples and taking part in neuroimaging studies will help us to learn more about ALS and related conditions. You will be someone related to a patient diagnosed with ALS or FTD who is known to have a familial type of ALS or FTD caused by a fault in the C9orf72 gene.

We are also recruiting *patients* with ALS or FTD. Comparing the samples from patients can help us to trace the genetic factors responsible for ALS and FTD.

We are also recruiting *healthy volunteers* who do not have any family history of ALS or FTD.

We are hoping to include a total of 1450 participants in this study.

Do I have to take part?

No. It is up to you to decide whether or not to take part. If you do take part, you will be given this information sheet to keep and you will be asked to sign a consent form. You are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of care you receive now or in the future.

We will ask you if you would be willing to be contacted about other studies in the future. You can decline to be contacted and this will not impact on your ability to participate in the current study or your legal rights or future clinical care.

What will happen to me if I decide to take part?

If you are interested in participating, a member of the study team will speak to you (in person, by video or over the telephone) about what the study involves. If you would like to take part, you will be invited to meet with a researcher by video or to travel to Oxford to participate in the study. If your family member attends the MND Clinic in Oxford, It may be possible to arrange this alongside your family member's routine clinic visit. If you are unable to travel to Oxford or undertake a video call, the study team may be able to arrange to visit you in your home to complete some of the study procedures. You will also be asked to visit your GP or local hospital to provide a blood sample.

If you provide consent to take part, we will ask you, as a minimum, to take part in the following:

- a brief health questionnaire.
- a small blood sample
  we may also ask you to complete questionnaires

We might also ask you to provide other samples as described in detail below. You can choose which sample type(s) you are happy to donate. You are free to donate whichever samples you feel comfortable providing.

We may ask if you would be willing to donate samples or undergo scans (e.g. MRI) on multiple occasions, as described in detail below. You are not obliged to give samples on more than one occasion, and giving a sample once does not mean you must continue to donate samples for this study in the future. Not everyone will be asked to take part in all aspects of the study.

You will be asked to nominate a study partner for the duration of the study who may be asked to provide additional information about your health and any symptoms relevant to the study. The study partner should be someone who knows you well, such as a spouse, partner, close friend or family member

1. Blood sample

An experienced phlebotomist or nurse will collect a small blood sample (approximately 75 ml, the equivalent of around 15 teaspoons), usually from a vein in your arm.

We may also ask your permission to take additional samples of blood at future times(up to 75 ml each time, the equivalent of around 15 teaspoons). These subsequent samples would be at approximately 12-24 monthly intervals. The samples will be used to identify not only which genes and other biological markers are expressed in blood, but more specifically those that are altered in patients as their condition changes over time. These changes will allow us to understand basic biochemical changes of the disease over time.

Blood samples may be taken at the John Radcliffe Hospital or at the Oxford Centre for Human Brain Activity (OHBA). If it is not feasible for you to travel to Oxford, we may be able to arrange for a researcher to visit you in your home and take a blood sample there.

Remote plasma monitoring:

We may also provide you with a kit to take small blood samples at home by finger prick (similar to that used for monitoring diabetes) to be sent to Oxford. This is optional, but if you choose to take part in this part of the study we will provide you with clear instructions on how to take the blood samples and send them to Oxford, and all of the equipment you need.

2. Skin sample (optional)

We may ask you if you are willing to donate a small skin sample. If you decide to take part in this part of the study, you will undergo a skin biopsy from the inner arm or outer thigh. A local anaesthetic injection will be used to numb the skin. A small piece of skin approximately 3-4 mm diameter will be taken. The biopsy may be closed with a stitch, or covered with a dressing which is left in place for 2-3 days. The procedure takes approximately 10 minutes. You will be observed for after the biopsy to make sure that any bleeding stops and then you will be able to return home.

Before deciding whether to donate a skin sample, it is important that you tell the researcher about any medication you are taking and any medical conditions you have, so that they can make sure it is safe for you to take part in this part of the study.

The skin cells will be grown and may be converted into stem cells, allowing us to carry out investigations looking at abnormal cellular functions. Stem cells are cells that can develop into any type of cell in the body if given the right chemical signals. We create induced pluripotent stem cells (iPSCs) by taking cells collected from samples of skin and treating them with chemicals to convert them into stem cells. These are therefore very different from embryonic stem cells, which are only found in a developing embryo. The iPSCs can be used to create a supply of the kinds of cells affected by specific diseases, called a cell line. We will create lines of nerve cells for use in researching ALS/FTD.

The skin cells we grow might be taken to collaborating laboratories, which may be outside the UK. This is to allow us to access the highly specialised skills available in the other laboratories to turn the skin cells into neuronal cells. Collaborators would only receive anonymised

samples; this means that they would not have any information that would be able to identify you personally.

Skin samples may be taken at the John Radcliffe Hospital or OHBA. If it is not feasible for you to travel to Oxford, we may be able to arrange for a researcher to visit you in your home and take a skin sample there.

3. Cerebrospinal fluid (CSF) (optional)

We may ask if you are willing to undergo a procedure called a lumbar puncture or LP. This is a very routine procedure in our hospital and is only ever done by highly trained staff who have done many such procedures.

A lumbar puncture involves taking a small sample of the fluid from around the lower part of the spine (CSF) with a fine needle (up to 20 ml, which is around 10-16% of the total amount, and is replaced by the body within a few hours). This procedure is done under a local anaesthetic to minimise discomfort.

This is done whilst you are sitting (or lying) comfortably on a hospital bed. We suggest that you rest lying flat for 30 minutes after the procedure. You may drive afterwards. The CSF sample is then sent for analysis. We may also ask your permission to take additional samples of CSF at future times(up to 20 ml each time). These subsequent samples would be collected every 12-24 months. .

Your sample will be used to measure several CSF components that may be altered in patients who have ALS or FTD and which may affect the function of nerve cells. The effects of the CSF on nerve cells grown in the laboratory will also be measured.

Lumbar punctures will take place at the John Radcliffe Hospital or at OHBA.

4. MRI scan (optional)

The MRI scanner is a tube about 60cm in diameter. We have two MRI scanners which differ in their magnetic field strength and each one provides different information. One scanner is at the Oxford Centre for Functional MRI of the Brain (WIN-FMRIB), and the other at the Oxford Centre for Clinical Magnetic Resonance Research (OCMR) which are buildings next door to each other. Another scanner is located at the Oxford Centre for Human Brain Activity (OHBA). Each scan is broken into different parts, each 10-30 minutes each, and in total lasts approximately 90 minutes from the time you enter the tube. MRI involves very powerful magnetic fields so we must ensure that there are no metal objects about your person, or implanted from previous surgery or accidents. After a questionnaire about possible metal implants, we will ask you to remove loose jewellery. We will provide a safe place to put any valuables, and we may ask you to change into clean pyjama-style clothes for the scan. For the scan you would lie on a cushioned bed, which would then be moved into the middle of the tube. We would help you on to the bed if mobility is difficult (including a hoist if needed), and ensure you are comfortable prior to starting. The scan is noisy (like a road drill) but we will provide earplugs and the researcher will ensure that they are fitted correctly and are comfortable. You will be able to speak to the radiographer at all times, and there is a 'panic button' you can press at any time if you want to stop the scan and be taken out. We would

remove you immediately if you felt uncomfortable in any way. We would not need to give you any injections during the scan, and MRI does not involve exposure to any ionizing radiation (e.g. X-rays). During the scan, we will measure your pulse and breathing rate non-invasively – this can improve the scan analysis later. You will mainly be asked to lie as still as possible, breathing normally, sometimes to look at a screen or to squeeze your fist gently.

The MRI scans would be carried out at the WIN (FMRIB), OCMR or the OHBA.

You may be asked to return for further MRI scans at an interval of 12-24 months.

5. MEG scan (optional)

MEG is a silent, non-invasive brain imaging technique that measures the magnetic fields .produced by nerve cells. Brain activity is measured by sitting comfortably upright under a helmet which contains sensitive detectors. MEG measurements can be affected by metal in the shielded room so you will be asked to remove any jewellery items, removable dental braces and any clothing that has metal parts or a metallic finish. If you are wearing glasses with metal parts, you will be given special non-metallic glasses to wear. Before you enter the scanner we will attach some slightly sticky electrode pads to your wrists to measure your heartbeat and around your eyes to measure eye movements. We also place small pads near the forehead and above the ears to record the position of your head in the scanner. During the measurement, it is possible to ask to stop at any time. The recording involves pressing a button on a box or squeezing your hand when asked, and other tests of memory and thinking, during which we will painlessly monitor your brain activity.

The MEG scans will take place at OHBA.

You may be asked to return for further MEG scans at an interval of 12-24 months.

6. Non-invasive neurophysiological testing (optional)

Electromyography (EMG), is a non-invasive way of measuring the electrical activity of nerves and muscles by temporarily attaching an electrode (small silver disc) to your skin. This allows us to measure the function of the motor nerves in your spinal cord and limbs. All EMG measurements in this study are recorded using electrodes on the surface of your skin and we will not insert any needles to record EMG.

We may ask you to take part in two types of EMG. In the first, several electrodes will be taped on the skin over muscles on your forearm so that we can measure electrical activity while you hold your arm steady. In the second type of EMG, brief (~0.2 milliseconds) electrical pulses are initially applied over your skin to stimulate motor nerves in the face, wrist, and leg. During the brief stimulation pulse, you will feel a tingling sensation at the face, wrist, or leg and the muscles in your eyelid, hand, or foot will twitch. We will then measure electrical activity from your muscles through attached surface electrodes on your face, hand and leg. We will ask you to briefly clench your jaw or use your hand and foot muscles at different points in the test.

You may be asked to return for further EMG scans at an interval of 12-24 months.

7. Activity Monitoring (optional)

We may ask you to wear a wrist-worn activity monitor, a small device that records body movements during normal daily activities such as standing, walking, cycling or running. It also captures inactive periods such as time spent sitting, lying down or sleeping. We will provide you with a separate information sheet and a way to send the monitor back to us if you choose to go ahead with it. We may ask you to repeat the activity monitoring every 6 months.

8. Computer Cognitive Testing (optional)

We may ask you to undertake additional tests of memory and thinking on an iPad, called "Ignite". It will take around 20-30 minutes to complete. If you come to Oxford for testing it may happen there, or we will send the iPad to you along with instructions and a way to send it back to us. We may ask you to repeat this every year.

Below is a summary of the types of tests outlined above. You may be asked to participate in all of these, or only some of these. It is your choice to decide which tests you would like to take part in.

Age	Blood	Skin	CSF	Remote plasma monitoring	MRI	MEG	EMG	Activity monitoring	iPad cognitive tests
45 years or over	Every 12 months	One sample only	Every 12 months	Every 3-12 months	Every 12 months	Every 12 months	Every 12 months	Every 6 months	Every 12 months
Under 45 years	Every 24 months		Every 24 months	Every 3-12 months	Every 24 months	Every 24 months	Every 24 months	Every 6 months	Every 12 months

No information that could identify you will be collected through the activity monitoring or Ignite application. The Ignite application was developed by University College London, meaning that data from Ignite will be collected on secure computers at University College London. The data will be transferred from University College London to secure computers at the University of Oxford where they will be linked to your research record. Activity monitoring data will be downloaded to secure computers at the University of Oxford on return of the activity monitor and linked to your research record.

What should I consider?

Before deciding whether to donate samples, it is important that you tell the researcher about any medication you are taking and any medical conditions you have, so that they can make sure it is safe for you to take part in the study.

This research project does not require any lifestyle restrictions (e.g. driving, dietary, drinking, taking part in sport). You can continue to take any regular medication, but it would be important for you to let us know what these are, and any new medications you might start during the course of the study. You can participate in this study even if you are involved in other research studies, but you should let the researchers know about any other studies in

which you are participating or planning to participate to make sure there are no conflicts.

What are the possible benefits of taking part?

There is no intended clinical benefit to you for taking part in this study. We cannot promise the study will help you but we hope that the information we obtain will eventually help to improve the diagnosis and treatment of people who carry a C9orf72 mutation.

What are the possible disadvantages and risks of taking part?

Blood samples:
There are small risks associated with needle injections. For most people, needle injections do not cause serious problems, however some people experience a small amount of swelling, bleeding or pain at the needle site or some people may feel faint. There may be minor temporary bruising at the site of removal. There is always a theoretical risk of introducing infection into the skin, blood or spinal fluid with any invasive procedure, but in practice the use of sterile single-use equipment by highly-trained staff makes this risk extremely remote. Any infection would be treated promptly with antibiotics.

Skin samples:
The biopsy itself is done following a local anaesthetic injection to numb the biopsy site. You should therefore not feel anything. Some people however may feel some mild discomfort. The biopsy site may heal with a small scar.

CSF samples:
The spinal fluid removal procedure (lumbar puncture or LP) is generally a very safe and trouble-free procedure. Although many people understandably worry beforehand that it might be very uncomfortable, this is not our usual experience, and highly-trained doctors perform this procedure routinely without any complications. LP can be briefly painful when the local anaesthetic is applied under the skin of the lower back, and occasionally as the needle is passed into the space between the bones it can cause a momentary feeling like an electric shock in your legs. In practice, when carried out by experienced staff (as it would be), there is rarely any significant discomfort for participants.

The removal of spinal fluid can however sometimes result in a temporary headache the day after the procedure. The headaches occur because of temporary low spinal fluid pressure due to leaking fluid from the needle hole, and is recognisable because it is better lying down. This complication affects 5-10% of people who have lumbar punctures to a mild extent. It is more common in those under 40 years of age. In rare cases the headache is persistent or severe enough to keep a person in bed for several days, and extremely rarely requires a second procedure to try to seal the hole preventing further fluid leak. In practice LPs are carried out on a daily basis at the John Radcliffe Hospital without complications, and all the necessary facilities and staff are available to deal with any unexpected problems.

MRI scan:
MRI is safe and non-invasive and does not involve any ionising radiation (x-rays). However, because they use a large magnet to work, MRI scans are not suitable for everybody. Because of this, you will be asked pre-screening safety questions to help determine if you are able to take part. For example, if you suffer from claustrophobia, you could not be scanned. Normally, MRI scanning for research purposes would not be performed without further investigation if you have a heart pacemaker, mechanical heart valve, mechanical implant such as an aneurysm clip, hip replacement, or if you carry other pieces of metal that have accidentally entered your body. While there is no evidence to suggest that MRI is harmful to unborn babies, as a precaution, the Department of Health advises against scanning pregnant women unless there is a clinical benefit. We do not test for pregnancy as routine so if you think you may be pregnant you should not take part in this study. As some of the scans are noisy, we would give you earplugs, head padding or headphones to make this quieter for you. It is important that these are fitted correctly as they are designed to protect your ears. In preparation for your scan and for your comfort and safety we may ask you to change into pocketless and metal free "pyjama-style" top and trousers, which are available in a range of sizes. You may keep your underwear and socks on, but you may be asked to remove any items of clothing that contain any metal. Metal jewellery, including body piercing, must also be removed. Eye shadow and mascara must also be avoided, since some types contain materials that can interact with the magnetic field. If you wish to wear eye makeup to your scan we can provide makeup removal wipes but you are advised to bring your own makeup to reapply. Lockers are provided to secure your personal belongings and clothing.

Some people scanned in MRI scanners, especially those with a stronger magnet, may experience a mild dizzy sensation as they are moved into the scanner. This is normal and the sensation starts to go away as soon as you are in the scanner.

It is important to note that we do not carry out scans for diagnostic purposes, and therefore these scans are not a substitute for a doctor's appointment. Our scans are not routinely looked at by a doctor; rather our scans are intended for research purposes only. Occasionally a possible abnormality may be detected. In this case, we would have the scan checked by a doctor. If the doctor felt that the abnormality was medically important, you would be contacted directly and recommended to have a hospital (NHS) diagnostic scan arranged. All information about you is kept strictly confidential.

MEG scan:
MEG is not like MRI and does not generate any noise or magnetic fields that might cause metallic objects to move or heat up. There are no known risks associated with MEG.

Non-invasive surface EMG:
Some EMG measurements involve stimulating the motor nerves at the face, wrist, and leg through briefly applied electrical pulses. This is very safe and used in diagnostic clinical practice. However, if you have an implantable cardioverter defibrillator (ICD) device, you will not take part in this type of EMG due to the small risk of the electrical pulses interfering with your device and triggering an irregular heart rhythm. This is not a risk if you do not have an ICD device.

Will my General Practitioner/family doctor (GP) be informed of my participation?

We will not routinely inform your GP of your participation in this study, but will ask your permission to contact your doctor if we find any results with clear implications for your current health. You will be asked to consent to this, and also to allow us to contact your GP to verify any information that you tell us about your medical history if required. If needed, we might contact your GP by secure email or telephone call to confirm eligibility if there are details that you are unable to provide.

Will my taking part in the study be kept confidential?

Yes. All the information about your participation in this study will be kept confidential. Responsible members of the University of Oxford [and the relevant NHS Trust(s)] may be given access to data for monitoring and/or audit of the study to ensure that the research is complying with applicable regulations. All will have a duty of confidentiality to you as a research participant and nothing that could reveal your identity will be disclosed outside the research site. We will ask you to consent to allow these people access to the information collected about you in the course of the study. All people looking at your records and the procedures for handling, processing, storage and destruction of your data are compliant with United Kingdom General Data Protection Regulation (UK GDPR) and the Data Protection Act 2018.

You will only be identified on your donated samples and study documentation using a unique study code that will be assigned to you. It will not be possible for anyone to be able to identify you from the samples or study database as all the data will be coded. Only the local study team at the John Radcliffe Hospital will be able to link you to the data in the study database. Any information that could identify you personally will be stored in locked offices at the local study site, under the custody of Prof Kevin Talbot and Prof Martin Turner. No information regarding the results of testing undertaken as part of this research will be fed back to individuals participating in this study.

Data collected during the course of the study may be passed on to other organisations, including commercial organisations, in pseudonymised form. This might also include anonymous quotations about your experience of taking part in this study, drawn from interactions with the research team during the course of the study visits. from participants.

All data will be stored securely by the research unit for at least 20 years after the study has been completed.

Will I be reimbursed for taking part?

Reasonable travel expenses for any visits that you make to the hospitals in Oxford in addition to visits you would normally make to attend your relative's normal appointments will be reimbursed on production of receipts, or a mileage and parking allowance provided

as appropriate. If you need to stay overnight in Oxford we can arrange modest hotel accommodation. We will aim to co-ordinate any visits with your family member's routine clinical visits if they attend the Oxford MND clinic, in which case you should not incur any extra expense as a result of your participation in this study.

There is no other payment for taking part in this study.

Will any genetic tests be done?

With your consent, genetic tests will be done on some of the samples you donate. We will analyse the samples to find out if there are some genes that are altered in people with ALS or FTD symptoms compared with people who do not have these symptoms, and to find out if some genes are altered as patients' symptoms change over time. No information about the results of any genetic testing done on your samples will be given to you. If you wish to find out your own genetic status, you will need to undergo separate genetic testing through the NHS clinical genetics service where appropriate support can be provided.

What will happen to the samples I give?

With your consent, the sample(s) that you give will be for research purposes and will be considered as a gift. Samples will be labelled with the study code, date and volunteer identifier only and it will not be possible to identify who you are from your samples alone.

The data and samples collected may be analysed by the Chief Investigator Dr Alexander Thompson and his scientific collaborators as part of this study. Your samples and data may be sent to University departments or commercial companies in the UK or abroad for analysis as part of this study. No details that could directly identify you would be sent with the data and samples. Sometimes, new methods to analyse data become available after a study has ended. Therefore we are asking for your permission to use your data in future studies, and to share data, such as your scan data, with other researchers.

With your permission, any sample remaining after the study has ended may be stored indefinitely in a Research Tissue Bank licensed by the Human Tissue Authority. You will be asked to consent for us to be able to use your stored samples for further health research. Occasionally, some of your sample may be sent for analysis to other laboratories, possibly outside the UK and EU. This could include hospitals, universities, non-profit institutions or commercial laboratories worldwide. All samples will be anonymised, which means that the person analysing your sample will not be able to identify you. If you agree to your samples being used in future research, your consent form will be held until the samples have been used up. You can still participate in this study if you do not wish your sample to be used in further health research.

What will happen to my data?

We will be using information from you and your medical records in order to undertake this study. United Kingdom Data protection regulation requires that we state the legal basis for processing information about you. Research is a task that we perform in the public interest. The University of Oxford, based in the United Kingdom as Sponsor, is the data controller. This means that we, as University of Oxford researchers, are responsible for looking after your information and using it properly. We will use the minimum personally-identifiable information possible. We will keep identifiable information about you for three years after the study has finished. We will store the research data and any research documents with personal information, such as consent forms, securely at the University of Oxford for up to 20 years after the end of the study as part of the research record.

The local study team will use your initials, date of birth, and contact details, to organise follow-up visits (if applicable) and to report any unexpected findings with clear implications for your current health (please see the section entitled "What if you found an unexpected abnormality?" below). They will keep identifiable information about you from this study for three years after the study has finished.

UK Data protection regulation provides you with control over your personal data and how it is used. When you agree to your information being used in research, however, some of those rights may be limited in order for the research to be reliable and accurate. Further information about your rights with respect to your personal data is available at https://compliance.web.ox.ac.uk/individual-rights

You can find out more about how we use your information by contacting the research team at acorn@ndcn.ox.ac.uk.

What will happen if I don't want to carry on with the study?

You can withdraw from the study at any time, without giving a reason. Your decision to withdraw will not affect your future care in any way. If you choose to withdraw from the study at any point, any data collected from you up until that time will continue to be used. Any remaining sample(s) will be destroyed if you request this, but data from any analysis that has already performed on your samples will continue to be used.

What will happen to the results of this study?

The results of this research may be presented at scientific meetings in the UK and overseas. It will not be possible to identify you from any of the data that will be presented. The data from the study may also be published in a medical journal. You will not be identified in any report or publication. The results of this study may lead to the development of patents and/or to commercial benefits for sponsors and researchers. A patent is a right to the exclusive use of an invention, such as a new test or new drug, for a fixed period of time. You would not be entitled to receive any personal or financial benefit from this.

What if you found an unexpected abnormality?

Research is still a long way from finding a simple "test for ALS or FTD". In theory however, our work might identify markers suggesting early signs of ALS or FTD in those without symptoms, or a more adverse prognosis in some of those with ALS or FTD. However, such findings would be based on the results from groups of participants, and could not be reliably interpreted for an individual. For this reason, we do not intend to discuss individual results with participants, but we will keep all participants informed about overall group-level findings, and inform the wider international scientific community.

Occasionally we do find something unexpected on the MRI scan. If so, we would discuss it with you if a consultant neurologist and a consultant neuroradiologist felt there were clear implications for your future health, and would then ask your permission to contact your GP to arrange any further tests as needed.

What if something abnormal is found in my genes?

It is not routine practice in the UK to recommend predictive testing for genetic forms of ALS/FTD. This is because there are no proven therapies to reduce the chance of developing the illness in the future. Knowing that you are very likely to develop such a serious illness later in life can be very difficult to live with. Significant uncertainty regarding the average age of onset and severity of disease further complicates our ability to predict what will happen to individuals who carry genetic changes. Nevertheless some individuals still want to be tested for example to assist family planning. Genetic counselling is mandatory prior to receiving predictive genetic results of this nature, particularly since it might have an effect on further family members.

Given the above, we propose to test your DNA for ALS-related mutations, but will not disclose the results to you. This will allow you to safely enter our study without having to find out your own genetic status. We guarantee that we will not accidentally disclose the results, since the individual with access to your genetic test results, the 'Genetic Guardian', will not have any direct contact with participants, and will keep the researchers who do have contact with you blind to your results. The Genetic Guardian works at the University of Oxford but does not have any other contact with the Oxford MND clinic or participants in our studies. We will also not disclose your genetic results to your family, General Practitioner, other doctors, or any insurance companies. Results will be held separate from your normal medical records on secure university computers that are only accessible to the Genetic Guardian.

The only circumstance in which we would 'unblind' your genetic results is if you develop symptoms of ALS or FTD in the future, and wish to know the genetic test results. This information might then be useful, but confirmation would still take place in an accredited NHS laboratory.

Entering into this study does not prevent you from changing your mind about seeking your genetic results at any stage. You will have to pursue this via the normal channels of an NHS clinical genetics service to ensure that you can benefit from genetic counselling.

Our genetic analysis will be focused on mutations that can contribute to ALS and FTD. We will not report back any information about unrelated mutations, for example those genetic changes that are linked to other medical conditions.

What if there is a problem?

If you wish to complain about any aspect of the way in which you have been approached or treated, or how your information is handled during the course of this study, you should contact Dr Alexander Thompson on 01865 228371 or by email alexander.thompson@ndcn.ox.ac.uk or you may contact the University of Oxford Research Governance, Ethics & Assurance (RGEA) office on 01865 616480, or the director of RGEA, email RGEA.Complaints@admin.ox.ac.uk

The Patient Advisory Liaison Service (PALS) is a confidential NHS service that can provide you with support for any complaints or queries you may have regarding the care you receive as an NHS patient. PALS is unable to provide information about this research study. If you wish to contact the PALS team at the John Radcliffe Hospital, please phone 01865 221473 or email PALS@ouh.nhs.uk.

The University of Oxford, as Sponsor, has appropriate insurance in place in the unlikely event that you suffer any harm as a direct consequence of your participation in this study. NHS indemnity operates in respect of the clinical treatment which is provided.

Who is organising and funding the study?

This research study is organised by the University of Oxford.

The funding for this study comes from the National Institute for Health Research – Oxford Biomedical Research Centre, and the Alan Davidson Foundation in a charitable gift to the Oxford MND Care and Research Centre.

Who has reviewed the study?

All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect participants' interests. This study has been reviewed and given favourable opinion by the London-Surrey Research Ethics Committee.

Participation in future research:

Independent from the current study, and if you consent, we may offer you the opportunity to participate in other studies. These studies will be explained separately, and you would give consent for them specifically. Agreeing to be contacted about future research does not oblige you to take part. You can decline to be contacted and this will not impact on your

ability to participate in the current study or your future clinical care. Your contact details would be held separately from the study data in a password protected database, on a computer in the Nuffield Department of Clinical Neurosciences. You have the option of removing your contact details at any time by contacting the research team.

Further information and contact details:

Please contact the ACORN team at the Oxford MND Care and Research Centre at acorn@ndcn.ox.ac.uk

Thank you for reading this information sheet and considering taking part in this study. If you decide to take part you will be given a copy of this information sheet and a PDF or paper copy of the signed consent form.