NCT04664205

University of North Carolina at Chapel Hill
Consent to Participate in a Research Study
Adult Participants

Consent Form Version Date: 09/17/21
IRB Study # 20-3100
Title of Study: Metabolic, Hormonal, and Physiological Characterization of Isoenergetic High Intensity Interval Training and Moderate Intensity Continuous Training in Adults with Type I Diabetes
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Funding Source and/or Sponsor: North Carolina Diabetes Research Center (NCDRC)

CONCISE SUMMARY

The purpose of this study is to understand how changing the intensity of exercise effects metabolism, hormones, and glucose control immediately after the 48 hours after.

Participation in this study will involve 4 in-person visits, separated by at least 7 days. These visits will require a total of 6-7.5 hours, over about 5 weeks. Measures of your body composition and fitness level will be measured during your first visit. Following this baseline testing, you will be asked to participate in 2 different types of exercise and one control session; during these sessions you will be asked to participate in high intensity exercise (HIIT), more moderate intensity continuous exercise (MICT), or no exercise (control). This exercise will be based on your fitness level; you will be asked to wear a mouthpiece for the beginning and end of the exercise. Additionally, a small amount of blood (~1.5 teaspoons) will be drawn prior to the exercise, immediately after, and 1-hr after the exercise to measure changes in your blood as it relates to fat and protein us. The control visit will consist of two blood draws, one when you arrive and one an hour later.

Throughout the study, you will be asked to wear a continue glucose monitoring device and a wrist-watch fitness tracker throughout the study to allow us to monitor your glucose levels and your usual physical activity. You will also be asked to keep track of what you eat for 3 days, with 1 of those days occurring the day prior to your exercise visit; this will help us to understand the influence of what you eat on the results.

During this study, you may experience a hypo- or hyperglycemic event due to the exercise, particularly in a fasted state. These exercise sessions will occur in the morning; you will be encouraged to manage these events as you typically would. The study team will also help you to manage the even. Additional risks involved include muscle soreness related to exercise, minor

bruising from the blood draw, and low-dose radiation from a single DXA scan. There are no direct benefits from participating, but you will receive information about your body composition, fitness level, and health.

Your participation in this study will help us to better understand the impact of varied intensity of exercise on metabolism and glucose control. If you are interested in learning more about this study, please continue to read below.

What are some general things you should know about research studies?

You are being asked to take part in a research study. To join the study is voluntary. You may choose not to participate, or you may withdraw your consent to be in the study, for any reason, without penalty.

Research studies are designed to obtain new knowledge. This new information may help people in the future. You may not receive any direct benefit from being in the research study. There also may be risks to being in research studies. Deciding not to be in the study or leaving the study before it is done will not affect your relationship with the researcher, your health care provider, or the University of North Carolina-Chapel Hill. If you are a patient with an illness, you do not have to be in the research study in order to receive health care.

Details about this study are discussed below. It is important that you understand this information so that you can make an informed choice about being in this research study. You will be given a copy of this consent form. You should ask the researchers named above, or staff members who may assist them, any questions you have about this study at any time.

What is the purpose of this study?

The primary purpose of this study is to compare the metabolic responses immediately and 1 hr after one bout of HIIT compared to MICT matched for total energy expenditure, vs no exercise (control; CON) in adults with type1 diabetes (T1D).

You are being asked to be in the study because you are a man or woman with type 1 diabetes for at least one year, a HbA1c <9%, are 18-51 years old, and have a BMI < 30 kg/m^2.

Are there any reasons you should not be in this study?

You should not be in this study if you have:

- Physician diagnosis of active diabetic retinopathy that could be worsened by exercise
- Physician diagnosis of peripheral neuropathy with numb feet
- Physician diagnosis of autonomic neuropathy

- Medications: beta-blockers, agents that affect hepatic glucose production such as beta-adrenergic agonists, xanthine derivatives; any hypoglycemic agent other than insulin.
- Severe hypoglycemic event defined as the individual requiring a third party of hospitalization in the last 6 months
- Diabetic ketoacidosis in the last 6 months
- Have a closed-loop pump and are not willing to use manual mode during exercise and 48 hours afterward
- Physician diagnosis of cardiovascular disease that would affect exercise tolerance
- Currently doing HIIT
- Severely impaired hearing or speech
- Are pregnant

How many people will take part in this study?

Approximately 14 people will take part in this study.

How long will your part in this study last?

If you enroll in this study, your participation will involve 4 in-person visits. These visits will amount to 6-7.5 hours.

The study last approximately up to 5 weeks:

- 1 screening and enrollment phone call (45 minutes)
- 1 baseline visit (45 minutes)
- 3 treatment visits (90-120 minutes each)

Participant Responsibilities:

While participating in this research study, you will need to:

- Be willing and able to follow the study directions and procedures
- Tell study staff about any side effects or problems
- Ask questions as you think of them
- Tell the investigator or the study staff if you change your mind about staying in the study

What will happen if you take part in the study?

All visits will take place in the Applied Physiology Lab located in Fetzer Hall (room 25) on UNC's main campus.

Screening and Enrollment Phone Call: ~45 minutes

You will complete a phone screening to determine your eligibility, answer any questions that you have, and obtain a verbal commitment to the study. Following this call you will be sent an electronic link to complete a written consent acknowledging your participation (this document) and a link to complete about your medical health history specific to your diabetes history, current diabetes management, other past, and current medial problems. We will also ask that you write down your most recent HbA1c will be recorded (taken within the previous 3 months). Upon

completion of this information, your health history will be reviewed by the study team study team; approval for your participation will be confirmed by communication with your personal physician or endocrinologist. Upon clearance from your physician, we will reach out to you to schedule your baseline testing.

Visit 1- Baseline Testing: ~45 minutes

You will be asked to arrive to the laboratory after an overnight fast (8 hr) and your usual dose of insulin administered the day prior, with no morning mealtime insulin the day of testing. Your height and weight will be recorded to obtain body mass index. Free parking will be provided for all testing and training visits in the Stallings Evans Parking lot located behind Fetzer Hall. If you are female, you will be asked to provide a urine pregnancy test prior to any testing.

1. **Body composition** (~15-20 minutes): We will measure your body fat, muscle, body water, and bone density as described below.
    - *Dual-energy X-ray Absorptiometry (DXA)* (10-15 min): Your body composition (amount of fat and muscle tissues, density of your bones) will be measured from a total body scan. For this test you will be asked to remove all metal and jewelry, and then will be asked to lie on your back on a table. During this test you will be exposed to a small amount of radiation. This amount of radiation is similar to the amount of radiation that you would receive from flying here to California.

    - *Bioelectrical Impedance Spectroscopy* (1 min): This test will determine your total body water. You will be asked to remove your socks and shoes and stand on a device while grasping hold of metal electrodes. A harmless electrical current, which you cannot feel, will then be conducted through the body.

2. **Cardiorespiratory fitness** (20-30 min): You will complete an exercise test on a stationary bike. You will be fitted with a mouthpiece and nose clip to help measure how much air you breathe out during the test. You will be asked to pedal until you feel like you can no longer continue. The test will start at an easy intensity, and the intensity will increase as the test goes on. To ensure your safety, we will monitor your heart rate and breathing rate continuously throughout the exercise test and for several minutes after the test has concluded. At the conclusion of the test, you will be allowed to cool down, stretch, and drink water as needed. This test will allow us to identify your fitness level and heart rate.
3. **Familiarization and Randomization** (10-15 min): After you have some brief rest from the exercise test, we will have you practice the interval exercise. We will have you practice a few intervals and cycle a few minutes at the individualized intensity for each respective exercise. You will also be asked, and provided with instructions, to practice one session (HIIT or MICT) on your own at home, under a usual fed state, prior to your visit to the lab. Each practice session will occur with CGM and wrist-watch activity monitoring.

Visit 2-4: Exercise Order *(~90 minutes to 120 minutes)*

You will be asked to complete 2 exercise sessions, and one control (no exercise) visit. The order of these visits will be randomize (like rolling a dice). Procedures will be the same for both exercise visits; the control visit will be slightly different, as there will be no exercise. There will be a minimum of seven days between each exercise trial.

1. **Continuous Glucose Monitoring (CGM)**: You will be given the option to monitor your interstitial glucose levels via your own CGM or through a Freestyle Libre Pro (Abbot Laboratories), which will be provided to you. In the case you decide to use your own CGM, the researchers will ask for you to share your data only for the dates you are involved in the study. If you decide to use the Freestyle Libre Pro, the sensor will be inserted subcutaneously on your upper arm 7 days before exercise for a period of up to 7 days post exercise. The results of CGM are for research purposes and will not be used for treatment purposes. You will continue treatment based on your physician's advice.

2. **Dietary Controls:** You will be asked to record your food intake on the three days, with at least one day occurring the 24 hrs prior to the exercise (HIIT, MICT, CON). You will be asked to consume a similar meal the evening prior to each exercise session. After the exercise session, you will receive a telephone call to ask you to report the food that you consumed in the 24 hrs following the exercise.

3. **Physical Activity:** You will be asked to wear a wrist-watch physical activity monitor (Garmin Vivosmart 4) for 7 days before exercise and up to 7 days post exercise in conjunction to measure your typical daily levels of physical activity.

4. **Blood Collection** (~5 minutes)**:** An individual trained in phlebotomy will collect approximately ~ 1.5 teaspoons of your blood upon arrival, immediately after exercise, and one-hour post exercise. For the control visit, a blood sample will be taken at baseline and 1 hour later. Blood will be collected to understand metabolism of fats and proteins, as well as for concentration of cortisol, glucagon, and insulin. Blood samples will be destroyed within two years of the analysis.

5. **Saliva Collection (females only)** (~5 minutes)**:** Estrogen concentrations will be determined using a small saliva sample. You will be asked to avoid brushing your teeth for 45 minutes prior and undergoing dental work for 48 hours prior to sample collection to avoid blood contamination. You will be asked to passive drool into a small straw to collect < ¼ of teaspoon of saliva.

6. **Exercise Details:** (~20- 30 minutes)
   During both exercise sessions, you will be asked to wear a mouthpiece (the same as worn during the exercise test) during the first and last 3 minutes of the exercise session. This will allow us to determine how much oxygen and carbon dioxide you breathe in and expire.

- HIIT Exercise (20 minutes): You be asked to warm up for 2 min at a self-selected intensity, followed by 10 alternating sets of one minute of pedaling hard at a resistance corresponding to 90% of your personal max exercise and one-minute of pedaling slowly at 50 watts (W). Heart rate and finger stick capillary glucose will be tracked throughout the duration of the exercise.
- MICT Exercise: You will be asked to cycle continuously at a workload corresponding to 65% VO_2peak (W) for ~20-30 minutes. Heart rate and finger stick capillary glucose will be tracked throughout the duration of the exercise.
- CON – No Exercise: No exercise will be performed. You will arrive to the lab following the same pre-testing guidelines as the exercise sessions. You will be asked to sit for about 60 minutes.

What are the possible benefits from being in this study?
Research is designed to benefit society by gaining new knowledge. There is little chance you will benefit from being in this research study. You will receive information about your body composition and your fitness level.

What are the possible risks or discomforts involved from being in this study?
You may experience a hypo- or hyperglycemic event due to the exercise, particularly in a fasted state. These exercise sessions will occur in the morning; you will be encouraged to manage these events as you typically would. The study team will also help you to manage the event. If low blood glucose occurs during a study visit (< 70 mg/dL), study personnel will be trained to administer 15 grams of an oral carbohydrate, and to repeat as needed every 10 minutes until the blood glucose level is > 70 mg/dL. If the blood glucose level is above 300 mg/dL during a study visit, study personnel will be trained to check for urinary ketones. After the exercise session, subjects will be instructed to take their usual dose of insulin or other diabetes medication as prescribed. If participants experience hypoglycemia or hyperglycemia outside of study visits, they will be advised to treat these situations per their usual diabetes care plan.

With any exercise, there is a small risk for syncope, as well as a cardiovascular event (rare; <1%). Because of the short nature of the high intensity bouts, risk of syncope is reduced; rest periods also allow for greater blood flow, reducing risk of syncope. To reduce the risk of a cardiovascular event, all exercise testing will be preceded by a medical history review and physician clearance. Additionally, there are 3 trained research personnel that will always be present during maximal testing, as well as a licensed medical professional on call and an operational AED (defibrillator) within 10 feet of the testing area. There may be some physical discomfort and/or soreness as a result of this increased physical activity with the exercise program in this study.

You may experience slight discomfort from the blood draw and there is potential for bruising, swelling, dizziness, and lightheadedness (rare). Participants with known dizziness or lightheadedness with blood draws will be asked to lie down during the draw to minimize risks. The risk for any exchange of blood borne pathogens is low (rare). All blood samples will be handled by individuals with blood borne pathogen and laboratory safety training. These

procedures follow the rules of universal precautions, and all investigators and research assistants have up to date training. Continuous glucose monitoring (CGM) procedure is routinely used in clinical practice. The main risks of CGM are local irritation from the sensor or tape.

Emotional distress and/or embarrassment may occur with the measurement of body composition and receiving high body fat results (rare). To minimize risk participants will be measured individually and results will be discussed in a private area, with no one but trained research staff present. This research study involves exposure to radiation from 1 DXA scan. Please note that this radiation exposure is not necessary for your medical care and is for research purposes only. For comparison, the average person in the United States receives a radiation exposure of 0.3 rem (or 300 mrem) per year from natural background sources, such as from the sun, outer space, and from radioactive materials that are found naturally in the earth's air and soil. The dose that you will receive from participation in this research study is less than amount you receive from these natural sources in one year. The amount of radiation you will receive in this study has a minimal risk and is below the dose guideline established by The University of North Carolina Radiation Safety Committee for research subjects. You will be given all necessary contact information for laboratory personnel and will be encouraged to report any adverse events experienced. There may be uncommon or previously unknown risks. You should report any problems to the researchers.

What if we learn about new findings or information during the study?

You will be given any new information gained during the course of the study that might affect your willingness to continue your participation.

How will information about you be protected?

You will not be identified in any report or publication about this study. We may use de-identified data and/or specimens from this study in future research without additional consent. These biospecimens will not be used for commercial profit. Although every effort will be made to keep research records private, there may be times when federal or state law requires the disclosure of such records, including personal information. This is very unlikely, but if disclosure is ever required, UNC-Chapel Hill will take steps allowable by law to protect the privacy of personal information. In some cases, your information in this research study could be reviewed by representatives of the University, research sponsors, or government agencies (for example, the FDA) for purposes such as quality control or safety.

By signing this informed consent document, you agree that some of the information generated by participating in this study and/or a copy of the consent form may be included in your medical record and that this information may be viewed by other physicians or caregivers who provide healthcare services to you. This will allow the doctors caring for you to know what study medications or tests you may be receiving as a part of the study and know how to take care of you if you have other health problems or needs during the study.

All the information that you give us and the results of the tests (measurements) will be kept private to the extent of the law. Your research files will be stored and locked in our research office and will only be available to the researchers on this study to ensure your privacy. All

computers that have data for this study will be password protected, and only study researchers will have access to these computers.

We will mark all of your records with an alphanumerical code, not your name. The file that links your name to your study identification code will be kept in a locked drawer. Only the principal investigator (PI) and special project staff will be able to link your name and code during the study. This information will be removed following completion of the study.

In results reported in academic journals or meetings, you will not be identified by name, by recognizable photograph, or by any other means without your specific consent. We will combine your facts with those of other people in this study so no one who reads a report from this study will be able to identify you. You, your health care provider, your insurance carrier, your employer and your family members will not have access to facts found during this study.

What will happen if you are injured by this research?

All research involves a chance that something bad might happen to you. If you are hurt, become sick, or develop a reaction from something that was done as part of this study, the researcher will help you get medical care, but the University of North Carolina at Chapel Hill has not set aside funds to pay you for any such injuries, illnesses or reactions, or for the related medical care. Any costs for medical expenses will be billed to you or your insurance company. You may be responsible for any co-payments and your insurance may not cover the costs of study related injuries.

If you think you have been injured from taking part in this study, call the Principal Investigator at the phone number provided on this consent form. They will let you know what you should do.

By signing this form, you do not give up your right to seek payment or other rights if you are harmed as a result of being in this study.

What if you want to stop before your part in the study is complete?

You can withdraw from this study at any time, without penalty. The investigators also have the right to stop your participation at any time. This could be because you have had an unexpected reaction, or have failed to follow instructions, or because the entire study has been stopped.

Will you receive anything for being in this study?

You will be receiving $125 for taking part in this study. Compensation will be prorated, with each visit compensated at $31.25. Free parking will also be provided for all testing and training visits. Any payment provided for participation in this study may be subject to applicable tax withholding obligations.

Will it cost you anything to be in this study?

It will not cost you anything to be in this study.

Who is sponsoring this study?

This research is funded by a pilot grant through the North Carolina Diabetes Research Center. This means that the research team is being paid by the sponsor for doing the study. The researchers do not, however, have a direct financial interest with the sponsor or in the final results of the study.

What if you have questions about this study?

You have the right to ask, and have answered, any questions you may have about this research. If you have questions about the study (including payments), complaints, concerns, or if a research-related injury occurs, you should contact the researchers listed on the first page of this form. A description of this clinical trial will be available on 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 website at any time.

What if you have questions about your rights as a research participant?

All research on human volunteers is reviewed by a committee that works to protect your rights and welfare. If you have questions or concerns about your rights as a research subject, or if you would like to obtain information or offer input, you may contact the Institutional Review Board at 919-966-3113 or by email to IRB_subjects@unc.edu.

Participant's Agreement:

I have read the information provided above. I have asked all the questions I have at this time. I voluntarily agree to participate in this research study.

_____
Signature of Research Participant

_____
Date

_____
Printed Name of Research Participant

_____
Signature of Research Team Member Obtaining Consent

_____
Date

_____
Printed Name of Research Team Member Obtaining Consent