ISU IRB: 23-150-00
Approved Date:
Expiration Date: 06/13/2024

INFORMED CONSENT DOCUMENT
Iowa State University
Department of Kinesiology

Title of Study: RESISTance Exercise for Depression Trial **(RESIST Study)**

Investigator: Dr. Jacob D. Meyer, PhD (Principal Investigator)

This form describes a research project. It has information to help you decide whether you wish to participate. Research studies include only people who choose to take part—your participation is completely voluntary. Please discuss any questions you have about the study or about this form with the project staff before deciding to participate. The purpose of this study is to understand how resistance exercise training influence brain blood flow and mental health. By participating in this study, you would engage in 16-weeks of resistance exercise training twice per week, followed by assessment visits at 26 and 52 weeks post-intervention. Risks may include physical discomfort, psychological stress, social stigmatization, or breach of confidentiality, each detailed below. Benefits may include personal health reports and 16-weeks of resistance training using state of the art equipment. Please carefully review this document to determine if you would like to participate and ask the research team if you have any questions while doing so.

Funding: This study is funded by a grant from the National Institute of Mental Health.

INTRODUCTION

The purpose of this study is to understand how resistance exercise training influences brain blood flow and mental health. Please note, participation in the study is no way a treatment for depression. You are being invited to participate in this study because:

- You are between 18-65 years old
- You are diagnosed with major depressive disorder with current depressive symptoms
- You are EITHER not taking any mental health medications or seeking other mental health treatment (e.g., behavioral, psychological) OR be on a stable mental health medication and/or treatment regimen for the past 8 weeks, and be willing to maintain that regimen for the duration of the study
- You have or will have physician clearance to participate in resistance exercise training

Due to the potential impact of certain conditions on study outcomes, you will be excluded from participation if you are:

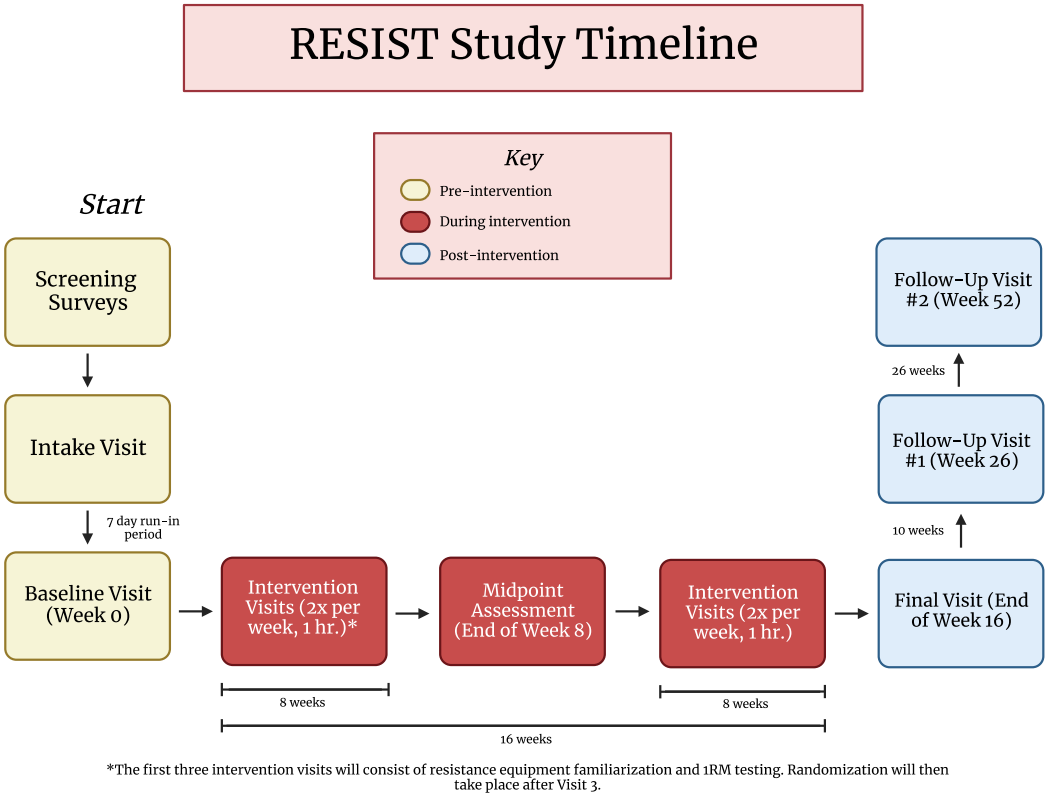
- Currently pregnant, nursing, or planning to become pregnant during the study
- Currently diagnosed with Substance Use Disorder
- Diagnosed with lifetime or current Psychosis, Mania, or Bipolar Disorder, via the SCID
- Class III+ or greater level of obesity (BMI≥40),
- Have high active suicidal ideation

- Currently meet resistance exercise training (RET) recommendations of exercising 2 days per week for the last 8 weeks
- Suffered a recent (within 3 months) severe concussion, in which you lost consciousness
- Currently have cardiovascular disease
- Currently have uncontrolled hypertension (blood pressure greater than 160/100 mmHg)
- Currently have uncontrolled diabetes
- Exhibit behavioral disturbance (e.g., aggression, mild-moderate cognitive impairment) or relationships with study team members (i.e., clinical interviewers) that would significantly interfere with study participation, as assessed by clinical research personnel

If you have any questions about the inclusion and exclusion criteria for this study, please ask the study staff now. Research staff will make inclusion/exclusion decisions regarding your participation based on your responses to questions during this Intake Visit. You will be excluded from participation if you are deemed ineligible to participate based on your responses.

DESCRIPTION OF PROCEDURES

If you agree to participate, you will be asked to complete an initial Intake Visit (today's visit), Baseline Assessment Visit, 16 weeks of resistance exercise training, a Midpoint (week 8), Final (week 16) and two Follow Up (weeks 26 and 52) Assessment visits (see figure below).



Prior to each Assessment Visit, we will ask that you abstain from alcohol, exercise and dietary supplements for 24 hours prior, are 4 hours fasted, and do not consume non-essential medication (i.e., typically over the counter medication not prescribed for chronic conditions, such as allergy medication, nutritional supplements, Advil, etc.) or caffeine the morning of testing because these substances can influence artery function. Please DO continue to take your prescribed medications. We will also ask that you wear loose fitting, comfortable clothing and tennis shoes for each study visit (Assessment Visits and RET Sessions) to complete body composition analyses, strength assessments and resistance exercises.

Intake Visit (2.5-3 hrs.)
During the Intake Visit, after reading and signing the informed consent document, you will complete questionnaires. You will then complete a clinical interview to verify eligibility. The clinical interviewer is an ISU Counseling Psychology Graduate Student, who has been trained and is supervised by Nathaniel Wade (licensed psychologist in the state of Iowa). Dr. Wade will not be present during the interview, but all clinical interviews will be video and audio-recorded for weekly supervision by Dr. Wade. Following, you will collaboratively create a mental health safety plan with the clinical interviewer to use during enrollment in the study.
After the clinical interview, you will complete more questionnaires. You will be given instructions over an activPAL accelerometer and asked to wear the device on your thigh for 7 days (24 hours/day) to assess activity levels. After one week, you will be asked to return for a Baseline Visit.

Baseline Visit (2.5-3 hrs.)
During the Baseline Visit, you will return the accelerometer and the data will be checked for valid wear time. If there is not enough data (i.e., at least 4 days of at least 10 hours of valid wear time/day determined using the activPAL software), you will be asked to re-wear the monitor and the Baseline Visit will be rescheduled. Next, a trained phlebotomist will collect approximately 2 teaspoons of blood. These samples will be drawn via venipuncture. Blood samples will be collected to examine alternative biomarkers associated with or potentially underlying treatment response. You will then complete questionnaires and anthropometric assessments. Anthropometric assessments will include height, weight, and a body composition analysis (described below).

You will then complete cerebrovascular assessments (each described below with pictures of each in the Cerebrovascular Assessments document behind the informed consent in this binder). We will assess vascular function while you lie on your back after 10 min of quiet rest in a dimly lit room. All of the vascular assessments described below are non-invasive (no needles, no blood). We will always measure your blood pressure first using the standard physician's office arm cuff, followed by simultaneous measurement of your neck blood flow, brain blood flow, blood pressure waveforms, heart rate variability, blood pressure variability, and exhaled carbon dioxide (i.e., these measures will take place at the same time in order to be more efficient). Although these measures are being conducted at the same time, only the probes at your temples measuring brain blood flow will remain on you for the entire testing period. We will then reassess brain blood flow and carbon dioxide levels while you perform 8 periods of paced-breathing followed by 20-second breath-holds. This test will give us information about how the arteries in your brain regulate blood flow.

Following, you will then complete grip strength assessments and resistance exercise equipment familiarization, detailed below. You will then receive health education and schedule all study visits.

Familiarization Procedures. You will complete familiarization with three exercise machines (chest press, lat pulldown, and leg press) at the baseline visit. A research team member will describe and demonstrate the correct form for each exercise first. Next, you will complete 2 reps at a very light intensity. The intensity will progress to a moderate-to-hard intensity so you are able to learn each movement and ask questions throughout the process. Familiarization for all other exercises will be completed during RET sessions one and two.

Resistance Exercise Training (RET Sessions; ~1 hr. each)
During the 16-week intervention period, you will complete RET twice per week. All exercises will be performed using state-of-the-art resistance exercise equipment, and all RET sessions will be fully supervised by a research staff member, available for questions and help at any time.

Each session will last ~60 minutes, beginning and ending with a 5-minute warm-up on a cycle ergometer or treadmill. The progression of this training will begin with a two-week

familiarization process to introduce you to the machines, teach correct lifting technique, ensure safety and comfort with each exercise, and complete estimated 1-RM testing on additional machines (e.g., bicep curl) to program the rest of your workouts. During each session, you will perform 3 sets of 8-12 repetitions on 9 different exercise machines, including leg press, hamstring curl, quadriceps extension, chest press, upper back, lat. pulldown, shoulder press, biceps curl, triceps extension, and one body/free-weight exercise (e.g., 3 sets planks for ~15-60 seconds, with or without additional weight placed on your back, depending on abilities). You will have a 1-min rest time between each set. The workload of your RET sessions will be tailored based on your group assignment and your estimated 1-RM (described below). You will either be randomized to the high- or low-dose RET group. Each group (high- and low-dose) will begin at different intensity levels, but both will progress in intensity throughout the intervention.

If you need to miss a session (e.g., traveling, holiday), we will also provide you with a set of exercise resistance bands to complete the session at home. We will provide instructions and have you practice each exercise during the first 2 weeks to ensure you are comfortable completing the resistance exercise session independently.

Midpoint, Final, and Follow-up Assessment Visits (~2.5-3 hrs. each)
You will return for a Midpoint, Final, and Follow-up Assessment Visit at the end of week 8, 16, 26, and 52 weeks, respectively, after re-wearing the activPAL activity monitor for 7 days. The monitors will be given to you during your RET Sessions prior to the Midpoint and Final Visit and we will ask you to pick it up prior to your Follow Up Visits. Assessments taken during these visits will be identical to those collected during the Intake and Baseline Visit. Each will begin with a clinical interview by a trained Clinical Interviewer, followed by a blood draw, questionnaires, and anthropometric assessments. Cerebrovascular and strength assessments will then be completed.

DESCRIPTIONS OF ASSESSMENTS:

Questionnaires: You will be asked to complete several questionnaires about your health (including sensitive medical history information), physical activity, how you are feeling and other psychological factors. Most questionnaires will be completed electronically, and all questionnaires will only be associated with your study ID number. You will be able to skip any questions that you do not feel comfortable responding to.

Body composition assessment: We will estimate your body fat using bioelectrical impedance, which estimates the composition of various tissues in the body (muscle vs fat) by determining the tissue's resistance to an electrical current. For this assessment, you will be asked to remove your shoes, socks, accessories, and all metal (e.g., watches, jewelry). You will also be asked if you have any implanted devices, such as a pacemaker. If you do, you will not complete this analysis and instead continue with the rest of the study visit. If not, you will complete the analysis. To do so, you will stand on a platform in barefoot (i.e., no socks/shoes) and hold onto the device's handles for ~60 seconds while a safe, painless electrical current flows through your body.

Cerebrovascular Assessments:

- **Blood pressure:** We will measure your blood pressure by placing an automated cuff around your upper arm after you have rested quietly for at least 5 minutes. The automated cuff will inflate and deflate slowly. This is the same measurement that is often done at the physician's office during a routine visit. Brachial blood pressure will be taken at least twice and additional blood pressures will be taken if values differ by more than 5 mmHg until blood pressure has stabilized (no more than 5 consecutive measures will be taken).
- **Arterial Stiffness:** We will place a very sensitive pressure sensor on your neck (carotid artery), wrist (radial artery), forearm (brachial artery), and hip (femoral artery). Using the blood pressure waveforms from this technique, we can assess how stiff different segments of your arteries are. This technique is non-invasive and takes 5-15 minutes.
- **Blood Flow:** We will measure your neck blood flow and brain blood flow using Doppler ultrasound. Probes like these are used clinically in the physician's office to measure brain blood flow and similar to those designed to look at babies in the womb. An ultrasound probe will be placed on your neck and 2 others will be placed on both sides of your head (near your temple, between your eye and ear) to assess neck artery stiffness and blood flow, and brain blood flow in two different arteries. The ultrasound probes on your temples will be secured with a headset in order to measure brain blood flow. Each ultrasound probe needs a small amount of hypoallergenic (not likely to cause an allergic reaction) gel at each site to help us get a clearer picture. This gel washes off very easily and is composed of salt and water.
- **End-tidal CO2:** We will measure the amount of carbon dioxide exhaled with each breath by putting a sterile plastic mouthpiece in your mouth and asking you to breathe normally but only through your mouth. In order to facilitate this, we will put a nose-clip on your nose to prevent air escaping through your nostrils. During this time, we will also clip a pulse-oximeter onto your finger to measure the amount of oxygen in your blood (similar to devices seen in physician's offices/hospitals).
- **Heart rate variability (HRV) and blood pressure variability (BPV):** We will assess continuous heart rate and blood pressure. Heart rate (HR) will be measured noninvasively via a standard electrocardiogram (EKG) by placing 3 electrodes on your torso. Blood pressure will also be measured non-invasively using a small inflatable cuff that will be placed around your middle finger and pointer finger (similar to a pulse oximeter that would be used in a doctor's office).

Strength Assessments:

- **Grip Strength:** Grip strength will be collected for a simple, quick, overall estimate of strength, assessed using a hydraulic hand dynamometer. For this assessment, you will squeeze the dynamometer twice to practice. Then, then you will squeeze the device as hard as possible. There will be three separate trials completed on each hand.
- **One Rep Maximum Estimate Strength Assessment (1-RM):** During the first two weeks of training and at subsequent assessment visits, we will do strength testing on two upper body (chest press and lat. pulldown) and one lower body

(leg press) major muscle groups. We will also have you complete strength assessments on all machines to program your workout. To do so, we will use an estimated 1-repitition max (1RM) testing method, which records the maximum amount of weight that can be lifted ~2-5 times with correct form, timing, and breathing. In these tests, you will begin by being shown the machines, proper form for each lift, and perform the lift 10 times (1 set, 10 reps) with light weight. You will then continue performing sets of 10 reps, gradually increasing weight until only 1-5 reps are performed to exhaustion (i.e., you cannot complete more than 1-5 reps). These values are used to calculate what we estimate a person's 1RM to be, or maximum amount of weight they can lift one time (i.e., if you complete 5 reps, that is generally ~87% of your true 1RM). The field-wide standard for reporting muscle-specific strength is 1RM values, and using an estimated 1RM protocol provides more rigorous, reliable results and is safer for non-expert lifters over conducting a true 1RM (i.e., continuing testing until one and only one repetition is able to be completed) protocol. Actual 1RM testing forces individuals to perform multiple near-maximal lifts and often results in greater variability in inexperienced lifters and can cause injury. Thus, to estimate 1RM values, a standard estimated 1RM testing protocol will be used as recommended by the American College of Sports Medicine and standard resistance training design.

RISKS OR DISCOMFORTS

There are some risks and/or discomforts you may experience during participation of this research study. Each risk is detailed below, along with a description of how the research team will attempt to minimize their occurrence.

Discomfort during or after resistance exercise training (RET) or strength assessments. Resistance exercise training and strength assessments are generally very safe and tolerable, even for inactive adults. The most common complication is delayed onset muscle soreness, characterized by pain and stiffness felt in muscles several hours to days after exercise. Very rarely musculoskeletal injury can occur because of improper lifting technique and/or from lifting weights that are too heavy. Other risks associated with general exercise include shortness of breath, feeling dizzy or fatigue. Extremely rarely a heart rhythm abnormality or heart attack may occur during exercise, requiring resuscitation and hospitalization. However, this is extremely uncommon during exercise sessions of individuals who pass study inclusion criteria that screens for contraindications to exercise. To reduce this risk, all research staff will be trained in first aid, location of the AED, and other safety protocols (see Exercise Emergency Action Plan for additional details). To further minimize these risks, the research team will teach proper form for all exercises and strength assessments, use individualized exercise prescription, closely supervise all sessions and assessments, and share tips on how to manage soreness. In addition, each session will begin and end with a 5-minute aerobic warm up/cool down (e.g., walking) on a treadmill to reduce injury.

Discomfort from cerebrovascular assessments. Cerebral and carotid Doppler ultrasound is non-invasive. The probe will be cleaned with disinfectant spray between the consecutive uses. There is a small risk that gel may come into contact with the eye as the cerebral measure is made approximately halfway between the eye and ear. To protect against this happening, we will use the least amount of gel possible to obtain the measurements. If gel does come into contact with the eye it may cause slight discomfort but it is not permanent. The gel is water soluble and actually designed to be used for eye exams (to examine retinal blood flow); therefore, it rinses out easily. There is a laboratory sink in close proximity to the cerebrovascular assessments that will serve as an eye-wash station if gel does come into contact with your eye. There is also a private restroom in close proximity that can be used if preferred.

Discomfort from femoral artery palpation. There is potential risk for discomfort from having a technician perform the femoral artery palpation required for the arterial stiffness assessment. We will have technicians of both sexes available during all assessments and you will be asked if you have a sex preference for the research personnel completing the assessment. In addition, we employ a number of techniques to try and ease any concern with the measurement. These techniques include:

- Showing where the pulse is located and having you try to find the pulse on yourself so you have a better idea where the technician will be placing the probe
- We palpate and measure the femoral artery pulse through (i.e. over) a pair of thin athletic shorts (meaning the probe and technician's hand is not directly against your skin; the lab maintains a number of clean, thin athletic shorts in a variety of sizes (S-XXL) in the event these need to be used). If we still cannot get the pulse waveforms we will place the probe inside the shorts pocket and try to again obtain the pulse (i.e. the probe and technician's hand are still are not directly touching skin but are placing thinner material between the probe and pulse).
- If that is not sufficient, we will ask you if we can place the probe under your shorts but on top of your underwear. Importantly, in this setting once we place the probe underneath the shorts the technician keeps their hands on top of the shorts to manipulate the probe (again, the technician's hand is not directly touching the skin).
- If you express any discomfort throughout this process, we will remove the probe and will skip the assessment.

Risks of the Blood Draws. There is a rare risk of fainting or dizziness. There is also a small risk of bruising or bleeding at the site of the needle (about 1 in 10 cases), and an extremely small risk (about 1 in 1000 cases) of infection. The total quantity of blood collected across all visits will be about 50 mL (~10 teaspoons), much less than that taken during a single donation at the Red Cross Center or a blood drive (500mL or ~101 teaspoons). On rare occasions, the needle may damage a nerve or the vein, causing the vein to become blocked. Additionally, there is a small risk of fainting or dizziness during and after the blood draws. These risks will be minimized by using trained phlebotomists to draw the blood and using sterile equipment in an area designed for the collection of blood samples. Two research staff members will be present in case the participant begins to feel faint or dizzy.

Psychologic stress from mental health questions. There may be limited psychological stress related to discussing mental health questions during the clinical interview. Dr. Meyer and Dr. Wade have supervised the training of the personnel who administer the clinical mental health interviews. Dr. Wade, a licensed psychologist in the state of Iowa, will provide guidance to the person performing the clinical interview to help them in minimizing any psychological distress that may be experienced while discussing mental health issues. For participant safety, during the Intake Visit, you will collaboratively create a safety plan with the clinical interviewer to provide support if dealing with suicidal thought any time throughout or after the study. Additionally, the research team will closely monitor suicidality throughout the study, both during assessment visits by the clinical interview and weekly via questionnaire. If any severe responses are encountered, the clinical interviewer will follow up with you to assess suicide severity and facilitate activation of your safety plan if needed. If unable to get ahold of you, emergency services will be contacted to perform a welfare check. If at any time during the study, it appears you may be an imminent threat to yourself, emergency personnel (either Iowa State University police or city police) will be contacted to help you transport to additional emergency services (e.g., community mental health services).

Social risk due to stigmatization. There may be some social risk regarding the disclosure of mental health information. The main risks are harm to reputation, embarrassment, or stigmatization if participation in the study becomes known, but given the study procedures, this risk is low. Nonetheless, strategies to reduce this risk include:

- Using a strategic study name that does not disclose the clinical outcome being evaluated in the study
- Having all assessment visits on an individual basis to minimize contact with other participants
- Having assessment visits performed in closed rooms to minimize the chance of being noticed by others
- Having the RET sessions occur in an exercise space that is advertised as hosting numerous studies. Signage and flyers for the multiple studies will be posted outside of the exercise space, and opaque paper will be used to over windows to the exercise area (i.e., covering widows for privacy during exercise)

Breach of confidentiality. Confidentiality will be a central value of this study. However, there are situations in which confidentiality might need to be breached. Research staff are permissive reporters, meaning they will voluntarily contact local authorities or other health service providers if you reveal (a) that a child or older adult is being abused or severely neglected, or (b) that you are an imminent threat to yourself or someone else. If a report is made, this may be a breach of your confidentiality. We are making you aware of this potential need to breach your confidentiality by informing you here, as well as having this specifically discussed with the clinical interviewer during the Intake Visit.

To further reduce all risks, all research personnel will have had extensive training and supervision prior to assisting with study visits. As noted above, all clinical interviewers are trained and supervised by Dr. Wade (licensed clinical psychologist in Iowa). Dr. Lefferts (Assistant Professor with over 10 years of experience conducting brain blood flow assessments) trains and supervises all lab-technicians completing the brain blood assessments. Each lab technician completed reliability testing on the brain blood flow

assessments, under direct supervision of Dr. Lefferts, prior to assisting with study visits. Dr. Lansing (Assistant Scientist with over 5 years of experience conducting physical activity interventions) trains and supervises study personnel on physical activity monitoring devices, body composition and strength assessments, and administering the RET program. All study personnel completed test outs on each assessment, under supervision of Dr. Lansing, prior to assisting with study visits. On-going training and supervision of these assessments will occur during the entire study duration. Please let the research team know now if you have any questions about the training of the research staff.

BENEFITS

As part of the study, you will receive health education during the Baseline Visit. This will include personalized health data, including physical activity summaries (e.g., average steps/day, average sedentary time per day, minutes of moderate and vigorous physical activity), body composition (e.g., percent fat mass, percent lean muscle mass), and cerebrovascular assessments (e.g., arterial stiffness, blood pressure, brain blood flow). These data will be collecting using state-of-the-art equipment, providing extremely detailed and accurate data. Such assessments are costly but will be provided free of charge for participation in this study. Additionally, you will receive normative values for each assessment, physical activity recommendations and information for strategies for improving physical and mental health.

As part of the intervention, you will also receive 16 weeks of structured exercise training using state-of-the-art exercise equipment with highly trained staff to teach proper lifting form and closely monitor exercise sessions. This may result in physical and mental health benefits.

We hope that the study will benefit society by helping us learn more about behavioral treatments for depression.

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

COSTS AND COMPENSATION

You will be compensated for travel to and from each study visit you attend at Research Park 6 and the Forker building in Ames, IA. Compensation will be distributed in the form of checks mailed to your home or mailing address every two weeks. Additionally, you will receive a $50 Visa gift card for each assessment visit you attend, up to $300.

You will need to complete a form to receive payment. Please know that payments may be subject to tax withholding requirements, which vary depending upon whether you are a legal resident of the U.S. or another country. If required, taxes will be withheld from the payment you receive. You will need to provide your address and may also need to provide your social security number (SSN; pending the amount you will be reimbursed for traveling to study visits) on the form in order for us to pay you. This information

allows the University to fulfill government reporting requirements. Confidentiality measures are in place to keep this information secure. You may forego receipt of payment(s) and continue in the research study if you do not wish to provide your social security number and address. Information regarding documentation required for participant compensation may be obtained from the Controller's Department: (515) 294-0457 or http://www.controller.iastate.edu.

In addition, you will receive prizes throughout the intervention for achieving intervention milestones (e.g., completing 1RM baseline testing, attending 8 sessions). These may include: a study tee-shirt, water bottle, hat, bag, workout towel, lanyard, and/or pin. You will also receive your own set of resistance exercise bands to use during the intervention for at-home workouts when necessary.

PARTICIPANT RIGHTS

Participating in this study is completely voluntary. You may choose not to take part in the study or to stop participating at any time, for any reason, without penalty or negative consequences. You can also skip any questions that you do not wish to answer. Participating or choosing not to participate will not affect your relationship with any of the study personnel or with your health care provider. You can continue receiving care from your primary health care provider regardless of your participation in the research. Your choice of whether or not to participate will have no impact on you as a student/employee of Iowa State University in any way. If you become pregnant during this study or if the medications you routinely take for psychological reasons change, please inform the staff, and you will be removed from the study.

If you have any questions *about the rights of research subjects or research-related injury*, please contact the IRB Administrator (515) 294-4566), the IRB Director (515) 294-3115), or IRB@iastate.edu.

RESEARCH INJURY

Please tell the researchers if you believe you have any injuries caused by your participation in the study. The researchers may be able to assist you with locating emergency treatment, if appropriate, but you or your insurance company will be responsible for the cost. Eligible Iowa State University students may obtain treatment from the Thielen Student Health Center. By agreeing to participate in the study, you do not give up your right to seek payment if you are harmed as a result of being in this study. However, claims for payment sought from the University will only be paid to the extent permitted by Iowa law, including the Iowa Tort Claims Act (Iowa Code Chapter 669).

CONFIDENTIALITY

Note: In this section, we will refer to both the National Institutes of Health (NIH) and the National Institute of Mental Health (NIMH). The NIMH is the federal agency funding this research; it is a sub-agency of NIH, which has a set of policies governing data collection, data sharing, and privacy/confidentiality for research to which the agency awards funds.

Records identifying participants will be kept confidential to the extent permitted by applicable laws and regulations and will not be made publicly available. However,

federal government regulatory agencies, the National Institute of Mental Health, auditing departments of Iowa State University, and the Institutional Review Board (a committee that reviews and approves human subject research studies) may inspect and/or copy study records for quality assurance and data analysis. These records may contain private information.

To ensure confidentiality to the extent permitted by law, the following measures will be taken. Only subject ID codes will be used for data processing and analyses. Physical activity, self-report measures, blood samples, and all assessments (anthropometric, cerebrovascular, and strength) will be de-identified and marked with subject ID code to minimize any risks of confidentiality.

Audio and video recordings from the clinical interviews will also be kept confidential. They will be automatically saved to the research team's Webex account cloud (password protected and only accessible to the research team). All recordings from the clinical interview will immediately be stored on ISU's secure, cloud-based storage system and then deleted from Webex altogether. All recordings will only be linked to your ID code and will never be shared outside the research team.

Additionally, we will use REDCap software which will eliminate the need for hard copies of each questionnaire to be filled out. Instead, questionnaires will be filled out on a computer and the data will be stored on a password-protected folder (on ISU's secure cloud-based storage system) with only subject ID codes linking each set of questionnaire answers to the participant. The individual information that you provide as part of this experiment will not be disseminated in any manner that may identify you. However, de-identified information from this experiment may be disseminated in journal articles, theses, and conference presentations.

CERTIFICATE OF CONFIDENTIALITY

Identifying information gathered about you during this research project is protected by a Certificate of Confidentiality from the National Institutes of Health. With this Certificate, researchers cannot be forced to share identifying information about you with anyone not connected to the research, even by a court subpoena. The researchers will use the Certificate to resist any court orders or legal demands.

Additionally, identifying information protected by the Certificate will not be shared outside of the research team, <u>except in the following instances</u>:

- If there is a law that requires disclosure (such as to report child abuse or communicable diseases, *but not for legal or other similar proceedings)*;
- If you have consented to the disclosure or sharing of information, including any disclosure or data sharing plans described elsewhere in this consent document; or
- For use in other scientific research, as allowed by federal regulations protecting research subjects; or
- To personnel of the NIH, when information is needed for auditing or program evaluation; or
- To meet the reporting requirements of the Food and Drug Administration, such as for studies of investigational medical devices or drugs; or

- To authorized individuals at Iowa State University if they need to verify that the research is being done correctly.

In addition, the researchers may share information if necessary to prevent serious harm to you or someone else; for example, if the researchers learn of ongoing child abuse or neglect, or the imminent threat of harm to you or others, they may share this information with the appropriate authorities.

You should know that a Certificate of Confidentiality does not prevent you from voluntarily sharing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

ADDITIONAL USE OF RESEARCH DATA, INCLUDING BLOOD SAMPLES

Data from this study will be submitted to the National Institute of Mental Health Data Archive (NDA) at the National Institutes of Health (NIH). More information about the NDA is below. In addition, information about your personal characteristics, such as your sex/gender, race, ethnicity, and age, must be reported to the National Institutes of Health (NIH), the parent agency of study's funding agency (the National Institute of Mental Health). The information we report to NIH will not include any information that could identify you.

Aside from sharing deidentified study data with NDA or NIH, there are no other known plans for future research using the data, but additional research questions may be explored with collaborators at Iowa State or at other institutions. For example, future research might include the analysis of cerebrovascular assessment to answer new research questions related to depression. In all future analyses, only de-identified data will ever be used.

Your blood samples will have your identity removed and will be securely and confidentially stored for potential future analyses of biomarkers, such as a protein or hormone when new research indicates it may be relevant (in treatment of depression or physiological response to exercise) after you have finished the study. In some cases, we may ask a collaborator or lab outside of the Iowa State research team to analyze the blood samples for us. We will not perform any genome sequencing of your samples. Whole genome sequencing is a process that maps out your specific DNA. You will not receive results from any analysis of blood samples.

Please be aware that we will not obtain additional permission from you for the uses of your de-identified data or blood samples described above.

The National Institute of Mental Health Data Archive (NDA)

Data from this study will be submitted to the National Institute of Mental Health Data Archive (NDA) at the National Institutes of Health (NIH). NDA is a large federal database where deidentified study data from many NIH studies are stored and

managed. Sharing your deidentified study data helps researchers learn new and important things about brain science more quickly than before.

Deidentified study data means that all personal information about you (such as name, address, birthdate and phone number) is removed and replaced with a code number. The study researchers will have to collect your personal information from you in order to make that code number. Creating the code number involves inputting your information into a secure federal tool that generates the code. The resulting code number is a series of numbers and letters. There is no information in the code that can be used to infer your identity (e.g. it does not contain your initials, date of birth, etc.). The study researchers will never send your personal information to NDA. Your blood samples and the audio/video recordings of the clinical interviews will NOT be included in any data submitted to the NDA.

It is possible that you will participate in more than one study that sends data to NDA. NDA can connect your data from different studies by matching the code number on your deidentified data from each study. This data matching helps researchers who use NDA data to count you only one time. It also helps researchers who use NDA to better understand your health and behavior without knowing who you are.

During and after the study, the study researchers will send deidentified study data about your health and behavior to the NDA. Other researchers across the world can then request your deidentified study data for different research projects. Those research projects may examine a wide variety of topics—some may be very different from the study in which you are currently participating.

Sharing your study data does have some risks, although these risks are rare. The study researchers will make every attempt to protect your identity before sending the data to NDA. However, there remains a possibility that someone could identify you or that unauthorized people might access your data and attempt to learn your identity.

Every researcher (and the institution to which they belong) who requests your deidentified study data must promise to keep your data safe and promise not to try to learn your identity. Experts at the NIH who know how to keep your data safe will review each request carefully to reduce risks to your privacy.
You may not benefit directly from allowing your study data to be shared with NDA. The study data provided to NDA may help researchers around the world learn more about brain science and how to help others who have problems with brain science. NIMH will also report to Congress and on its website about the different studies using NDA data. You will not be contacted directly about the study data you contributed to NDA.

You may decide now or later that you do not want your study data to be added to NDA. You can still participate in this research study even if you decide that you do not want your data to be added to NDA. If you know now that you do not want your data in NDA, please tell the study researcher before leaving the visit today. If you decide any time after today that you do not want your data to be added to NDA, call or email the study staff who conducted this study, and they will stop sharing your study data with NDA.

However, once your data is part of NDA, the study researchers cannot take back the study data that was shared before they were notified that you changed your mind.

If you would like more information about NDA, it is available on-line at http://nda.nih.gov.

Please initial to indicate your choice:

_____ YES, my deidentified study data may be added to the NDA

_____ NO, do NOT add my study data to the NDA

QUESTIONS
You are encouraged to ask questions at any time during this study. For further information ***about the study,*** contact Dr. Meyer at (515) 294-1386 or jdmeyer3@iastate.edu.

Pregnancy
This study does not allow the participation of female subjects who are pregnant. Female subjects are therefore asked to sign the following statement before proceeding. Please sign this statement only if you are certain you are not pregnant and do not plan on becoming pregnant during your inclusion in this study. If you are not certain or are trying to become pregnant, please do not sign this statement.

I confirm that I am not pregnant and do not plan on becoming pregnant during my inclusion in this study. If I become aware that I am or was pregnant during my inclusion in this research, I will promptly inform the investigators.

Participant Signature _____ Date: _____

Maintain Contact Information
Aside from the present research study, Dr. Meyer's laboratory and others in the Kinesiology department routinely conduct research on physical activity, exercise and wellbeing. If you are interested in being contacted about studies in the future, please indicate so below.

____ Yes, please keep my contact and demographic information and contact me regarding future studies that I may be eligible to participate in

_____No, I would not like to be contacted regarding future research opportunities, please destroy my contact information at the conclusion of the study

FINAL CONSENT AND AUTHORIZATION PROVISIONS
Your signature indicates that you voluntarily agree to participate in this study. When you sign this document, you are stating that the experiment has been fully explained to you, and that you understand that the data obtained from this study are to be used for research purposes only, not for the evaluation or diagnosis of any disorder, and that such data will remain confidential, except as required by law. You are also stating that you have been given the time to read the document, had the opportunity to ask

questions concerning all aspects of the procedures, and that your questions have been satisfactorily answered. Your signature indicates that you are aware that participation is voluntary, and that you may withdraw your consent at any time.

I, the undersigned, hereby consent to be a participant in the project described above conducted in the Department of Kinesiology at Iowa State University.

Participant Name (printed) _____
Participant Signature _____ Date: _____

Investigator Statement
I certify that the participant has been given adequate time to read and learn about the study and all of their questions have been answered. In my opinion, the participant understands the purpose, risks, benefits and procedures included in this study and has voluntarily agreed to participate.

Research Personnel Signature: _____ Date: _____