The effect of high intensity acute exercise on peptide levels in humans

PARTICIPANT INFORMATION SHEET

We invite you to participate in an exercise intervention study aimed at identifying novel exercise regulated peptides. Your participation in the research is entirely voluntary (your choice). If you do agree to take part, you may contact the investigators to withdraw from the research at any time, without having to give a reason. You can also request that any samples or data you provide for this research be withdrawn prior to the publication of any results.

Who can take part?

You can take part if you are a male, aged 18-35 years of age, and are healthy. You must be willing to exercise vigorously and visit the University of Auckland (Grafton) 2 times over 1-2 weeks. The duration of these visits varies from 90 minutes to 4 hours.

The study will involve the collection and analysis of muscle and blood samples. Many iwi, hapu, and whānau disagree with gene testing of tissue samples due to issues with the loss of rights to your whakapapa. However, it is acknowledged that individuals have the right to choose. We encourage you to consult with your friends and whānau, especially around the gene testing process and the collection of your muscle tissue before agreeing to participate. If you have any cultural requirements or questions that relate to your potential participation in this project, please ask the research team before signing this document. It is the role of the investigators to ensure that you understand all procedures and risks: please feel free to ask any questions.

Who designed the trial?

This trial was designed by research staff at the University of Auckland. The researchers conducting this trial are interested in understand the molecular mechanisms through which exercise improves health.

Background

It is not clear how exercise improves health. Organs in our body (particularly muscle) send chemical messengers (such as hormones, metabolites and peptides) in response to exercise, and these chemical messengers play a role in the health promoting effects of exercise. Here, we will test whether peptides that are regulated by exercise are involved in regulating our adaptive responses to exercise and how your genes effect the response of these peptides to exercise.

What is the aim of the research?

The aim of the research is to assess the effects of high intensity exercise on muscle and blood levels of peptides.

What happens if I decide to take part?
This research requires 2 visits.

**Visit one (screening 1-1.5 hr)**
This will take place in person at the University of Auckland Grafton campus at 85 Park Road, Grafton. We will discuss this participant information sheet with you and if you wish to participate you will be asked to sign an informed consent form. You will be asked some questions about your health, have your height and weight measured, and undergo a DEXA scan which will give you information about your bone, fat and muscle mass. DEXA scans will expose you to a small amount of radiation, but this is no more than you would be exposed to as background in a normal day. You will also be asked to perform an aerobic fitness test to determine your maximal exercise capacity. You will cycle continuously on a stationary bike with incrementally increasing workloads until exhaustion (12 to 20 minutes) and your expired breath will be collected through a mouthpiece. A blood sample will also be collected before and after the test.

**Visits two (4 hours)**
Depending on your results from visit one, you may be given the opportunity to provide muscle samples during visit two. You do not have to provide muscle sample, it is your choice.

This visit will take place at least 48 hours after the first visit. We ask that you abstain from exercise for at least 48 h before this visit. We also ask that you do not eat anything after 10 pm the night before, and arrive to the laboratory in the morning having only consumed water (not coffee, tea or juice). During this visit you will complete 10 repetitions of 60 s high intensity stationary bike cycling with 75 s rest between each repetition. If you elect to provide muscle samples, muscle biopsies will be taken from your thigh muscle. You will be given local anaesthetic to prevent you from feeling pain and a small 4mm incision will be made, then a muscle sample the size of a small pea will be collected; you may still feel a deep pressure sensation. Your leg might be sore for a few days after the procedure. We will collect muscle samples immediately before, immediately after and 3 h following exercise. There will be a total of **THREE MUSCLE BIOPSIES** over the course of the study.

Regardless as to whether you provide a muscle sample, a small needle will also be placed into your arm vein. This is slightly painful and can cause discomfort. This needle has a plastic cannula that will be left in your arm vein. This too is a little uncomfortable and you will not be able to fully bend your arm. The researcher will take blood before, halfway through, and every 30 min for 3 h following exercise to measure hormones, peptide, genes, proteins, metabolites and mitochondrial function in your blood to determine your metabolic response to exercise. The total amount of blood taken in each for each of these visits will be no more than 150 ml. You will also be asked to provide a urine sample pre and post exercise.

**Follow-up care**
Research personnel will contact you after the final study visit to check how you are feeling. The muscle biopsy site may take several days to fully heal, if you experience any symptoms such as bruising or pain contact the research personnel via telephone.

**The risk and benefits of the research**
Overall there are no major risks associated with taking part in this research. There is low risk associated with the DEXA. We are exposed to very low amounts of radiation
all the time from the sun and other sources in our everyday lives. The DEXA scan involves exposure to a similar amount you normally experience in one day.

There are minor risks involved in muscle biopsy, including bleeding, bruising, muscle soreness or infection. Our research staff will explain all of this to you in detail, and you will be welcome to ask questions. You may feel some discomfort from the biopsies on the day after the study. Again, staff will be available to answer any questions and advise you about any problems that you may experience.

While there is a risk of injury (such as muscle strain) or feeling faint/nausea associated with high intensity exercise, in healthy individual undertaking stationary cycle riding we believe this to be negligible.

There are slight risks associated with blood sampling. These are minimised by having all procedures undertaken by a qualified phlebotomist using accepted antiseptic technique. There is a small chance of minor bruising as a result of insertion of the catheters or venepuncture. Very occasionally, however, there can be infections. We consider the risk extremely low given the aseptic/barrier techniques used.

The research will be stopped should any harmful effects appear or if research investigators feel that it is not in your best interest to continue. Any symptoms that you may experience will be recorded as part of the trial.

In the unlikely event of a physical injury as a result of your participation in this study, you may be covered by ACC under the Injury Prevention, Rehabilitation, and Compensation Act 2001. ACC cover is not automatic, and your case will need to be assessed by ACC according to the provisions of the Injury Prevention, Rehabilitation, and Compensation Act 2001. If your claim is accepted by ACC, you still might not get any compensation. This depends on a number of factors, such as whether you are an earner or non-earner. ACC usually provides only partial reimbursement of costs and expenses, and there may be no lump sum compensation payable. There is no cover for mental injury unless it is a result of physical injury. If you have ACC cover, generally this will affect your right to sue the investigators. If you have any questions about ACC, contact your nearest ACC office or the investigator. You are also advised to check whether participation in this study would affect any indemnity cover you have or are considering, such as medical insurance, life insurance and superannuation.

**Will there be genetic testing?**

We will measure the amount of some of your genes, proteins and metabolites because they can change after exercise and may provide a biomarker of the exercise response. There is no one gene that determines your fitness or exercise capacity, but a number of small changes which contribute to your ability to adapt to exercise.

Studying genes involves looking at the DNA which is the genetic code that is found inside the body’s cells. We are investigating how differences in DNA may affect how the body responds exercise, and how this might determine the health benefits you get from exercise.

DNA is prepared from a sample of your blood. If you want, we can arrange for a karakia when your left-over blood or DNA is disposed of. Please indicate this in the Consent Form. From the DNA we will compare the genes which control how your respond to exercise. We will **NOT** decode and record your entire genetic code, but will focus just
on genes that there is a reason to believe that they may be involved in controlling how you respond to exercise.

When DNA is made, it is a clear liquid in a test-tube. Your genetic code is inside the DNA. In the past we have used labour intensive laboratory methods to look at certain genes in the liquid DNA. However, by using the latest technology we can now ‘decode’ the DNA in the liquid into a ‘sequence’ which is stored on a computer. We can then more easily look at the genes we are interested in. Your genetic information is protected on computers at The University of Auckland. It is important to know that there is no one gene that determines your health or response to exercise, but a number of small changes which contribute to the exercise response. We will NOT be testing other genetic diseases that you could be carrying. Our genetic testing will NOT provide any information on heritage.

**What will happen with my blood and muscle samples?**

We will analyse your blood, urine and muscle samples in New Zealand for hormone, peptide, protein, gene, metabolite levels and mitochondrial function. A portion of your blood and muscle sample will also be sent to Prof. Pinchas Cohen's laboratory in the USA for analysis of additional peptide levels. Blood and muscle samples will be stored in secure freezers in an access-restricted area at the University of Auckland, until analysis is completed. Samples will be stored in the same facility as animal tissue. There will be no future unspecified research made on your samples without your prior approval. After completion of the study, we will keep your contact details for 10 years but you will only be contacted in the unlikely event that we would like to perform further unspecified analysis. If we cannot contact you at this time we will not perform this analysis. After these analyses have been performed on your tissue samples, it will not be possible to return any unused samples to you, although you are welcome to request their return prior to any analysis.

Your samples will be kept until the end of the analysis for a total of 10 years. At the end of this time a medical waste contactor will dispose of your tissue. If you would like a karakia performed at this time, please indicate so in the consent portion of this form. Any samples for disposal by karakia will be clearly marked. It is possible that the entire sample may be used for analysis, in that case there will be no need for disposal and a karakia is not possible. All samples sent overseas will be used in analysis, and therefore no disposal will be required.

**Confidentiality**

Research files, data and all other information that you provide will remain strictly confidential. This data will be used for scientific publication and presentations. No material that could personally identify you will be used in any reports on this research. All computer records will be password protected. Upon completion of the research your records will be stored for at least 10 years in a secure place, before being destroyed by the principle investigator or co-investigators. If this is not possible for any reason the head of the principle investigators department or otherwise designated research will take responsibility for this process. A copy of your results will be given to you upon completion of the research at your request. Data from this study will not be used for any future research.
Trial Payments

There will be no financial cost to you for taking part in the trial. In addition to a comprehensive fitness assessment and body composition analysis you will receive a gratuity of either a $50 (if no muscle biopsies were taken) or $200 (if biopsies were taken) in the form of Westfield vouchers.

Finally

Thank you for considering your participation in this study

Ngā Tāngata hei whakapānga atu - For more information please contact:

Troy Merry, Department of Molecular Medicine and Pathology, The University of Auckland, 85 Park Rd. Grafton
Telephone: 09 923 9008   Email: t.merry@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@hdc.org.nz

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

This research has received Ethical Approval from the Southern Health and Disability Ethics Committee

The investigators of the research are:

Dr. Troy Merry,
Department of Molecular Medicine and Pathology
The University of Auckland, New Zealand
Telephone: 09 923 90086   Email: t.merry@auckland.ac.nz

Prof David Cameron-Smith,
Human Nutrition Unit and Liggins Institute
The University of Auckland, New Zealand
Telephone: 099231336   Email: d.cameronsmith@auckland.ac.nz

Dr. Cameron Mitchell
Liggins Institute
The University of Auckland, New Zealand
Telephone: 099236606    Email: Cameron.mitchell@auckland.ac.nz
Please keep this information sheet for your records.
CONSENT FORM

I have read and I understand the Participant Information Sheet and wish to take part in the research entitled “The effect of high intensity acute exercise on peptide levels in humans”, which is designed to investigate the effects of exercise on tissue peptide levels.

I have had the opportunity to discuss this research with the investigator. I am satisfied with the answers I have been given.

1. I have had the opportunity to use support from a family (whanau) member or a friend to help me ask questions and understand the research.
2. I understand that taking part in this research is voluntary (my choice), and that I may withdraw from the research at any time and this will in no way affect my future or continuing health care.
3. I understand that blood and muscle samples will be collected and sent overseas for analysis and will not be able to be returned to me.
4. I understand that the treatment or investigation will be stopped if it should appear harmful to myself.
5. I understand the risks associated with partaking in this research.
6. I have had time to consider whether to take part.
7. I know whom to contact if I have any side effects from the research.
8. I know whom to contact if I have any questions about the research.
9. I agree not to restrict the use of any data or results that arise from this research provided such a use is only for scientific purpose(s)

Participant to complete: Please circle as appropriate

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<thead>
<tr>
<th>Statement</th>
<th>Yes</th>
<th>No</th>
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<tr>
<td>I consent to participate in the “The effect of high intensity acute exercise on peptide levels in humans” study</td>
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<td>I wish for a karakia to be said at the time of my tissue disposal</td>
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<td>I wish to receive a copy of the results. I understand that there may be a delay between data collection and the publication of the research results</td>
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<td>I understand that my tissue samples may be stored for up to 10 years and some of the samples will be sent overseas.</td>
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<td>I understand that there will be genetic analysis done one my DNA samples</td>
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CONSENT FORM

Participant to complete:

I ______________________________ Print full name
of ______________________________ Print address
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hereby consent to take part in this research which is designed to investigate the effects of high intensity exercise on muscle and blood levels of peptides.

________________________________ Signature of Participant
________________________________ Date

Research Personnel to complete:

________________________________ Full name of Principal Investigator
________________________________ Signature of Principal Investigator
________________________________ Contact telephone number for PI

Research Personnel to complete:

________________________________ Project explained by
________________________________ Project role
________________________________ Signature
________________________________ Date

A copy of this consent form is to be given to the participant and to be kept in their research file.

APPROVED BY THE HEALTH AND DISABILITY ETHICS COMMITTEE
Reference Number 16/STH/116