

## *PARTICIPANT INFORMATION SHEET*

### **Study Title: Brain Ventricular Lactate and Cortical Glutathione Levels in Fibromyalgia Syndrome.**

#### ***Investigators:***

**Dr Richard Kwiatek**, MBBS, FRACP. Consultant Rheumatologist. Palmerston, North Adelaide (Phone 8267 1767)

**Dr Samuel Whittle**, MBBS(Hons), MCLinEpi, FRACP. Senior Consultant Rheumatologist, The Queen Elizabeth Hospital (Phone 8222 6688)

**Dr Barbara True**, MD(USA), FRACP. Consultant Rheumatologist. Wakefield House, Adelaide (Phone 8232 2844)

**Mr Benjamin Crouch**, BSc(Hon). Medical Physicist. Royal Adelaide Hospital, Adelaide

#### ***Introduction:***

You have been asked to take part in the above clinical research study. This is because you are **either** a current private patient of Dr Kwiatek, Dr Whittle or Dr True and have uncomplicated fibromyalgia syndrome not on medications **or** have been suggested to be healthy, not exercise regularly and possibly interested in taking part in the above study as a healthy control (or match).

This Participant Information Sheet and Consent Form tells you about the research project. It explains the purpose of the research, procedures and risks involved. It also describes information about you that will be obtained, how that information will be used and with whom it will be shared. Knowing what is involved will help you decide if you want to take part in the research. Please read this information carefully. Ask questions about anything that you don't understand or want to know more about. Before deciding whether or not to take part, you might want to talk about it with a relative, friend or your local doctor.

Participation in this research is voluntary. If you don't wish to take part, you don't have to. You will receive the best possible care whether or not you take part. If you decide you want to take part in the research project, you will be asked to sign the Consent Form.

By signing it you are telling us that you;

- Understand what you have read
- Consent to take part in the research project
- Consent to have the tests that are described
- Consent to use of your personal and health information as described

You will be given a signed and dated copy of this Participant Information Sheet and Consent Form to keep.

### ***Purpose of the Study:***

You are invited to participate in this research study, which is being conducted to attempt to confirm and extend the results of a recent study performed in New York (Natelson BH et al. “Effect of Milnacipran Treatment on Ventricular Lactate in Fibromyalgia: A Randomized, Double-Blind, Placebo-Controlled Trial.” Journal of Pain 2015; Volume 16: Pages 1211-9).

This overseas study found that an important metabolic chemical (lactic acid) is increased in the brains of people with fibromyalgia syndrome, suggesting that altered fundamental chemical processes in the brain might be contributing to the symptoms of sufferers, with potential therapeutic implications.

For many years, research into the debilitating fibromyalgia syndrome has been hampered by a lack of objective markers of the disease, both for diagnosis and for disease severity.

Whilst several other brain-involving illnesses have been shown to have abnormal lactic acid levels (and glutathione levels, which will also be measured in this study), confirmation of similar changes in fibromyalgia syndrome will prove that the disorder is associated with pathology in the brain, although not necessarily unique to fibromyalgia.

However, preliminary work by the same New York group in the related disorder of chronic fatigue syndrome suggests that lactic acid and glutathione levels might also correlate with symptom severity in at least the chronic fatigue syndrome. The current study will attempt to more definitively confirm that this is the case in fibromyalgia syndrome, by testing for both chemicals in a larger number of people with fibromyalgia than those previously tested with chronic fatigue syndrome. It will therefore help determine if levels of lactic acid and glutathione can be used as objective markers of disease severity in fibromyalgia, independent of psychological distress.

### ***Study Procedures:***

Involvement in the study, for both fibromyalgia and healthy control subjects, will require two visits during business hours –

- (i) For all potential healthy controls, at Palmerston Surgery, 37 Barton Terrace East, North Adelaide, for up to half an hour, for a general discussion with Dr Kwiatek, a brief physical examination by Dr Kwiatek and signing of the attached Consent Form, to be arranged by ringing 8267 1767. However, prior to this appointment, potential healthy controls will be asked to fill out a simple questionnaire, either by telephone or email, to confirm their healthy status and probable suitability for the study, and therefore appropriateness of attending Palmerston Surgery to meet Dr Kwiatek.

For private fibromyalgia patients of Drs Kwiatek, Whittle and True, for up to half an hour, for a general discussion and signing of the attached Consent Form with their respective private rheumatologist, at Palmerston, The Queen Elizabeth Hospital and Wakefield House, respectively, to be arranged by ringing their respective rooms (see *Investigators*, above).

- (ii) At Clinical and Research Imaging Centre, Northern Pod, SAHMRI Building, North Terrace, Adelaide, for a 45-minute magnetic resonance imaging (including spectroscopy) scan of the brain, to be arranged by ringing 8267 1767.

At visit (i), all participants will receive a booklet of standard questionnaires, to be filled out carefully in their own time, and a stamped, addressed envelope, for posting the completed questionnaires. These questionnaires could take up to two hours to complete, especially for participants with fibromyalgia. They will be asking questions about pain, fatigue, sleep, cognition (thinking), psychological distress and general health, and, if problems exist with any of these, how they affect the participant's life.

After visit (i), but before visit (ii), arrangements will be made for you to have, at a mutually convenient time, an approximately half-hour telephone interview with Dr Barbara True. Using the Structured Clinical Interview of the Diagnostic and Statistical Manual of Mental Disorders – Version 5 (SCID-5-Clinical Version), Dr True will ask you a series of standardized screening questions to help determine if you are likely to have a significant psychological disorder which might compromise your involvement in this brain scanning study.

### ***Risks and Discomforts:***

Magnetic resonance imaging (including spectroscopy) is a safe procedure (no exposure to ionising radiation), as long as simple, routine precautions are followed, such as removal from self of all magnetic materials, including jewellery, and exclusion if neurostimulators, pacemakers, intraocular or intracranial metal are present.

However, it is generally recommended that magnetic resonance imaging be avoided in pregnancy, unless absolutely necessary, and so, if relevant, we require effective contraception be used throughout involvement in this study.

Some parts of this study's magnetic resonance imaging scan will be somewhat noisy, but noise-suppressing headphones will be supplied. Also, a distress button is provided to press if there are any problems whilst in the scanner.

Although some people can experience claustrophobia whilst in a magnetic resonance imaging scanner, that used at the Clinical and Research Imaging Centre is of wide bore, minimising this risk.

In the event of an unexpected and unrelated abnormality being detected on any magnetic resonance imaging, the results will be disclosed to the participant and also the participant's GP.

### ***Possible Benefits:***

This study aims to make a significant contribution in determining if lactate and glutathione levels in the brain can be used as an objective marker of disease severity in the controversial disorder of fibromyalgia. It also aims to provide confirmatory evidence that fibromyalgia involves objective pathological processes in the brain. As such, it will not provide treatment for individuals with fibromyalgia, but should add significantly to the already considerable international efforts to advance the scientific understanding and management of this disorder.

### ***Voluntary Participation / Right to Refuse or Withdraw:***

There is no obligation for you to be involved in this study. If you do not participate your normal treatment plan will be followed. If you decide to participate in the study and later feel that you no longer wish to be part of it, you may withdraw from the study at any time without prejudice to any current or future medical treatment.

***Confidentiality:***

Your records relating to this study and any other information received will be kept strictly confidential. However, the study's investigators and, when necessary by law, other authorised agencies, may inspect the records related to the study. In the unlikely event you are admitted to hospital as a result of an adverse event resulting from this study, your treating doctor may require access to your study records.

Your identity will not be revealed to any party other than the investigators and your confidentiality will be protected in any reviews or reports of this study which may be published. Your information will be stored and maintained in accordance with Australian Privacy Legislation.

Your general practitioner will be notified of your participation in this study and of any clinically relevant information noted by the study's doctors during its conduct.

***Costs:***

Participation in this study involves no out-of-pocket expenses. The study is being funded by its investigators, including the costs for the magnetic resonance imaging.

As this study is neither externally funded nor sponsored, there will be no payment for involvement.

***Illness or Injury:***

If, as a result of being in this study, you become ill or are injured, please immediately contact Dr Kwiatek. He will then give you all necessary information and arrange treatment.

***Compensation for Injury:***

In the unlikely event of something untoward occurring, participants of this study will be covered by the Medical Indemnity Insurance policies of the private practices of Drs Kwiatek, Whittle and True, respectively, and the Indemnity Insurance of the Clinical and Research Imaging Centre.

***Termination of the Study:***

Participants are free to withdraw from the study at any time, and can do so without explanation.

***Investigators' Benefits:***

The investigators of this study are receiving no payment from any party for their involvement.

***Results of the Study:***

Participants will be provided with abstracts (summaries) of all presentations (at scientific conferences or in scientific journals) of the study's results and, upon request, explanation of these in lay terms will

be given by the study's Principal Investigator, Dr Kwiatek. Provision of individual results can be also negotiated through Dr Kwiatek, but may be relatively uninterpretable in the individual case.

***Consent:***

Your study doctor is required to provide you with all information regarding the nature and purpose of the research study and its risks/benefits, and you should be given the opportunity to discuss these. It is emphasised that you are free to withdraw anytime and that if you do not participate you will not suffer any prejudice.

***Advice and Information:***

If you have any further questions regarding this study, please do not hesitate to contact Dr Kwiatek on 8267 1767.

The Bellberry Human Research Ethics Committee has reviewed and approved this study in accordance with the National Statement on Ethical Conduct in Human Research (2007) – incorporating all updates. This Statement has been developed to protect the interests of people who agree to participate in human research studies.

Should you wish to discuss the study or view a copy of the Complaint procedure with someone not directly involved, particularly in relation to matters concerning policies, information or complaints about the conduct of the study or your rights as a participant, you may contact the Committee Chair, Bellberry Human Research Ethics Committee on 08 8361 3222.

All study participants are to be provided with a signed and dated copy of the Participant Information Sheet and Consent Form for their personal records.

## *CONSENT FORM*

### **Study Title: Brain Ventricular Lactate and Cortical Glutathione Levels in Fibromyalgia Syndrome.**

I, \_\_\_\_\_, the undersigned, hereby voluntarily consent to my involvement in the research project titled Brain Ventricular Lactate and Cortical Glutathione Levels in Fibromyalgia Syndrome.

I acknowledge that the nature, purpose and risks of the research project and alternatives to participation have been fully explained to my satisfaction by Dr \_\_\_\_\_.

Specifically, the details of the procedure(s) proposed and the anticipated length of time it will take, the frequency with which the procedure(s) will be performed and an indication of any discomfort that may be expected have been explained to me.

- I freely agree to participate in this research project according to the conditions in the Participant Information Sheet which I confirm has been provided to me.
- I understand that my involvement in this study may not be of any direct benefit to me.
- I have been given the opportunity to have a member of my family or another person present while the study is explained to me.
- I have been told that no information regarding my medical history will be divulged to unauthorised third parties and the results of any tests involving me will not be published so as to reveal my identity.
- I understand that access may be required to my medical records for the purpose of this study as well as for quality assurance, auditing and in the event of a serious adverse event and I consent to this access.
- I understand that I am free to withdraw from the study at any stage without prejudice to future treatment. 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.
- I am 18 years of age or over.
- I consent to my treating Doctor/s being notified of my participation in this study and of any clinically relevant information noted by the study doctor in the conduct of the study.
- I declare that all my questions have been answered to my satisfaction.
- I have read, or have had read to me, and I understand the Participant Information Sheet, version 5, dated 4th February 2018.

**NAME OF STUDY PARTICIPANT:** \_\_\_\_\_

**SIGNATURE OF STUDY PARTICIPANT:** \_\_\_\_\_

**DATE:** \_\_\_\_\_

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**Declaration by Principal Investigator (PI) or Co-Investigator (CI):**

A verbal explanation of the research project, its procedures and risks has been given to the participant and I believe that the participant has understood that explanation.

**NAME OF PI or CI:**

**SIGNATURE OF PI or CI:** \_\_\_\_\_ **Date:** \_\_\_\_\_

The Principal Investigator or Co-Investigator must provide the explanation and provision of information concerning the research project.

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***USE THIS SECTION ONLY IF REQUIRED***

*Refer TGA Note for Guidance on Good Clinical Practice July 2009 clause 4.8.9 outlining when an impartial witness is required.*

**SIGNATURE OF WITNESS:** \_\_\_\_\_ **DATE:** \_\_\_\_\_

**FULL NAME OF WITNESS:** \_\_\_\_\_

**ADDRESS:** \_\_\_\_\_

I declare that I have been present when the research was explained to the above-named participant and to the best of my observation and belief was understood and the consent freely given.