Participant Information Sheet

Study title:	Brain Responses in Individuals with Rheumatoid arthritis pain	
Principal investigator:	**Name: Dr Ram Mani** **Department: School of Physiotherapy** **Position: Senior Lecturer**	Contact phone number: 034793485

Introduction

Thank you for showing an interest in this project. Please read this information sheet carefully. Take time to consider and, if you wish, talk with relatives or friends, before deciding whether or not to participate. If you decide to participate we thank you. If you decide not to take part there will be no disadvantage to you and we thank you for considering our request.

What is the aim of this research project?

The brain and spinal cord respond in a special way to your sore joints and other areas of the body. These responses make a significant contribution to persistent pain.

This research aims to measure how the nervous system responds to touch/pressure on painful joints or other body areas, and to identify the kinds of things that may affect how much pain you might feel.

This information would help us develop specific treatments that would help reduce and manage pain.

Who is funding this project?

This research has been funded by the University of Otago Research Grant.

Who are we seeking to participate in the project?

We are seeking 50 individuals with rheumatoid arthritis and 50 healthy individuals.

Rheumatoid arthritis: Adults (between 25-75 years old), who are currently living with rheumatoid arthritis and have persistent pain (that has lasted for more than three months) in at least one or more joints are invited to participate in the study. Persistent pain is the pain that is present almost every day, but the intensity of the pain may vary. This includes persistent pain that is reduced by treatment.

Healthy individuals: Adults (between 25-75 years old), who **do not have pain** (in the last 3 months) are invited to participate in the study.

Exclusion criteria for both groups: You are not eligible to participate if you have the following condition(s): Infective arthritis, Joint injections (steroids) in the last month, Steroid medications (>10mg) in the last month, cold-sensitive conditions (e.g. Raynauld's disease, reflex sympathetic dystrophy), underwent joint replacement or spinal or shoulder surgeries, brain injury or disease (e.g. Stroke and Multiple Sclerosis), spinal cord injury or disease, nerve injuries or neuropathies in the limbs (having sensory loss/numbness and muscle weakness), soft-tissue injuries (in the last 3 months), pregnancy or 6 months post-labour, skin conditions, difficulty or inability to read English, attention and

cognitive disorders, uncontrolled hypertension and heart failure, or history of acute myocardial infarction.

You will be screened for the above-mentioned conditions by the assistant research fellow either by phone or by email to determine your eligibility to participate in this study.

If you participate, what will you be asked to do?

You will be required to attend 2 sessions, taking a maximum of 30-45 minutes at the 1st session and 120 minutes at the 2nd session (1 week later from your first session), at the School of Physiotherapy in Dunedin. A female research fellow, with a health professional background, will administer all testing procedures.

Session-1: You will be given an activity monitor (also known as an accelerometer), which should be worn at your waist level for the next 7 days during waking hours. Accelerometers are small electronic devices (about the size of a matchbox) that records how much you move throughout the day. You will be asked to keep a daily log of how long you wear the accelerometer each day for 7 days. You will then be asked to return the activity monitor and diary when you come to 2nd session at the School of Physiotherapy. Your height, weight, waist and hip circumference, will also be recorded and you will also fill questionnaires.

Session-2:

1. Recording your brain activity: At the beginning of the session, you will have to wear a cap on your head with electrodes imbedded into it. Electrode gel will be applied for recording better signal quality. The electrodes in the cap, which is connected to computer, will record your brain activity when you are resting (for 10 minutes) with your eyes closed at the beginning of the session.

2. Testing your sensation: Following recording the brain activity, simple test procedures recording your ability to perceive a range of sensations will be administered over the painful body part and at distant locations (non-painful body part) for comparison purposes. You are asked to bring shorts, or pants or singlet (depending upon your painful body part) that are able to be easily rolled in order to expose the body region (e.g. knee joint) for testing purposes. You will be asked to lie or sit and the skin of the painful joint or body region will be exposed in order for sensation testing to be performed. Each area will first be tested to ensure that you can feel normal light touch. The following test procedures will be administered.

Repeated light touches with a thin and blunted nylon filament/tooth pick/brush - You will be simply asked to tell us whether you are feeling a sensation of touch or of pain. If you feel pain on repeated touches, you will asked to rate your intensity of pain in a 0-10 point scale.

Repeated light touches of a blunt tip plastic calliper 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.

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 body part when you are resting, as well as immediately following 2 minutes of hand immersion in cold-water bath maintained at ~ 12^{o}c.

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.

3. 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. 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.

4. Questionnaires:

Rheumatoid arthritis group: You will be asked to complete questionnaires about yourself (age, gender, education, ethnicity, well-being), and your pain (nature/intensity/coping strategies) and how much this affects your daily life, current medication history (including pain relief), sleep, fatigue levels and the presence of other health issues, if any (e.g. mood, diabetes and other diseases, if any). You will also be asked about your thoughts associated with pain. The amount of physical activity and sitting time during a typical weekday and weekend in the past 7 days, choices, confidence and readiness to take part in physical activity, social support and participation, will also be recorded.

Healthy participants: You will be asked to complete questionnaires about yourself (age, gender, education, ethnicity, and well-being). Other areas of questioning include general health, sleep, fatigue, cognition, emotions, health beliefs and perceptions, resilience and the presence of other health issues, if any (e.g. mood, diabetes and other diseases, if any). The amount of physical activity and sitting time during a typical weekday and weekend in the past 7 days, choices, confidence and readiness to take part in physical activity, social support and participation, will also be recorded.

5. Blood samples:

Rheumatoid arthritis group: A qualified professional at the Southern Community Laboratories, Dunedin, will collect a sample of your blood (5 ml) at the session-2. Blood samples will be immediately transported to the Department of Physiology, where the samples will be stored in -80ºC freezer, and further processed to derive measures of disease activity. In addition, the research fellow would gentle palpate your joints to record the presence of soreness. Together with the blood levels of inflammatory markers and number of tender/swollen joints, your RA disease severity will be determined.

Healthy participants: A qualified professional at the Southern Community Laboratories, Dunedin, will collect a sample of your blood (5 ml) at the session-2. Blood samples will be immediately transported to the Department of Physiology, where the samples will be stored in -80ºC freezer, and further processed to derive measures of inflammation. The levels of inflammatory markers will be compared against the RA group and to relate it to your sensory responses and brain activity data.

You may decide not to take part in the project without any disadvantage to yourself of any kind. Your participation is entirely voluntary.

You will be provided a petrol voucher at the end of the session (*value of $30*) for travel expenses associated with taking part in the study.

Is there any risk of discomfort or harm from participation?

We do not anticipate any form of discomfort that would last following test procedures, particularly the sensation of pain during the pressure to pain sensation testing procedure. You may feel mild pain, tingling, or pins and needles sensation in your hand during or immediately following immersion in 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 procedures. A slight reddening of skin may stay following the pressure to first pain testing, and it should disappear within hours of testing.

Your brain activity is recorded using the electrode cap, which is totally a safe and harmless procedure. Although there is no electricity is applied through electrodes and there is very little chance, that EEG will trigger a seizure. Application of electrode gel may cause inconvenience and you are offered to use the shower facilities at the School of Physiotherapy.

Your blood sample (5 ml) will be collected at session-2. We believe this procedure has very minimal risk considering the experience of the staff at the southern community laboratories collecting the blood. However, every precaution will be taken to make sure the collection procedure is aseptic and risk free.

What specimens, data or information will be collected, and how will they be used?

Your responses to a range of sensory stimulus (as described above) over the painful/non-painful body part/joint will be recorded. Your brain responses during rest will be recorded. These data will be used to measure the level of natural pain inhibitory functions. Questionnaire data will provide information about yourself, and your disease/condition (pain) including pain intensity and interference in function, current medication history (for pain relief) and the presence of other health issues, if any (e.g. stress levels, depression, anxiety, diabetes and other diseases, if any). You will also be asked about your thoughts that are associated with pain (e.g. fear of movement). Your height, weight, waist and hip circumference, and the amount of physical activity and sitting time, will be recorded to understand the relationships with pain, and sleep. The level of inflammatory markers from the blood samples will be used to measure your current disease (i.e. RA) activity.

Blood samples will be securely stored until 3 years after the publication of results, following which they will be destroyed through the Standard University disposal methods, OR; disposed with appropriate karakia (based on your choice). Following research completion, all the collected data (anonymised) will be compared against the level of inflammatory markers who do not have pain (healthy participants) and/or other types of pain (e.g. osteoarthritis).

What about anonymity and confidentiality?

Only a summary of the gathered data will be mentioned in the completed research report. Every attempt will be made to preserve your confidentiality and anonymity. On arrival to the School of Physiotherapy, University of Otago, you will be given a unique identification code, and your data will be linked to that code only. Only study personnel will have access to any personal information. All study information will be coded, and stored in secure locked filing cabinets for 10 years, then destroyed. 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. You are most welcome to request a copy of the results of the project if you wish.

If you agree to participate, can you withdraw later?

You may withdraw from participation in the project at any time and without any disadvantage to yourself of any kind. You will have full rights to correct or withdraw the information until the research is completed or until the time when we begin to analyse the data.

Any questions?

If you have any questions now or in the future, please feel free to contact either:

Dr Divya Adhia **Research Fellow** **Surgical Sciences, Dunedin School of Medicine, University of Otago, Dunedin**	Contact free phone number: 0800 295 774 Email: brainandjointpainstudy@otago.ac.nz
Dr Ram Mani **Senior Lecturer** **School of Physiotherapy, University of Otago, Dunedin**	Contact phone number: 03 479 3485

Dirk De Ridder **Professor** **Department of surgical sciences, University of Otago, Dunedin.**	Contact phone number: 03 474 0999 extension 9337
Associate Professor Rajesh Katare **Department of Physiology, University of Otago, Dunedin.**	Contact phone number: (03) 479 7292

This study has been approved by the University of Otago Human Ethics Committee (Health). If you have any concerns about the ethical conduct of the research you may contact the Committee through the Human Ethics Committee Administrator (phone +64 3 479 8256 or email gary.witte@otago.ac.nz). Any issues you raise will be treated in confidence and investigated and you will be informed of the outcome.

Brain Responses in Individuals with Rheumatoid arthritis Pain

Principal Investigator: Dr Ram Mani (ramakrishnan.mani@otago.ac.nz and 034793485)

CONSENT FORM FOR PARTICIPANTS

Following signature and return to the research team this form will be stored in a secure place for ten years.

Name of participant: ……..

1. I have read the Information Sheet concerning this study and understand the aims of this research project.
2. I have had sufficient time to talk with other people of my choice about participating in the study.
3. I confirm that I meet the criteria for participation which are explained in the Information Sheet.
4. All my questions about the project have been answered to my satisfaction, and I understand that I am free to request further information at any stage.
5. I know that my participation in the project is entirely voluntary, and that I am free to withdraw from the project at any time without disadvantage.
6. I know that as a participant I will be required to visit the School of Physiotherapy for two sessions (at the beginning and a week later) to complete the questionnaires that will measure details as listed in the information sheet. I will wear the activity monitor for a week following my visits to the School of Physiotherapy. At the completion of the study period, I will return the accelerometer to the School of Physiotherapy.
7. I know that as a participant I will be asked to respond to various sensory testing procedures, and carry out simple physical tasks. I understand that I may feel mild to moderate pain during few sensory testing procedures, which usually does not last following the procedures.
8. I understand I have to wear an electrode cap (with gel applied to record clear signals) that will be used to record my brain activity during rest with my eyes closed.
9. Five millilitres of my blood sample will be collected and analysed in the study for the measuring the inflammatory levels in your body.

10. At the end of the study, I consent to any remaining samples being disposed of using:

    ☐ Standard disposal methods, OR;

    ☐ Disposed with appropriate karakia

11. I understand the nature and size of the risks of discomfort or harm which are explained in the Information Sheet. Application of electrode gel may cause inconvenience and I am offered to use the shower facilities at the School of Physiotherapy.
12. I know that the questionnaire will explore my physical and mental well-being and that if the line of questioning develops in such a way that I feel hesitant or uncomfortable I may decline to answer any particular question(s), and/or may withdraw from the project without disadvantage of any kind.
13. I know that when the project is completed all personal identifying information will be removed from the paper records and electronic files which represent the data from the project, and that these will be placed in secure storage and kept for at least ten years.
14. I understand that the results of the project may be published and be available in the University of Otago Library, but I agree that any personal identifying information will remain confidential between myself and the researchers during the study, and will not appear in any spoken or written report of the study.
15. I know that I will be given a petrol voucher (*a value of 30$*) as a reimbursement for the travel expenses associated with study participation.
16. I know that there is no other remuneration offered for this study, and that no commercial use will be made of the data.
17. I wish to have a copy of my results at the end of the study: Yes/ No
18. Please specify a contact person (a friend or a relative), in case of an emergency during the study participation at the School of Physiotherapy. The contact details will be deleted from the file following your visit.

    Name and contact phone number of a friend or relative:

Signature of participant:	Date:

Signature of the researcher:	Date: