Exercise-stimulated Muscle Glucose Uptake in Upper Body Obesity

NCT04532814

May 23, 2024

MAYO CLINIC

Name and Clinic Number

Approval Date: **May 23, 2024**
Not to be used after: **May 22, 2025**

RESEARCH PARTICIPANT CONSENT AND PRIVACY AUTHORIZATION FORM

Study Title: Exercise-stimulated muscle glucose uptake in upper body obesity

IRB#: 20-002949

Principal Investigator: Dr. Michael D. Jensen and Colleagues

Key Study Information

This section provides a brief summary of the study. It is important for you to understand why the research is being done and what it will involve before you decide. **Please take the time to read the entire consent form carefully and talk to a member of the research team before making your decision.** You should not sign this form if you have any questions that have not been answered.	
It's Your Choice	This is a research study. Being in this research study is your choice; you do not have to participate. If you decide to join, you can still stop at any time. You should only participate if you want to do so. You will not lose any services, benefits or rights you would normally have if you choose not to take part.
Research Purpose	The purpose of this research is to compare insulin resistance in closely matched upper body obese and normal weight, sedentary participants. You have been asked to take part in this research because you are 18-55 years of age and are likely to have muscle metabolism characteristics that will help us learn more about diabetes-related conditions.
What's Involved	Study participation involves a screening visit where we will review the informed consent, perform a DEXA scan to measure body fat, a CT scan of your abdomen, draw a screening blood sample and have you participate in a bicycle exercise test. If the test results show you are eligible for the study we will ask you to be admitted to the hospital for an overnight stay, followed the next morning by a study that includes an intravenous infusion of insulin and glucose. If the results of this study show you are still eligible to participate you will be asked to take part in two additional exercise studies. One study will be an

	outpatient visit with a high intensity, intermittent bicycle exercise bout to use up the sugar in your muscles. Following this exercise test you will be required to eat a low carbohydrate diet from the CRTU kitchen for two days and then return for the second exercise study. This exercise study will be done following an inpatient overnight visit and will include two muscle biopsies and blood sampling.
Key Information	The risks associated with taking part in this study are completely described later in this form, be sure to review them carefully. You will be carefully monitored throughout this study for side effects which may affect your willingness to participate. The most important side effects for you to be aware of if you are in this study are the risk of hypoglycemia or low blood sugar and pain from the muscle biopsies. Our study is for research purposes and will not improve your health. The tests and procedures in this study that are performed for research are paid by the study. However, you and/or your insurance will need to pay for all other tests and procedures that you would have as part of your clinical care, including co-payments and deductibles.
Learn More	If you are interested in learning more about this study, read the rest of this form carefully. The information in this form will help you decide if you want to participate in this research or not. A member of our research team will talk with you about taking part in this study before you sign this form. If you have questions at any time, please ask us.

Making Your Decision

Taking part in research is your decision. Take your time to decide. Feel free to discuss the study with your family, friends, and healthcare provider before you make your decision. Taking part in this study is completely voluntary and you do not have to participate.

If you decide to take part in this research study, you will sign this consent form to show that you want to take part. We will give you either a printed or electronic copy of this form to keep. A copy of this form will be put in your medical record.

For purposes of this form, Mayo Clinic refers to Mayo Clinic in Arizona, Florida and Rochester, Minnesota; Mayo Clinic Health System; and all owned and affiliated clinics, hospitals, and entities.

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Contact Information

If you have questions about …	You can contact …
▪ Study tests and procedures ▪ Materials you receive ▪ Research-related appointments ▪ Research-related concern or complaint ▪ Research-related injuries or emergencies ▪ Withdrawing from the research study	**Principal Investigator:** Dr. Michael D. Jensen **Phone:** (507) 255-6515 **Study Team Contact:** Pamela Reich **Phone:** (507) 255-6062 **Institution Name and Address:** Mayo Clinic Department of Endocrinology Endocrine Research Unit Joseph 5-194 200 First St SW Rochester, MN 55905
▪ Rights of a research participant	**Mayo Clinic Institutional Review Board (IRB)** **Phone:** (507) 266-4000 **Toll-Free:** (866) 273-4681
▪ Rights of a research participant ▪ Any research-related concern or complaint ▪ Use of your Protected Health Information ▪ Stopping your authorization to use your Protected Health Information ▪ Withdrawing from the research study	**Research Participant Advocate (RPA)** **(The RPA is independent of the Study Team)** **Phone:** (507) 266-9372 **Toll-Free:** (866) 273-4681 **E-mail:** researchparticipantadvocate@mayo.edu
▪ Billing or insurance related to this research study	**Patient Account Services** **Toll-Free:** (844) 217-9591

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

Why are you being asked to take part in this research study?

You are being asked to take part in this research study because you are between 18-55 years of age and because you are likely to have muscle metabolism characteristics that will help us learn more about diabetes-related conditions.

Why is this research study being done?

Adults who gain most of their excess weight in the abdominal area typically do not process sugar (glucose) normally in their muscle in response to insulin, especially compared to lean adults. We know that some of this is due to differences in how fat cells release fat molecules into the bloodstream, which in turn affects muscle metabolism. We don't know whether fat molecules in the bloodstream are handled differently by those with abdominal fat gain compared with lean adults. By measuring how muscle handles fat molecules in the bloodstream and how that relates to the ability of insulin and exercise to help the muscle use glucose, we will help understand the interaction between fat cells and muscle as it relates to diabetes-related diseases.

Information you should know

Who is Funding the Study?
The National Institutes of Health/National Institute of Diabetes and Digestive and Kidney Diseases, is funding the study and will pay your study doctor or the institution to cover costs related to the study.

Information Regarding Conflict of Interest:
Your healthcare provider may be referring you to this research study. If your healthcare provider is also an investigator on this study, there is the chance that his or her responsibilities for the study could influence his or her recommendation for your participation. If you prefer, your healthcare provider will be happy to refer you to another investigator on the research study team for you to decide if you want to participate in the study and to see you for the research study activities while you are in the study.

How long will you be in this research study?

You will be in this study for a screening visit and up to three study visits if you qualify to continue on with the study. There will be two overnight visits in the Clinical Research and Trials Unit (CRTU) at Saint Marys Hospital. The total duration of study participation from screening to final study visit may last anywhere between 2-8 weeks.

What will happen to you while you are in this research study?

If you agree to be in the study, you will be asked to participate in the following:

All of the tests and procedures will be performed unless you have performed similar testing/procedures recently. The investigator will determine if these tests and/or procedures need to be repeated.

For both the Screen Day and the Study Days, you will report to the Clinical Research and Trials Unit (CRTU), located on the 5th floor of Domitilla building, St. Marys Hospital. The Screen Day and the first Study Day activities may occur on the same day. If you are a female of child bearing potential you will need to have a negative pregnancy test prior to both the screen and study days.

Visit 1: Screen Day (about 3 hrs):
When you arrive at the CRTU, after fasting for 12 hours, you will review the informed consent. When all of your questions have been answered and if you agree to participate, you will sign this form, and complete the following tests and procedures:

- Your height, weight, blood pressure and heart rate will be measured.
- You will have blood drawn from your arm to determine your fasting glucose and lipid profile.
- You will have a body composition (DEXA) scan where you will lie on a table, fully clothed, while a machine moves over your body. This test takes 20-30 minutes. The machine uses a small amount of x-rays to measure how much fat and muscle you have. You will also meet with a registered dietician to discuss the types of meals you will need to consume prior to the overnight stay.
- Later that day or on a separate visit, your maximal physical exertion level will be examined by measuring how much oxygen your body can use during an exercise bout on a stationary bicycle. The exercise bout involves gradually increasing how much effort

you need to pedal the bicycle until you are peddling as hard as you can. During this test, a clip will be placed on your nose and you will breathe through a mouthpiece.
Also, during this exercise bout, your heart rate and blood pressure will be monitored closely. To do this, you will have blood pressure measurement using a cuff placed around your upper arm and periodically inflated. You will also have an EKG.

- A single x-ray picture of your abdomen will be taken using a CT scan. For this test you will lie on a table which will be passed through a large, open circular tube.
- If these results indicate you are eligible for the study the next step is an inpatient study visit.

Visit 2: Insulin Clamp (overnight stay): You will be given 3 days of meals from the metabolic kitchen for 3 days prior to this visit. You will report in the late afternoon/early evening to the Clinical Research and Trials Unit at Mayo Clinic Hospital – Rochester, Saint Marys Campus where you will be provided an evening meal. That evening, one IV catheter (plastic tube) will be placed in a large arm vein for infusions of salt water.

The following morning, another intravenous catheter (plastic tube) will be placed in a vein in your hand. Your hand will be placed in a large clear box with warm air keeping the hand warm.

You will receive an intravenous infusion of a small amount labeled, stable (nonradioactive) fat and glucose (sugar) molecules to allow us to measure how your body releases and takes up fat and sugar.

You will receive an intravenous infusion of insulin (a hormone that is normally present in the body) for two hours through a vein catheter in your arm. It is used in this study to keep the amount of insulin in your blood at a certain level. Additional sugar solution will be given to keep your blood sugar levels in a normal range (goal 90-95 mg/dL).

You will remain in bed throughout the study day, but will be instructed to move your legs at 15-minute intervals to avoid complete immobility. You may get up to use a bedside commode or use a urinal. Blood samples will be drawn throughout this visit. No more than 450 mL of blood will be taken during the entire study, including all study days. We will measure the rate at which your body burns calories while you are laying still, also known as indirect calorimetry. During this procedure, a clear plastic hood with air holes in it will be placed over your head. You will be able to breathe fresh air through this hood. This will be done for 20 continuous minutes and will be done twice.

You will be offered something to eat before you leave. Depending upon the results of this measurement you will be invited to participate in the subsequent study visits.

Study Visit 3 (outpatient visit, approximately 2.5 hours): You will participate in a high intensity bicycle exercise bout designed to reduce the amount of sugar in your muscles.

After this exercise study visit, you will be fed a very low carbohydrate (sugar) diet from the Clinical Research and Trials Unit for one or two days to prevent sugar from increasing in your muscles before the second exercise visit. During these one or two days of low carbohydrate diet, we will provide all materials to test your urine twice a day during a video call visit with our research staff. This will ensure that the amount of carbohydrate you are eating is correct.

You will need to stop taking any aspirin or ibuprofen from three days before to three days after the next overnight stay.

Study Visit 4 (overnight stay): You will be asked to report in the late afternoon/early evening to the Clinical Research and Trials Unit at Mayo Clinic Hospital – Rochester, Saint Marys Campus where you will be provided an evening meal. That evening, one IV catheter (plastic tube) will be placed in a large arm vein for infusions of saline.

You will be transferred to the Department of Radiology where a catheter (a small plastic tube placed in a blood vessel) will be placed in an artery in your arm to measure blood pressure and draw some blood. You will receive a local anesthetic (numbing medicine) prior to insertion of the catheter to minimize discomfort. Also, catheters (a small plastic tube placed in a blood vessel) will be placed in an artery and a vein in your leg. You will receive a local anesthetic (numbing medicine) prior to insertion of the catheter to minimize discomfort. You will then be transferred back to the CRTU. Blood will be withdrawn from these catheters or blood pressure measured. You will receive an intravenous infusion of a small amount labeled, stable (nonradioactive) fat and glucose (sugar) molecules to allow us to measure how your body releases and takes up fat and sugar. Also, a green dye (indocyanine green) will be infused into the catheter in the leg artery for measurement of leg blood flow. This compound is commonly used to measure blood flow in people.

An abdominal fat and a muscle biopsy of your thigh will be taken before and after exercise. During this exercise study we may need to give you sugar water through the catheter in your arm vein to keep your blood sugar normal.

During this study you will be asked not to engage in strenuous activity (exercise) for 24 hours prior to each of the visits.

What are the possible risks or discomforts from being in this research study?

As with all research, there is a chance that confidentiality could be compromised; however, we take precautions to minimize this risk.

- DEXA Scan, CT scan, X-ray: You will be exposed to a small amount of radiation in this research study. The amount of radiation you will receive has a low risk of harmful effects.
- Insertion of small catheters (plastic needles) into arteries and veins: The most common complications of inserting a small catheter in the arm and leg is a bruise and pain at the site of catheter placement which may last up to 3 weeks after removal of the catheter. Occasionally, you may experience nausea and dizziness during the procedure, and a tingling and/or pain in your hand, which usually goes away in two weeks. The most serious complication of these procedures is a decrease in blood flow to the forearm and hand caused by a clot or spasm of the artery. The chances of this occurring are less than 1 in 4,000, and a variety of treatments will be available in the unlikely event that this should occur. In the unlikely event of a major complication we would obtain an immediate (less than15 minutes) vascular surgery consultation for treatment. There is an extremely rare, but reported risk of embolism (blood clot or air) that can be introduced from the arterial line which can cause neurologic or arm problems.
- Fat and Muscle biopsy: The most common risks of a muscle biopsy include pain and muscle cramping. Discomfort from the muscle biopsy is very common and may last from 2 days to 2 weeks or longer. The most common risk of fat biopsy includes pain, a small dent and bruising at the site of the biopsy. The bruising is very common and may last one to two weeks. Less common risks of both muscle and fat biopsies include bleeding, infection, a small scar, and numbness of the skin around the site of the biopsy. The chance of these risks is less than 1% (1 in 100). Care will be taken to reduce the chance of these risks. There is also a chance that you may have an allergic reaction to the lidocaine used for local anesthesia.
- Withdrawal of blood from the arterial catheter: There is no known risk associated with drawing 450 cc of blood from a healthy person.
- Heart rate and blood pressure monitoring: There are no known risks associated with heart rate, oxygen saturation, and breathing monitoring.
- Insulin infusion: You will be closely monitored for any adverse reactions related to low blood sugar (hypoglycemia) and if symptomatic, the study will be promptly stopped and you will be appropriately treated. The glucose levels proposed are within safe limits. Side effects include: confusion, nausea, hunger, tiredness, perspiration, headache, heart

palpitations, numbness around the mouth, tingling in the fingers, tremors, muscle weakness, blurred vision, cold temperature, excessive yawning, irritability, and loss of consciousness. A study doctor will be available at all times during the study. You will be frequently monitored and glucose infused to keep blood sugar within normal levels.

- Exercise: The risks associated with vigorous exercise include abnormal heartbeats, shortness of breath, nausea, dizziness and in very rare circumstances heart attack, stroke, or death.
- Blood draw: The risks of drawing blood include pain, bruising or in rare cases infection at the site of the needle stick
- Venous catheterization (IV): Placement of a venous catheter involves the risk of infection, bruising, blood clots, or vessel perforation. The risks from this procedure are very small and are reduced by use of trained personnel.
- Indocyanine green infusion: if you are allergic to iodine you may have a severe allergic reaction to indocyanine green; you should not participate in this study if you are allergic to iodine or iodine containing compounds.

Are there reasons you might leave this research study early?

You may decide to stop at any time. You should tell the Principal Investigator if you decide to stop and you will be advised whether any additional tests may need to be done for your safety.

In addition, the Principal Investigator or Mayo Clinic may stop you from taking part in this study at any time:

- if it is in your best interest,
- if you don't follow the study procedures,
- if the study is stopped.

If you leave this research study early, or are withdrawn from the study, no more information about you will be collected; however, information already collected about you in the study may continue to be used.

We will tell you about any new information that may affect your willingness to stay in the research study.

What if you are injured from your participation in this research study?

Where to get help
If you think you have suffered a research-related injury, you should promptly notify the Principal Investigator listed in the Contact Information at the beginning of this form. Mayo Clinic will offer care for research-related injuries, including first aid, emergency treatment and follow-up care as needed.

Who will pay for the treatment of research related injuries?
Care for such research-related injuries will be billed in the ordinary manner, to you or your insurance. Treatment costs for research-related injuries not covered by your insurance will be paid by Mayo Clinic.

What are the possible benefits from being in this research study?

You won't benefit from taking part in this research study. It is for the benefit of research.

What alternative do you have if you choose not to participate in this research study?

This study is only being done to gather information. You may choose not to take part in this study.

What tests or procedures will you need to pay for if you take part in this research study?

You won't need to pay for tests and procedures which are done just for this research study.

These tests and procedures are:

- DEXA scan
- CT scan
- Exercise testing
- Catheter insertions
- Breathing tests
- Blood draws
- Muscle/fat biopsies
- Overnight hospital stays
- Urine testing
- Insulin
- Pregnancy test, as required

However, you and/or your insurance will need to pay for all other tests and procedures that you would have as part of your clinical care, including co-payments and deductibles.

If you have billing or insurance questions call Patient Account Services at the telephone number provided in the Contact Information section of this form.

Will you be paid for taking part in this research study?

You will receive $ 50 for the screening visit, $ 250 for the inpatient visit, $300 for the outpatient exercise visit and $700 for the inpatient overnight exercise visit. If you are able to complete the entire study, you will receive up to $1300.

Payment for participation in research is considered taxable income and reportable to the Internal Revenue Service (IRS). Accounts Payable at Mayo Clinic will be given your name, address and Social Security number in order to issue a check for your study participation. If you receive research payments totaling $600 or more in a calendar year, a tax Form 1099 will be sent to you. For Mayo Clinic employees, research payments are included in your paycheck with applicable taxes withheld and reported on your Form W2 after calendar year-end.

Will your information or samples be used for future research?

Unless you give your permission below, your information or samples collected for this study will not be used or shared for future research, even if the identifiable information such as your name, Mayo Clinic number or date of birth is removed.

We would like to keep your information and samples for future research. You can still take part in this current study even if you don't want your information or samples used for future research.

Researchers at Mayo Clinic who aren't involved with this study may ask to use your information and/or samples for future research. Researchers at other institutions may also ask for a part of your information and/or samples for future studies. Unless you indicate otherwise, the future research may be on any topic. No direct benefits to you are expected from the future research. Your information and/or samples will only be shared consistent with your consent, and with all applicable laws and regulations.

If you approve release of your information and/or samples by checking 'yes' below, Mayo may send the information and/or samples to researchers who request them, but Mayo will not send your name, address, phone number, social security number, or any other identifying information with the information and/or samples. Your information and/or samples may be sent with a code, and only the researchers for this study at Mayo Clinic would be able to link the code to you.

Some future studies may examine your DNA, the genetic information you inherited from your parents (genetic testing). If there are findings which may be useful for your health care, the researchers may contact Mayo Clinic, so Mayo Clinic can give you the option of learning the results. You would be given general information on the potential risks, benefits, and costs of choosing to learn about the findings.

To support future research, de-identified genetic information may be placed in databases accessible by the internet. Some of the information may be available to anyone using the internet, and some will be released only to approved researchers. Combined study information (including genomic summary results) may be published, but the information will not identify you.

Even though information traditionally used to identify you will not be shared, people may develop ways in the future to allow someone to link your genetic information back to you. For this reason, confidentiality cannot be guaranteed.

It is also possible that reidentified information could be used in discriminating ways, and there could be additional unknown risks. We will make every effort to protect your confidentiality.

Please read the following statements and mark your choices:

1. I permit my information and samples to be stored and used in future research of muscle metabolism at Mayo Clinic:

☐ Yes ☐ No Please initial here: _____Date: _____

2. I permit my information and samples to be stored and used in future research at Mayo Clinic to learn about, prevent, or treat any other health problems:

☐ Yes ☐ No Please initial here: _____Date: _____

3. I permit Mayo Clinic to give my information and samples to researchers at other institutions:

☐ Yes ☐ No Please initial here: _____Date: _____

You may withdraw your consent for future use of your information and/or samples at any time, by writing to the Principal Investigator at the address provided in the "Contact Information" section of this consent form.

Your information and/or samples would be removed from any repository where they are stored, if possible. Information and/or samples already distributed for research use will not be retrieved.

How will your privacy and the confidentiality of your records be protected?

Mayo Clinic is committed to protecting the confidentiality of information obtained about you in connection with this research study. All data generated by your study visits will be coded and de-identified. All hard copy data will be kept in secure locked file cabinet which will only be accessible by authorized study staff. All electronic data will be password protected and only accessible by authorized study staff. If some information is reported in published medical journals or scientific discussions, it will be done in a way that does not directly identify you. If the results of the research are made public, information that identifies you will not be used.

During this research, information about your health will be collected. Under Federal law called the Privacy Rule, health information is private. However, there are exceptions to this rule, and you should know who may be able to see, use and share your health information for research and why they may need to do so. Information about you and your health cannot be used in this research study without your written permission. If you sign this form, it will provide that permission (or "authorization") to Mayo Clinic.

Your health information may be collected from:

- Past, present and future medical records.
- Research procedures, including research office visits, tests, interviews and questionnaires.

Your health information will be used and/or given to others to:

- Do the research.
- Report the results.
- See if the research was conducted following the approved study plan, and applicable rules and regulations.

Your health information may be used and shared with:

- Mayo Clinic research staff involved in this study.
- Other Mayo Clinic staff involved in your clinical care.
- The Mayo Clinic Institutional Review Board that oversees the research.
- Federal and State agencies (such as the Food and Drug Administration, the Department of Health and Human Services, the National Institutes of Health and other United States agencies) or government agencies in other countries that oversee or review research.

How your information may be shared with others:

While taking part in this study, you will be assigned a code that is unique to you, but does not include information that directly identifies you. This code will be used if your study information is sent outside of Mayo Clinic. The groups or individuals who receive your coded information will use it only for the purposes described in this consent form.

If the results of this study are made public (for example, through scientific meetings, reports or media) information that identifies you will not be used.

In addition, individuals involved in study oversight and <u>not</u> employed by Mayo Clinic may be allowed to review your health information included in past, present, and future medical and/or research records. This review may be done on-site at Mayo Clinic or remotely (from an off-site location). These records contain information that directly identifies you.

However, the individuals will not be allowed to record, print, or copy (using paper, digital, photographic or other methods), or remove your identifying information from Mayo Clinic.

Is your health information protected after it has been shared with others?

Mayo Clinic asks anyone who receives your health information from us to protect your privacy; however, once your information is shared outside Mayo Clinic, we cannot promise that it will remain private and it may no longer be protected by the Privacy Rule.

Your Rights and Permissions

Participation in this study is completely voluntary. You have the right not to participate at all. Even if you decide to be part of the study now, you may change your mind and stop at any time. You do not have to sign this form, but if you do not, you cannot take part in this research study.

Deciding not to participate or choosing to leave the study will not result in any penalty. Saying 'no' will not harm your relationship with your own doctors or with Mayo Clinic.

If you cancel your permission for Mayo Clinic to use or share your health information, your participation in this study will end and no more information about you will be collected; however, information already collected about you in the study may continue to be used.
You can cancel your permission for Mayo Clinic to use or share your health information at any time by sending a letter to the address below:

Mayo Clinic
Office for Human Research Protection
ATTN: Notice of Revocation of Authorization
200 1st Street SW
Plummer Building, PL 3-02
Rochester, MN 55905

Alternatively, you may cancel your permission by emailing the Mayo Clinic Research Participant Advocate at: researchparticipantadvocate@mayo.edu.

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Please be sure to include in your letter or email:

- The name of the Principal Investigator,
- The study IRB number and /or study name, and
- Your contact information.

Your permission for Mayo Clinic to use and share your health information lasts until the end of this study, unless you cancel it. The study does not end until all data has been collected, checked (or audited), analyzed, and reported. Because research is an ongoing process, we cannot give you an exact date when the study will end. Sometimes this can be years after your study visits and/or activities have ended.

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Enrollment and Permission Signatures

Your signature documents your permission to take part in this research.

	/ /	: AM/PM
Printed Name	Date	Time

Signature

Person Obtaining Consent

- I have explained the research study to the participant.
- I have answered all questions about this research study to the best of my ability.

	/ /	: AM/PM
Printed Name	Date	Time

Signature