Impact of acute exercise on brain insulin sensitivity in middle-aged to older adults

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CONSENT TO TAKE PART IN A RESEARCH STUDY

Title of Study: Impact of acute exercise on brain insulin sensitivity in middle-aged to older adults

Principal Investigator: Steven K. Malin, PhD

Research Summary: This consent form is part of an informed consent process for a research study. It will provide info to help you decide if you want to do this study. It is your choice to participate. Exercise improves how muscles respond to the hormone insulin (i.e. insulin sensitivity). However, the effect of exercise on brain responses to insulin is unclear.

Purpose: We will assess how exercise changes brain responses to insulin in adults. We will use brain imaging (MRI). Brain blood flow before and after a nose spray of insulin will be done. We will also test how insulin impacts memory and health. People will be asked to visit Rutgers University about 6 times. These visits consist of two screening visits, 2 conditions (rest and exercise), and 2 testing visits. Testing will be conducted at Rutgers Brain Health Institute. Visits will range from about 1 to 6 hours during 1) the initial screening, 2) fitness test (2nd screening) and measures of body fat and muscle, as well as 3) brain imaging and a glucose tolerance test. Tests will be performed after the two conditions. People will be randomized to these conditions (e.g. flipping a coin).

Risks/Benefits: There are no direct benefits for being in this study. Possible risks include tiredness from exercise, pain from needle placement for blood work, and mild discomfort from devices like MRI, insulin spray, etc. You do not have to participate. You do not have to be in this study to receive medical care.

This consent form will provide details about the study and what will be asked of you. If you have any questions now or during the study, you should feel free to ask. You should expect to be given answers that you understand. After your questions have been answered and you wish to participate in the study, you will be asked to sign this consent form. You are not giving up any legal rights by taking part in this research or signing this consent form.

Who is conducting this study?
Dr. Steven K. Malin, PhD is the Principal Investigator of this study. The Principal Investigator is in charge of the research. Yet, there are other people who are part of the research team that help do the research.

Dr. Malin is located at 70 Lipman Dr, Loree Gymnasium New Brunswick NJ 08901 and may be reached at: (848) 932-7054 or steven.malin@rutgers.edu.

The Principal Investigator or another member of the study team will ask you to sign this informed consent. You will be given a copy of the signed consent form to keep.

Sponsor of the Study
Brain Health Institute and the School of Arts & Sciences, Rutgers University

Why is this study being done?
In the United States, about 6.5 million adults aged 65 and older have dementia. Dementia refers to poor abilities to think, remember, and reason (i.e. cognitive function). There are different forms of dementia, and Alzheimer's disease is the most common. Dementia occurs due to changes in the brain. Dementia risk is increased by poor brain responses to insulin (otherwise known as brain insulin resistance). Since genetics and aging cannot be reversed, it is important to look at physical activity and/or diet as possible treatments.

Exercise reduces Alzheimer's Disease risk. Exercise training for 8 weeks was recently shown to improve brain responses to insulin. Yet, people also lost body fat. This makes it difficult to know how much of this effect was due to exercise alone. This work was also in younger adults. Since no data is available in middle-age to older adults, we look to fill this gap in knowledge.

This study's purpose is to test if one exercise session affects brain responses to insulin. This will be measured by brain blood flow (MRI). We will also test thinking, blood sugar levels, heart rate, and blood pressure before and during a sugary drink (i.e. oral glucose tolerance test). Info from this study may improve exercise recommendations for brain health.

Who may take part in this study and who may not?
Non-smoking adults between 40 and 80 years old and body mass index (BMI) of 25-45 kg/m^2 may take part. People will be free of chronic disease, and blood work will be done to confirm you do not have kidney/liver disease. People who are not currently engaged 150 minutes of exercise per week or more may participate. People who have lost or gained weight recently, have a history of significant disease (e.g. congestive heart failure, cancer, etc.), are currently pregnant, or on weight loss medications are not eligible for safety reasons.

Why have I been asked to take part in this study?
You meet the criteria above. Your decision to participate in this study is yours. You do not have to participate.

How long will the study take and how many subjects will take part?
This study will require about 6 study visits. The study takes about 25 hours in total over about 1 month. Each visit will last between **1-6** hours depending on tests done. There are 2 Screening Visits, 2 Intervention Visits, and 2 Test Visits. We can split up some of the visits, if need be, for your convenience.

Up to **48** people will be in this study.

What will I be asked to do if I take part in this study?
Note: All tests in this form is for research purposes only. In light of COVID-19, we will follow safety checks set by the university guidelines until we are told not to. These checks will be done at the time of in person visits. They include a temperature check and questions related to exposure yourself or to others with COVID-19. Face masks should also be worn unless otherwise indicated.

*Note: Screening visits 1 and 2 can be combined to help you.

Visit 1 - Screening at the Clinical Research Center (CRC) or Institute for Food, Nutrition and Health (IFNH) or Foran Hall (Day 1) (lasts about 2-3 hours)

If you agree to participate, you will sign this consent form before any tests take place. We will complete screening tests to make sure you qualify safely for the study. You are to be fasted (nothing to eat or drink after midnight, water is ok) for blood work. Screening includes:

- Health history and Physical Activity Readiness Questionnaire (PAR-Q) that will take about 30 minutes to complete
- Vital signs (blood pressure, heart rate).
- Cognitive screening via Montreal Cognitive Assessment (MoCA) test. It helps assess memory, attention, and focus. This will take about 5-10 mins to complete.
- Your height, weight, and waist will be measured.
- Blood draw will also be performed for laboratory testing.
- Body mass index (BMI) will be calculated. It must be between 25-45 for you to participate.

We will also measure blood flow in your arm and neck as well as blood pressure in the arm. Here are the tests:

- *Common carotid artery intima-media thickness (CCA-IMT)*
  - This test measures neck blood vessel (i.e. carotid artery) thickness.
  - This test uses an ultrasound device to measure the size of the blood vessels in the neck that deliver blood to

the brain. Ultrasound is a procedure that creates a picture image using sound waves. Unlike X-rays, ultrasound does not involve radiation.
    - Before the test, you will be asked to lie down on a bed quietly for about 15 minutes. During this time, you will be connected to heart rate monitoring device. Then an ultrasound probe will be lightly pressed against your neck. Images will be taken for about 5 minutes.
    - This procedure takes about 10 minutes. We will complete this measure after the completion of other testing during the screening and again after 30 minutes.

- *Common carotid artery blood flow and diameter*
    - This test allows us to measure the size of blood vessels in the neck and blood flow traveling through the vessel (i.e. carotid artery) in the neck to the brain.
    - This procedure also uses an ultrasound device to measure the quantity of blood flow moving through the carotid artery as well as the size of the vessel. This test will be completed immediately following CCA-IMT in the same position lying flat on the bed.
    - This procedure takes about 5 minutes. Images will be taken for about 2 minutes. We will complete this measure following the completion of other testing during the screening and again after 30 minutes.

- *Brachial artery blood flow and diameter*
    - This test measures blood flow and size in the arm (i.e. brachial artery) using an ultrasound device.
    - You will remain flat on your back in the bed. This measure will be completed after the neck artery blood flow measure.
    - This procedure takes about 5 minutes to complete. We will complete this measure following the completion of other testing during the screening and again after 30 minutes.

- *Augmentation Index*
    - This measures the blood flow and pressure in a vessel. This vessel is called the aorta. It takes blood to the body from the heart. We will use a device from SphygmoCor.
    - This is done by placing a blood pressure cuff on your arm. The blood pressure cuff will inflate three different times.
    - This will take about 5 minutes. We will complete this measure following the completion of other testing during the screening and repeat measurements after 15 and 30 minutes.

PLEASE NOTE: If you are a woman who is able to bear a child, you will have a pregnancy test that must be negative in order to participate – this will be determined via urine collected at the screening.

Visit 2 - Screening at the Clinical Research Center (CRC) or IFNH or Foran Hall
(will last about 1-2 hours)

IMPORTANT: You must fast (not eat; water is ok) for 10-12 hours before this visit. The second screening visit will take place at the CRC:

- Review of your medical history.
- A questionnaire about feelings of stress. This takes about 5 minutes to complete.
- A nose spray of insulin will be provided. You will take two sprays in each nostril over 2 minutes via the VianaseTM device.
- Blood sugar levels will be measured by a fingerstick at 0, 30 and 120 minutes after the spray.
- Physical exam and vital signs (blood pressure, heart rate) will be conducted in person or virtually by Zoom.
- Resting electrocardiogram (ECG) to see the electrical activity of your heart will also be done.
- Measures of vessel thickness and blood flow in the arm and neck will be repeated as done in Visit 1. This will be done before the nose spray and about 30 minutes after the spray. Blood pressure will be assessed before the spray as well as about 15, 30, and 90 minutes after the spray.

If you continue to qualify for the study, the remainder of the visit will involve:

A. Body Composition and Resting Metabolism:

- You must be fasting for 4-10 hours.
- Your weight will be measured without shoes and minimal clothing.
- Your waistline will be obtained with a tape measure to test how much fat is in the stomach area.
- We will measure the total amount of fat and muscle in your body with the DXA in the hospital. DXA is a machine that uses a small dose of radiation to create pictures of the inside of your body.
- You will be required to wear clothes without metal on them (including zippers and bras with an underwire). If your clothes have metal, we will ask that you change into clothes provided by the lab
    - If issues occur with the DXA machine, we will measure the total amount of fat in your body with the BodPod® in the IFNH. The BodPod® looks like a large white egg and has a window on the door. It analyzes the way air is moved within the machine.
    - We will provide a swimsuit and cap for you to wear during this test. This is to standardize your results. You will not get wet at any time. You will enter the device and sit down. A door will close while you sit still. You are asked to breath normally.
- Resting metabolic rate will be done to determine how many calories you burn. While laying down you will wear a canopy (cover) that is connected to a device (Indirect calorimetry) to measure your carbon dioxide (CO_2) and oxygen. These measures are then used to calculate the number of calories you burn in a day to determine food needs.

B. Treadmill exercise testing for cardiovascular fitness (i.e. VO2max):

- You will be asked to perform a maximal exercise test in the CRC or the IFNH. This will be done on a treadmill. If difficulties exist with the treadmill, a stress test will first be done on a bike in the CRC. Then the maximal test will be done in the IFNH. The test will start with low speed, and the resistance, or incline, will increase every 2 minutes. You will be asked to go until you feel exhausted.
- During the test, you may have electrocardiogram (ECG) heart and blood pressure checking if at risk.
- We will measure your metabolic rate, like done during rest. During exercise, you will wear a facemask that is connected to a device (indirect calorimetry) to assess carbon dioxide (CO_2) and oxygen.
- You will receive the results of your test after the completion of the study.
- When done, you will be provided with an **accelerometer.** The accelerometer is a small device, similar to a pedometer, that is worn on your belt. It records the amount of activity you perform. The device is to be returned.

C. Diet logs and appetite questionnaires

- You will fill out a daily record of your eating habits for 3 days before the intervention and before testing days. You will also answer questions that test your response to the food you eat prior to rest and after the exercise intervention. This takes about 30 minutes to complete.

The following questionnaires will be completed at Visit 2. If unable to for any reason, they will be completed at later visits.

D. Physical Activity questionnaire*:*

- *Minnesota Leisure Time Physical Activity:* This is a checklist of 60 activities you may have participated in over the last 12 months. This takes about 10 minutes to complete.

E. Quality of life questionnaires

- *Physical activity enjoyment*: This will help understand your feelings about exercise. This takes about 5 minutes to complete.
- *Sleep History*: This will help understand sleep patterns. This takes about 5 minutes to complete.
- Morningness-Eveningness questionnaire: This will help understand your daily activity pattern preference. This will take about 5 minutes.
- *Veteran Rand-36*: This assesses overall stress, anxiety, overall happiness, etc. This questionnaire will have you think about your quality of life. This takes about 10 minutes to complete.
- *Perceived Stress Acute*: You will be asked to complete questions related to stress since last night. This will take about 5 minutes to complete.

RANDOMIZATION

You will be randomly assigned (i.e. flip of a coin) to start with rest or exercise conditions. You have an equal chance of being assigned to any one of the groups. You cannot which one you do first. After the first condition, the other condition will be completed about one week later.

Visits 3-6 - TESTING

Common Instructions Across Study Test Visits 3-6

- Maintain your normal activity levels.
- You will be provided the same diet on the day before the MRI and both conditions made of 55% carbohydrate, 30% fat, 15% protein.
- **You must not drink alcoholic or drinks with caffeine for at least 24 hours before the study test visits.**
- You must not use allergy, pain-related medicines (over the counter or prescription), or vitamins for at least **24 hours** prior to each testing visit. Prescription meds may be taken after testing.
- You must not perform any high intensity exercise (outside of this study) for **72 hours** prior to each test day.
- **The tests must be performed in the fasted state. You may not eat or drink anything (except water) after about 9:00 pm the night before.**
- Arrive at the Brain Health Institute by 6:30-9:00am on the morning of each test.

REST AND/OR ACUTE EXERCISE INTEREVENTION (Visit 3 and 5) (approximately 1.5 hours)

You will perform a 1 hour period of rest or a single session of supervised at moderate to high intensity exercise on a treadmill. This will be in the IFNH and/or CRC in the late afternoon. Heart rate and a rating of how hard you are working will also be collected. You will be asked to avoid food/caffeine for about 3 hours prior to the visit. Water will be allowed Exercise and rest conditions will be conducted approximately one week apart based on when you are free.

A. **Blood and Urine Collection at Visits 4 and 6:**

- After an overnight fast and before brain images, weight, blood pressure and heart rate will be taken. An IV line will then be placed into a vein in either the forearm or hand.
- An IV is a small flexible tube that is inserted into a vein guided by a needle. Once the tube is in place, the needle is removed and replaced with cap. This IV allows blood to be drawn or fluids to be given.
- The IV catheter will be in your arm for the remainder of each visit (about 6 hours). It will be removed before you leave the Brain Health Institute.
- Blood taken will be tested to measure sugars, fats, and hormones.
    - Visits 4 and 6: about 11 tablespoons of blood will be drawn per visit.
    - Additional blood (about ½ tablespoon) may be drawn to verify results of the screening visit as determined by the investigator.
- You will be provided with a plastic container and asked to collect one urine void on visit 4 and 6.

B. **Brain Images, Cognitive Tests and Glucose Metabolism to be done at Visits 4 and 6 (approximately 5 hours):**

- This series of tests will take about 5 hours.
- After an overnight fast, you will meet at the Brain Institute.
- Weight, blood pressure, and heart rate will be collected after about 5-10 minutes of quiet rest.
- A stress questionnaire will be given. This takes about 5 minutes to complete.
- You will then complete tests related to memory and attention using an iPad (e.g. the NIH Toolbox). This will take about 25 minutes.
- Fasting blood draws will be completed.
- After fasting blood work, you will be placed in a whole-body MRI scanner. After a 1-minute of rest to set up the machine and get you in place in the scanner, there will be an image for about 5 minutes to measure the shape of the brain. After this, will measure blood flow in the brain for about 45 minutes.
- After the scan, blood pressure and heart rate will be measured again. You will be provided the insulin spray into your nose as described above for the screening. This is to see how insulin impacts the brain.
- About 30 minutes later, we will repeat blood pressure, heart rate, and brain images, and cognitive tests.

- Then, the 75g sugar drink will start. This is used to help determine how quickly sugar is removed from the blood. Thirty minutes after you drink the sugar, four more blood draws will be taken at 30, 60, 90, and 120 minutes. We will also take heart rate and blood pressure at these times.
- Feelings toward different foods will also be collected at time of blood draws.
- After the tests are complete, you will be provided some food and allowed to leave.

END OF STUDY:

After subjects have completed Visit 6, the study will be complete.

Study Screening and Testing Schedule Visit Overview

Study Visit	Screening Visit 1	Screening Visit 2	Intervention (Rest/ exercise) Visit 3	Testing: Brain Image Visit 4	Intervention (Rest/exercise) Visit 5	Testing: Brain Image Visit 6
Informed Consent	X					
Vessel Thickness, Blood Flow, and Blood Pressure Measures	X	X				
Blood Draw, Vital Signs	X			X		X
History, Physical, Electrocardiogram		X				
Body Composition (DXA)		X				
VO2peak (Treadmill testing)		X				
Insulin spray		X		X		X
Diet Record		X				
Appetite Questions		X		X		X
Quality of Life Questions		X				
Accelerometer		X	X		X	
Heart Rate Monitors		X	X		X	
MRI				X		X
Oral Glucose Tolerance Test (OGTT)				X		X
Cognitive Tests	X			X		X
Urine Collection				X		X

Exercise sessions will be performed at the CRC, Loree Gymnasium, or IFNH on Cook-Douglass Campus and supervised by a researcher. You will be asked to wear a heart rate monitor. Movement trackers will be provided after Screening Visit 2.

What are the risks of harm or discomforts I might experience if I take part in this study?

Research studies often involve some risks. We will do all we can to prevent bad results for you.

Risks and side effects related to the study procedures include:

Likely

- Tiredness and soreness associated with exercise.
- Soreness associated with the IV.
- Mild to moderate discomfort (e.g. pain, tingling, and/or numbness) in the forearm and hand during the 5 minutes when the blood pressure cuff is inflated.

Less Likely

- There may be mild skin irritation caused by the application of electrodes for the heart monitor.
- Possible reaction to the glucose drink such as nausea or feeling sick to your stomach
- Exercise may result in pain of the muscle/tendons in your legs.
- Drop in blood sugar below 70mg/dl (hypoglycemia).

Rare but serious risks related to exercise

- Abnormal blood pressure responses
- Faintness, dizziness, or irregularities in heart rate or heart rhythm.
- Heart attack, stroke, or even death (the risk of death during or immediately after an exercise test is less than 1 in 10,000). Every effort will be made to minimize risks during each exercise session. Emergency equipment and trained researchers will be present during the exercise tests.

Blood draw and IV catheter placement: When a needle is inserted into a vein/skin there will be some temporary pain (common) and possible bruising. Infection is very rare as your skin is cleansed prior to needle insertion. Only sterile needles are used. Some people also feel dizzy when they have their blood drawn.

If the people doing the study are exposed to your blood or body fluids in a way that could give them a disease, your blood may be tested. The tests might check for: hepatitis, HIV (Human Immunodeficiency Virus), or other infections. You and the person exposed would be told the test results. However, your name would be kept private. If your test is positive for these disease, we will tell you how to find help. You may want help in understanding what the results mean for you.

ECG: Men may need to have a small amount of chest hair shaved off for the ECG pads to stick correctly. A small amount of the stickiness might stay on your skin. You can easily remove this with soap and water or an alcohol wipe. It may also remove hair.

Urine Collection: There are no risks to collecting urine samples. However, some people may find it embarrassing to collect samples.

Risk of Saline Flush: Saline clears blood from the IV catheters when they are not in use. Saline is a salt solution. There are no known risks to saline flush other than mild pain at the injection site.

Study Diet: You may find it difficult to stick to a special diet. You might have to fight cravings to eat or drink items that are not part of the provided research diet.

Questionnaires: You might find it boring to complete the questionnaires. There is the potential risk of loss of privacy. Every effort will be made to keep your info private. However, this cannot be guaranteed. Some of the questions we will ask you for this study may make you feel uncomfortable.

Accelerometer: You might find it difficult, uncomfortable, or unsightly to wear the activity monitor for periods of time.

Indirect Calorimetry: For some people, the plastic cover over their heads makes them feel anxious. This feeling is brief and will go away when the canopy is removed. The canopy is “see through” and does not restrict movement.

Intranasal Insulin Spray: This is the nose spray of insulin. It is tolerated well by most people. But it could affect the nose area. Nose soreness, sneezing, nosebleed, headaches, and dizziness have been reported. The risk of low blood sugar is very low.

Oral Glucose Tolerance Test: You could react to drinking this amount of sugar. These reactions could include nausea, low blood sugar, sweating, or an increase in blood pressure.

In the event of a medical emergency, study personnel will call the Rutgers Emergency Services line and physician on call

for immediate assistance.

DXA Scan: This study involves radiation exposure from DXA scans of your body. You experience background radiation every day. Background radiation comes from space and naturally occurring metals. The radiation dose you will receive in this study will be less than 1 day worth of this natural radiation. This radiation dose is what you will receive from this study only. It does not include any exposure you may have received or will receive from other tests. The risk from this dose is considered small. This radiation exposure is not necessary for your medical care. Yet, it is necessary to obtain the research info desired.

MRI Risks: The magnetic field made by the MRI has no known health risks in healthy adults. There are risks for certain populations (e.g. those with pacemakers). You will be screened for other objects of concern (e.g. piercings, metal implants, iron based tattoos). The magnet may make you anxious or be uncomfortable to sit in. It may also be loud. You will be given ear plugs. You will be given a button to press if you need to exit the scanner. The study team will review your MRI screening questionnaire. This is to make sure completing the scan is not risky.

Incidental findings: The MRI is for research purposes only. It does not give a diagnosis. Yet, the MRI exam could reveal something abnormal. Scans at the Center for Advanced Human Brain Imaging Research (CAHBIR) are screened for images that do not look normal. If there is any sign of something that looks abnormal, the scan will be reviewed by a medical doctor (i.e. University Radiology Group (URG)). The medical doctor provides a brief written report with their thoughts. If the finding is concerning, the medical doctor will provide a recommendation for medical follow up. The study PI, Dr. Malin, will tell you about this report.

Reproductive Risk: If you become pregnant during the study, you should notify the study doctor as soon as possible. While there no evidence of birth defect or complications, you will be encouraged to exit the study.

Drug to drug interaction: You should share all medicines, herbal products, vitamins, or food supplements prior to starting this study. You should also avoid new drugs if possible. Please tell the study doctor if so, and you might be able to stay on these medicines in the study.

A caution about giving too much blood:
Because of the amount of blood being taken, you should not give blood for other reasons while in the study. You should wait 2 months after the study before donating blood.

Unforeseeable risks: There may be risks or side effects related to the study that are unknown at this time. You will be notified of any significant new findings that become known that may affect if you want to do the study. Contact the study project manager Daniel Battillo at (daniel.battillo@rutgers.edu) if you have any symptoms or problems.

Are there any benefits to me if I choose to take part in this study?
You will not receive any direct benefits from being in this study. Yet, info researchers get from this study may help others in the future. Society in general will benefit from greater understanding of the importance of exercise with or without insulin spray in the nose to make the brain or body healthier.

What are my alternatives if I do not want to take part in this study?
You do not have to be in this study to be treated for your illness or condition. You can get the usual treatment even if you choose not to be in this study. The usual treatment would include careful follow-up with your primary care physician.

How will I know if new information is learned that may affect whether I am willing to stay in the study?
During the study, you will be updated about any new info that may affect whether you still want to be in the study. You will be contacted if new info is learned that affects you.

Will I receive the results of the research?
During the study your study leader will let you know of any test results that may be important to your health. Your study leader will tell you new findings that may be important for your health. These may help you decide if you want to continue in the study. The final results of the research will not be known until all the info from everyone is combined and reviewed. At that time, you can ask for more info about the study results. After the study is over, you will receive your own results.

These may include your amount of body fat and muscle, fitness, and the effects of exercise on blood sugar after the sugary drink).

You will also be shown and receive a picture of your brain from the MRI session. The images from this study are limited and are not gathered to find out problems in the brain. Yet, if your scan reveals an unusual finding, we will have a medical doctor look at your scan at no charge to you. If the medical doctor thinks that there is something in the scan that should be looked at more, we will convey this message to you at no charge. We try to get such review done within a week of the scan. We cannot promise this will always happen within a week. This finding may cause you stress. Therefore, we typically do not share info about any observed concerns until a medical doctor has looked at the scan. Because these scans are for research only, there will only be a very brief report if something is seen. Neither Dr. Malin, nor the medical doctor, will contact your physician or insurance company about the findings. But, if you request it, and sign a release of information form. We can then provide your doctor with the pictures and medical doctor's brief report of the area of concern. If needed, we can also provide a referral to a doctor or clinic who specializes in looking at and treating the problem seen in the scan.

Will there be any cost to me to take part in this study?
All of the tests outlined this research study will be provided at no cost to you or your health insurance. You will be responsible for the cost of travel to come to any study visit. We will pay for your parking during the study.

Will I be paid to take part in this study?
You will be paid up to $300 for the study. If you only complete 1 condition with MRI, you will be paid up to $150 via a check. You will receive payments based on your selection below. You will be paid by check provided by the study team. Rutgers takes about 4-6 weeks to process these checks. The payment may be reported to the IRS as income.

Completion of screening and Visits 3 and 4 MRI Conditions:	$150
Completion of Visits 5 and 6:	$150
Total payment:	**$300**

By agreeing to be in this study, you are donating your blood for research. This gives up any property rights you may have in them. The results of this research from your donated material may have commercial value. But you will not receive any payments.

How will information about me be kept private or confidential?
All efforts will be made to keep your info private. But total privacy cannot be guaranteed. We will keep files in locked cabinets/rooms and use password protected devices. You will be provided an ID number that minimizes use of your name to protect your privacy.

The info collected from you might be published in a medical journal. This would be done in a way that protects your privacy. No one will be able to find out from the article that you were in the study.

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 info that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

What are your responsibilities in the study?
You have certain responsibilities to help ensure your safety, including:

- Be completely truthful about your health history and answer all of the study-related questions completely.
- Follow all instructions given.
- You should tell the study doctor or study staff about any changes in your health or the way you feel.
- Tell the study doctor or study staff as soon as possible if you have to take any new medications. This includes anything prescribed by a doctor or medication that you can buy without a prescription (over-the-counter). This also includes herbal supplements and vitamins. The study doctor will let you know if you can take these medications.
- You cannot drink alcohol 24 hours prior to study tests. We ask you to avoid alcohol during the study.
- You cannot eat or drink foods that contain caffeine 24 hours before testing. Coffee, tea, soda, and chocolate have caffeine. Please ask a study member if you have questions.

- We also ask that you avoid any structured exercise for 24 hours before testing. Please keep your exercise to your normal everyday activities.

What will happen to my information or blood samples collected for this research after the study is over?
After the tests for the study are completed, there may be samples left over. Normally, these leftover samples would be thrown away. We ask that you let us keep them for future research. After info that could identify you has been removed, de-identified samples collected for this research may be used by us or other investigators for other research purposes. We would not get new informed consent from you.

If you agree, samples collected for research will be added to our freezers for storage. The samples will be used for to be determined future research on disease prevention. As we learn more, new research questions and new types of research may be done.

Along with samples, researchers will maintain your health info. Combining info from the samples with info from your health records may help this research. For this research, the following types of info could be included: heart rate/blood pressure, lab results, age, gender, medications you are taking, whether or not you have diabetes, family history of cardiovascular disease and other known medical disease. We would maintain health info and samples until used. Your info will be kept secured and in locked rooms.

_____Please check here if you agree to us storing your sample for future analysis.

_____Please check here if you DO NOT agree to us storing your sample for future analysis.

What will happen if I am injured during this study?
You will be exposed to certain risks of personal injury, which include descriptions outlined above in "risks". In addition, new adverse effects of exercise/insulin spray could be found. These could result in personal injury. The University will help you find medical treatment if you get hurt or sick from the study. The subject's health insurance carrier or other third-party payer will be billed for the cost of this treatment, if the University shall not submit to federally funded programs. These include Medicare, Medicaid or CHAMPUS, for reimbursement first, if submission to such programs is prohibited by law. No financial compensation will be provided by the University. No other type of assistance is available from the University. Yet, by signing this form, you are not giving up any legal rights to seek further compensation.

What will happen if I do not wish to take part in the study or if I later decide not to stay in the study?
It is your choice whether to take part in the research. You may change your mind and stop the study at any time. Your relationship with the study staff will not change. You may do so without penalty and without loss of benefits you have been told you will receive.

Even if you do not change your mind, the study leader can take you out of the study. Some reasons for doing so may include:
a) Your study physician is concerned about your health.
b) You do not follow the instructions of the study doctor or study staff.
c) The study sponsor closes the study for safety, administrative or other reasons.

If you decide to stop being in the study, we will ask you to contact the study coordinator (contact information listed below) by telephone, email, or written letter. If you decide to withdraw from the study for any reason, you may be asked to return for at least one additional visit for safety reasons.

Who can I contact if I have questions?
If you have questions about taking part in this study or if you feel you may have suffered a research related injury, you can contact the researchers listed below to:

Steven K. Malin, Ph.D. (Principal Investigator)
Department of Kinesiology and Health
Division of Endocrinology, Metabolism, and Nutrition
Rutgers University, New Brunswick, NJ 08901, (848)
932-7054; steven.malin@rutgers.edu

Daniel Battillo, B.S. (Study Manager)
Department of Kinesiology and Health
Rutgers University, New Brunswick, NJ 08901,
(848)-932-7059; daniel.battillo@rutgers.edu

EMERGENCY HEALTH CONTACT *if problems occur:*

- In case of emergency, call 911 or go to the nearest Emergency Department
- During business hours, contact Dr. Shah, MD at (732) 235-6337. After hours or on the weekend, call (732) 401-5445 to reach Dr. Shah. Please DO NOT text as they will not be forwarded to Dr. Shah. Only phone calls please.

- If you have questions, concerns, problems, information, or input about the research or would like to know your rights as a research subject, you can contact the Rutgers IRB or the Rutgers Human Subjects Protection Program.

    - Phone: (973) 972-3608 or (732) 235-2866 or (732) 235-9806.
    - Email: irboffice@research.rutgers.edu.
    - Write: 335 George Street, Liberty Plaza Suite 3200, New Brunswick, NJ 08901.

PERMISSION (AUTHORIZATION) TO USE OR SHARE HEALTH INFORMATION THAT IDENTIFIES YOU FOR A RESEARCH STUDY

The next few paragraphs tell you about how investigators want to use and share identifiable health information from your medical record in this research. Your information will only be used as described here or as allowed or required by law. If you sign this consent form, you agree to let the investigators use your identifiable health information in the research and share it with others as described below. Ask questions if there is something you do not understand.

What Is the Purpose of The Research and How Will My Information Be Used?
The purpose of collecting and using your health information for this brain and exercise study is to help researchers answer the questions that are being asked.

What Information About Me Will Be Used?

If you sign this form, we may collect any or all of the following information about you:

- Personal info such as name, address and date of birth.
- Your health info is required for this study. This may include a review of your medical records and test results from before, during, and after the study from any of your doctors or health care providers. This may include mental health care records, substance abuse records, and/or HIV/AIDS records.
- Social Security number ONLY IF you are being paid to be in this study

Who May Use, Share or Receive My Information?
The research team may use or share your info collected or created for this study with the following people and institutions:

- Rutgers University Investigators Involved in The Study.
- The Rutgers University Institutional Review Board and Compliance Boards.
- The Office for Human Research Protections in the U.S. Dept. of Health and Human Services
- Hospital Personnel (e.g. CRC nurses) as necessary for clinical support if needed due to, for instance, risks mentioned
- Non-Rutgers Investigators on the Study Team for blood analysis/interpretation (e.g. Uta Erdbrugger at University of Virginia, Dimitrios Kapogiannis from NIH, etc.).

Those persons or organizations that receive your information may not be required by Federal privacy laws to protect it. They may share your information with others without your permission, if permitted by law.

Will I Be Able to Review My Research Record While The Research Is Ongoing?
No. We are not able to share information in the research records with you until the study is over. To ask for this information, please contact the Principal Investigator, the person in charge of this research study.

Do I Have to Give My Permission?
No. You do not have to permit use of your information. But, if you do not give permission, you cannot take part in this study. (Saying no does not stop you from getting medical care or other benefits outside of this study.)

If I Say Yes Now, Can I Change My Mind and Take Away My Permission Later?
Yes. You may change your mind and not allow the continued use of your information at any time. If you take away permission, your information will no longer be used or shared in the study. But we will not be able to take back information that has already been used or shared with others. If you say yes now but change your mind later, you must write to the researcher and tell him or her of your decision. This is: Dr. Steven K. Malin, PhD in the Department of Kinesiology and Health at Rutgers University ((848) 932-7054; steven.malin@rutgers.edu).

How Long Will My Permission Last?

There is no date when your permission will end. Your health information may be studied for many years.

AGREEMENT TO PARTICIPATE

Subject Consent:

I have read this entire consent form, or it has been read to me, and I believe that I understand what has been discussed. All of my questions about this form and this study have been answered. I agree to take part in this study.

Subject Name (Print):_____

Subject Signature:_____Date:_____

Signature of Investigator/Individual Obtaining Consent:

To the best of my ability, I have explained and discussed all the important details about the study including all of the information contained in this consent form.

Investigator/Person Obtaining Consent (Print):_____

Signature:_____Date: _____