DOES PERIPHERAL NEUROINFLAMMATION PREDICT CHRONICITY FOLLOWING WHIPLASH?

PARTICIPANT INFORMATION SHEET

Chief Investigator

Professor Andrew Dilley PhD

Address: Department of Neuroscience
Brighton and Sussex Medical School
Trafford Centre
University of Sussex
Falmer
Brighton BN1 9RY

Phone: 01273 877094 Email: a.dilley@bsms.ac.uk

Dear Participant

We would like to invite you to take part in our research study. Before you decide it is important that you understand why the research is being done and what it would involve for you if you took part. We ask you to have a read through this information sheet. If you have any questions and would like to discuss the study, please do not hesitate to contact the study team. Contact details can be found at the end of this information sheet.

Talk to others about the study if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

1. What is the purpose of the study?

We are interested in whether nerves in the neck and arm become inflamed following a whiplash injury. In particular, we are interested in whether inflammation of these nerves causes some patients to develop chronic pain in their neck or arms.

Following a whiplash injury to the neck, many people experience arm and neck pain. For some of these patients, the pain may become chronic, which is when the pain persists for more than three months. Such chronic pain can be difficult

to treat, which is partly because we do not fully understand what is causing the pain. It is also difficult to determine which patients will develop chronic pain, and therefore how to treat these patients appropriately. Experiments that we have performed in our laboratory suggest that the nerves in the neck and arm may be inflamed in some patients following a whiplash, and that this inflammation may be causing pain. Inflammation is the body's response to an injury.

In this study, we want to determine whether inflammation of the nerves in the neck and arm is a cause of pain soon after a whiplash injury. We also want to find out whether simple clinical tests can be used to identify patients who have nerve inflammation, and whether those patients with nerve inflammation go on to develop chronic pain. If this study is successful, we may be able to better predict which patients develop chronic pain. Our findings may also help clinicians determine the best treatment for these patients.

2. Who is organising and funding the research?

This study is a collaboration between the Brighton and Sussex Medical School and Oxford University. It is funded by the charity Versus Arthritis.

3. Why have I been invited?

You have been invited because you have recently had a whiplash injury.

We will be recruiting patients with a whiplash injury within one-month following a motor vehicle collision. Healthy volunteers will also be recruited to compare to patients.

You will not be able to take part in this study if you are under the age of 18 or over 65. You will also not be able to take part if you have a history of neck or arm pain lasting more than 3 months that required treatment, or suffer from a neurological condition (for example, a condition that affects the brain), rheumatoid arthritis, or a different autoimmune disease (such as psoriasis or lupus). Also, you cannot participate if you have had a previous diagnosis of a nerve injury or diabetes, are currently taking steroids, or you are pregnant or deemed unsuitable to have Magnetic Resonance Imaging (MRI).

4. Do I have to take part?

No, you do not have to take part; it is up to you to decide. If you do decide to take part, you will be asked to sign a consent form at the start of the first appointment. You are free to withdraw at any time without giving a reason. Taking part in this study will not affect your current treatment.

5. What will I have to do?

If you are interested in participating in this study, we would be grateful if you could contact the study team by email or phone as soon as possible. Contact details are at the end of this information sheet.

Screening call

After you have contacted the study team, a member of the team will organise a time for you to take part in a telephone screening call. During the call, we will answer any questions that you may have about the study. We will then ask you a series of questions about your whiplash injury, which will help us determine whether you fit the criteria to take part in this study. We will also ask you a few questions that will help us determine whether you are eligible for magnetic resonance imaging (MRI). The screening call will take approximately 15 minutes.

If you are suitable for the study, and you are still interested in participating, we will arrange a time for you to attend a clinical appointment at the Clinical Imaging Sciences Centre, which is at the Brighton and Sussex Medical School on the University of Sussex Campus in Falmer, or the Nuffield Department of Clinical Neurosciences at the John Radcliffe Hospital in Oxford.

We will also send you a series of questionnaires to complete to bring along to your appointment. These will be used to determine how the neck injury is affecting you and will provide us with information about the sort of pain you are experiencing, and how much distress it is causing you. If you cannot complete these questionnaires before the appointment, you will have the opportunity to complete them during the appointment, or at home after the appointment. If you prefer, we can email you an electronic version of the questionnaires to complete. The questionnaires will take approximately 45 minutes to complete.

Clinical appointment within one month following injury

During your appointment, you will be given an opportunity to discuss the study with a member of the study team. If you agree to take part, you will be asked to sign a consent form. After you have consented to take part in the study, we will ask you for the completed questionnaires or give you the opportunity to complete them.

You will then be assessed by a member of the study team. This assessment will involve the following:

Clinical examination

This will involve checking your clinical history and diagnosis, as well as performing some standard clinical tests that will look at movements in your neck and arm. Your muscle strength and reflexes will also be examined. The clinical

examination will take approximately 30 minutes.

Magnetic resonance imaging (MRI)

You will undergo a series of MRI scans to look at the nerves in your wrist and neck. You will be given a short break between each set of scans. The MRI will take approximately 1 hour.

In preparation for your scan, and for your comfort and safety, we may ask you to change into a pocketless and metal free "pyjama-style" top and trousers, which are available in a range of sizes. You may keep your underwear and socks on, but we would ask ladies to remove underwired bras. If you have a suitable sports type bra you may wear this instead. Metal jewellery, including body piercings, must be removed. Eye shadow and mascara must also be avoided. If you wish to wear eye makeup to your scan, we can provide makeup removal wipes. Lockers are provided to secure your personal belongings and clothing.

You will be asked to lie on your back in the MRI scanner and to keep as still as possible for the duration of each set of scans.

When scanning your wrist, your forearm and wrist will be positioned in a wrist coil with your arm at your side or above your head. The wrist coil is like a large bracelet. It is padded on the inside and fits firmly round your wrist, but not too tight, and should not cause any discomfort. When scanning your neck, your head will be supported comfortably by a head/neck coil, which is similar to a padded helmet.

The MRI scanner makes a variety of loud noises. You will be given ear protectors to wear to filter out the majority of this noise.

You will also be given a call button to press if at any time you wish the scan to stop.

Sensory testing

This will involve using equipment to identify the moment you can feel a temperature (warm or cold) or pressure that is applied to the skin, and when you decide that it feels painful. At this point, the sensory test is stopped. Sensory testing will take approximately 40 minutes.

Clinical tests to assess how a nerve responds to stretch and pressure

These clinical tests will involve your arm and head being moved into different positions. They also involve using slight pressure to press over parts of the limb to assess for tenderness. They will take approximately 20 minutes.

Blood test

As part of the assessment, a small blood sample (approximately 30ml) will be taken from a vein in your arm. Your blood sample will be coded with an ID number and stored in a freezer located at the Brighton and Sussex Medical School or Oxford University. Samples will be tested for chemicals that are produced during inflammation. We will also look for specific genes or molecules that may be

associated with developing chronic pain. If you have agreed, part of your blood sample will be stored for future research into chronic pain.

Taking a blood sample is standard clinical practice. However, some people may develop a small bruise, which will disappear within a few days. As some people may feel lightheaded when a small blood sample is taken, we will position you comfortably on a bed or chair. The blood test will take approximately 10 minutes.

Six months following you whiplash injury

After six months, we will contact you again. We will send you the questionnaires to complete. You may also be invited back for a second clinical appointment. During this appointment, you will have a repeat MRI scan and clinical assessment, which will include taking another small blood sample.

6. What are the possible benefits of taking part?

There will not be any direct benefits to you from taking part in this study. It is important to understand that the results from this study will not provide a diagnosis. Furthermore, we will be unable to provide feedback on your individual MRI or blood results. For these reasons, it will not be possible to use your results as part of any legal or insurance claim. If you would like feedback of the overall research findings, then once the study has been completed, this can be provided. Also, study updates will be provided on the following webpage: www.bsms.ac.uk/whiplash.

You will not receive payment for participating in this study. However, once all questionnaires have been completed, your name will be entered into a draw for one of five £100 Amazon vouchers. In addition, we will reimburse reasonable travel expenses.

7. Are there any possible disadvantages or risks of taking part?

There are no disadvantages to taking part in the study. However, the clinical appointment will take approximately three hours of your time. If you decide not to take part, your current treatment will not be affected in any way.

Magnetic Resonance Imaging (MRI) is a very safe procedure and does not involve radiation. During your initial assessment you will have been screened to ensure that you are suitable to have an MRI.

The images that will be acquired are not for diagnostic purposes and this examination should not be considered an alternative to a normal medical consultation. However, very rarely something may be found in the images and an expert opinion sought. If there are any unexpected findings that need further tests, your will be contacted through your GP or directly by a neurologist to

arrange a formal diagnostic scan. If you have any concerns about this, please contact a member of staff.

During the clinical assessment of your arm and neck, you may sometimes feel slight pain or discomfort. However, this should not last long and we will stop if you ask us to.

Having blood taken is a routine and very safe procedure. Occasionally, it may cause bruising, or you may feel lightheaded. If you feel unwell or any pain, then we will stop. We will also stop if you ask us to.

We may extract DNA from your blood to study the potential relationship between specific genes and the risk of developing chronic pain. The DNA stored by the researchers will not have information that identifies you. However, your DNA is unique to you, so it can never be completely anonymous. Sometimes the genes that we inherit increase the risk of health conditions, for instance, heart disease or rare forms of cancer. In people whose risk is known to be higher than average, there is action that can be taken to reduce the risk of these conditions developing or causing problems in the future. In doing this research, it is possible that we may by chance find genetic changes in your sample that may increase the risk that you have of developing one of these conditions. This kind of genetic change is termed an incidental finding. You can decide whether you want to be informed about such medically actionable findings. If a medically actionable finding is identified and you opted to be informed, then a clinically qualified member of the research team will arrange an appointment with you to discuss the findings.

8. What will happen to the blood samples if I give permission for their use in future research?

We will ask for your permission to keep your anonymised samples beyond this study. This will be optional. The blood samples will either continue to be stored in secure freezers within laboratories at the Brighton and Sussex Medical School and Oxford University and used by local researchers in other ethically approved projects. The samples may also be transferred to a tissue bank (e.g., Oxford Brain Bank or the Imperial College Healthcare Tissue Bank), which is a facility used to store blood samples. The blood samples will then be used in ethically approved research projects in the area of musculoskeletal, neurological and pain research, which have been approved by the biobank access committee. This research may take place in hospitals, universities, non-profit institutions or commercial laboratories worldwide. All personal information that could identify you will be removed or changed before information is shared with other researchers or results are made public.

9. What about confidentiality?

All the information about you having taken part in this study, and all information collected during the research, will be kept strictly confidential. Your name and address will be removed from the data, so that you cannot be recognised from it. All personal details will be stored securely in compliance with EU General Data Protection Regulation (GDPR) and the Data Protection Act (2018) for a maximum of 10 years, after which it will be destroyed. Study data will be given a number and will not be linked to personal details.

Some parts of the data collected for the study will be looked at by authorized radiologists that are not directly involved with the research. Individuals from the NHS Trust and regulatory authorities may also look at your medical records to check the accuracy of the study. All will have a duty of confidentiality to you as a research participant.

10. What will happen if I do not want to carry on with the study?

You are free to withdraw at any time and without giving a reason. If you decide to withdraw or not join the study, this will not affect the standard of care you receive. We will also be happy to discuss with you what will happen to any data that has been collected up to the point of your withdrawal from the study. If you withdraw from the study, unless you state otherwise, any blood samples which have been collected whilst you have been in the study will continue to be used for this research. You are free to request that your blood samples are destroyed at any time during or after the study. At the end of your study, if you have agreed, your tissue will be kept in a fully anonymised manner. At this stage, samples cannot be withdrawn anymore, as we will not be able to trace them back to you.

11. What if there is a problem?

If you have any concerns about any aspect of this study or complaints about the way you have been treated during the study or possible harm you might suffer, you should ask to speak with the researchers who will do their best to answer your questions. The researchers contact details are provided at the end of this information sheet.

If you remain unhappy and wish to complain formally, you can contact the University Research Governance Officer at the University of Sussex (Dr Antony Walsh; email: researchsponsorship@sussex.ac.uk).

12. Harm

The University of Sussex has insurance in place to cover their legal liabilities in the unlikely event harm should arise from this study.

13. What will happen to the results of the research study?

The results of the study will be written up and published in scientific journals and presented at scientific and medical conferences.

14. Who has approved this study?

This study has received ethical approval from *the Brighton and Sussex Medical School Research Governance and Ethics Committee (BSMS RGEC*) and the *National Research Ethics Committee [London - Brighton & Sussex Research Ethics Committee] for conduct in the NHS.*

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

Contact Details:

Brighton and Sussex Medical School study lead:

Professor Andrew Dilley PhD

Address: Department of Neuroscience
Brighton and Sussex Medical School
Trafford Centre
University of Sussex
Falmer
Brighton BN1 9RY

Phone: 01273 877094 Email: a.dilley@bsms.ac.uk

Oxford University site lead:

Dr Annina Schmid, PhD

Address: Nuffield Department of Clinical Neurosciences
John Radcliffe Hospital
West Wing Level 6
Oxford
OX3 9DU

Phone: 01865 223254 Email: annina.schmid@ndcn.ox.ac.uk