Document Coversheet

Study Title: Effects of Unloading and Sleep Restriction on Balance Regulation and Quadriceps Structure and Contractile Function

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Consent and Authorization to Participate in a Research Study

KEY INFORMATION FOR:

Effects of unloading and sleep restriction on balance regulation and quadriceps structure and contractile function

We are asking you to choose whether or not to volunteer for a research study about how unloading and sleep restriction affect muscle strength and voluntary activation of muscle. We are asking you because you are a healthy person between the ages of 18 and 50 years old who regularly participates in exercise. This page is to give you key information to help you decide whether to participate. We have included detailed information after this page. Ask the research team questions. If you have questions later, the contact information for the research investigator in charge of the study is below.

WHAT IS THE STUDY ABOUT AND HOW LONG WILL IT LAST?

During space flight, astronauts are exposed to many stimuli (such as unloading and loss of sleep) that can affect their physical performance. These stimuli may combine to impair muscle strength and balance and increase risks of falls and injuries during exploration missions on the moon or Mars. By doing this study, we hope to improve mission performance, safety, and health of astronauts in extraterrestrial exploration missions

This study aims to determine size, strength, and voluntary activation of thigh muscles as well as and balance regulation in response to prolonged disuse with and without sleep restriction. To do this, we will measure the strength, efficiency, and activation of the quadriceps with several tests. We will also measure quadriceps size by MRI and your ability to maintain balance while standing on one leg and stepping down from a step.

By doing this study, we hope to learn if how muscle unloading and sleep restriction combine to affect strength and ability to maintain balance. This could help improve our understanding of what is happening to the muscle of people who suffer unloading and loss of sleep (for example, astronauts or those in a hospital). Your participation in this research will include 3 total visits, each lasting 2-2 ½ hours, and last about 2 weeks. The total amount of time you would commit to this study would be about 6 to 7.5 hours although research protocols will affect your daily life for the duration of the study.

WHAT ARE KEY REASONS YOU MIGHT CHOOSE TO VOLUNTEER FOR THIS STUDY?

You might want to take part in this study if you are curious about your quadriceps strength and muscle size. As part of this study, you will gain information about your quadriceps strength and muscle mass. This information may be interesting to you in terms of managing your health and fitness. You might also want to participate to help improve the scientific community's understanding of how the human body responds to combined unloading and sleep loss.

WHAT ARE KEY REASONS YOU MIGHT CHOOSE NOT TO VOLUNTEER FOR THIS STUDY?

You might not want to participate if you are unwilling or unable to limit your sleep or are worried about the effects of sleeping less for three nights in a row. You might not want to participate if you are unwilling or unable to walk exclusively with crutches for two weeks. Two weeks of unloading may significantly affect your daily life and could reduce muscle size and strength of one leg. We will help you understand how to follow research procedures to allow you to evaluate if this is something you are able to do. Additionally, you might not want to participate if you are worried about electrical stimulation of the thigh muscles. Some individuals experience some discomfort during this procedure, but this effect goes away in a few minutes.

If these are concerning to you, the only choice is to not participate in this study. If you are not comfortable with this type of exercise and electrical stimulation after a practice session, you may choose to withdraw from the study at that time.

DO YOU HAVE TO TAKE PART IN THE STUDY?

If you decide to take part in the study, it should be because you really want to volunteer. You will not lose any services, benefits, or rights you would normally have if you choose not to volunteer.

If you are a student and you decide not to take part in this study, your choice will have no effect on your academic status or class grade(s).

WHAT IF YOU HAVE QUESTIONS, SUGGESTIONS OR CONCERNS?

If you have questions, suggestions, or concerns regarding this study or you want to withdraw from the study contact Lance Bollinger, PhD of the University of Kentucky, Department of Kinesiology and Health Promotion at 859.257.7904 or lance.bollinger@uky.edu. If you have any concerns or questions about your rights as a volunteer in this research, contact staff in the University of Kentucky (UK) Office of Research Integrity (ORI) between the business hours of 8am and 5pm EST, Monday-Friday at 859-257-9428 or toll free at 1-866-400-9428.

DETAILED CONSENT:

ARE THERE REASONS WHY YOU WOULD NOT QUALIFY FOR THIS STUDY?

You would not qualify for this study if you have any of the following:

- Are not between the ages of 18 and 50
- Are shorter than 5 feet tall (females) or 5 and a half feet tall (males)
- Are taller than 6 and a half feet tall
- Have a waist circumference less than 21 and a half inches or greater than 35 inches (females)
- Have a waist circumference less than 29 and a half inches or greater than 40 inches (males)
- Have a body mass index of less than 18.5 or greater than 29.9
- do not regularly sleep between 7 and 9 hours each night
- do not regularly participate in exercise
- blood clotting disorder
- heart rhythm problem
- heart, lung, kidney disease or diabetes
- are pregnant or have given birth in the past 6 months
- have taken oral contraceptives within the past 3 months
- high blood pressure (resting blood pressure of > 140 over > 90)
- have undergone sex-affirming therapies (hormone therapy and/or sexual reassignment surgery)
- have had a low back or leg injury or surgery in the past 6 months
- have a diagnosed sleep disorder
- have been prescribed medication to help sleep
- muscle, bone, or joint injury in the past six months
- neurological disorder which affects balance (such as multiple sclerosis or Parkinson's disease)
- Implanted devices such as but not limited to a pacemaker, internal defibrillator, or cochlear implants that could negatively be affected by electrical stimulation

WHERE WILL THE STUDY TAKE PLACE AND WHAT IS THE TOTAL AMOUNT OF TIME INVOLVED?

The research procedures will be conducted at the human performance laboratory in the Multidisciplinary Science Building (Rm. B04A) at the University of Kentucky. Some research procedures will be conducted at other locations, but we will guide you to these facilities. You will need to come 3 times during the study. Each of those visits will take about 2-2 ½ hours. The total amount of time you will be asked to volunteer for this study is 6-7.5 hours over the next 2 weeks. However, the research procedures will also affect your day-to-day life for the duration of the study.

WHAT WILL YOU BE ASKED TO DO?

You will be asked to walk using crutches and specially supplied shoes for the entire length of the study. This will keep your left leg suspended in the air at all times. You will be asked not to use your left leg muscles at all (or as minimally as possible) for the entire study. For the last three days of the study, you will be asked to either maintain your usual sleep or to restrict your sleep to only 5 hours per night. To monitor sleep, you will also be asked to wear a wrist worn sleep monitoring device for the entirety of the study. We will also ask you to complete a sleep questionnaire each morning of the study. Before and after this intervention, you will be asked to perform a series of tests to measure quadriceps size, strength, and activation. We will also measure your balance during single leg stance and after stepping down from a platform. At the end of the study, you will have an MRI of your thigh muscles.

Screening: On the first visit, we will ask you to answer a few items about your health history and current exercise habits to ensure it is safe for you to be part of the study. Additionally, we will give you a wrist worn device to wear that will track sleep. We will then familiarize you with the equipment used and the tests we will conduct (described below). We will provide you with specialized shoes and crutches to use throughout the study and help you get comfortable with using this equipment during daily activities such as walking, climbing and descending stairs, and transitioning between sitting and standing.

Unloading intervention: For the entire study, you will wear the shoes provided and walk using crutches. You should treat your left leg as though it could not move on its own or support your body weight. You should use your arms or right leg to move your left leg at all times throughout the study. You may want to use elevators or escalators when possible. You will be asked to (as much as possible) maintain daily activities throughout the study. If you exercise, you will be asked to only use your right leg for exercise. These procedures may be challenging to follow. The research team will communicate with you via phone call or email to assess compliance and provide encouragement or guidance for this procedure.

There is a small risk of blood clot with this unloading. To reduce risk of clot formation, you will need to do a few things. First, you will take an aspirin pill (81 mg) once every day. This is a low level of medication that has been recommended by a physician overseeing the study. To maintain regular blood flow, you will also be asked to wear specially designed compression stocking on your left leg throughout the study (this will be provided by the research team). You should wear the compression stocking as much as possible whenever you are on your feet throughout the study, but you can remove it to bathe. You can also reduce risk of blood clot formation by ensuring that you stay adequately hydrated throughout the day and maintaining your typical physical activity level.

We will contact you every day by phone, text, or email (whichever you prefer) to ask about compliance with unloading and screen for negative symptoms such as swelling, discoloration, tenderness/pain, and elevated temperature of your unloaded leg. If you have symptoms, we might ask you to have a blood test to look for evidence of blood clotting. If you develop symptoms of blood clotting, you will be removed from the study and referred to a physician**. If you experience discoloration (redness), an increase in temperature, or pain in your left leg, you should seek immediate medical attention.**

After 10 days of unloading, we will measure the size and temperature of your calf muscles. If you have followed the recommended protocol, you left calf should be larger and cooler than your right calf. If so, we will randomly assign you to either a regular or restricted sleep intervention. If the size and temperature of your left leg are not different from the right leg, you will be removed from the study at this time.

Exercise: As much as possible, you should follow your regular exercise program, except that only your right leg should be used for exercise. You will be given instructions, and familiarized with a series of passive, range of motion exercises that you will complete twice per day for the duration of the study. We will provide an elastic strap that you will use to help you perform these exercises. You should keep the muscles of your left leg as relaxed as possible during these exercises. The total time expected for these passive exercises is about 15 minutes per day. You should record all exercise in an exercise record book that we provide for you.

Sleep: At the beginning of the study, we will give you a wrist worn device to measure your sleep. We will ask that you wear this every night of the study. We will also ask you to complete a sleep diary report about your sleep within the first hour after you wake up each day. For the first 10 days of the study, we will ask you to sleep for 9 hours each night between 9:00pm and 6:00am. You will complete a six-item sleep diary each morning of the study right after you wake up.

After 10 days of unloading, we will inform you whether you have been randomized to the regular or restricted sleep group. If you are randomized to the regular sleep group, you will continue to follow the same sleep pattern for the next three nights. If you are randomized to the restricted sleep group, you will be asked to sleep for only 5 hours each night for three consecutive nights (between the hours of 1:00am and 6:00am). You will be asked not to take naps during the daytime if you are in the restricted sleep group. You should not consume additional caffeine during this phase of the study. All sleep procedures will be done at your regular place of residence.

Muscle Strength Testing: All muscle testing will be performed on both legs on the morning after the final night of the study (between the hours of 8:00 and 11:00a). You should not exercise for 24 hours before muscle strength testing and you should not consume any caffeine prior to this muscle strength testing session. We will place sensors (to measure muscle activity) on both of your thighs. We will shave the areas and rub them with an abrasive sponge and alcohol to make sure the area is clean for a good connection. You will sit on a knee extension machine like a chair. Your ankle will be secured to the device with a padded strap. We conduct a series of tests to measure muscle strength and activation. Each test will be performed 3-5 times. First, we will

ask you to extend your knee as hard as you can. Your leg will not move during this test. Based on your strength, we will ask you to extend your knee with given amount of force. We will tell you how hard to push and you will have a visual screen to guide you. You will do this at six different efforts, each one harder than the last. Each effort will last 10 seconds and you will be able to rest for one minute between each effort. The hardest effort will be 90% of your maximal strength. Most subjects can hold this level of force for 10 seconds with only minor trouble.

Next we will place two gel electrodes, one on your upper thigh and the other close to your knee. These will be connected to a specially designed device that will deliver a small electrical shock to your thigh. This device is made specifically for this purpose and all electricity delivered is a safe amount. Although you will feel this electrical shock, most subjects say this does not hurt. We will gradually increase the intensity of this stimulus until your thigh twitches which will cause your leg to extend. We will continue to increase the intensity of the shock until your force output no longer increases. This will tell us how much electricity you will need to for the next test. The next test will consist of 3 shocks: before, during, and after a maximal knee extension effort. We will repeat this test 3-5 times. We will instruct you when to relax and when to extend your leg and provide verbal encouragement throughout this test. After all muscle testing procedures have been completed on one leg, we will repeat this process on the opposite leg.

Balance Assessment: You will then complete a series of balance assessments. During these tests, you will have small sensors adhered to the skin over your thigh and calf muscles with double-sided tape. Before each assessment you will be given the opportunity to practice the test. During the first assessment, you will stand still on one leg for 15 seconds. You will repeat this test on both legs with your eyes open and with your eyes closed. You will do this barefoot and with shoes that we will provide for you.

During the second balance assessment, you will step off a 12-inch wooden platform and land on a force platform. As soon as you land, you will have to hold your landing position as best as you can for 10 seconds. You will repeat this test three times for each leg. We will provide specific shoes for you to wear during this test.

Muscle imaging: Before the study starts, we will ask if you have any implanted medical devices, metal in your eye or brain and other questions to ensure it is safe for you to have an MRI scan. We will repeat these questions at the end of the study before the MRI procedure in case anything changes over the course of the study.

After you have completed the entire unloading and sleep intervention (13 days), we will measure thigh muscle size and quality with magnetic resonance imaging (MRI). We will ask you to wear clothing suitable for an MRI procedure such as athletic attire without metal zippers or decorations. If you do not have this type of clothing, we will give you disposable shorts and a gown. We will assist you in getting to the MRI facility (Whitney Hendrickson Cancer Facility). You will lie on your back in the MRI scanner with a coil placed on top of your thighs. You will enter the scanner feet first. Your legs will enter the scanner so that we can collect images of your thigh muscles. It is unlikely that your head will enter the scanner. We will try to make you as comfortable as possible during this procedure by providing pillows, blankets, ear plugs, and headphones to limit the noise of the scanner. It may be possible to listen to your choice of music during this procedure. We will acquire images over approximately 30 minutes. During this time, we will ask you to stay awake and as still as possible.

Follow up: To assess the long-term impact of this study, we will follow up with you by phone call 30 days after the study is over. If you experience a fall or medical complication as a result of this study, we will ask you to report this during this phone call.

WHAT ARE THE POSSIBLE RISKS AND DISCOMFORTS?

The major sources of risk and discomfort for this study involve the unloading and sleep restriction interventions. The major health risk is the potential to develop deep vein thrombosis (DVT) – a blood clot in your leg – from prolonged disuse of one leg. These instances are very rare, but can have serious health effects such as pulmonary embolism and death. Risk of this condition are reduced by continuing to engage in your regular exercise, wearing a compression stocking, taking aspirin daily, and completing the assigned range of motion exercises. If you experience symptoms of DVT, you should seek immediate medical attention. Sleep restriction may impair your mental function. You may wish to avoid use of heavy equipment or refrain from driving, if you are performing sleep restriction. Other potential sources of risk and discomfort include a cold sensation from gel electrodes and electrical shock. In rare cases, some people may develop a rash or irritation where the patches were placed as a reaction to the adhesive in these electrodes. The table below will help you understand the

likelihood and severity of the risks and discomforts.

Potential Consequences	Likelihood	Symptoms	Severity	Course of action
Deep vein thrombosis	Rare	Leg swelling Leg pain, cramping, pain, or soreness Change in skin color of leg Elevated temperature of leg	Serious, potentially life threatening	Seek immediate medical attention
Loss of muscle size and strength	Expected to happen	Smaller size of left leg Muscle weakness Harder to complete daily activities	Not severe. Most subjects lose about 5% of muscle size and 15-20% of strength during similar studies	Resume typical exercise program. Loss of muscle size and strength typically return in about 1-2 months after similar studies.
Reaction to adhesive	Occasional	Rash on skin	Not severe	Bandage area and provide first-aid care as needed
Muscle soreness	Occasional	Pain in leg within 24-48h of exercise	Mild interference with daily living activities and other exercise	Remain physically active, avoid prolonged sitting, stretch affected muscles
Discomfort from electrical stimulation	Occasional	Pain in groin area	Not severe	Contact research team if you are concerned. We will guide you through the proper action.
Increased feelings of sleepiness or tiredness	Often	Fatigue Difficulty focusing	May impact activities such as operating heavy machinery as well as performance on any tests or assessments	Ask others for help with transportation

In addition to risks described in this consent, you may experience a previously unknown risk or side effect.

WILL YOU BENEFIT FROM TAKING PART IN THIS STUDY?

You will not receive any direct benefit from taking part in this study. Although exercise is known to improve health, the level of exercise involved in this study is unlikely to significantly improve your health.

IF YOU DON'T WANT TO TAKE PART IN THE STUDY, ARE THERE OTHER CHOICES?

If you do not want to be in the study, there are no other choices except not to take part in the study.

WHAT WILL IT COST YOU TO PARTICIPATE?

There are no financial costs to participating in this study. All research procedures (MRI and blood tests if needed) and equipment (shoes, crutches, sleep monitor, aspirin, compression stockings,) will be paid for by the research team. It is likely that you will lose some muscle mass (about 5%) and strength (about 15%) in your left leg as a direct result of the unloading intervention. With modest exercise training, it is likely that this loss of muscle strength could be recovered in one to two months.

WHO WILL SEE THE INFORMATION THAT YOU GIVE?

When we write about or share the results from the study, we will write about the combined information. We will keep your name and other identifying information private.

We will make every effort to prevent anyone who is not on the research team from knowing that you gave us information, or what that information is. Your data will be saved in hard copy form in a locked file cabinet in a room with a locked door. Electronic records of your data will be stored on password protected computers and will not contain any personal identifying information.

You should know that in some cases we may have to show your information to other people. For example, the law may require or permit us to share your information with:

- authorities or a mental health professional if you pose a danger to yourself or someone else (e.g. suicidal thoughts).

To ensure the study is conducted properly, officials of the University of Kentucky may look at or copy study records that identify you.

CAN YOU CHOOSE TO WITHDRAW FROM THE STUDY EARLY?

You can choose to leave the study at any time. You will not be treated differently if you decide to stop taking part in the study.

If you choose to leave the study early, data collected until that point will remain in the study database and may not be removed.

The investigators conducting the study may need to remove you from the study. You may be removed from the study if:

- you are not able to follow the directions,
- we find that your participation in the study is more risk to you than a scientific benefit

ARE YOU PARTICIPATING, OR CAN YOU PARTICIPATE, IN ANOTHER RESEARCH STUDY AT THE SAME TIME AS PARTICIPATING IN THIS ONE?

You may take part in this study if you are currently involved in another research study. It is important to let the investigator/your doctor know if you are in another research study. There are some studies which may limit your ability to participate in this study. You should discuss this with the investigator/your doctor before you agree to participate in another research study while you are in this study.

WHAT HAPPENS IF YOU GET HURT OR SICK DURING THE STUDY?

If you believe you are hurt or if you get sick because of something that is due to the study, you should call Lance Bollinger, PhD at 859.257.7904 immediately. Dr. Bollinger will help determine what type of treatment, if any, is best for you at that time.

It is important for you to understand that the University of Kentucky does not have funds set aside to pay for the cost of any care or treatment that might be necessary because you get hurt or sick while taking part in this study. Also, the University of Kentucky will not pay for any wages you may lose if you are harmed by this study.

Medical costs related to your care and treatment because of study-related harm will be your responsibility.

You do not give up your legal rights by signing this form.

WILL YOU RECEIVE ANY REWARDS FOR TAKING PART IN THIS STUDY?

You will receive a $500 check as compensation for your participation after you have completed all research

procedures.

WHAT IF NEW INFORMATION IS LEARNED DURING THE STUDY THAT MIGHT AFFECT YOUR DECISION TO PARTICIPATE?

We will tell you if we learn new information that could change your mind about staying in the study. We may ask you to sign a new consent form if the information is provided to you after you have joined the study.

WILL YOU BE GIVEN INDIVIDUAL RESULTS FROM THE RESEARCH TESTS?

Generally, tests done for research purposes are not meant to provide clinical information. We will provide you with individual research results concerning sleep quality and quantity, muscle strength, and muscle activation.

Do you give permission for us to contact you about research results or incidental findings that are determined to be important to you/your family's health? (Incidental findings are unforeseen findings discovered during the course of the research that may affect you or your family's health).

☐ Yes ☐ No _____Initials

You may also withdraw your consent to be contacted with information about research results or incidental findings by sending a written request to Dr. Lance Bollinger at 201 Seaton Bldg, Dept. of Kinesiology and Health Promotion, Lexington, KY 40506

WILL WE CONTACT YOU WITH INFORMATION ABOUT PARTICIPATING IN FUTURE STUDIES?

The research staff would like to contact you in the future with information about participating in additional studies. If so, it will be limited to two times per year.

Do you give your permission to be contacted in the future by _____Dr. Lance Bollinger regarding your willingness to participate in future research studies?

☐ **Yes** ☐ **No** **Initials**_____

WHAT ELSE DO YOU NEED TO KNOW?

If you volunteer to take part in this study, you will be one of about 30 people to do so at the University of Kentucky.

WILL YOUR INFORMATION BE USED FOR FUTURE RESEARCH?

All information (e.g., your name or date of birth) will be removed from the data collected in this study. However, a link or code to your identity will be kept during the study period. At the end of the study period, any link / code to your identity will be destroyed. Therefore, while your data may be shared with other researchers, there will be no way to link these data to you. Any use of your data for future research or shared with other researchers will not contain identifiable information.

INFORMED CONSENT SIGNATURES

This consent includes the following:

- **Key Information Page**
- **Detailed Consent**

You will receive a copy of this consent form after it has been signed.

_____ _____

Signature of research subject **Date**

_____

Printed name of research subject

_____ _____

Printed name of [authorized] person obtaining informed consent Date