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School of Medicine

EFFECT OF AN EXERCISE TRAINING PROGRAM ON METABOLIC FLEXIBILITY IN OLDER ADULTS WITH PREDIABETES

Informed Consent Form to Participate in Research

Gary Miller, PhD, Principal Investigator

SUMMARY

You are invited to participate in a research study. The purpose of this research is to determine if exercise can promote metabolic flexibility, or your muscles ability to alter the use fats and carbohydrates for energy. You are invited to be in this study because you are over the age of 60. Your participation in this research will involve two separate 30-minute screenings at the Department of Health and Exercise Science Wake Forest University testing laboratories. An exhaustive description of the study will be provided to you at the end of your first screening visit. If you consent to the research study at this point in time, you will be asked to come back for the second 30-minute screening visit. If you still qualify for the study after your second screening visit, you will be presented with a menu from the Clinical Research Unit. You will be able to indicate your food preferences at this time. If you consent to the provided menu, we will then schedule a time for you to pick up three days of food at the Wake Forest Baptist Medical Center Clinical Research Unit. You are asked only to eat the meals and snacks provided to you for the three days leading up to the baseline testing visit. After the baseline testing visit, you will begin a 6-week exercise training program which will take place at the Department of Health and Exercise Clinical Research Center. The program will gradually increase from walking three times a week for an hour each day and build up to five 1-hour sessions per week. Following training, there will be one more 30-minute appointment at the Department of Health and testing laboratory, and two 2-hour follow-up tests at the Wake Forest Baptist Medical Center Clinical Research Unit. Before each of the 2-hour follow-up tests, you will again be asked to pick up 3-days of food from the Clinical Research Unit and consume those meals and snacks as indicated for the three days leading up to each test. The food and testing procedures will be similar to the baseline testing visit.

During the 30-minute visits to the Department of Health and Exercise testing laboratory you will do a graded exercise test in which you will incrementally work up to your maximum exercise capacity on a treadmill. These tests typically require about 8-12 minutes of exercise. The baseline and follow-up testing visits at the Wake Forest Baptist Medical Center Clinical Research Unit will consist of blood draws, and a test in which we measure the amount of oxygen your body is using at rest, during 20 minutes of moderate exercise, and then after the exercise period. We ask that you report to the lab for testing in a fasted condition, that is not eating or drinking anything besides water for the previous 8 hours. The 3-days of food you will pick-up and eat before these tests is considered a high-fat diet. Again, we ask that you only consume the meals and snacks provided by the study for the three days leading up to each of the three testing visits. All research studies involve some risks. A risk to this study that you should be aware of is bruising or temporary pain following the blood draws, muscle and joint soreness from the exercise tests and exercise training, and potential gastrointestinal distress and fatigue from the diet. You may or may not benefit from participation in this study, as a regular exercise regimen

can improve health. We hope the information learned from this study will benefit other people in the future.

Your participation in this study is voluntary. You do not have to participate in this study if you do not want to. You will not lose any services, benefits, or rights you would normally have if you choose not to participate.

The remainder of this form contains a more complete description of this study. Please read this description carefully. You can ask any questions if you need help deciding whether to join the study. The person in charge of this study is Gary Miller, PhD. If you have questions, suggestions, or concerns regarding this study or you want to withdraw from the study you may contact Gary Miller at [redacted] or [redacted].

If you have any questions, suggestions or concerns about your rights as a volunteer in this research, contact the Institutional Review Board at [redacted] or the Research Subject Advocate at Wake Forest at [redacted].

INTRODUCTION

You are invited to participate in a research study about metabolic flexibility. Metabolic flexibility is the ability of an individual to switch your use of energy for the body between different fuel sources, such as carbohydrates and fat. We are specifically interested in how exercise training affects the muscle's ability to switch energy sources from carbohydrates to fats with a high fat diet. This is pertinent, as people with metabolic diseases such as type 2 Diabetes Mellitus struggle to switch from one source of energy to another. Research studies are designed to gain scientific knowledge that may help other people in the future. You are being asked to take part in this study because you are over sixty years of age. Your participation is voluntary. Please take your time in making your decision as to whether or not you wish to participate. Ask the study staff to explain any words or information contained in this informed consent document that you do not understand. You may also discuss the study with your friends and family.

WHY IS THIS STUDY BEING DONE?

The purpose of the study is to determine if a 6-week exercise training program promotes exercise-induced metabolic flexibility, that is, the ability to switch fuel sources for energy, in older prediabetic adults.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

Twenty (20) people at 1 research site will take part in this study.

WHAT IS INVOLVED IN THE STUDY?

Participants will come to the Department of Health and Exercise Science research laboratory for the initial screening visit (approximately 30 minutes long). Here you will review consent forms with research staff and sign them if you would like to participate in the study. If you agree to participate, a finger stick will be taken to measure HbA1c values. This will help us determine if volunteers have prediabetes. If HbA1c values do not indicate prediabetes, you will not be able to

participate in the study. Your height and weight will be obtained at this visit if you qualify for the study. As part of the exclusion criteria you are asked to not consume for 3 days prior to exercise testing products that contain caffeine, such as coffee, energy drinks, nutritional supplements, and other-the-counter medications like certain pain relievers. You are also asked to not use over-the-counter decongestants such as pseudoephedrine as they may affect how much energy you use. You may speak with your doctor to see if it is safe for you not to take these types of medications for 3 days prior to the testing visits.

Those who qualify to participate in the study will come to a second screening at the Department of Health and Exercise Science research laboratory in Worrell Professional Center (approximately 30 minutes). Here we will perform a graded exercise stress test. You will wear a face mask hooked to a machine that collects the amount of oxygen and carbon dioxide you exhale. The test begins with measurements of oxygen and carbon dioxide during resting, sitting, and with hyperventilation. ECG and blood pressure will be measured throughout the testing. We will then have you walk on a treadmill at a brisk pace under the supervision of a physician and an exercise physiologist. While you are walking, the grade of the treadmill will be increased at a rate of 1%/minute or 2%/minute, depending on your fitness level, until you have built up to your maximum intensity. You will stay at this high intensity level for approximately 1 minute. Heart rate and ECG are continuously monitored, and blood pressure is recorded every 2-3 minutes during the test and throughout a 6-minute recovery period. This will help us to determine if you are healthy enough to participate in this study and to establish the exercise intensity for subsequent exercise tests and for the exercise training program.

After the two screening visits, we will begin the study tests. The first test will take place approximately 4-10 days after the graded exercise test. We ask that you eat only meals and snacks provided by the Wake Forest Clinical Research Unit for the 3 days prior to the testing visit. The foods provided to you are consistent with a high fat diet (20% of kcals from carbohydrate, 65% fat; 15% protein). We will schedule a time for you to go to the Clinical Research Center at Wake Forest Baptist Medical Center and pick up 3 days' worth of high-fat prepared food. This pickup will occur four days before your testing visit. We ask that you consume these foods as instructed for the three days prior to your visit. If you have food allergies or aversions to the provided food, you will not be able to participate. The night before your visit you will be asked to fast for 8 hours. We also ask that you abstain from caffeine and exercise for 24 hours before these tests. On the day of the visit, participants will be asked to come to the Clinical Research Unit at the Wake Forest Baptist Medical Center for a 20-minute submaximal exercise test. This visit will last about 2 hours. During this time, you will have the following measurements taken:

Gas exchange: You will be asked to wear a face mask hooked to a machine that measures the gases you exhale. You will wear this mask while laying down for 15 minutes. Following this 15-minute resting period, we will have you walk on a treadmill for 20 minutes at a moderate intensity of about 50% of your maximum capacity. After exercise, we ask that you keep the mask on for 30 minutes as you relax, and we will continue to measures the gases you exhale.

Blood Samples: You will have multiple blood draws from a catheter throughout the duration of the testing visit. A registered nurse will insert the catheter into your arm at the beginning of the visit so that we can easily obtain blood samples. If you agree to the study, 1 teaspoon of blood will be collected prior to any exercise so that we can measure insulin, glucose, fats, and lactate in the blood during rest. As you exercise for 20 minutes (see "gas exchange") we will collect 1 tsp of blood using the catheter at 5, 10, 15, and 20 minutes into exercise. One more teaspoon of blood will be taken through the catheter, 30 minutes after the end of the exercise period. At this time, the mask and catheter will be removed by the nurse. In the event that placement of the catheter is unsuccessful, needles will be used to collect samples at times 0 (prior to initiation of exercise), 20 (immediately at the end of the exercise), and 50 (30 minutes after the end of exercise).

Exercise Training Program: For 6 weeks between the two testing visits, participants will attend an exercise training program. You will begin walking 3 days a week for 1 hour at 50% of your maximum intensity. This is considered a moderate exercise intensity. Eventually, you will build up to 5 days a week. You will exercise under trained supervision at the Department of Health and Exercise Science Clinical Research Center for 1 hour on Monday, Wednesday, Friday sometime between 6:00 AM and 9:00 AM. When you are ready to add on more days, you can come to the same setting for 1 hour each Tuesday and Thursday between 5:30 PM and 7:00 PM.

After the training program you will participate in a series of follow-up visits.
Graded Exercise Test: The first visit following the exercise training program will take approximately 30 minutes. It will consist of a second graded exercise stress test at the Wake Forest research laboratory in Worrell Professional Center. This is similar to the Graded Exercise Test performed at the beginning of the study.
Follow-up test 1: Approximately 4-10 following the graded exercise test, the first follow-up test will occur and be identical to the submaximal baseline test. Again, in preparation for your visit, you will pick up foods provided by the research staff four days before your visit and eat them for the three days leading up to your visit. You will be asked to only consume the provided food for the days instructed. We are requesting that you do not consume other food items during these three days before testing. These foods will be identical to the diet consumed before the baseline testing visit. You will come to the Wake Forest Baptist Medical Center Clinical Research Unit for 2 hours to have the following measurements taken: amount of oxygen and carbon dioxide exhaled (during 15 minutes rest, 20 minutes at 50% of your maximum capacity as determined by your first VO2 max test, and 30 minutes post-exercise) and blood samples for blood glucose, lactate, insulin, and fats. The speed of the treadmill will be the same as used during the initial submaximal exercise test.
Follow-up test 2: The second follow-up test will take place at the Wake Forest Baptist Medical Center Clinical Research Unit. This will take place approximately 4-10 days after the first follow-up test. It will be identical to Follow-Up Test 2 described immediately above, except this time you will exercise at 50% intensity as determined by your second graded exercise test performed after your exercise training program. This will also be at a moderate exercise intensity. Three days' worth of food will be provided in preparation for this visit as well.

As indicated above, as part of this research study, you will be asked to provide a biological specimen (blood).

If you agree to participate in this study, you will have approximately 1 teaspoon of blood withdrawn from a vein for a total of 18 times (6 times at the baseline testing, 6 times at the second follow-up test, 6 times at the third follow-up test). The total amount of blood withdrawn during the study will be approximately 18 teaspoons.

The research that may be performed with your blood sample is not designed to help you specifically. There is no personal benefit to you from taking part in this aspect of the research study. It might help people who have diseases at some point in the future, but it is not known if this will happen. The results of the research performed with your tissue will not be given to you or your doctor. The results will not be put in your medical record. The research using your blood sample will not affect your care. In the future, research on your specimen may involve whole genome sequencing.

How Long Will I Be in the Study?

You will be in the study for approximately 8-10 weeks. Six weeks will be dedicated to the exercise regimen. Testing will happen prior to and after the training program.

You can stop participating at any time. If you decide to stop participating in the study, we encourage you to talk to the investigators or study staff first to learn about any potential health or safety consequences. There are no anticipated serious health consequences of sudden withdrawal from the study.

What Are the Risks of the Study?

You may experience discomfort, bruising and/or bleeding where the needle is inserted for the blood drawing. Occasionally some people become dizzy lightheaded or feel faint. Infection may occur on rare occasions. Frequent donation of blood can result in low iron in your blood (iron deficient anemia).

You also may experience claustrophobia while wearing the facemask of the gas measurement device. Although not common, individuals may become anxious while wearing the mask.

The graded exercise test could provoke significant symptoms like sudden chest pain, sudden changes in blood pressure, loss of coordination, mental confusion or extreme shortness of breath. Changes may also be seen on ECG. The exercise test will be stopped if such signs or symptoms occur. Potential complications and side effects of exercise include disturbances of heart rhythm (rapid heart rates or severe changes in the rhythm of your heart), heart attacks, heart failure, and decreases in blood pressure. In addition, musculoskeletal problems, severe fatigue, dizziness, fainting and body aches have been reported from exercise tests. Safety monitoring will include ECG monitoring, measuring your blood pressure and continuous supervision by qualified study staff.

The graded exercise tests and VO_2 max tests are performed on a treadmill. Falling on the treadmill is a risk.

The submaximal exercise tests and the exercise training will be at a moderate walking intensity. Potential risks are small but musculoskeletal problems, fatigue, dizziness, fainting and body aches have been reported from this level of exercise. Safety monitoring will include measuring your blood pressure and heart rate and continuous supervision by qualified study staff during the submaximal exercise tests and exercise training.

You could experience an allergic reaction to the meals provided given prior to the day of the lab. Please seek medical attention (call 911) if an allergic reaction occurs during the study and notify research staff. You will be asked about potential food allergies prior to starting the studies to reduce the risk of this happening.

Because the meals provided before testing visits are high in fat, you could experience gastrointestinal issues, feel sluggish or fatigued, and experience constipation. You could experience foodborne illness if you store foods improperly. The Clinical Research Unit will explain how to store all foods when you pick them up to minimize this risk.

If you avoid consuming caffeine during the period around the exercise testing you may experience caffeine withdrawal that may result in headaches, fatigue, anxiety, and poor concentration. Withholding over-the-counter decongestant medications or pain relievers may also lead to side effects, such as increased congestion and possibly headaches from the congestion, and lack of pain relief. It is recommended that you speak with your physician to make sure it is safe for you not to take these products for 3 days prior to testing visits.

Taking part in this research study may involve providing information that you consider confidential or private. All information will be kept in a locked room in a locked drawer where only authorized personnel are permitted to enter or on a password-protected computer. Only authorized people will have access to research records. All files will be kept in a locked drawer in a locked room. After your initial visit, all forms will be deidentified and only reference your unique study identification number. Your name will no longer be attached to the collection forms. There is still however a possibility that personal information collected in this study could be stolen. This information could include name, date of birth, phone number, and email. When the research data are no longer scientifically useful, they will be destroyed.

Being in this study will take up some of your personal time. We will try to schedule your visits at convenient times for you.

WHAT HAPPENS IF I EXPERIENCE AN INJURY OR ILLNESS AS A RESULT OF PARTICIPATING IN THIS STUDY?

Should you experience a physical injury or illness as a direct result of your participation in this study, Wake Forest University School of Medicine maintains limited research insurance

coverage for the usual and customary medical fees for reasonable and necessary treatment of such injuries or illnesses. To the extent research insurance coverage is available under this policy the reasonable costs of these necessary medical services will be paid, up to a maximum of $25,000. Wake Forest University Baptist Medical Center holds the insurance policy for this coverage. It provides a maximum of $25,000 coverage for each claim and is limited to a total of $250,000 for all claims in any one year. The Wake Forest University School of Medicine, and the North Carolina Baptist Hospitals, Incorporated do not assume responsibility to pay for these medical services or to provide any other compensation for such injury or illness. Additional information may be obtained from the Medical Center's Director of Risk and Insurance Management, at [redacted].

If you are injured, the insurer may require information such as your name, social security number, and date of birth in order to pay for your care. This is because the insurer is required by law to report any payments made to cover the care of any persons who are members of a government insurance plan to the Department of Health and Human Services.

You do not give up any legal rights as a research participant by signing this consent form. For more information on medical treatment for research related injuries or to report a study related illness, adverse event, or injury you should call Gary Miller at [redacted] or [redacted].

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

If you agree to take part in this study, there may or may not be direct benefit to you. We hope the information learned from this study will benefit other people in the future.

WHAT OTHER CHOICES ARE THERE?

This is not a treatment study. Your alternative is to not participate in this study.

WHAT ARE THE COSTS?

All study costs, including any study supplements and procedures related directly to the study, will be paid for by the study. Costs for your regular medical care, which are not related to this study, will be your own responsibility.

WILL YOUR RESEARCH RECORDS BE CONFIDENTIAL?

The results of this research study may be presented at scientific or medical meetings or published in scientific journals. Your identity and/or your personal health information will not be disclosed unless it is authorized by you, required by law, or necessary to protect the safety of yourself or others. There is always some risk that even de-identified information might be re-identified.

Participant information may be provided to Federal and other regulatory agencies as required. The Food and Drug Administration (FDA), for example, may inspect research records and learn your identity if this study falls within its jurisdiction.

If you choose to participate in this study, your medical record at Wake Forest University Baptist Medical Center will indicate that you are enrolled in a clinical trial. Information about the

research and any medications or devices you are being given as a participant may also be included in your medical record. This part of the medical record will only be available to people who have authorized access to your medical record. If you are not a patient at this Medical Center, a medical record will be created for you anyway to ensure that this important information is available to doctors in case of an emergency.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this Web site at any time.

WILL YOU BE PAID FOR PARTICIPATING?

If you attend all testing visits, you will be compensated $125. You will receive $25 at each of the following appointments attended: screening visit 2 (your first graded exercise test), baseline submaximal exercise test, follow-up graded exercise test, follow-up submaximal exercise test 1, and follow-up submaximal exercise test 2.

WHO IS SPONSORING THIS STUDY?

This study is being sponsored by Wake Forest University Department of Health and Exercise Science and the Translational Science Center. The sponsor is providing money or other support to Wake Forest University Health Sciences to help conduct this study. The researchers do not, however, hold a direct financial interest in the sponsor or the product being studied.

WHAT ABOUT MY HEALTH INFORMATION?

In this research study, any new information we collect from you and information we get from your medical records or other facilities about your health or behaviors is considered Protected Health Information. The information we will collect for this research study includes**:**

-Graded exercise stress test results
-Blood pressure, ECG, and heart rate
-Gas exchange results
-Information from your medical chart such as current medications.
-Height, weight, and body mass index
-Age
-Blood glucose, insulin, nonesterified fatty acids, Hba1c and lactate

If this research study involves the diagnosis or treatment of a medical condition, then Protected Health Information collected from you during this study may be placed in your medical record, and may be used to help treat you, arrange payment for your care, or assist with Medical Center operations.

We will make every effort to keep your Protected Health Information private. We will store records of your Protected Health Information in a cabinet in a locked office or on a password protected computer.

Your personal health information and information that identifies you (“your health information”)

may be given to others during and after the study. This is for reasons such as to carry out the study, to determine the results of the study, to make sure the study is being done correctly, to provide required reports and to get approval for new products.

Some of the people, agencies and businesses that may receive and use your health information are the research sponsor; representatives of the sponsor assisting with the research; investigators at other sites who are assisting with the research; central laboratories, reading centers or analysis centers; the Institutional Review Board; representatives of Wake Forest University Health Sciences and North Carolina Baptist Hospital; representatives from government agencies such as the Food and Drug Administration (FDA), the Department of Health and Human Services (DHHS) and similar agencies in other countries.

Some of these people, agencies and businesses may further disclose your health information. If disclosed by them, your health information may no longer be covered by federal or state privacy regulations. Your health information may be disclosed if required by law. Your health information may be used to create information that does not directly identify you. This information may be used by other researchers. You will not be directly identified in any publication or presentation that may result from this study unless there are photographs or recorded media which are identifiable.

If required by law or court order, we might also have to share your Protected Health Information with a judge, law enforcement officer, government agencies, or others. If your Protected Health Information is shared with any of these groups it may no longer be protected by federal or state privacy rules.

Any Protected Health Information collected from you in this study will be kept in the research records and will be kept for at least six years after the study is finished. At that time any research information not already in your medical record will either be destroyed or it will be de-identified. You will not be able to obtain a copy of your Protected Health Information in the research records until all activities in the study are completely finished.

You can tell Gary Miller, PhD that you want to take away your permission to use and share your Protected Health Information at any time by sending a letter to this address:

Gary Miller, PhD
[redacted]

However, if you take away permission to use your Protected Health Information you will not be able to be in the study any longer. We will stop collecting any more information about you, but any information we have already collected can still be used for the purposes of the research study.

By signing this form you give us permission to use your Protected Health Information for this

study.

The data for this study will be kept private and confidential to the extent allowed by federal and state law.

WHAT ARE MY RIGHTS AS A RESEARCH STUDY PARTICIPANT?

Your participation in this study is completely voluntary. You may choose not to take part in this study, choose not to answer specific questions, or leave the study at any time. There will be no penalty or loss of benefits to which you are entitled if you choose not to give your permission to take part or you withdraw from the study.

You will be given any new information we become aware of that would affect your willingness to continue to participate in the study.

Information that identifies you may be removed from the data or specimens that are collected as part of this study and could be used for future research or shared with other without additional consent.

WHO CAN I TALK TO IF I HAVE QUESTIONS?

For questions about the study or in the event of a research-related injury, contact the study investigator, Dr. Gary Miller at [redacted] or [redacted]

The Institutional Review Board (IRB) is a group of people who review the research to protect your rights. If you have a question about your rights as a research participant, or you would like to discuss problems or concerns, have questions or want to offer input, or you want to obtain additional information, you should contact the Chairman of the IRB at [redacted].

You will be given a copy of this signed consent form.

SIGNATURES

I agree to take part in this study. I authorize the use and disclosure of my health information as described in this consent and authorization form. If I have not already received a copy of the Privacy Notice, I may request one or one will be made available to me. I have had a chance to ask questions about being in this study and have those questions answered. By signing this consent and authorization form, I am not releasing or agreeing to release the investigator, the sponsor, the institution or its agents from liability for negligence.

Subject Name (Printed):_____

Subject Signature: _____ Date: _____Time:_____ am pm

Person Obtaining Consent (Printed):_____

Person Obtaining Consent:_____ Date:_____ Time:_____ am pm