MRC National Survey of Health and Development

Neuroimaging sub-study (London)

Invitation to participate

We are inviting you to take part in a new round of health information collection. This is a clinical sub-study that will complement the regular home visits and postal questionnaires.

Before you decide if you would like to participate, it is important for you to understand why the research is being done and what it will involve. Please take whatever time you need to discuss the study with your family and friends. Your participation is voluntary.

For this clinical sub-study, the research team responsible for the MRC National Survey of Health and Development (NSHD) is collaborating with neurologists who work at the National Hospital for Neurology and Neurosurgery, and Institute of Neurology at University College London (UCL).

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What is the Neuroimaging sub-study about?

For most people health changes gradually with age, often in subtle ways that we scarcely notice. We have already studied those changes by comparing the measures of health taken throughout your early life, and in adulthood. From that we learned a lot about the processes of ageing, building on our knowledge of how factors across life influence health and function. Now we would like to measure health again, with a particular focus on memory and thinking, using a variety of measures to look at brain structure and function.

The specific aims of the Neuroimaging sub-study are firstly to identify the brain changes that accompany healthy ageing; and secondly to see if we can detect brain changes that in due course might help predict who is at risk of developing dementia, and Alzheimer's disease in particular.

We will then explore the genetic, environmental and lifestyle factors that contribute to this increased risk. We aim to be able to identify preventive measures to maintain good health and activity for as many years of later life as possible, and so to influence national health policy. We hope also to gain valuable biological information about early cognitive (memory and thinking) decline, which may in due course help determine how best to design drugs to prevent Alzheimer's disease and other forms of dementia, and how best to conduct drug trials aiming to see if these therapies are effective.

Why have I been invited to participate?

The Neuroimaging study is a clinical sub-study of the MRC National Survey of Health and Development (NSHD), the British 1946 birth cohort study. You have been invited to participate because you are a member of this cohort study who attended a clinic visit at age 60–64 and because you may have expressed an interest in taking part in additional sub-studies.

Do I have to take part?

No, your involvement is voluntary and it is up to you to decide if you would like to participate in this sub-study. If you decide not to participate this decision will not in any way affect your ability to continue to participate in the main NSHD data collections, or any other NSHD clinical sub-study. It will not affect any NHS treatment you receive if you do not take part.

What will I have to do if I take part?

Participating in the Neuroimaging sub-study will involve you making two trips to London, two years apart. We will find dates that suit you, reimburse you for any travel expenses, provide meals and refreshments, and will arrange for up to two nights' stay in a hotel for each visit. We would encourage you to bring a partner or someone who knows you well. The person accompanying you would also have all their travel and accommodation expenses reimbursed.

At each visit we would like to:

1) ask you about your health, medications and any concerns you have about memory; perform a neurological examination; and test your walking;

2) perform some tests of memory and thinking;

3) assess your sense of smell, and perform some tests of vision and hearing;

4) take blood and urine samples; and

5) perform a brain scan.

These assessments would all be performed in one day. More detail concerning what is involved with each of these investigations is provided below.

Pre-visit discussion

If you are interested in taking part, we would first give you the opportunity to discuss what is involved with a member of the research team by telephone. He or she will explain what the study involves, answer any questions you have, and will ask you some questions about your health and your medical history to ensure you are eligible to participate (e.g. make sure there is no reason why you cannot have an MRI brain scan). If, following this discussion you are eligible and willing to take part, we will arrange convenient dates for you to come to London.

The visits

On the day of your visit you will be asked to come to the Leonard Wolfson Experimental Neurology Centre which is housed within the National Hospital for Neurology and Neurosurgery, where you will meet the researchers involved in the Neuroimaging sub-study. This is a brand new facility specifically designed for studies of this kind. You will have the opportunity to discuss any questions or concerns you have about participating at that stage. If you decide to enter the Neuroimaging sub-study, you will be asked to complete and sign a research consent form. We will give you a copy of the consent form to keep. You will also be asked to nominate a family member or friend who you would like to act as your consultee in the future, should you lose the ability to provide consent.

A typical overview of the day is as follows:

Arrive at National Hospital for Neurology and Neurosurgery
Greeting and refreshments

↓

Consent and history
approximately 1 hour – this will include giving a blood and urine sample

↓ 15 minute break

Physical examination
approximately 1 hour

↓ 15 minute break

Tests of memory and thinking
approximately 1 hour

↓

Lunch
approximately 1 hour

↓

Tests of smell, hearing and vision
approximately 1 hour

↓

Transfer to PET/MRI scanning department
15 minute walk or short taxi ride

↓

Brain scan (PET/MRI)
approximately 1 hour

End of day

↓ 2 year interval

Repeat testing identical to visit 1

Clinical assessments

We will ask you to provide details of your family tree including familial history of dementia, Alzheimer's disease and Parkinson's disease and any medications you are taking. We will ask you some questions about your memory and thinking skills and, with your permission, will also ask the person accompanying you (or someone close to you who we can contact by telephone) to provide further information about your memory and thinking. With your permission, we will discuss other relevant research studies, which you may wish to consider or receive further information about, including the possibility of post-mortem brain donation. This part of the study will take no more than one hour, with suitable breaks.

With your permission, we will measure your height, weight, blood pressure, and perform a standard neurological examination, which we will video. The videos will be used for research purposes only and all original recordings will be destroyed; digitized copies will be stored on a secure server at UCL. We will ask you to take off your shoes and socks and allow us to examine your arms and legs, but you will not need to undress. We would like you to do some walking tests while wearing an accelerometer which is a small device attached to your lower back with adhesive tape. These assessments will together take no more than one hour, with suitable breaks.

Tests of memory and thinking

We will perform a variety of tests of memory and thinking. Some of these will be paper and pen assessments; others will be computer based. These assessments will take no more than one hour, with breaks if necessary.

Tests of vision, hearing and smell

Aspects of vision will be tested using a new smartphone-based application, which will measure acuity (sharpness of vision), colour vision and contrast sensitivity (ability to distinguish subtle differences between light and shade, important, for example, when driving at night). These tests are quick and easy: you will not need to take off your spectacles or remove your contact lenses (if you wear them), and there is no need for you to have eye drops put in.

Your hearing will be tested by measuring the faintest sounds you can hear. We will play you four different tones in each ear through headphones, each at different levels of loudness and softness, and each time we'll ask you to raise a finger when you hear a sound, and lower it when you can no longer hear it. In addition, we will test the ability of your brain to make sense of more complex, overlapping sounds by playing you words spoken against a background of babble (a bit like a cocktail party) and asking you to say the words you hear. This will take 25–30 minutes.

We will assess your sense of smell using a standard test which involves asking you to identifying a number of different scents. You may be asked to complete this test in your own time, and we will provide a stamped envelope if required.

These assessments together will take no more than one hour.

Donating blood, DNA and urine

With your permission, we will take a blood sample (55mls, equivalent to 4 tablespoons), and collect 20mls (2 tablespoons) of urine. Some of the blood will be sent to the laboratories for immediate measurements (including blood count, kidney function and glucose); and some of the blood and urine will be stored in the Institute of Neurology and used to try and develop new tests for detecting early dementia. The remainder of the blood will be used to extract DNA, which will be sent for decoding. This decoded information will then be safely and securely stored by the study team, and used to try and work out the genetic causes of early dementia.

What are the risks of having a blood test?

Blood taking is a routine and very safe procedure and will be performed by trained personnel. Some people can feel faint during the procedure, which will therefore be performed sitting or lying down. There is a small risk of bruising.

Any results from studies using DNA will not be documented in patient notes of any kind or be available to outside entities (e.g. insurance companies).

Brain scanning

What type of scan will I have?

At the end of the day, we will invite you to have a brain scan on a special PET/MRI scanner housed at University College Hospital. The scanner is about a 15 minute walk from the Leonard Wolfson Experimental Neurology Centre: you will either be accompanied there on foot or by taxi as required. This scanner allows PET and MRI scanning to be done at the same time. PET stands for Positron Emission Tomography. A PET scan can be used to demonstrate if certain proteins are building up in the brain. MRI stands for Magnetic Resonance Imaging and produces an electronic picture of brain structure created using a strong magnet instead of an X-ray.

Before you have a scan, the researchers will ask you some questions to make sure it is safe for you to have the MRI. Metal items may interfere with the MRI and some can be potentially hazardous. These include but are not confined to: cardiac pacemaker, aneurysm clip(s), implanted insulin/drug pump, neurostimulator (TENS unit), hearing aid/cochlear implant, surgical clip or staple(s), heart valve prosthesis, dental braces or any type of removable dental items. It is essential that you tell the study team if there is any possibility that you might have metal in your body. You will be asked to remove any dentures, hair clips, combs, earrings, and necklaces just before you enter the scanner. Women will be asked to remove an underwired bra. You can eat and drink as normal before a PET/MRI scan.

Why am I having this scan?

In this study we are using the PET scan to look at the levels of a protein (β amyloid) that occurs in the ageing brain and Alzheimer's disease. The scan will use a very small amount of radioactive substance called Florbetapir to show up the protein (β amyloid). The MRI scan allows us to assess brain structure, connections and blood flow, and to see if there have been any damage to the blood vessels.

What will happen before, during, and after the scan?

Before you enter the scanner, a small cannula (tube) will be inserted into one of the veins in your hand or arm. When you are ready to go into the scanner you will be asked to lie flat on your back on the scanner bed, which will then slide into the scanner. A small dose of Florbetapir will be injected through the cannula just as the scan starts. You will be able to press a button when you are in the scanner to tell the study team if you feel uncomfortable or want the scan to stop. You will need to lie as still as possible during the scan as this helps to ensure that the images we collect are of a good quality.

The scanner makes loud knocking noises during the scan; we will provide you with earplugs which will help to reduce the level of noise for you. The scan will take no more than one hour to complete. Before you leave

the scanning department, you will be given time to rest and ask any questions you may have about the study. The day after the scan we will telephone you to see how you are and to answer any further questions you may have. We will give you a telephone number for you to call if you have any problems or concerns and wish to speak to one of the researchers in the interim.

What are the risks of the scan?

Many hundreds of people have been imaged using Florbetapir, which has proven to be very safe. The side-effect, affecting approximately 1 in 100 people, is headache. Florbetapir was licensed for clinical use in Europe in January 2013. There have been no known harmful reactions to Florbetapir compounds. Despite this, there is still the possibility of a rare allergic reaction. Venous cannulation is a routine medical procedure that has minimal risk when performed by trained personnel. A cannula is a flexible tube containing a needle that is inserted into a vein in your hand or arm. The Florbetapir will be injected through the cannula. Some people feel lightheaded following insertion of a cannula and there is a risk of fainting. To minimize these effects, the cannula will be inserted in the vein while you are lying down. Having a cannula inserted can cause some discomfort and there is a very small risk of blood clots, bruising and infection.

Florbetapir is a radioactive substance and you will receive a radiation dose from it. The total amount of radiation that you will receive will be 7mSv, which is 3 times the normal radiation to which people living in Britain are exposed to over one year (2.5mSv), and is equivalent to driving an extra 7000 miles in a year. The additional risk of death from cancer if you were to live another 30 years is extremely low (estimated to be ~1 in 3000). As with all studies involving radioactivity, specific permission has been obtained to ensure that the levels of radiation to which you will be exposed are safe, and a nominated expert nuclear medicine doctor at the Institute of Nuclear Medicine will oversee this part of the study. We have previously performed research scans using this tracer on healthy volunteers without any complication. You may feel claustrophobic or uncomfortable lying in the PET/MRI scanner. You can ask to stop the scan at any time.

Please inform one of the researchers if you have had any research or clinical scans in the last 12 months as this may affect your eligibility to take part in the Neuroimaging sub-study.

Ending involvement in the Neuroimaging sub-study

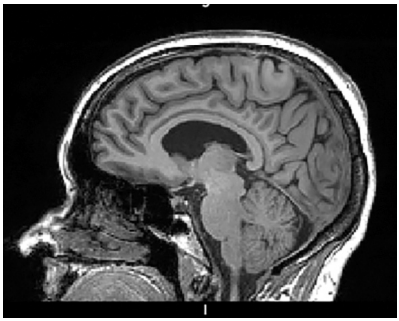
You can decide to end your involvement in this sub-study at any time. A decision to withdraw would not affect any ongoing care, or stop you from continuing with the main NSHD data collections. Information about you that has already been collected as part of your involvement in the Neuroimaging sub-study may be retained. If at any point during your participation, the Chief Investigator or the study sponsor or the director of the study determines that it is not in your best interest to continue the study, or if it is determined that no further valuable data can be obtained, they will stop your participation in the study, with no cost or consequence to you. This would be explained to you at the earliest possible opportunity.

Involvement of your General Practitioner (GP)

When you consent to participate in the Neuroimaging sub-study we will ask for your consent to inform your GP of your involvement in the study and to feed back the results of certain tests. If you are not happy for your GP to know that you are participating in this study it will not be possible for you to enter the study.

What are the possible benefits of taking part?

If during the course of the Neuroimaging sub-study we determine that you do have significantly elevated blood pressure, we will inform you and your GP. We will also inform you and your GP if any of the routine blood tests show any significant abnormalities that it would be in your interest to know about; or if the neurological examination reveals any significant abnormalities that the investigators consider it would be in your interest to know. We will not routinely provide you or your doctor with the results of the brain scans as they are for research purposes only, but will let you and your doctor know if there are any major abnormalities on the MRI scan (e.g. the presence of a tumour or a large aneurysm) which might affect your clinical care. You should be aware that being in a research study does not take the place of routine physical examinations or other appointments with your doctor, and should not be relied upon to diagnose or treat medical problems.



New Information

New information acquired during the course of the research that may affect your involvement in the Neuroimaging sub-study will be discussed with you as soon as possible after the findings become available to the study Chief Investigator.

Confidentiality and use of information

Any information collected during the Neuroimaging sub-study will be kept strictly confidential. Assessment and test results will be stored on a secure, confidential computer network on the UCL system, accessible only to members of the study team. We shall collaborate in our studies with research and clinical scientists in other centres in Britain and overseas, and they will have access only to anonymous computer-based information. Only members of the research and clinical team will have access to identifiable information. We shall keep the information for the foreseeable future in order to continue our studies of ageing. We will protect your personal information in accordance with UCLH NHS Trust Information Governance policy; the handling, processing, storage and destruction of data will be conducted in accordance with the UK Data Protection Act (1998) to ensure that confidential information is safeguarded.

Expenses and Payments

You will not receive any payment for participating in this study. However, travel and hotel costs and the costs of meals/drinks during your visit, for you and the person accompanying you, will be reimbursed. We will discuss your travel arrangements with you and either arrange or help you to arrange travel and hotel bookings for you and the person accompanying you.

What if there is a problem?

If you or your relatives have any concerns about the Neuroimaging sub-study you can speak to a member of the research team who will do their best to answer any questions. Contact details are at the end of this information booklet.

If you wish to complain, or have any concerns about any aspect of the way you have been approached or treated by members of staff you may have experienced due to your participation in the research, National Health Service or UCL complaints mechanisms are available to you. Please ask a member of the research team if you would like more information on this.

In the very unlikely event that you are harmed by taking part in this study, compensation may be available to you. If you suspect that the harm is the result of the Sponsor's (UCL) or the hospital's negligence then you may be able to claim compensation. After discussing with the research team, please make the claim in writing to Dr Jonathan Schott who is the Chief Investigator for the Neuroimaging sub-study and is based at the Institute of Neurology. The Chief Investigator will then pass the claim to the Sponsor's Insurers, via the Sponsor's office. You may have to bear the costs of the legal action initially, and you should consult a lawyer about this. NHS Indemnity does not offer no-fault compensation i.e. for non-negligent harm, and NHS bodies are unable to agree in advance to pay compensation for non-negligent harm.

What will happen to the results of the research study?

We shall, as in the past, continue to publish the results of our research in medical and research journals, and let you know each year (with the birthday card) what we have published and where. References to all the publications will continue to be available on our web site (**www.nshd.mrc.ac.uk**). No one in the study will be identifiable in any report or publication.

Who is organising and funding the research?

The Neuroimaging sub-study is being organised by researchers at the MRC National Survey for Health and Development, the Institute of Neurology and the Institute of Nuclear Medicine, UCL. It is sponsored by UCL. Funding for the study is from the Wolfson Foundation, Alzheimer's Research UK, and the Medical Research Council. AVID Radiopharmaceuticals (a subsidiary of the pharmaceutical company Eli Lilly) are supplying the Florbetapir tracer at no cost, but have had no part in the design of the study, and will have no influence over the way in which results are published.

Who has reviewed the study?

This research project has been reviewed by the London Queen Square Research Ethics Committee [14/LO/1173].

What happens next?

If you are interested in taking part, a member of the research team would like to talk to you on the phone and answer any questions you may have about the study and to discuss any medical conditions that may affect your participation. Following this discussion, and if you agree to participate, a member of staff from the research unit will contact you to arrange a mutually convenient time for your first visit and organise travel and overnight accommodation if needed.

If you have any queries about your appointment please contact:

Ms Claudia Cramer
Box 16
Institute of Neurology
London
WC1N 3BG

Telephone: 020 344 84773
Mobile: 07557 393419
Fax: 020 3448 3104

If you have any queries about the NSHD please contact:

Dr Michelle Byford or
Dr Andrew Wong
MRC National Survey of Health and Development
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33 Bedford Place
London
WC1B 5JU

Telephone: 020 7670 5700
Fax: 020 7580 1501

E-mail: **m.byford@ucl.ac.uk**
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Web: www.nshd.mrc.ac.uk

Location of the Leonard Wolfson Experimental Neurology Centre

The Leonard Wolfson Experimental Neurology Centre is located in the Albany Wing of the National Hospital for Neurology and Neurosurgery, Queen Square. The main entrance is the first left on the ground floor.

Directions to the National Hospital for Neurology and Neurosurgery, Queen Square, London, WC1N 3BG

The nearest tube station is Russell Square (Piccadilly Line). Buses 68, 168 and 188 serve the Institute. The nearest mainline train stations are Euston, King's Cross and St. Pancras International.

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