The Connection Between Increased Thrombotic Risk and Parkinson's Disease

Participant Information Sheet for Healthy Volunteers

Invitation

We would like to invite you to take part in a research study.

Before you decide if you would like to participate, take time to read the following information carefully and, if you wish, discuss it with others such as your family, friends, colleagues, doctor or nurse.

Please ask a member of the research team, whose contact details can be found at the end of this information sheet, if there is anything that is not clear or if you would like more information before you make your decision.

What is the purpose of the study?

The main purpose of this study is to investigate whether small cells in the blood called platelets are more easily activated, or "switched on", in patients with Parkinson's disease than in those without. Blood platelets are the smallest cells in your blood, and one of their main functions is to prevent you from bleeding if you become injured. You may have seen their effect if you had a cut or scrape on your skin that after a short while stopped bleeding. Although blood platelets are meant to protect you from bleeding, if they are too easily activated, they can sometimes lead to unwanted effects like blood clots.

A few research groups have shown that individuals living with Parkinson's may experience an increased risk of blood clots in their lower legs and brain. You may not have heard of this before, and to date there are quite few research articles on this topic. The studies have estimated that patients could experience nearly three times higher risk for stroke caused by blood clots in the brain in comparison to individuals without Parkinson's. Another study looked at blood clots in the legs of individuals living with Parkinson's, and they found that 20% of the individuals had a blood clot in the lower leg without symptoms. Researchers have not been able to find the exact cause to why some individuals experience an increased blood clot risk. We hypothesise that the blood platelets become activated by inflammation, something that is often increased in individuals living with Parkinson's, and that this may be one cause for the increased risk of blood clots.

This study consists of up to two visits at Aston University. In the first visit, we would like to collect a blood sample from you and compare the how easily your blood platelets become activated and form clots in comparison to those individuals with Parkinson's. Should you wish to, you can also attend a second visit where we test your reaction speed, test your memory, and look at your blood vessel health. We want to learn whether platelets that are more "switched on" can be related to the health of your brain and blood vessels.

We will also look at your DNA in the blood sample to find out if there are specific changes, also known as mutations, that might explain any differences that we may find. We will only analyse your DNA for changes in specific genes related to platelets being “switched on”, we will not sequence all your DNA or analyse it in a way that makes it possible to find out who you are.

Our results will give new understanding of how blood clots form in patients with Parkinson’s and what treatments can prevent them from happening. We will also learn about how blood clotting is related to vessel and nerve health, which can give us new knowledge on how Parkinson’s occurs and gets progressively worse. Long term, we hope that our results contribute to new potential treatments and ways to identify who might be at risk of blood clots and stroke.

Why have I been invited?

You are being invited to take part in this study because of any of the following reasons:

- You may have read about the study online or seen any of our advertisement and contacted us for further information.

- You may have approached us by e-mail or in person because you heard about the study and you want to find out more.

- You may have been approached, prior to, or when you attended a clinical appointment with a member of your family or friend.

To participate in this study you must be

- 18 years of age or over.

- willing and able to give informed consent in English.

You will **not be eligible** to take part if you:

- have been diagnosed with a bleeding disorder, particularly a platelet disorder. These include Bernard-Soulier syndrome, Glanzmann's thrombasthenia, Haemophilia, or von Willebrand disease.

- have been diagnosed with any neurodegenerative disease, diabetes, or rheumatoid arthritis, have other chronic conditions that are not under control, or have suffered a recent vascular event, meaning a blood clot (e.g. heart attack, stroke, or blood clot in the lungs) or a major bleeding where you needed to be given new blood (less than 1 year ago at time of enrolment).

- have used any non-steroid anti-inflammatory drugs (e.g. ibuprofen, naproxen, diclofenac), or blood-thinning medicines that inhibit platelets like aspirin or clopidogrel in the past 14 days before the blood sampling on the day of enrolment to the study. These drugs can interfere with our laboratory tests.

What will happen to me if I take part?

If you decide to take part in this study, you will first be asked to carefully read through this information and ask any questions you may have. You will then be invited to sign the consent form.

You will also be asked to donate a blood sample of maximum 30 ml (about two tablespoons) from a vein in your arm.

We will also collect the following data about you:

- Your age.
- Your sex at birth.
- If you had any blood clots or severe bleeding (also known as haemorrhage) before.

We expect your visit to take about 30 minutes if you decide to participate in this study. The visit would take place at Aston University. For the first visit we will invite 265 healthy volunteers.

OPTIONAL Second Visit: Should you wish, you can participate in a second study visit and this will take place at Aston University. It will be a slightly longer visit taking up to two hours.

The purpose of this visit is to find out more about your blood vessels, memory, and how fast your brain can send signals. The data from the tests in this will further help us understand how the blood's ability to form clots from the first visit can be related to the health of the blood vessels and the brain. At the start of the visit, you will have the opportunity to ask any further questions you may have, and we will seek your consent again before any tests begin.

- We will take pictures of the back of the back of your eyes (retina) using a machine. This is known as an "Optical Coherence Tomography". No eye drops are necessary for this assessment. This test takes about 10 minutes.
  Potential risks: Retina imaging is a standard clinical optometric procedure that is non-invasive and does not require any drug treatments. On occasion, an image undertaken for research purposes may show abnormal findings. If you consent, any incidental findings would be reviewed by a qualified clinician (a clinical optometrist), and if found relevant to your health, they would contact your GP to inform them. Your GP would then decide whether to speak to you and/or refer you to a hospital clinician for further investigation if appropriate.

- We will measure the blood flow in your fingers by measuring the finger temperature as we inflate and deflate a blood pressure cuff on your arm. This measurement is known as "Digital Thermal Monitoring". This test takes about 7 minutes.
  Potential risks: We will also use a blood pressure cuff on your arm, when the cuff is inflated it might give a pinching sensation to your arm and skin.

- We will use test called "Montreal Cognitive Assessment" (MOCA) to assess your attention, memory, and thinking speed. In this test a team member will ask you simple questions and ask you to draw and write with a pen on paper. This test takes about 15 minutes.
  Potential risks: The assessment will be performed at your own pace in a quiet room. You can take breaks or ask any questions when you want or need to. Some individuals may find tests stressful, if you at any point feel too stressed or uncomfortable, please notify the research team member and we will pause or stop the test.

- We will measure how quick you respond to an image whilst we record the activity of your brain with wires placed on your scalp. This is also known as an "Electroencephalogram", also known as EEG. The test involves paying attention to an image presented on a computer screen whilst pressing buttons. This test takes about 30 minutes in total, including instructions and fitting of electrodes on your skin. ***Potential risks****:* While electroencephalogram is a safe and non-invasive procedure, a little discomfort could happen when we prepare your skin for the electrodes. To get a good signal we need to gently clean your skin before we put the electrodes on. We will also put a paste on your skin for the electrodes to be able to pick up the relevant signals. Even when very rare, it is possible that some participants develop a skin reaction to the cleaning substances or conductive paste. To minimise discomfort, the cleaning of your skin will be carried out by a trained member of the research team as gently as possible. If you have a skin reaction, then we will immediately stop the procedure.

Please note that the Optional Second Visit requires access to your scalp for the EEG reading. Most individuals find they do not need to wash their hair immediately after an EEG, but in case you wish to clean yourself afterwards, we will offer shampoo, towel, and showering facilities. If you require, for any reason, a research team member of a gender that corresponds with yours, please let us know and we will accommodate this.

We will invite up to 65 of the healthy volunteers from the first visit for this part of the study. If you are interested in attending the second visit, you can leave your contact details on the consent form and we may contact you to arrange an appointment at Aston University. If you do not hear from us within 30 days after your first visit, it means that we have finished recruiting for the second visit.

Do I have to take part?

No. It is up to you to decide whether or not you wish to take part.

If you do decide to participate, you will be asked to provide informed consent.

You can halt your participation in the research at any time by telling the researcher and any data collected up to that point will not be used.

If you wish to withdraw your data after participation, you can do so by contacting the research team. If you withdraw your data after participation, you would no longer be contacted directly by the research team regarding this study. Any information or samples that were previously collected would be destroyed or securely removed. Limited information about you would be retained for audit purposes and your signed consent and withdrawal would be archived. Withdrawing your data from the study would prevent your information from contributing to future analyses, but it may not be possible to remove them from analyses that have already been performed and/or published. Although all information about you would be rendered unusable for research, it may not be possible to remove all stored data due to the requirement for computer backups. If you have not actively withdrawn from the study, then the data will continue to be used. It will not be possible to withdraw data after the end of the study, 31/10/2028, as the data will be anonymised.

If you are interested in participating in this research, you will be provided with a consent form that you will need to sign and return to the research team. You can return the consent form as a paper copy in person to the research team when you attend the visit, and you will be provided with a copy of the fully signed form.

As this study is exploratory, and the results cannot be used to guide an individual's treatments, you will not receive your individual results back from this study.

Will my taking part in this study be kept confidential?

Yes. A code will be attached to all the data you provide to maintain anonymity. Analysis of your data will be undertaken using coded data.

If we need to collect personal data (such as a name and contact details) we will only use this for the purposes outlined in this participant information sheet.

If you are interested in being invited for future research, we will retain your contact details for this purpose. We are also interested in contacting you again within 5 years' time to ask about your clinical status. You can remove your details at any time by contacting the research team.

The data we collect will be stored in a secure document store (paper records) or electronically on a secure encrypted mobile device, password protected computer server or secure cloud storage device.

To ensure the quality of the research, Aston University and the University Hospitals Birmingham NHS Foundation Trust may need to access your data to check that the data has been recorded accurately e.g. for the purposes of audit. If this is required, your personal data will be treated as confidential by the individuals accessing your data.

For the Optional Second Visit, we will ask you if you want to provide your GP address. On occasion, an image undertaken for research purposes may show abnormal findings in approximately 1 in every 100 individuals. These are called incidental findings and, in many cases, may be of little or no clinical significance. If you want to, we can contact your GP regarding any clinically relevant incidental findings in your retina. If you say yes to this option, any incidental findings will be reviewed by a qualified clinician (a clinical optometrist), and if found relevant to your health, they will contact your GP to inform them. Your GP will then decide whether to speak to you and/or refer you to a hospital clinician for further investigation if appropriate.

What are the possible benefits of taking part?

Although you may find participation in this study interesting, it is unlikely that there will be any direct benefits for your health as a result.

This study is exploratory, and it cannot guide an individual's treatment or tell us whether an individual has a higher or lower risk for getting a blood clot.

However, we hope that the findings of this study will allow us to understand if there is a relationship between the ability of the blood to form blood clots and neurodegenerative diseases such as Parkinson's.

What are the possible risks and burdens of taking part?

First visit

Donating a blood sample can feel uncomfortable. About 10% of individuals that donate a blood sample may experience a small bleeding under the skin that results in a bruise which disappears over time. A very small number of people (1 in every 1000) may also experience an infection. If you experience any persisting discomfort after your blood sample donation, please contact your general practitioner.

What will happen to the results of the study?

You will not receive your individual results back from this study.

The results of this study may be published in scientific journals and/or presented at conferences. If the results of the study are published, your identity will remain anonymous. Upon completion of the study a lay summary can be forwarded to you. Should you wish to receive a copy, please provide your contact information on the consent for or contact a member of the research team.

The anonymised data from this study will be shared with other scientists and research groups using data repositories (databases) when we publish our study results, as described in Appendix A. This means that the data from this study can be used to conduct further research. We do this so that no data will come to waste, and so that the data from this study will help as many other studies as possible.

What will happen to any samples that I provide?

The samples will be stored at Aston University using your unique identification code and used in accordance with the Human Tissue Act, which ensures appropriate management of all human materials.

With your permission any samples remaining at the end of the study will be retained in an anonymised form for future research. Any future research involving the samples will require review by a research ethics committee before it commences.

Expenses and payments

No expenses or other payments will be made.
If you attend the **OPTIONAL Second Visit**, you will receive £20 in gift vouchers as a thank-you for your time.

In some cases, it might become difficult for us to get a good EEG reading of the signal due to the volume of hair or hairstyle you have. If we are unable to get a good EEG reading, we may have to stop the measurement. Even if we stop the measurement, you will still be given the £20 in gift vouchers for your time.

Who is funding the research?

The study is being funded by the British Heart Foundation.

Who is organising this study and how is my data being used?

Aston University is organising this study and acting as data controller for the study. Research data will be used only for the purposes of the study or related uses identified in this Information Sheet or Appendix A.

Who has reviewed the study?

This study was given a favorable ethical opinion by London - Harrow Research Ethics Committee.

What if I have a concern about my participation in the study?

If you have any concerns about your participation in this study, please speak to the research team and they will do their best to answer your questions. Contact details can be found at the end of this information sheet.

If the research team are unable to address your concerns or you wish to make a complaint about how the study is being conducted you should contact the Aston University Research Integrity Office at research_governance@aston.ac.uk or via the University switchboard on +44 (0)121 204 3000.

Research Team

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Thank you for taking time to read this information sheet. If you have any questions regarding the study please don't hesitate to ask one of the research team.

How will we use information about you?

We will ask you about information about yourself for this project.

This information will include your:

- Age.
- Sex at birth.
- If you had any blood clots or severe bleedings, also known as haemorrhages, before.

People will use this information to do the research or to check your records to make sure that the research is being done properly.

People who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead.

We will keep all information about you safe and secure.

Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study.

What are your choices about how your information is used?

- You can stop being part of the study at any time, without giving a reason, we would then remove research data we stored about you. It may not be possible to remove them from analyses that have already been performed and/or published.
- We need to manage your records in specific ways for the research to be reliable. This means that we won't be able to let you see or change the data we hold about you.
- If you agree to take part in this study, we will use your data for scientific publications in peer reviewed journals. As it is a requirement from many scientific journals and research funders, the anonymised data from this study will be shared on data repositories. Data repositories are online databases for research data, like for example the Aston Data Explorer, or the Open Science Framework.

Where can you find out more about how your information is used?

You can find out more about how we use your information

- at www.hra.nhs.uk/information-about-patients/
- our webpage available at www.aston.ac.uk/dataprotection
- by asking one of the research team
- by sending an e-mail to dp_officer@aston.ac.uk, or
- by ringing us on +44 (0)121 204 3000.