Participant Information Sheet

Study title: Influence of Exercise Training on Chemoreflex Sensitivity

Locality: Auckland
Sponsor: University of Auckland

Lead investigator: Thalia Babbage
Contact phone number: 09-373 7599 | ext. 86320

You are invited to take part in a study on [x]. 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 8 pages long, including the Consent Form. Please make sure you have read and understood all the pages.

WHAT IS THE PURPOSE OF THE STUDY?

There is a significant burden of disease in New Zealand arising from chronic heart diseases such as coronary heart disease, heart failure, and high blood pressure. There is new evidence that specialised receptors in the body that respond to changes in blood gas levels (i.e., chemoreceptors) are over-active in chronic heart diseases. This leads to worsening symptoms, reduced quality of life and poor outcomes. There are currently no treatments available that are non-invasive and free from harsh side effects, despite the potential clinical benefit of targeting these chemoreceptors. The purpose of the present investigation is to understand whether exercise training can be used as a novel therapy for cardiovascular disease conditions.

In this study, we are particularly interested in the effect of training history (e.g., endurance, resistance or untrained) on chemoreflex function in young, healthy
individuals. We hope that this information will prove insightful into the mechanisms behind observed benefits to exercise training and will also aid in understanding the exercise prescription for future investigations in patient populations.

This study is being conducted by Thalia Babbage (Doctoral Candidate, University of Auckland), Dr James P Fisher (Principal Supervisor, University of Auckland), Prof. Julian Paton (Co-supervisor, University of Auckland), Dr Nicholas Gant (Investigator, University of Auckland) and Dr Ana Luiza Carrari Sayegh (Postdoctoral Research Fellow, University of Auckland).

For further information please contact Thalia Babbage, Principal Investigator (Email, thalia.babbage@auckland.ac.nz, Phone, 09 373 7599 | Ext 86320).

Ethical aspects of this study have been reviewed and approved by Health and Disability Ethics Committee Protocol number [20/CEN/176].

**WHAT WILL MY PARTICIPATION IN THE STUDY INVOLVE?**

We are inviting 3 groups of people to participate.

- **Endurance** trained individuals - performing >4 hours of endurance exercise training on 2 or more days per week, for more than 12 months continuously.
- **Resistance** trained - performing >4 hours of resistance training on 2 or more days per week, for more than 12 months continuously.
- **Untrained** - not performing any regular physical activity for more than 12 months continuously.

You have been invited to participate because you potentially fit into one of these 3 groups of people.

For safety and scientific reasons you are ineligible to participate in this study if you are: younger than 18 years old or older than 45 years old, are pregnant, are a smoker, have a body mass index <18 (weight in kilograms divided by height in metres squared), or have a significant medical condition (e.g. heart failure, lung disease). An investigator will carefully check the inclusion/exclusion criteria with you and answer any queries.

Participation involves one familiarisation visit (~60 min) and one experimental visit (~3 hours) where you will come to the **Exercise Nutrition and Metabolism Laboratory, Department of Exercise Sciences, University of Auckland**. The general procedure of participating is as follows:

Once you have read this form, an investigator will contact you to make sure that your questions have been answered and check that you understand what is involved. They will then schedule a familiarisation visit with you.

**Familiarisation / screening visit**

At the familiarisation visit (~60 min) an investigator will further explain the nature of the procedures, answer any remaining questions and ask you to complete the Consent Form below. You will be asked to complete a pre-screening for physical activity (Get Active Questionnaire) and health / physical activity questionnaires. Then, providing you meet the study inclusion/exclusion criteria, you will be enrolled into the study. Body weight and height will be measured, and then you will be familiarised with the study procedures.
At the screening visit, you will also complete a handgrip strength test using a hand held dynamometer. You will then complete a graded maximal exercise test to measure your endurance capacity. During this test you will be required to perform incremental exercise on a motorised treadmill, while wearing a mouthpiece, nose clip and headset which will allow analysis of your breathing. Your heart rate will also be monitored during the test. The exercise test takes ~10-15 minutes.

Experimental visit
You will attend a single experimental visit that will last ~3 hours. This will be conducted at the Exercise Nutrition and Metabolism Laboratory. For premenopausal women, this visit will be scheduled to occur during the first five days of your menstrual cycle or during the low hormone phase of contraceptive pill use. Prior to the study visit the following pre-study stipulations apply:

- No food intake for 2 hours prior to the study.
- No caffeine (e.g., coffee, coke, red bull) for 12 hours before the study.
- No alcohol on the day before the study and the day of the study.
- No exercise after 8:00pm the evening before the study and no exercise on the day of the study.
- No 'over the counter' (e.g. paracetamol) medications on the morning of the study.

The following procedures will be conducted while you rest on a comfortable chair.

Experimental Protocol
You will be asked to sit in a comfortable chair for the duration of the test. After a resting baseline period of ~15 minutes, we will assess your "peripheral" and "central" chemoreceptor sensitivity using two short (~5 minutes) gas mixture trials. One gas mixture will contain low oxygen to target the stimulation of your peripheral chemoreceptors. The other gas mixture will contain high carbon dioxide and high oxygen to target stimulation of your central chemoreceptors. After each trial you will be asked to rate your breathing sensation using a simple 0-10 scale.

Measured Variables
Throughout the experimental procedures described in the paragraph above we will continuously monitor your breathing and cardiovascular system. Breathing will be monitored with a lightweight mask covering your mouth and nose, or a mouthpiece with a nose clip. Your heart rate will be measured using a 3-lead electrocardiogram by placing sticky electrode patches on your chest. Your blood pressure will be monitored by a small blood pressure cuff around the finger, and another around your upper arm. A lightly placed finger-clip will monitor your blood oxygen saturation. Blood flow of the large arteries in your brain will be measured using two probes placed lightly on your temples with the help of an adjustable headband and gel.

**WHAT ARE THE POSSIBLE BENEFITS AND RISKS OF THIS STUDY?**

**Benefits:** It is unlikely that there will be a direct benefit to you from participating in this study. However, we will be happy to talk to you about the data collected (e.g., your heart rate, blood pressure). The information we will gather from all the people taking part in this study will help us to understand the effect of exercise training on peripheral chemoreflex sensitivity, which can be implicated in chronic heart disease conditions. The
results of this study will translate to patient population research, with understanding of the effect of specific exercise training histories on central and peripheral chemoreflex function and exercise prescription for patient populations.

**Risks and Discomforts:** The risks associated with the procedures are minimal. The research team are experienced with all the procedures employed. Further, your heart rate, blood pressure, breathing and oxygen levels will be carefully monitored by an investigator throughout the study. The experimental protocol will be stopped if untoward symptoms develop, or at your request.

Hypoxia and hypercapnia are used to stimulate the peripheral and central chemoreceptors, and may produce feelings of breathlessness, light-headedness or dizziness. The risk of this is low, and further minimised by being applied for a short period of time (5 minutes), but if this does occur symptoms rapidly reverse (in a few seconds) by breathing normal room air again.

Maximal exercise testing can involve sensations similar to those that may occur during strenuous exercise, including fatigue, muscle soreness, breathlessness, chest pain, fainting, vomiting and headache. A risk of fall is also present due to increasing gradient and speed throughout the test. To mitigate these risks, you will be monitored continuously throughout the test.

**COVID-19:** This study will not be conducted while New Zealand is at Alert Levels 3 and 4. The study will proceed at Alert Levels 1 and 2, undertaking and adhering to institutional guidance from the University of Auckland regarding practices to minimise the risk of transmission. This will include the researchers wearing personal protective equipment and maintaining appropriate physical distance when able. All equipment will be cleaned between participants, and surfaces wiped down. If you feel unwell on the day of your scheduled testing, have been in close contact with a confirmed or probable case of COVID-19, or have returned from overseas in the 14 days prior to your scheduled testing, please do not come in for assessment.

**WHO PAYS FOR THE STUDY?**

As a participant in this study you will not incur any costs. A $50 voucher will be provided to participants for their participation.

**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.
Detection of Abnormalities: The measures made are for research and are not a medical exam or diagnostic test. There is a small possibility that we may incidentally find an abnormality that is clinically significant, such as a heart rhythm abnormality. In the event of this, you will be informed of this and will be advised to consult your general practitioner. If you do not wish to know about this type of finding, please do not participate.

WHAT ARE MY RIGHTS?

Your participation in this study is entirely voluntary. You are free to decline to participate, or to withdraw from the research at any practicable time, without experiencing any disadvantage. You have the right to access information collected about you as part of the study. You will be informed of any new information related to the study that becomes available during the study that may have an impact on their health. Your identity will be kept strictly confidential and you will not be identified in the publication of the research findings.

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

Confidentiality: All information collected about you during the course of the research will be secure. Your name will appear on the attached Consent Form, which will then be coded with a Participant Identification Number. Other study data will then be stored using this Participant Identification Number and not your name. The de-identified study data will be shared with other researchers on the project. Your de-identified data may be used in future studies by other researchers only with the permission of the Lead Investigator, Thalia Babbage. The full results of the studies being conducted will not be known until after the last participant has been tested and the data analysed (up to three years). The results will be reported in professional publications and meetings, but will not be published in a form that identifies individual participants. If you are interested in receiving a summary of the results, please indicate as appropriate on the consent form below.

Data storage, retention, destruction and future use: Electronic data will be stored on a password protected University of Auckland server. Primary research data will be preserved and accessible for ten years, in confidence to appropriate individuals.

HDEC Auditing: an approved auditor appointed by New Zealand Health and Disability Ethic Committees, or any relevant regulatory authority or their approved representative may review your medical records for the sole purpose of checking the accuracy of information recorded for the study, for auditing purposes.

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, position: Dr James P. Fisher
Telephone number: 09 373 7599 | Ext 86320
Email: jp.fisher@auckland.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

If you require Māori cultural support, talk to your whānau, iwi, hapu or kaumatua in the first instance. Alternatively, you may contact the administrator for He Kamaka Waiora (Māori Health Team) by telephoning 09 486 8324 ext. 2324.

If you have any questions or complaints about the study, you may contact the Auckland and Waitematā District Health Boards Māori Research Committee or Māori Research Advisor by phoning 09 486 8920 ext. 3204.

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
Consent Form

Please tick to indicate you consent to the following

I have read, or have had read to me in my first language, and I understand the Participant Information Sheet.

I have been given sufficient time to consider whether or not to participate in this study.

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.

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.

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.

I consent to the research staff collecting and processing my information, including information about my health.

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 ☐ No ☐

I agree to an approved auditor appointed by the New Zealand Health and Disability Ethic Committees, or any relevant regulatory authority or their approved representative reviewing my relevant medical records for the sole purpose of checking the accuracy of the information recorded for the study.

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.

I understand the compensation provisions in case of injury during the study.

I know who to contact if I have any questions about the study in general.

I understand my responsibilities as a study participant.

I wish to receive a summary of the results from the study. Yes ☐ No ☐
**Declaration by participant:**
I hereby consent to take part in this study.

**Participant’s name:**

**Signature:** ___________________________ **Date:** ___________________________

**Declaration by member of 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:** ______________________________________________________

**Signature:** ___________________________ **Date:** ___________________________

**Ethical aspects of this study have been reviewed and approved by the Health and Disability Ethics Committee [20/CEN/176] on [25/08/2020] for [x] years.**