HAVEN Research Study

Investigating the relationships between HAemostatic function, VEssel health, and Neurocognitive health

Invitation to participate in a research study

This is an invitation to take part in a research study about blood vessel health and brain health in older people. Before you agree to take part, 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. Ask us if there is anything that is not clear or if there's anything else you would like to know. Take time to decide whether you want to take part, or not. You may like to discuss it with friends or relatives, or with your GP.

Aims of the study

The purpose of this study is to investigate whether the way our blood naturally clots can affect the health of the blood vessels around the body and in the brain, and how this relates to our cognitive function in older life. Previous research has shown that cardiovascular health conditions (like high blood pressure, heart disease, and diabetes) are linked to brain health and cognitive function in older adults. There is some evidence that certain regions of the brain that are involved in memory may be particularly affected. However, we do not yet know exactly how blood vessel health can affect the brain. In particular, we don't know whether overall cardiovascular health affects only the blood vessels in the brain, the brain cells, or the ability for blood vessels and brain cells to work together in a co-ordinated way. This research study will investigate these relationships. One of our goals is to see if there are substances in the blood that can help to identify and protect individuals at risk of developing brain health problems in later life.

Am I eligible to take part?

You **ARE** eligible to take part in this study if you are:

- Over 50 years of age

You are **NOT** eligible to take part in this study if you have any of the following:

- Any clinically diagnosed psychiatric or neurological condition (e.g. schizophrenia, depression, autism, etc)
- Diagnosed cardiovascular disease, diabetes, liver disease, or hypertension
- Diagnosed bleeding disorder (e.g. platelet function defects, haemophilia)

- Any metal implanted in your body
- Currently take anticoagulant or antiplatelet medication (e.g. clopidigrel, ticagrelor, warfarin, rivoroxaban)
- Suffer from claustrophobia (the brain scanner is an enclosed space)

Do I have to take part?

This is completely your decision, participation in this study is voluntary. If you choose to participate you will need to sign a consent form. After signing the consent form you are still free to withdraw from the study at any time. You will not need to give a reason why, and it will not affect your relationship with the University of Reading or any of the researchers involved in the study.

What will I have to do if I take part?

Participation in the study will require you to visit the University of Reading on two occasions, for approximately 2.5 hours each time. Information about each of the procedures in the study is provided below.

Visit 1 (approx. 2 hours 30 min)

Before your visit

On the day before your visit, please avoid doing strenuous exercise or drinking alcohol, and try to get a good night's sleep. We will give you a diet diary to complete so we know what foods you have eaten on that day. We will also ask you to eat a specific meal the evening before your visit, and will provide you with the meal. On the day of your visit, it is important you don't have anything to eat or drink (other than water) before you come in. This is because eating and drinking can affect some of the tests we need to conduct at the beginning of the visit. We will give you a meal at the end of your visit and will be able to accommodate dietary requirements.

Video study session (30 minutes)

You will watch a video of a TV programme lasting about 30 minutes. We will ask you to watch the video closely and concentrate throughout, since later you will be given a memory test involving the video. We are particularly interested in how your memory works, and the regions of your brain that are involved in memory.

Blood sample (15 minutes)

We will take a blood sample from your arm. We will take 30ml of blood (about 2 tbsp). This blood sample will be taken by someone who is trained and experienced to do so. We will use this blood sample to measure how your blood clots and your blood sugar, blood fat and haemoglobin levels.

Cognitive tasks (15 minutes)

This will be a test of your short-term memory - your ability to memorise things the researcher tells you. The researcher will give you a list of words and you will have to repeat the list from memory.

Brain scan (1 hour 30 minutes)

You will have a brain scan in an MRI scanner to measure your brain structure and function (MRI stands for magnetic resonance imaging). You will be in the scanner for approximately 1 hour, although we will allow 1 hour 30 min in total to make sure you have time to ask questions and feel comfortable.

Resting measures. You will first be asked to relax in the MRI scanner while a researcher takes resting measurements of your brain including brain structure and blood flow to different areas of your brain.

Memory test. After these measurements are complete you will be given a memory test on the video you watched earlier. You will complete this test while in the MRI scanner, and we will be able to take measurements of how your brain is functioning while you complete the test. The memory task will take about 20 minutes.

Visual test. Finally, you will be shown flashing images on a screen while in the MRI scanner. We will be able to take measurements of how your brain is functioning while you view the images. The visual test will take about 5 minutes.

Visit 2 (approx. 2h)

Before your visit

On the day before your second visit, you will need to follow the same procedures as you did for your first visit. Specifically:

- Avoid doing strenuous exercise
- Avoid drinking alcohol
- Try to get a good night's sleep
- Complete a diet diary (we will provide this)
- Eat a specific meal the night before you visit (we will provide this)

On the day of your visit, do not eat or drink anything (other than water) before you come in. We will give you a meal at the end of your visit and will be able to accommodate dietary requirements.

Blood sample (15 minutes)

We will take a blood sample from your arm. We will take 30ml of blood (about 2 tbsp). This blood sample will be taken by someone who is trained and experienced to do so. We will use this blood sample in the same way as in Visit 1, which will allow us to determine whether and how much the measurements of interest change over time.

Blood vessel function (30 minutes)

'Laser Doppler Imager' (LDI) is used to measure vascular function. Two small Perspex rings containing a small amount (~2.5 ml) of two liquids will be placed on your forearm and a very small current will be applied to allow the chemicals to pass through the skin barrier ('iontophoresis'). The chemicals stimulate the small blood vessels located under the skin to relax and increase the flow of blood. The LDI will continually monitor this response over 20 min by using a clinical laser to scan the rings on your arm. In total, LDI will take approximately 30 min per measurement. The action of the chemicals on your blood vessels is short-term and restricted to the small area of skin (approx. 10 cm) where they are applied. The procedure is pain-free; however, it is usual for some participants to experience some redness and irritation after iontophoresis but this should only last for 10 min. Throughout the LDI measurement, participants will be required to wear suitable eye protection and the researchers will ask you to remove or cover any jewellery on your measurement arm. Creams and lotions should also not be used on your arms as this can affect the measurement.

Travel (15 minutes)

The blood vessel function assessment is completed at a different building on campus to the other assessments. A researcher will accompany you to the building where you will have your brain scan (in a car if more comfortable). A researcher can also take you back at the end of the visit, should you wish.

Brain scan (1 hour)

You will have a brain scan in an MRI scanner to measure your brain structure and function (MRI stands for magnetic resonance imaging). You will be in the scanner for approximately 30 min, although we will allow 1 hour in total to make sure you have time to ask questions and feel comfortable.

Resting measures. You will first be asked to relax in the MRI scanner while a researcher takes resting measurements of your brain. This will be quicker than the resting measures at your first visit.

Brain blood vessel health. Finally, to measure your brain blood vessel health, we will test how the blood vessels in your brain respond to changes in carbon dioxide. This test will have two parts. You will need to breathe from a large bag containing slightly higher-than-normal levels of carbon dioxide (5%) for 5 minutes. You will then have to breathe faster-than-normal (30 breaths per minute) for 5 minutes, which will reduce your carbon dioxide levels to lower-than-normal.

Expenses and payment

You will receive £40 for your time and contribution to the research.

What are the benefits of taking part?

Participation of the current study will enable you to:

1. Obtain an image of your brain
2. Obtain information about your body and health
3. Experience what it is like to participate in a laboratory testing environment
4. Contribute to scientific research into body and brain health as we age
5. Contribute to the training of student researchers who are collaborating on the study

Participation in this research will have no direct health benefits for you. None of the tests or procedures in the study can be used for the purposes of diagnosing or managing illness.

What are the possible disadvantages and risks of taking part?

There are some risks associated with participating in this study. These risks are:

Common (about 25% chance)

- *Blood vessel function test - Redness or itching.* During this technique, a weak electrical current will deliver drugs to your skin blood vessels. This non-invasive technique is safe, but sometimes causes brief redness or itching which will go away within 20–30 minutes after the procedure.

Less common (less than 10% chance)

- *Blood sample – bruising.* There is a chance (about 1 in 50) that venous blood sampling may leave a bruise on your arm. The risk of this will be minimised because the researcher taking your blood will be trained and experienced.

Rare (less than 1% chance)

- *Brain scan - breathing higher-than-normal levels of carbon dioxide.* This can result in short-term and mild side effects. These include nausea, flushing, hyperventilation (breathing faster than normal), anxiety, sensory stimulation, and feelings of panic. To reduce these risks, trained staff will monitor you for these symptoms before, during, and after this test, and will stop the test if you begin to experience any of these symptoms.
- *Brain scan – claustrophobia.* The MRI scanner is a confined space, and it is possible you may suffer psychological stress, anxiety, or claustrophobia. The risk is expected to be 1 in 200 (0.5%). If you know you suffer from claustrophobia we will not complete an MRI scan on you. Whilst you are in the scanner, we will provide you with a panic button which you can press to stop the scan at any time.

There is more information about what it is like to have an MRI scan in the MRI Participant Information Sheet which you have received alongside this information.

Confidentiality and the use of my data

All information collected about you in the course of this study will be kept strictly confidential. It will not be possible to identify you from data that may be shared with the scientific community, or that may be included in any report or publication of the study.

The organisation responsible for protection of your personal information is the University of Reading (the Data Controller). Queries regarding data protection and your rights should be directed to the University Data Protection Officer at imps@reading.ac.uk, or in writing to: University of Reading, Information Management & Policy Services, Whiteknights House, Pepper Lane, Whiteknights, Reading, RG6 6UR, UK.

The University of Reading collects, analyses, uses, shares and retains personal data for the purposes of research in the public interest. Under data protection law we are required to inform you that this use of the personal data we may hold about you is on the lawful basis of being a public task in the public interest and where it is necessary for scientific or historical research purposes. If you withdraw from a research study which processes your personal data, dependent on the stage of withdrawal, we may still rely on this lawful basis to continue using your data if your withdrawal would be of significant detriment to the research study aims. We will always have in place appropriate safeguards to protect your personal data.

If we have included any additional requests for use of your data, for example adding you to a registration list for the purposes of inviting you to take part in future studies, this will be done only with your consent where you have provided it to us and should you wish to be removed from the register at a later date, you should contact Dr Gabriella Rossetti at g.m.rossetti@reading.ac.uk.

You have certain rights under data protection law which are:

- Withdraw your consent, for example if you opted in to be added to a participant register
- Access your personal data or ask for a copy
- Rectify inaccuracies in personal data that we hold about you
- Be forgotten, that is your details to be removed from systems that we use to process your personal data
- Restrict uses of your data
- Object to uses of your data, for example retention after you have withdrawn from a study

Some restrictions apply to the above rights where data is collected and used for research purposes.

You can find out more about your rights on the website of the Information Commissioners Office (ICO) at https://ico.org.uk

You also have a right to complain the ICO if you are unhappy with how your data has been handled. Please contact the University Data Protection Officer in the first instance.

Your personal data and consent form will be kept for 5 years before being destroyed.

Who has reviewed the study?

This study has been reviewed by the University of Reading University Research Ethics Committee (UREC) and given a favourable opinion for conduct.

What if new information becomes available?

If new information becomes available that might influence your decision to be in the study you will be provided with a new Participant Information Sheet to explain it, and if you still want to take part you will be asked to sign a new consent form.

Who do I contact if I have a complaint?

If you have any complaints or comments regarding the study, you can contact the study principal investigator Professor Anastasia Christakou by email: a.christakou@reading.ac.uk. Complaints or comments can be made at any stage of your participation in the study.

What if I change my mind about taking part?

If for any reason you wish to withdraw from this study, you are free to do so at any point (even during a laboratory test) without giving a reason, and no pressure will be put on you to remain in the study. If for any reason you lose the ability to consent to the research during the programme, then you would be withdrawn from the study. Identifiable data already collected with consent would be retained and used for scientific study, but no further data would be collected.

Questions?

Please ask us if you have any questions. You should not sign the form consenting to take part in the study if you still have unanswered questions or any doubts. Please feel free to contact one of the researchers below.

Dr. Gabriella Rossetti (study lead): g.m.rossetti@reading.ac.uk

Prof. Anastasia Christakou (principal investigator): a.christakou@reading.ac.uk

Thank you for considering participating in this research

Research Team

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