Brain blood vessel health: What is the influence of atrial fibrillation, high blood pressure and age?

(Cerebral vasomotor regulation in atrial fibrillation. CVR-AF)

HEALTHY VOLUNTEERS INFORMATION SHEET

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Please contact Dr. James Fisher on 0121 414 8011 or j.p.fisher@bham.ac.uk if you have any questions about this study.

You are being invited to take part in a research study at City Hospital (Sandwell and West Birmingham Hospitals NHS Trust), which is looking at how brain blood vessel health is influenced by atrial fibrillation, high blood pressure and age. This leaflet explains why the project is being done and provides details of what happens during the study. It is important that you read this if you are interested so that you understand what is involved. Do discuss it with friends, family, your general practitioner (GP) and you can, of course, contact us if you have any questions.

1. **What is the purpose of the study?**
Atrial fibrillation is one of the most common forms of an abnormal heart rhythm. Atrial fibrillation increases the risk of stroke but the reasons for this are not fully understood. Research is needed to better understand the reasons for this increased risk so strategies to reduce it can be devised effectively. Our work has recently shown that the ability of the arm blood vessels to dilate (i.e. widen) is less in atrial fibrillation patients. However, it is unknown if the blood vessels in the brains of atrial fibrillation patients are similarly altered. We will also investigate how high blood pressure and age may also affect brain blood vessel function.

2. **Why have I been chosen?**
We are inviting 3 groups of people to participate.
   A) Patients with atrial fibrillation
   B) Patients with normal heart rhythm and high blood pressure
   C) People with normal heart rhythm and normal blood pressure

You have been invited to participate because you have a normal heart rhythm and normal blood pressure (group C). The study procedures are exactly the same for each group of participants.

3. **Do I have to take part?**
It is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part 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.

4. **What will happen to me if I agree to take part?**
Participation involves one study morning where you will come to City Hospital. More details are provided below.

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The general procedure of participating is as follows:

4.1 Before consent
Once you have read this form, a research doctor and/or the Chief Investigator (Dr. James Fisher) will talk to you personally, by e-mail or by phone to make sure that all of your questions have been answered and will take great care to check that you fully understand what is involved before consent is taken. We will schedule a visit for you to come to the City Hospital, Birmingham so we discuss the study further, gain your informed consent and undertake the study.

4.2 Study day
This study will monitor your heart, blood vessels and breathing. For this we will examine you at rest, and during brief manoeuvres. The visit will take place in the morning, starting between 8 am and 10 am, and will last approximately 3 hours. The visit will be arranged for a day that is convenient for you.

In preparation for the study you will be asked to follow these restrictions prior to reporting for the Study day:

- No food intake for 12 hours (overnight) prior to the study.
- No caffeine (e.g. coffee, coke, red bull) for 12 hours before the study.
- No alcohol on the day before the study and on the morning of the study.
- No exercise after 8:00pm the evening before the study and no exercise on the morning of the study.

After you have been fully informed about the study we will ask you to give your consent to participate by signing a consent form.

The sessions consist of the following:

A. Your height and weight will be measured and you will be asked briefly about your health status (e.g., atrial fibrillation, high blood pressure).

B. **Routine blood test from your arm:** We would require approximately 40 millilitres of blood (2-3 tablespoons).

C. **Cognitive function:** You will be asked to complete four short cognitive (mental) tasks on an iPad device. These tasks are:
   i. **Motor Screening Task** (2 min): You will be asked to touch a flashing cross on screen when it is presented.
   ii. **Paired Associates Learning** (8 min): Boxes are displayed on the screen and open one by one in a randomized order to reveal patterns hidden inside. The patterns are then displayed in the middle of the screen, one at a time, and you will be asked to touch the box where the pattern was originally located. If you make a mistake, the patterns are re-presented to remind you of their locations.
   iii. **Spatial Working Memory** (5 min): The test begins with coloured boxes being shown on the screen. You will be asked to find one ‘token’ in each of the boxes and use them to fill up an empty column on the screen. The computer will never hide a token in the same coloured box, so once a token is found in a box you shouldn’t return to that box to look for another token.
   iv. **Attention Switching Task** (8 min): One at a time arrows will appear on the right or left side of the screen and you will be asked to make a right or left response.

D. **Arm blood vessel function:** The flow-mediated dilatation technique will be used to assess your arm blood vessel function. This involves the ultrasound examination (similar to scan done for pregnant women) of a large artery in the arm at rest and following compression and release of a blood pressure cuff around the forearm. A gel is used to assist with scan quality.
E. **Cardiovascular and breathing monitoring:** Your heart rate will be measured using an electrocardiogram by placing several sticky electrode patches on your chest. Your blood pressure will be monitored by a small blood pressure cuff around the end of your finger, and another around your upper arm. Breathing will be monitored with a lightweight mouthpiece covering your mouth and nose.

F. **Brain blood flow assessment:** An ultrasound examination of the large arteries supplying blood to your brain will be made using a probe placed lightly on the side of your neck with the help of a gel. After this a small ultrasound probe will be positioned on your temple and held lightly in place with the help of an adjustable headband and gel. Your brain blood flow will then be assessed during the following; a) lying quietly, b) breathing two gas mixtures with a small amount of added carbon dioxide, c) paced mild over-breathing, d) opening and closing the eyes, and e) moving from a crouching to a standing position [e.g., 5 second crouch, 5 second stand]. Rest periods will be conducted between each short manoeuvre. All manoeuvres are safe and convenient to perform.

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**Experimental protocol:** (Approximate times are shown on the right)
G. Physical activity monitoring and health questionnaires. At the end of the study visit you will be given a matchbox-sized device that can measure movement (physical activity monitor). You will be asked to wear this over the following 7 days (except during water-based activities). In the daytime the device can be fixed to a belt around the waist and at night it can be moved to a strap around the ankle. A stamped addressed envelope will be provided to enable you to return the device. You will also be given some health questionnaires to complete before you leave the laboratory. However, if you prefer these may be completed at home and returned in the envelope provided.

5. Who is excluded from taking part in this study?
For safety and scientific reasons the following exclusion criteria is used. You cannot take part if you are or have:
- Taking ‘over the counter’ or prescription medications
- Major illness (e.g., cancer, kidney or liver disease)
- Suffered a recent heart attack or stroke
- Respiratory disease such as chronic obstructive pulmonary disorders
- Neurological or inflammatory disease
- Viral illness in the last 2 weeks (e.g., flu).
- Pregnant or think you might be pregnant
- Taking hormone replacement therapy
- Intravenous drug use or alcohol intake >28 units/week
- Uncontrolled thyroid disorder
- Currently using oral nitrates
- Under 18 years of age

Please inform the chief investigator straight away if you have any of the conditions above.

6. What are the possible disadvantages and risks of taking part?
Studies are carried out by trained researchers who are experienced with all the procedures described, thus reducing possible disadvantages and risks. Potential disadvantages and risks related to the experimental measurements and procedures include:

Placement of a thin tube in a vein for blood samples: You may experience some discomfort and/or minor local bruising. Breathing carbon dioxide: There is a chance that during this test you may feel breathless or light-headed, but if this does occur symptoms rapidly reverse (in a few seconds) by breathing normal room air again. To minimise any risks all investigations are conducted in a clinical research department, where trained nursing and medical employees are based. Overnight fast: As the food you consume may affect the measurements we make you are asked to fast overnight. This may mean that you feeling hungry during the assessments. A mid-study snack (e.g., biscuit) can be offered if needed, but please note that you will be offered a more substantial hot or cold post-study meal.
7. What are the possible benefits of taking part?
There is no personal benefit to taking part. The information we will gather from all the people taking part will help us to understand how atrial fibrillation, high blood pressure and ageing influence brain blood vessel health. We hope that this will help us understand why people with atrial fibrillation are at an increased risk of stroke and help us to identify ways to reduce such problems.

8. Will my travel expenses be reimbursed?
Yes. For participating in this study we will cover the costs of your transport to the Hospital and car parking costs.

9. What if something goes wrong?
If something goes wrong during the study, we will stop immediately and a doctor will examine you and act accordingly. The City Hospital site has its own dedicated cardiovascular research department, where trained nursing and medical employees are based, whose duty it is to provide the appropriate level of care for patients. There is suitable equipment and expertise within the department in the unlikely event of an emergency situation. If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions (Dr James Fisher, 0121 414 8011, j.p.fisher@bham.ac.uk). If you wish to make a formal complaint you can do this by contacting the Patient Advice and Liaison Service team (PALS, 0121 507 5836).

10. Will my taking part in this study be kept confidential?
All information collected about you during the course of the research will be kept strictly confidential. This information will be identified according to a unique ID assigned to you when you start the study and known only to those directly involved with this project. The blood sample will be stored in a locked and protected laboratory at the Department of Cardiovascular Sciences, City Hospital. These samples will be stored using your unique ID. With your permission samples will be used in future research. With your permission, your medical notes will be accessed and your GP will be informed that you are taking part. We will also let your GP know of any problems that may be identified in the course of this study (for example a high blood pressure level that you and they did not know you had).

11. What will happen to the results of this research study?
The full results of the studies being conducted will not be known until the last participant has been tested, which may take up to 4 years. The results will be reported in professional publications and meetings but you will not be identified by name. If you are interested in receiving a summary of the results, please contact the Chief Investigator (Dr. James P. Fisher). Contact details are given at the head of this sheet.

12. Who is organising and funding the research?
This study is funded by the British Heart Foundation and is supported by Sandwell and West Birmingham Hospitals NHS Trust and the University of Birmingham.

13. Who has reviewed the study?
This study has been reviewed by the British Heart Foundation, NHS Research Ethics Committee and by local hospital Research and Development departments.

14. What if I have more questions or do not understand something?
If you have any further questions, do not hesitate to ask the investigators conducting the study (Dr James Fisher, 0121 414 8011, j.p.fisher@bham.ac.uk). If you would like to discuss participating in this study with somebody who is not directly related to the study, please contact Sister Ronnie Hayes (0121 507 6657) or the Patient Advice and Liaison Service team (PALS, 0121 507 5836).

15. What happens now if I decide to take part?
If you want to take part please contact Dr James Fisher (0121 414 8011, j.p.fisher@bham.ac.uk) to make an appointment.

This Information Sheet is yours to take home
Thank you for taking the time to consider taking part in this research