THE UNIVERSITY OF SYDNEY

Brain and Mind Centre
Sydney Medical School

ABN 15 211 513 464

Luke Henderson
Professor

Room 126, M02F
The University of Sydney
NSW 2006 AUSTRALIA
Telephone: +61 2 9351 7063
Email: luke.henderson@sydney.edu.au
Web: http://www.sydney.edu.au/

Chronic Migraine and the Brain

PARTICIPANT INFORMATION STATEMENT

(1) What is the study about?

You are invited to participate in a study exploring the brain mechanisms underlying chronic migraine. We hope to learn more about how the chronic migraine brain functions and what regions are responsible for precipitating and perpetuating the condition. You were selected as a possible participant in this study because you have expressed an interest in being part of our research.

(2) Who is carrying out the study?

The study is being conducted by Professor Luke Henderson, Dr Noemi Meylakh and Associate Professor Kevin Keay at the University of Sydney and Professor Vaughan Macefield at the Baker Institute Melbourne. The study commenced in March 2020 and will end in March 2024.

(3) What does the study involve?

Approximately 2.5 hours prior to the MRI session, you will be texted to stop eating and drinking with the exception of water. We will ask you to come to the Melbourne Brain Centre Imaging Unit at the University of Melbourne for one session which includes an MRI scan. We will firstly ask you to complete a number of questionnaires that will, if you are a migraine sufferer, provide us information about the quality of your migraines, the impact your migraines have on daily functioning and sleep, your psychological state and some general background and medical questions. If you are a control subject, you will be asked to complete a number of questionnaires that will provide us information about your psychological state and some general background and medical questions. You will then be asked to have an MRI scan.

This is a non-invasive, painless procedure, which involves you lying in a magnetic resonance scanner (the MRI machine). MRI equipment has been in routine clinical use for over two decades and is approved by the Australian Therapeutic Goods Administration, the European Union and the USA Food and Drug Administration for this purpose. You will lie on a motorised bed which is then moved into an open chamber which generates the magnetic field. The chamber is small. Some people find it claustrophobic. You will be screened by questionnaire for contraindications to scanning, such as presence of a pacemaker, metal shards or other metal implants. You will be required to remain still in the chamber for about 45 minutes. The scanner makes loud banging noises during this procedure, but you will be given ear-plugs to minimize disturbance.

Whilst lying on the MRI bed, a small heating device will be placed on your toe, and a fine cannula will be inserted into a right leg muscle. A brief pin-prick may be felt on insertion of the cannula but this will last only for a couple of seconds. We will carefully prepare the skin with alcohol swabs and the strictest standards of hygiene will be observed. The cannulas are disposable and sterile. The cannulas will be connected to a 1ml syringe filled with 5% hypertonic saline (sterile salty water) which produces brief pain. This technique is widely used for experimental muscle pain and is extremely safe.

During an initial MRI scanning session, the small device on the toe will be heated until you feel pain. Prior to the MRI scanning we will show you how this device works. We will heat it until it is painful so that you know what to expect both on the right cheek and the toe. We aim to elicit moderate pain levels. This pain will last for 10-20 seconds and will be repeated a number of times during the scanning session at three sites including the toe, right cheek and thumb. We can remove this thermode at any time to stop the pain if you wish. In addition, during one MRI scan, a small injection of this hypertonic saline (0.2-0.5 ml) will be made over 20 seconds into the muscle to induce brief pain. This pain will last approximately 3-5 minutes. Although we aim to make this pain of moderate intensity, in some cases the pain induced by this injection may become severe. If this occurs and you want to cease the pain experiment, we can inject a local anaesthetic which will immediately cease the pain caused by the hypertonic saline injection. At the end of the MRI scan, you will be asked to rate the pain intensity on a scale of 1-10 with zero denoting “no pain at all” and 10 representing “the worst imaginable pain”. You will also be asked to draw the pain location on a standard diagram.

The thermode temperatures used in this study are used routinely in human pain experiments and are not high enough to cause any skin damage. Furthermore, the temperature of the thermode is computer controlled and has an in-built safety mechanism. You may however, experience some redness in the lips after the MRI scanning session has finished. This will return to normal within a few hours. In addition, a small injection of sterile hypertonic saline is a standard method of muscle pain induction and has been widely used for decades without a published adverse incident. This procedure is well tolerated, with many volunteers willing to come back several times to participate in similar experiments. You may experience some discomfort in the injected muscle for a few hours after the end of the MRI session. This will disappear and will leave no adverse effects on your muscle.

Following the MRI session, you will be asked to travel to the Baker Heart and Diabetes Institute for an EEG recording and blood collection. Prior to blood collection, you will undergo a non-invasive EEG recording, where you will be fitted with a 32 channel EEG head cap, and EEG signals will be recorded continuously for 10 minutes with eyes closed. Following this, if you have ticked the box for “blood sample” on the consent form, we will then take a small blood sample so that we can assess inflammatory and genetic markers in your blood that regulate pain. The genetic marker we are testing is extremely common and has no impact on your health or that of your family and relates to how your brain processes pain.

Travelling between the University of Melbourne and the Baker and Heart Diabetes Institute can take place one of the following ways:

1. If you have driven yourself to the University of Melbourne and do not wish to leave your car or return to the University, you may drive yourself to the Baker and Heart Diabetes Institute. The researcher/s will travel separately. Alternatively, if you would like to leave your car at the University of Melbourne, transport will be organized for you to the Baker Institute and back to the University of Melbourne. The researcher will book a taxi service for you and the researcher/s will accompany you. The researcher/s will pay for the taxi using a credit card.

2. If you did not drive to the University of Melbourne, transport will be organized for you to the Baker Institute. The researcher will book a taxi service for you and the researcher/s will accompany you. The researcher/s will pay for the taxi using a credit card. Following blood collection, you will be offered the option of a paid taxi service back to the University of Melbourne accompanied by the researcher/s. If you do not wish to return to the University you will need to organize their own transportation. If this is the case, the researcher/s will ask that you wait 30 minutes and drink water to ensure they feel okay before travelling. If they have fainted post-venepuncture, the researcher/s will insist that a taxi service be called to take them home, and the researcher/s will accompany them. The researcher/s will pay for the taxi using a credit card.

Following the completion of the venepuncture session, the researcher/s will ask that you wait 30 minutes and drink water to ensure that you feel okay before either driving home or travelling unescorted via other transportation. If you are taking a taxi service back to the University of Melbourne with the researcher/s, you will not be asked to wait 30 minutes. If you have fainted post-venepuncture, the researcher/s will insist that a taxi service be called to take you home, and the researcher/s will accompany you. The researcher/s will pay for the taxi using a credit card.

This blood collection procedure is optional, therefore if you do not wish to participate in this part of the study, do not tick the box next to “blood sample” on the consent form. If you do not consent to blood collection, you will not be required to fast prior to the MRI session.

You may be asked to return for a second MRI, blood and EEG session to see if your brain changes as your migraine frequency changes.

(4) How much time will the study take?

In the interest of time, we ask that you complete the following questionnaires within the week prior to arrival to your MRI session, online via REDCap on the link provided to you via email. The paperwork will include a general clinical history including age, age of onset of migraine and when migraines moved from episodic to chronic migraine, current medication and intensity, location and frequency of migraine attacks including the dates of your migraines in the month leading up to the study. In addition, you will be asked to fill out a migraine diary describing the quality, intensity and location of your last migraine. You will be asked to complete the Migraine Disability Assessment Test (MIDAS) and Headache Impact Test (HIT-6) to assess the impact of migraines on daily functioning. You will then be asked to complete a number of questionnaires including the Becks Depression Inventory (BDI), Pain Catastrophizing Questionnaire (PCS), State/Trait anxiety questionnaires, and the Depression, Anxiety, Stress Scale (DASS). These questionnaires will be used to assess your psychological state. You will be asked to complete the Pain and Sleep Questionnaire 3 Question (PSQ-3) to assess how migraine pain has affected your sleep, and finally you will be asked to complete the Cardiff Anomalous Perceptions Scale and Conlon's Visual Discomfort Scale to assess how your migraines have affected your vision. You will have the option to complete the paperwork on arrival to your MRI session if you prefer.

Following the completion of all paperwork, you will be prepared for the MRI session. During this 15-minute preparation session, you will be shown how the thermode works including a test phase to elicit moderate pain levels. You will then have 60 minutes inside the MRI. Therefore, this part of the study will take approximately 1.5 hours.

If you have consented to participate in the blood sampling procedure, you will need to allow for approximately an extra 1.5 hours. Travel from the University to the Baker and Heart Diabetes Institute can vary between 20-40 minutes depending on time of day and traffic. The EEG will take around 20 minutes, blood taking procedure will take around 20 minutes, and then participants will be asked to stay for 30 minutes afterwards unless they are being escorted back to the University by the researcher/s. The travel back to the University is around 20-40 minutes. Therefore, this part of the study can take a varying period of time between 1-2 hours.

We will reimburse you $60 in the form of a pre-paid visa card to cover your travel expenses (not including travelling between the University of Melbourne and the Baker and Heart Diabetes Institute) and incidentals.

(5) Can I withdraw from the study?

Being in this study is completely voluntary - you are not under any obligation to consent and - if you do consent - you can withdraw at any time without affecting your relationship with The University of Sydney or Melbourne. During the MRI scanning session, you can stop the experiment at any time without prejudice.

(6) Will anyone else know the results?

All aspects of the study, including results, will be strictly confidential and only the researchers will have access to information on participants. Each subject will be assigned a code and all identifying features on each questionnaire, blood sample and brain image will be removed and replaced with this code. Only Prof Luke Henderson and Dr Noemi Meylakh will have access to this code which will be kept inside a lock cabinet in room 119 of the Brain and Mind Institute at the University of Sydney. All

questionnaires will be stored, and brain images processed on computers at the same location which is kept locked at all times. The results from the questionnaire, blood and brain image analyses will only be available to researchers directly involved in the research. Although a report of the study may be submitted for publication, individual participants will not be identifiable in such a report.

Since brain MRI is most commonly used in diagnosing neurological diseases, we may find unexpected pathology. In that event, a radiologist, who will look at all images obtained during your scanning session, will provide a report. It is standard policy to release the report to the researcher in charge of this study (Prof Luke Henderson) who would then be responsible for any follow up. If abnormalities should be found, Prof Luke Henderson would be responsible for advising you of the abnormal report and liaising with you for the submission of the report to your primary health care provider.

If any unexpected results should arise from your psychiatric testing, Prof Luke Henderson would be responsible for advising you of the abnormal scores and liaising with you for your GP's contact details. Your GP will then be notified of your scores and will get in touch with you to organize an appointment.

(7) Will the study benefit me?

We cannot and do not guarantee or promise that you will receive any benefits from the study

(8) Can I tell other people about the study?

Yes

(9) What if I require further information about the study or my involvement in it?

When you have read this information, Prof Henderson, Prof Macefield or Dr Meylakh will discuss it with you further and answer any questions you may have. If you would like to know more at any stage, please feel free to contact Prof Henderson (Phone: +61 2 9351 7063; email: luke.henderson@sydney.edu.au) or Dr Meylakh (Phone: +61 2 9351 0796; email: noemi.meylakh@sydney.edu.au).

(10) What if I have a complaint or any concerns?

Any person with concerns or complaints about the conduct of a research study can contact The Manager, Human Ethics Administration, University of Sydney on +61 2 8627 8176 (Telephone); +61 2 8627 8177 (Facsimile) or ro.humanethics@sydney.edu.au (Email).

This information sheet is for you to keep