Participant Information Sheet

Brain Signature of Pain in Knee Osteoarthritis

Lead investigator: Dr. Ramakrishnan Mani

Coordinating investigator: Jerin Mathew

Study Site: School of Physiotherapy, University of Otago, Dunedin, New Zealand

Contact phone number: 03 474 0999, ext; 58847

Ethics committee ref.: 21/CEN/63

You are invited to take part in a study investigating the brain activity patterns in people with knee osteoarthritis (KOA) pain. Whether or not you take part is your choice. If you don't want to take part, you don't have to give a reason, and it won't affect the care you receive. If you do want to take part now, but change your mind later, you can pull out of the study at any time.

This Participant Information Sheet will help you decide if you'd like to take part. It sets out why we are doing the study, what your participation would involve, what the benefits and risks to you might be, and what would happen after the study ends. We will go through this information with you and answer any questions you may have. You do not have to decide today whether or not you will participate in this study. Before you decide you may want to talk about the study with other people, such as family, whānau, friends, or healthcare providers. Feel free to do this.

If you agree to take part in this study, you will be asked to sign the Consent Form on the last page of this document. You will be given a copy of both the Participant Information Sheet and the Consent Form to keep.

This document is six pages long, including the Consent Form. Please make sure you have read and understood all the pages.

VOLUNTARY PARTICIPATION AND WITHDRAWAL FROM THIS STUDY

Taking part in the study is completely voluntary, including that you are free to decline to participate, or to withdraw from the research at any practicable time, without experiencing any disadvantage. We do not seek any reason or explanation for your withdrawal at any stage of the study.

WHAT IS THE PURPOSE OF THE STUDY?

Knee osteoarthritis (KOA) is a highly prevalent, chronic condition causing disabling symptoms, such as joint pain, physical and psychological dysfunction, and reduced quality

of life. People with KOA often experience persistent joint pain resulting in a significant impact on them, their whānau, and the wider community.
The purpose of this study is to investigate whether any changes in brain activity exists when compared to healthy individuals without pain. We are also interested in exploring whether such changes in brain activity are linked to your knee pain and functional levels. This study will bring a better understanding of the role of brain activity changes in KOA pain and help researchers design and investigate new treatment strategies to normalize brain activity to manage persistent joint pain in people with KOA.

If you have any questions about the study, you may contact Jerin Mathew at the School of Physiotherapy by email jerin.mathew@postgrad.otago.ac.nz or telephone *03 474 0999*, ext:58847.

The study has received ethical approval from the Health and Disability Ethics Committee (HDEC). Ref.:

HOW IS THE STUDY DESIGNED?

This study is intended to recruit 44 people with KOA and the same number of age and gender-matched healthy people. You will be requested to visit (once) the School of Physiotherapy, University of Otago, Dunedin campus for eligibility confirmation and assessment. The preliminary eligibility screening will be performed via an online survey or through a phone call whichever is suitable for you.

On your visit, you will be requested by the researcher to complete a set of questionnaires and undergo assessment procedures. The details of the measures and assessments are explained in the following sections.

WHO CAN TAKE PART IN THE STUDY?

Inclusion criteria: Adults aged 44 to 85, who had been diagnosed to have degenerative KOA by a doctor/physiotherapist and experiencing knee joint pain for a minimum duration of three months will be eligible to participate in the study.

Healthy individuals without pain will be invited for the study for comparison purposes.

Exclusion criteria: The participants will be excluded if they have one of the following situations/conditions.

- Inflammatory joint diseases.
- Lower limb trauma: Fractures and any soft-tissue injuries in the past 3 months or still recovering or undergoing treatments for the injury.
- Underwent knee joint replacements
- Underwent surgery or other invasive procedures for the knee in the last three months or scheduled to undergo surgery in the next 3 months.
- Undertaken any steroid injections to the knee joint in the past three months or oral steroids in the previous month.
- Any neurological disorders, including neuropathy.
- Cognitive disorders (e.g., Dementia)
- Psychiatric diseases (e.g., depression major)
- Difficulty or inability to read or understand English or provide informed consent.

- Pregnancy or six months post-labor.

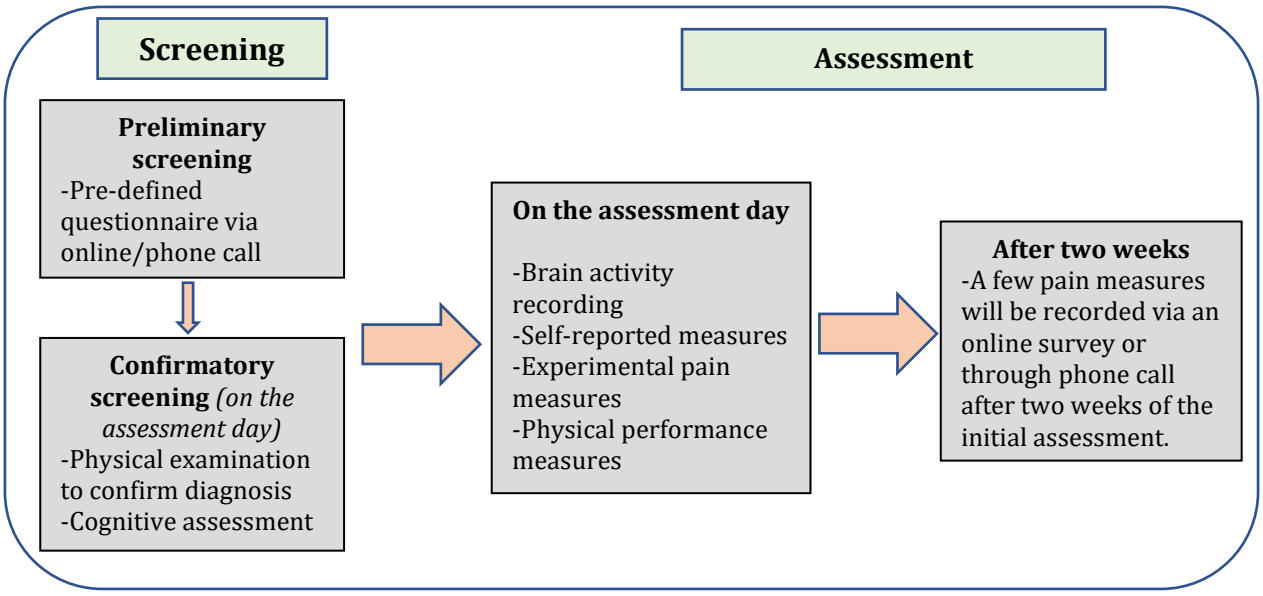
You will be instructed to abstain from alcohol for 24 hours before the assessment session and abstain from caffeinated beverages/nicotine products or heavy meals one hour before the study session. You will also be requested to avoid the use of any hair products (hair gel, hair spray, hair conditioner, etc.) on the day of the study session to achieve good brain signals.

You may continue to undergo treatments for KOA during the study period (the period from eligibility screening till the completion of assessment session). You will be prompted to report any changes in treatment, including any changes in the intake of medications during the study period.

WHAT WILL MY PARTICIPATION IN THE STUDY INVOLVE?

- The study phases are summarized in figure 1.

Figure 1; Study design and measures



Preliminary screening: The preliminary screening process will be conducted either via an online survey or through the phone based on your preference. If you do not hold a diagnosis about your KOA, this will be confirmed with physical examination on the assessment day through undergoing simple clinical assessment. Following eligibility screening, you will be invited to attend a 90-minute session at the School of Physiotherapy to undergo the assessments, as described below.

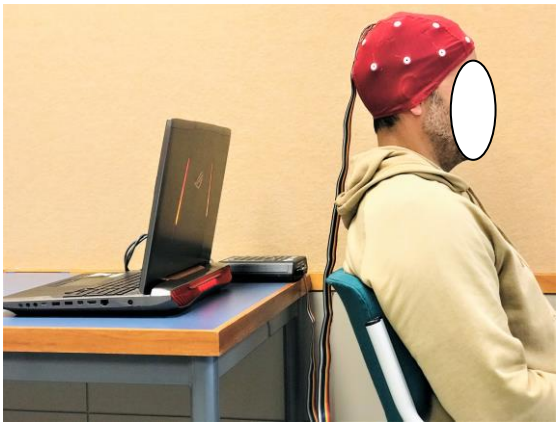
On the assessment day: Written informed consent will be obtained from you before the assessments.

Confirmatory/final screening: A member of the research team will conduct the assessments. A simple paper-based test called the Montreal Cognitive Assessment (MoCA) will be carried out for screening any cognitive problems. Volunteers scoring a total score of 26 or more will be included in the study.

Questionnaires: You will be asked to complete questionnaires about yourself (age, gender, education, ethnicity, well-being), and your pain (location, nature, intensity, function, thoughts about pain and coping strategies) about your and how much this affects your daily life, current medication history (including pain relief), sleep, psychological states, the extent of social support, and the presence of other health issues if any. Your physical activity levels

and sitting time in the past 7 days; height, weight, waist and hip circumference, leg/hand dominance will be recorded.

Brain activity recording: After completing the questionnaires, you will be asked to wear a cap with electrodes attached to it (see Picture 1), and the assessment is called electroencephalography (EEG). Electrode gel will be applied for recording better signal quality. According to Māori culture, the head is considered sacred *"he tapu te upoko"* and the brain is regarded as the *wairua* (soul). The researcher will obtain permission from you before touching your head. You will rest in a comfortable chair with your eyes closed for 10 minutes, and your brain activity will be recorded.



Picture 1. Brain wave testing setup

Testing your sensation: After recording the brain activity, the following simple test procedures will be administered over the painful knee and at a distant location (non-painful body part) for comparison purposes. **Repeated light touches** with a thin and blunted nylon filament - you will be simply asked to tell us whether you feel a sensation of touch or pain. If you feel pain on repeated touches, you will be asked to rate your intensity of pain on a 0-10-point scale, where 0=No pain and 10=Worst imaginable pain. **The pressure to pain sensation testing**: Pressure will be gradually applied by using a rubber-tipped pressure device. You will be asked to indicate immediately when the pressure sensation changes to discomfort or when you first feel pain. This procedure will be carried out over the painful knee when you are resting, as well as immediately following 2 minutes of hand immersion in a cold-water bath maintained at ~ 6 degrees Celsius. **Touch discrimination:** Repeated light touches of a blunt tip plastic caliper tool, increasing and decreasing the distance of two points - You will be asked to tell us if you feel one or two points of touch. **Vibration threshold:** Your ability to detect vibration will be tested using a tuning fork placed on the top of your shoulder. **Body part recognition task-** An iPad/tablet app will be used to record your performance accuracy on determining which side (left or right) of the image (a body part) appears on the screen. **Cold sensitivity:** Your sensitivity to cold will be tested by massaging the knee area with an ice cube, for 10 seconds.

Physical performance: You will be asked to perform simple physical tasks (e.g., repeated sit-to-stand) that either will be timed or observed to rate your performance. You will be asked to cover as much distance as you could walk in a six-minute time frame. You will also be asked to rate your knee discomfort on a 0 (no discomfort) to 10 (extreme discomfort) numeric scale, immediately before the task and once after each minute of walking. To measure your exercise capacity, you will be asked to walk as far as you can for six minutes on a level surface in the School premises.

Post-assessment: You will be contacted by the researcher after four weeks of the assessment session requesting you to complete questionnaires about your pain and function, which would take a maximum of 5 minutes to complete. This will be recorded via a brief online survey or via a phone called based on your convenience.

WHAT I CAN AND CANNOT DO DURING THE STUDY PHASES?

You are asked to bring shorts or pants that can be easily rolled up to expose your painful knee joint for sensory testing purposes.

The brain activity can be affected by various factors as listed below. Therefore, we request that you ***avoid***:

- Eating large meals for 2 hours before the session
- Drinking alcohol for 24 hours before the session
- Smoking for 4 hours before the session
- Consuming caffeinated drinks for 1 hour before the session
- Applying any hair products (oil, gel) before the session.

Take medications or undergo treatments as normal.

You will be provided with some refreshments (e.g., crackers, tea, or juice) after the assessment session.

WHAT ARE THE POSSIBLE RISKS OF THIS STUDY?

Previous studies show that brain activity recording is safe. There are no known risk or adverse events associated with brain activity recording procedure used in this study. Your brain activity is recorded using the electrode cap, which is a safe and harmless procedure. Application of electrode gel may cause inconvenience, and you are welcome to use the shower facilities at the school.

We do not anticipate any form of discomfort for pain sensation testing that would last following the test procedures. You may feel mild pain, tingling, or pins and needles sensation in your hand during or immediately following immersion in a cold-water bath. These ranges of sensations should normally disappear immediately following the testing. You will be closely monitored for your responses during sensory testing procedures, and sufficient rest periods will be provided between each testing procedure. A slight reddening of the skin may stay following the pressure to first pain testing, and it should disappear within hours of testing.

WHO PAYS FOR THE STUDY?

This study is funded by the Mark Steptoe Memorial Trust Grant-in-Aid (School of Physiotherapy, University of Otago) and student investigators research funds (internal and external).

WILL ANY COSTS BE REIMBURSED?

To recognize the actual or reasonable costs involved in participating in this project, all participants will be reimbursed $50 for completing the survey and attending the testing session.

WHAT IF SOMETHING GOES WRONG?

If you were injured in this study, you would be eligible **to apply** for compensation from ACC just as you would be if you were injured in an accident at work or at home. This does not mean that your claim will automatically be accepted. You will have to lodge a claim with ACC, which may take some time to assess. If your claim is accepted, you will receive funding to assist in your recovery.

If you have private health or life insurance, you may wish to check with your insurer that taking part in this study won't affect your cover.

WHAT ARE MY RIGHTS?

- You are a volunteer in this study and are free to withdraw from the research without experiencing disadvantage.
- You have the right to access information collected about you as part of the study.
- We will tell you if any new information becomes available during the study that may impact your health.
- You will have full rights to correct or withdraw the information until the research is completed or until we begin to analyse the data.
- We will store all the information collected about you securely, and it will only be accessed by the research team (coordinating investigator, lead investigator, and co-investigators). We will use identification numbers to store information collected from you, making data anonymous.

WHO HAS ACCESS TO MY DATA AND HOW IT IS MANAGED?

The study researchers and auditors from regulatory bodies as required by law will have access to your data. Every attempt will be made to preserve your confidentiality and anonymity. All personal data will be coded and stored either in a locked filing cabinet or electronically with password protection. It will be held by the research team at the School for Physiotherapy for a period of ten years after the completion of the study. It will then be destroyed as per the University of Otago policies. Any personal information [such as names, contact details, email address] held on the participants for practical purposes during the study period will be destroyed once the study is completed.

The data collected from this study may be used in future research to answer a different question.

The data management protocol for this study will be followed at all times in managing any collected data.

WHAT HAPPENS AFTER THE STUDY OR IF I CHANGE MY MIND?

We will write up the findings from the study in a PhD thesis, and these may be published in a scientific journal, or presented at a conference. We will not reveal any personal information about participants when we report results. Data will be presented in the statistical form, and every effort will be made to ensure anonymity.

WHO DO I CONTACT FOR MORE INFORMATION OR IF I HAVE CONCERNS?

If you have any questions, concerns or complaints about the study at any stage, you can contact:

Name: Jerin Mathew **Position**: PhD Candidate **Department:** School of Physiotherapy, University of Otago, Dunedin.	**Phone number:** 03 474 0999, ext:58847 **Email**: jerin.mathew@postgrad.otago.ac.nz
Name: Dr Ramakrishnan Mani **Position**: Senior Lecturer **Department:** School of Physiotherapy, University of Otago, Dunedin	**Phone number:** 03 479 3485 **Email**: ramakrishnan.mani@otago.ac.nz
Name: Professor Dirk De Ridder **Position**: Professor in Neurosurgery **Department:** Department of Surgical Sciences, University of Otago Dunedin.	**Phone number:** 03 470 9337 **Email**: dirk.deridder@otago.ac.nz
Name: Dr Divya Adhia **Position**: Research Fellow **Department:** Department of Surgical Sciences, University of Otago, Dunedin.	**Phone number:** 03 470 9337 **Email**: divya.adhia@otago.ac.nz

If you want to talk to someone who isn't involved with the study, you can contact an independent health and disability advocate on:

Phone : 0800 555 050
Fax : 0800 2 SUPPORT (0800 2787 7678)
Email : advocacy@advocacy.org.nz

For Māori health support please contact :

Name, position
Telephone number
Email

You can also contact the health and disability ethics committee (HDEC) that approved this study on:

Phone: 0800 4 ETHICS
Email: hdecs@moh.govt.nz

Brain Signature of Pain in Knee Osteoarthritis

Consent Form

Please tick to indicate your consent to the following

Please only include yes/no boxes if the statement is truly optional (i.e – that a person could still participate if they answer no).

I have read, or have had read to me in my first language, and I understand the Participant Information Sheet.	Yes ☐
I have been given sufficient time to consider whether or not to participate in this study.	Yes ☐
I have had the opportunity to use a legal representative, whanau/ family support or a friend to help me ask questions and understand the study.	Yes ☐
I am satisfied with the answers I have been given regarding the study and I have a copy of this consent form and information sheet.	Yes ☐
I understand that taking part in this study is voluntary (my choice) and that I may withdraw from the study at any time without this affecting my medical care.	Yes ☐
I consent to the research staff collecting and processing my information, including information about my health.	Yes ☐
If I decide to withdraw from the study, I agree that the information collected about me up to the point when I withdraw may continue to be processed.	Yes ☐
I understand that my participation in this study is confidential and that no material, which could identify me personally, will be used in any reports on this study.	Yes ☐
I understand the compensation provisions in case of injury during the study.	Yes ☐
I know whom to contact if I have any questions about the study in general.	Yes ☐
I understand my responsibilities as a study participant.	Yes ☐
I wish to receive a summary of the results of the study.	Yes ☐ No ☐
I understand data collected from me in this study may be used for future research.	Yes ☐ No ☐
I know that I will be given a voucher (a value of $50) as a reimbursement for the travel expenses associated with study participation.	Yes ☐
I am aware that auditors from HDEC and other regulatory bodies have access to both sets of data (identifiable and non-identifiable)	Yes ☐

Please specify a contact person (a friend or a relative), in case of an emergency during the study participants at the School of Physiotherapy. The contact details will be deleted from the file following the final follow-up assessment.

Name and contact phone number of a friend or relative:

Declaration by participant:

I hereby consent to take part in this study.

Participant's name:

Signature: Date:

Declaration by a member of the research team:

I have given a verbal explanation of the research project to the participant and have answered the participant's questions about it.

I believe that the participant understands the study and has given informed consent to participate.

Researcher's name: Jerin Mathew

Signature: Date: