Exercise in Adolescents with Insulin Resistance: A Path to Improved Brain Health?

NCT04154865

2/9/2021

University of Wisconsin-Madison
Consent to Participate in Research
and
Authorization to Use Protected Health Information for Research

Study Title for Participants: Exercise in Adolescents with Insulin Resistance: A Path to Improved Brain Health?

Lead Researcher: William G. Schrage, Ph.D
608-262-7015

Where Lead Researcher works: School of Education
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Invitation

If you are the parent or legal guardian of a minor who is invited to take part in this study, your child can participate in the study only if you give your permission. We will also ask your child if he/she is willing to take part in the study. In this consent form, “you” means the child who takes part in the study.

We invite you to take part in a research study about how insulin resistance— the body’s reduced ability to use the hormone, insulin— affects the brain. We are inviting you because you are between the ages of 12-18 and may or may not have insulin resistance.

The purpose of this consent and authorization form is to give you the information you need to decide whether to be in the study. It also explains how health information will be used for this study and for other research in the future, and requests your authorization (permission) to use your health information. Ask questions about anything in this form that is not clear. If you want to talk to your family and friends before making your decision, you can. When we have answered all your questions, you can decide if you want to be in the study. This process is called “informed consent.”

Important things to know about any research study:

Taking part in research is voluntary. You can choose not to be in this study, or stop at any time.

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If you decide not to be in this study, your choice will not affect your healthcare or any services you receive. There will be no penalty to you. You will not lose medical care or any legal rights.

Study Summary

What is this study about?

We want to find out if brain blood vessels of adolescents with insulin resistance respond the same as adolescents without insulin resistance. Also, we want to find out if exercise can increase brain blood flow in adolescents with insulin resistance, and if this is related to memory and thinking abilities.

What will happen during the study?

You will undergo a series of memory and thinking tests at one visit. At another visit, you will do a breathing test while we measure the blood flow in your brain using a small probe placed on your temple. You will then do a few memory and thinking tests, exercise on a stationary bike, and then do some more memory and thinking tests.

How much time will I spend on the study?

You will complete some questionnaires online at home. Then you may come to the University of Wisconsin 3-4 times for a total of about 3.5-5.5 hours.

The online questionnaires will take 30-60 minutes.
The first time will be a “screening” visit lasting 1-1.5 hours.
The second visit will be for memory and thinking tests lasting 2-3 hours.
The third visit will be for the breathing test lasting 30-60 minutes
The fourth visit is the exercise visit, which will last about 1-1.5 hours.

Could taking part in the study help me?

Being in this study will not help you directly. But your participation in the study may benefit other people in the future by helping us learn more about how insulin resistance affects brain health.

What are the main risks of taking part in the study?

All procedures have possible risks. The risks of this study are low, and we will watch for any problems during the procedure so that we can stop if necessary.

For this study, the main risks to know about are:

- We do not know if DEXA scans are safe during pregnancy, so if you think you might be pregnant, you should not be in the study.

- You might feel uncomfortable or anxious with some of the questionnaires and cognitive tests. You may skip any questions you do not feel comfortable answering.
- You might be uncomfortable getting your blood drawn.
- The breathing test may make you feel breathless. You can stop the test at any time.
- You might be uncomfortable during exercise. You can stop the test at any time.

How is research different from health care?

When you take part in a study, you are helping to answer a research question. Test results will not be used for your health care.

Questions about the study?
Contact the research team:
Aaron Ward 608-263-6308
William Schrage 608-262-7015

Questions about your rights as a research participant? Have a complaint about the research?
Contact University of Wisconsin Hospital and Clinics Patient Relations Representatives at 608-263-8009.

More information about this study

Why are researchers doing this study?

The purpose of this research study is to collect measurements to determine the effect of insulin resistance on the brain and on blood flow to the brain. We are doing this research because recent data suggests that the brain is affected by insulin resistance (i.e. the body's reduced ability to use the hormone insulin effectively), even at a young age.

This study is being done at the University of Wisconsin-Madison (UW-Madison). A total of about 20 people will participate in this study.

Funding for this study is provided by the Department of Kinesiology at the UW-Madison.

What will happen in this study?

If you decide to participate in this research study, the researchers will ask you to complete some questionnaires online (0.5-1 hour) and then visit the UW-Madison 3 to 4 times for about 5.5-8 hours total. Your visits will include the following:

Screening Visit (2-2.5 hours)
This visit will include online questionnaires which will take about 30-60 minutes you can do at home. If you are eligible, you will be asked to come to the UW-Madison for physical measurements, a blood draw, an ultrasound and carbon dioxide (CO_2) tolerance test, DEXA scan, and a maximal exercise test. You will be asked to fast before the in-person visit.

If you participated in another study in our lab and had a screening visit in the past 180 days, we can use the information from that screening visit and you will NOT need to repeat those same procedures.

Thinking and Memory Testing Visit (about 2-3 hours)
Memory and thinking tests will be used to assess your memory and other thinking abilities. Some questionnaires will evaluate aspects of your health, mood, and attitudes. Your parent/guardian will be asked questions about you too, and these questions include potentially sensitive information such as alcohol and drug use. You will be asked to fast before the visit.

If you participated in another study in our lab and performed these tests, we can use the information from that study and you will NOT need to repeat these procedures.

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Ultrasound and Breathing Test Visit (about 0.5-1 hour)
This visit will include an ultrasound of a blood vessel in your brain and a CO_2 breathing test. You will be asked to fast before the visit.

Ultrasound and Exercise Visit (about 1-1.5 hours)
This visit will include an ultrasound of a blood vessel in your brain, exercise, and some memory and thinking tests. You will be asked to fast before the visit. You must do the maximal exercise test before this visit.

Study Procedures

Fasting: You will be asked to fast for at least 4 hours prior to each visit. We ask that you refrain from vigorous exercise for 24 hours, and refrain from caffeine and NSAIDs like Ibuprofen for at least 24 hours prior to the visit. You may and should drink water as normal.

Questionnaires: We will ask you and your parent or guardian questions about your health and about your physical activity levels.

Body Measurements: We will take measurements of your height, weight, and hip and waist circumference.

DEXA Scan (Body Composition): DEXA is a type of x-ray scanner. The DEXA scan is done to determine body composition (amount of body fat). The scanner is a clinical scanner like many hospitals have for measuring bone density and body fat, and is operated by trained research staff.

Exercise Test: This test is used to measure your fitness. You will exercise on a stationary bike with increasing effort in 2-minute intervals until you cannot increase effort any more. You will wear a heart rate monitor (ECG), and mouthpiece or mask that will capture your breath but will allow you to breathe normally.

Moderate Exercise: This is used to see if you can improve your memory and thinking test scores immediately, and to see how much the blood flow to your brain increases. You will exercise on a stationary bike at a moderate intensity (50% of your maximal effort) for 20 minutes. You will wear a heart rate monitor (ECG), and mouthpiece or mask that will capture your breath but will allow you to breathe normally.

Blood Draw: A trained and certified person will take blood from a vein in your arm or hand. We will collect about 30 mL of blood (about 2 tablespoons). The blood samples we collect are used to determine various substances in your blood including blood sugar and cholesterol levels.

Thinking and Memory Testing: Memory and thinking tests will be used to assess your memory and other thinking abilities. Some questionnaires will evaluate aspects of your

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health, mood, and attitudes. Your parent/guardian will be asked questions about you too.

Ultrasound: A small non-invasive probe will be placed on your temple to measure the blood flow through a blood vessel in your brain. A headband will be fitted on your head to help hold the ultrasound probe. On the screening visit, we will make sure we can find a good signal from the blood vessel. On the study visit, this will be used to measure the blood flow in that blood vessel.

CO_2 Test: You will breathe two gasses with higher amounts of CO_2 and normal levels of oxygen. On the screening visit, this will be used to make sure you can tolerate the test. On the study visit, this will be used to investigate how your brain blood flow responds to the CO_2.

Vital Sign Measurement: We will measure your heart rate with ECG, blood oxygen levels with a finger or ear clip, blood pressure with a cuff on your upper arm, and your breathing with a mouth piece or mask.

Summary of study visits and procedures

	Screening Visit	Cognitive Testing Visit	CO_2 Challenge Visit	Exercise Visit
Fasting	X	X	X	X
Questionnaires	X			
Body Measurements	X			
Blood Draw	X			
DEXA Scan	X	X (if needed)	X (if needed)	X (if needed)
Exercise Test	X	X (if needed)	X (if needed)	
Cognitive Tests		X		X
Moderate Exercise				X
CO_2 Test	X		X	
Vital Signs	X		X	X

You may skip any question on the questionnaires or the cognitive tests that you do not wish to answer.

Protected health information (PHI) used in this study

Protected health information, also called PHI, is information about your physical or mental health that includes your name or other information that can identify you, like your date of birth or medical record number. To do this study, we will use the following kinds of PHI:

Results of tests or procedures done as part of the study
Things you tell the researchers about your health

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Information currently in your medical records as well as information added to your medical records during the course of this study. This information could include glucose and insulin levels, and general medical history. We will get this information from your health care providers such as Dr. Aaron Carrel.

How long will I be in this study?

You will be part of the study for about 1 week to 6 months, depending on your availability and staff availability.

The researchers may take you out of the study, even if you want to continue, if:

- your health changes and the study is no longer in your best interest
- you do not follow the study rules or no longer meet the requirements to be in the study
- the study is stopped by the sponsor or researchers

How is being in this study different from my regular health care?

This study is not part of your health care.

Do I have to be in the study? What if I say "yes" now and change my mind later?

No, you do not have to be in this study. Taking part in research is voluntary. This means that you decide if you want to be in the study. If you decide now to take part, you can choose to leave the study at any time.

If you decide to be in the study, the researchers will tell you about new information or changes in the study that may affect your willingness to continue in the study.

Let the researchers know if you choose to leave the study.

If you decide not to take part in the study, or if you choose to leave the study, your choice will not affect any treatment relationship you have with healthcare providers at UW-Madison, UW Health or any affiliated organizations, or any services you receive from them. No matter what decision you make, and even if your decision changes, there will be no penalty to you. You will not lose medical care or any legal rights.

Your authorization for researchers to use your protected health information (PHI) will continue indefinitely. However:

- You can choose to take back your authorization for researchers to use your health information. You can do this at any time before or during your participation in the research.

- If you take back your authorization, information that was already collected may still be used and shared with others, but the researchers will no longer be able to collect NEW information about you.
- If you take back your authorization, you will not be able to take part in the research study.
- To take back your authorization, you will need to tell the researchers by writing to the Lead Researcher, William G. Schrage at Department of Kinesiology, Medical Sciences Center, 1300 University Ave., Madison, WI 53706.

Will being in this study help me in any way?

Being in this study will not help you directly. Your participation in the study may benefit other people in the future by helping us learn more about how insulin resistance affects brain health.

This study is not a substitute for your regular medical care. You should continue to see your regular medical providers.

Will I receive the results of research tests?

All of the tests that are part of this study are for research purposes only. Because of this, we will not tell you or your doctors the results of these research tests.

Pregnancy Status (females only): You will be asked in private, away from your parent/guardian, if you are pregnant or may be pregnant. Your answer will not be shared with your parent/guardian unless there is suspicion of abuse, in which case the results will be disclosed to appropriate authorities.

Thinking and Memory Tests: The thinking and memory tests you will complete in this study may show that you are experiencing symptoms of emotional distress such as depression or suicidal thoughts. Your answers will be safeguarded as described below.

Ultrasound: The ultrasound that is used in this study does not take an image of your blood vessels or brain; it only measures the blood flow. The results of the ultrasound will NOT be reviewed by a physician and you will not be told the results.

There may be benefits to learning such results (such as early detection and treatment of a medical condition), but there are risks as well (such as problems with getting insurance or a job or feeling worried about a finding for which no treatment is required or appropriate). If you believe you are having symptoms that may require clinical attention, you should contact your primary care physician.

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What are the risks?

Fasting: Fasting may make you feel hungry, irritable, or fatigued. Refraining from NSAID use may cause increased pain, but this can be reduced by using acetaminophen or non-drug methods.

Questionnaires and Cognitive Tests: Some of the questions you will be asked on the questionnaires and cognitive tests are personal and may cause anxiety, distress, embarrassment, feelings of sadness, or discomfort. You may skip any questions you do not feel comfortable answering, but it is important for you to give your best effort.

Pregnancy Screening: You will also be asked whether you may be pregnant. The DEXA scan may be harmful to a fetus. Women who are pregnant or plan to become pregnant during the study should not participate. If you are a minor, we will have this conversation privately away from your parents. Your parents will not be informed whether or not you may be pregnant.

Blood Draw: There may be some discomfort, minor bruising, dizziness, or fainting associated with having blood taken. There is also a very small chance of infection (less than 1%) at the needle puncture site.

DEXA Scan: DEXA uses x-ray radiation to determine lean mass and fat mass, as well as bone mineral density. The radiation exposure from this scan is about 7 microsievert. To give you an idea about how much radiation you will get, we will make a comparison with an every-day situation. Everyone receives a small amount of unavoidable radiation each year. Some of this radiation comes from space and some from naturally-occurring radioactive forms of water and minerals. This research gives his or her body the equivalent of about 1 days' worth of this natural radiation.

Exercise Test and Moderate Exercise: You may feel tired, fatigued, or breathless. Also, the mouthpiece or face mask may be uncomfortable. The risk of a serious complication like a joint injury, heart problems, or death is very rare.

CO_2 Test: You may feel breathless. Also, the mouthpiece or face mask may be uncomfortable. This procedure is considered very safe.

Vital Sign Measurements: The risk of the blood pressure test is minimal. You may experience a few seconds of discomfort as your arm is squeezed by the blood pressure device.

Breach of Confidentiality: There is a risk that your information could become known to someone not involved in this study. Information about you provided by your parent or guardian will include sensitive information such as alcohol and drug use. If a breach of

confidentiality happens, it could be embarrassing, stigmatizing, have legal effects, affect your relationships with family and friends, affect your employment, or make it harder to get insurance or a job.

Will being in this study cost me anything?

There will be no cost to you for any of the study activities or procedures. If you need treatment for side effects while you are on the study, you or your insurance will need to pay for this treatment.

Will I be paid or receive anything for being in this study?

We will pay you up to $70 for the screening visit and $20/hr for the study visits. Payment will be provided at the end of each study visit. If you complete all the study visits, you will receive $140 to $180 for being in this study. If you choose to leave or we take you off the study for any reason, you will receive $20 for the online questionnaires; $10 for the screening visit blood draw; $10 for the DEXA scan; $20 for the maximal exercise test; $10 for the CO_2 familiarization; and $20/hr for any of the study visits up that point for your time, rounded to the nearest half hour. You will receive the payment, not your parent/guardian.

What happens if I am injured or get sick because of this study?

If you are injured or get sick because of this study, medical care is available to you through UW Health, your local provider, or emergency services, as it is to all sick or injured people.

If it is an emergency, call 911 right away or go to the emergency room.
For non-emergency medical problems, contact your regular health care provider.
Call the Lead Researcher, William G. Schrage, at 608-262-7015 to report your sickness or injury.

How will researchers keep my research information confidential?

We have strict rules to protect your personal information and protected health information (PHI). We will limit who has access to your name, address, phone number, and other information that can identify you. We will also store this information securely. We may publish and present what we learn from this study, but none of this information will identify you directly without your permission.

However, we cannot promise complete confidentiality. Federal or state laws may permit or require us to show information to university or government officials and to our study sponsors, the Department of Kinesiology responsible for monitoring this study. This includes access to your medical records so that study monitors, auditors, the Institutional Review Board and regulatory authorities can verify study procedures and/or

data. These groups will maintain your confidentiality. By signing this consent form, you and your parent/guardian (if applicable) are authorizing this access to your records. We may also have to tell appropriate authorities, such as child protective services or health care providers, if we learn during the study that you or others are at risk of harm (for example, due to child or elder abuse, or suicidal thoughts).

Authorizing the research team to use your PHI means that we can release it to the people or groups listed below for the purposes described in this form. Once your health information is released outside UW-Madison or UW Health it may not be protected by privacy laws and might be shared with others. Also, with appropriate institutional permissions and confidentiality protections, we might use information and biospecimens that we collect during this study for other research or share with other researchers without additional consent or authorization from you or your legally authorized representative.

Who at UW-Madison can use my information?

Members of the research team
Offices and committees responsible for the oversight of research
Personnel who schedule or perform medical tests or procedures, handle accounting and billing, or do other tasks related to this study

Who outside the UW-Madison may receive my information?

U.S. Office for Human Research Protections

Will information from this study go in my medical record?

A medical record will be created for you if you do not already have one. Some of the information we collect for this study will go in your medical record. This includes blood cell count (known as a complete blood count with differential) and insulin levels. Both you and your UW Health providers will be able to see these results. All other information we collect for this study will NOT go in your medical record.

What will happen to my data after my participation ends?

We will keep your blood samples, blood test results, and MRI data for an indefinite period of time, meaning we have no plans of ever destroying your blood samples or data. Keeping data or biospecimens for future research is called “banking.” The banked data will be kept in a secure location for use by researchers. The data that will be banked will be obtained during the course of the study; you will NOT need to undergo any additional procedures. The banking of samples and data is required for participation in the study.

This is what will happen with your banked data:

We will use the samples and data in future research projects about insulin resistance. We may also use them for other types of research.
The samples and data may be shared with other researchers at the University of Wisconsin-Madison.
The banked samples and data will be labeled with a code instead of your name.
When we give your samples or data to other investigators for research projects, they will not be able to use the code to figure out which samples or data are yours.
The research team will maintain a link between your samples or data and your identifiable information kept by the study team.
You can request to have your samples or data removed from the bank by contacting the research team at any time.

This is what will NOT happen with your banked samples or data:

Banked samples or data will not be shared with your health care providers or used in your treatment outside this study.

The risk related to banking of samples and data is a breach of confidentiality. There is a risk that your information could become known to someone not involved in this study. If this happens, it could affect your relationships with family and friends, affect your employment, or make it harder to get insurance or a job.

What if I have questions?

If you have questions about this research, please contact the Lead Researcher, William G. Schrage, at 608-262-7015. If you have any questions about your rights as a research subject or have complaints about the research study or study team, contact UW Health Patient Relations at 608-263-8009. The Patient Relations Representatives work with research subjects to address concerns about research participation and assist in resolving problems.

Optional study activities

This part of the consent form is about additional research activities that you can choose to take part in. Things to know about these activities:

They are optional. You can still take part in the main study even if you say “no” to any or all of these activities.
These activities will not help you directly. We hope the results will help us and others understand how insulin resistance affects the brain and blood vessels.
We will not tell you the results of these optional activities, and we will not put the results in your medical records.
Taking part in the optional activities will not cost you anything.

Indicate your choice of “yes” or “no” for each of the following research activities.

Our lab and our collaborators may have studies in the future that you may qualify for. Only we will contact you regarding these studies. Is it okay to contact you with information about future studies?

Yes, you may contact me in the future about studies.

No, you may NOT contact me in the future about studies.

The risks of these optional procedures is a potential breach of confidentiality. There is a risk that your information could become known to someone not involved in this study. If this happens, it could affect your relationships with family and friends, affect your employment, or make it harder to get insurance or a job. Only authorized personnel in the Lead Researcher's laboratory will have access to this information. Your information will be locked in secure filing cabinets within restricted-access spaces or stored in digitally encrypted databases. The link between the code and your information will be protected as described previously.

To take back your authorization for these optional activities, you will need to tell the researchers by writing to the Lead Researcher, William G. Schrage at Department of Kinesiology, Medical Sciences Center, 1300 University Ave., Madison, WI 53706.

Agreement to participate in the research study

You do not have to sign this form. If you refuse to sign, however, you cannot take part in this research study.

If you sign the line below, it means that:

- You have read this consent and authorization form describing the research study procedures, risks and benefits.
- You have had a chance to ask questions about the research study, and the researchers have answered your questions.
- You want to be in this study.
- You give authorization for your protected health information to be used and shared as described in this form.

_____
Printed Name of Subject (age 15-18)

_____ _____
Signature of Subject (age 15-18) Date

_____
Printed Name of Parent/Guardian

_____ _____
Signature of Parent/Guardian Date

_____ _____
Signature of Person Obtaining Parental/Guardian Permission and Authorization and Child Assent Date

****You will receive a copy of this form****