UNIVERSITY OF Southampton
School of Medicine

Southern Health NHS
NHS Foundation Trust

Memory Assessment and Research Centre
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Participant and Study Partner Information Sheet

Full Study Title:	Gaining new insight into the pathogenesis of Alzheimer's disease: investigating the role of the locus coeruleus using neuromelanin-sensitive MRI
Brief Title:	Investigating the Locus Coeruleus in Alzheimer's Disease using MRI
Sponsor:	University of Southampton

You are being invited to take part in a research study. Before deciding to participate it is important for you to understand why the research is being done and what it will involve. This information sheet has been written to tell you why this study is being done and what will be required of you if you decide to take part. It will also tell you what the potential benefits and risks of taking part are to enable you to make an informed decision about whether you would like to take part in this study.

Please take your time and read this information sheet carefully. You may discuss this study with your family, friends, GP or others involved in your care if you find it helpful in making your decision. If anything you read is not clear or you would like more information, please do not hesitate to contact a member of the research team who will be able to answer any questions you may have.

Thank you for taking the time to read this information sheet and for considering taking part.

Who is conducting the study?

This study is conducted by researchers from the Faculty of Medicine, University of Southampton. Some of the data from this study will be collected and used as part of an educational qualification. Our research team include;

Dr Ruihua Hou, Senior Research Fellow in Psychiatry
Dr Angela Darekar, the lead for MRI Physics
Professor Simon Liversedge, Professor of Experimental Psychology
Professor Clive Holmes, Professor of Biological Psychiatry
Miss Rebecca Ollington, PhD student

What is the purpose of this study?

The locus coeruleus (LC) is a tiny nucleus in the brain stem. Evidence from animal and post-mortem studies suggest that the LC is damaged in Alzheimer's disease with some arguing that it is one of the first brain areas to be damaged. Recently, a new high-resolution Magnetic Resonance Imaging (MRI) technique has been developed which allows us to see this small structure on a brain scan. This pilot study aims to test how successful this new MRI technique is at detecting signal intensity in the LC in people with Alzheimer's disease and to examine the quality of these images. It aims to see whether there are differences in the LC signal on the MRI scans between people with Alzheimer's disease and age-matched healthy control subjects.

Changes in pupil size and responses to light and other physiological measures e.g. heart rate and blood pressure, have previously been used as indirect measures of LC activity. This study will therefore also look at the link between changes in the signal intensity of the LC as shown on the MRI scan and these other biological and physiological measures.

The LC produces an important chemical called noradrenaline (NA). Current treatments for Alzheimer's disease do not affect this chemical. This study will advance our understanding of the role of the LC and NA in Alzheimer's disease which may lead to the development of new treatment targets.

Why have I been invited?

You have been invited to take part in this study because you have a diagnosis of mild cognitive impairment or mild to moderate Alzheimer's disease and have registered your interest in volunteering for research.

Do I have to take part?

Participating in this study is entirely voluntary. You do not have to participate in the study and if you decide not to take part the standard of your medical care and your legal rights will not be affected.
If you do decide to take part we will ask you to sign a consent form to confirm that you understand the study and agree to take part. You will be given a copy of this consent form for your records.

After signing the consent forms you are still free to change your mind and you may withdraw from the study at any time and you do not have to give a reason for doing so.

What will happen to me if I take part? What will I have to do?

There will be a telephone screening stage and a total of 3 visits for testing sessions that you and your study partner will need to attend.

During the screening stage, your eligibility and diagnosis will be reviewed and validated.

Visit 1 will last approximately 2-2.5 hours and will take place at the Memory Assessment & Research Centre, Moorgreen Hospital.

Study procedures at this visit include:

- discussing the study and signing the consent forms
- taking a medical history and reviewing your current medications;
- taking some physiological measures e.g. heart rate, blood pressure, respiration rate. These measures will be taken at rest, on standing, after doing mental arithmetic and after your hand has been in ice water for 90 seconds. performing an electrocardiogram (ECG) to measure the activity of your heart.
- giving a blood sample (approximately 15ml, equivalent to one tablespoon).
- performing some tests which assess your memory, thinking ability and sleep quality

Visit 2 will last approximately 1-1.5 hours and will take place at the imaging centre at Southampton General Hospital. You will undergo a MRI scan which involves lying still in a machine for up to 1 hour.

Visit 3 will last approximately 2 hours and will take place in the Psychology Department at the University of Southampton. You will be asked to complete a short reading test while your eye movement is recorded by a remote eye-tracker, in addition, your pupil size and responses will be recorded.

What is your study partner required to do during the study?

You need a study partner to participate in this study. Your study partner does not need to be related to you, but should be someone who knows you well enough and spends enough time with you to be able to answer questions about your mood, thinking ability and everyday functioning. They will also need to accompany you to all three visits.

At Visit 1 which will last approximately 2-2.5 hours and will take place at the Memory Assessment and Research centre they will:

- discuss the study with research staff and sign the consent form
- aid in providing information about your medical history and current medications
- provide information about your mood, thinking ability, sleep quality and everyday functioning

What will happen to the blood sample that I give?

A blood sample will be taken at the Memory Assessment & Research Centre. A total of 15ml (approximately 1 tablespoon) of blood will be taken. Usually all of the blood can be obtained at the same time which means you should not get an extra needle prick.

We would like to use the blood sample to investigate the blood cells that work as part of your immune system.

One of the blood samples will also be used for genetic testing. Information gathered from genetic testing may help researchers to investigate how it links to the LC signal intensity. At present, the results of genetic testing are difficult to interpret in terms of prognosis for an individual, and therefore you will not be told the results of the genetic testing. This is not an optional blood test, i.e. you will be required to have this blood test if you wish to take part in the study, and you will be asked to give consent for this to take place.

Blood samples will be analysed by the local laboratory at Southampton General Hospital. The samples will be stored in a safe location and will not be labeled with any information that would identify you directly. A participant number that is linked to your information will be used instead. Your samples will be destroyed according to the standard procedures of the laboratory as soon as possible after the study is completed and results are available to the Sponsor.

One of the samples taken will be kept for use in future research projects. This is an optional blood sample and you do not have to agree to do this in order to take part in this study. If you do give permission for this sample to be taken, the sample will be labelled with your patient identification number and will be stored for a maximum of 8 years after the end of the study. Any sample remaining at that time will be destroyed safely and securely. If you decide to

withdraw from the study for any reason, you can request that the samples you have given are destroyed safely and securely.

What are the possible disadvantages and risks of taking part?

Time and effort to attend testing sessions are the main disadvantages of taking part in this study. You will have rest periods during testing, if needed, and are free to stop any test or procedure at any time. Study staff will be fully trained to administer the neuropsychological tests and have testing experience within a clinical trials setting.

Taking blood samples:
During the study, blood will be drawn to perform a variety of tests. The risks of drawing blood include temporary discomfort from the needle in the arm, bruising, swelling at the needle site, and, in rare instances, infection.

Conduct of cognitive tasks:
The conduct of cognitive tasks could be tiring for you. You may experience nervousness, tiredness or boredom during the mental testing. Sufficient breaks will be provided between the tasks to minimise the effects of this.

Undergoing MRI scan:
The MRI scan will last up to 45 minutes. Although the procedure is not associated with any pain, it can be loud which people sometimes find discomforting. You may feel slightly claustrophobic. Both the research team at the Memory Assessment and Research Centre and the imaging staff at Southampton General Hospital will go through a checklist to ensure a health and safety procedure is followed and there are no risks involved.

What are the possible benefits of taking part?

There are no other direct expected benefits to you taking part in this study but you may feel satisfaction in knowing that your participation may help others in the future. You will be contributing to a knowledge base of the role of the locus coeruleus in the development of Alzheimer's disease and your involvement may help to develop new intervention targets to improve clinical outcomes and quality of life of patients with Alzheimer's disease in future.

Your MRI brain scan will be reviewed by a radiologist. If any pathological findings are made, i.e. if anything unusual is found, plans will be in place for you where further support or a referral is needed.

Who has reviewed the study?

The study has been reviewed by an independent Research Ethics Committee (REC Ref:

16/NW/0675). The members of the NHS Research Ethics Committee will assess all of the details of the study and every effort will be made during and after the study to ensure your safety and to ensure that the research team will respect and protect your rights, wellbeing and dignity throughout the study and after completion of the study. The NHS Research and Development team at Southern Health NHS Foundation Trust have also reviewed and approved this study.

What if there is a problem?

Southern Health NHS Foundation Trust as well as University of Southampton provides insurance in case you are injured or become ill as a result of taking part in this study.

If you think you have become hurt or sick as a direct result of taking part in the study, you should contact the research team at the Memory Assessment and Research Centre in Southampton on **02380 475206** during office hours, or the on-call member of the Southampton research team on **07773 355969** if it is out of hours.

In the unlikely event that your participation in this study results in a medical problem, your doctor will explain the treatment options available and where you can go to get information and treatment.

If you have any concerns about your participation in the study or wish to make a complaint, please contact Isla Morris, Research Integrity and Governance Manager, Research Governance Office, Corporate Services, Building 37, Highfield Campus, Southampton SO17 1BJ. Telephone: 02380 595058 email: rgoinfo@soton.ac.uk .

Further information on your rights as a research subject and on the complaints procedure can also be provided by the Complaints and Patient Advice and Liaison Services (PALS) team, 5 Sterne Road, Tatchbury Mount, Calmore, Southampton, SO40 2RZ. Telephone: 02380 874065.

Will my taking part in the study be kept confidential?

You will be given a unique study number. All information recorded that is to be included in the analysis will be anonymised and coded using this number and your initials only. Your main clinical medical records will be stored at the Memory Assessment and Research Centre (Southern Health NHS Foundation Trust). These records will be kept in a locked cabinet in a locked office within a locked unit and will be kept confidential in line with the trust's information governance and data protection policies. All blood samples stored will be identifiable only by the unique study number.

MRI scans will be acquired as part of this research trial, but not as part of the diagnostic pathway. However, the standard structural MRI scans will be reviewed and reported by a Consultant Neuroradiologist, to check for any incidental findings. If any clinically significant

findings are found, a procedure will be followed to manage this. This will involve a letter and report being sent to your GP, with the expectation that this will be followed up via the usual clinical management pathway. MRI data will be anonymised before being extracted from clinical systems for research analysis. This data will be stored securely for the duration of the study and archived in line with trust policy.

If you take part it will be necessary for qualified members of the University of Southampton, Southern Health NHS Foundation Trust, the Research Ethics Committee and applicable regulatory authorities to have access to your medical records to check that the information from the study has been recorded accurately. By signing the consent form you are giving permission for this to happen.

If the results are published all of your records will be kept confidential and your name will not be disclosed to anyone outside of the research team at MARC and the imaging site at the Southampton General Hospital.

Paper and other manual files will be archived securely and destroyed after a period of 15 years. Appropriate access controls will be in place to ensure that access to confidential research information is restricted to those who need access within the research team.

We will notify your GP about your participation in the study if you consent to this.

Early withdrawal from the study

The entire study could be discontinued at any time by the following entities: study doctors, the Ethics Committee, the University of Southampton or Southern Health NHS Foundation Trust if the safety of research participants is found to be at too much risk.

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

You may decide to stop participating in the study at any time without giving any reason. A decision to withdraw will not affect the care you receive. If you decide to withdraw, please tell the study staff. The study staff will discuss with you the best way to stop your participation in this study.

Your study doctor or the study sponsor may take you out of the study if they think it is in your best interests or if you do not follow the study instructions.

In the event of a loss of capacity, the research team would retain tissue and personal data collected and continue to use it confidentially in connection with the purposes for which consent is being sought. If you withdraw from the study the information you have already provided will be kept confidential.

What will happen to the results of the research study?

A written report detailing the results will be submitted to the regulatory authorities with the aim to publish them in a scientific journal. These publications and reports will not identify you. If you would like a copy of the results you can tell the researcher who will make them available to you at the end of the study after publication.

Expenses and payments

There will be no additional cost to you as a result of being in the study. There is no payment for taking part in this study. Any travel expenses will be reimbursed.

Who is organising or sponsoring the research study?

The research is being organised by researchers from the Faculty of Medicine, University of Southampton and conducted at the Memory Assessment and Research Centre (MARC), Tom Rudd Unit, Moorgreen Hospital.

The University of Southampton is sponsoring this study and is responsible for the proper conduct of this study.

The study is being funded by Alzheimer's Research UK.

Contact details for further information

If you would like to discuss your potential involvement in this research further please contact:

Name: **Rebecca Ollington**
Email address: rebecca.ollington@nhs.net
Telephone: 02380 475206
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Tom Rudd Unit, Moorgreen Hospital, Botley Road, Southampton, SO30 3JB