Document:
Informed Consent Form

Official Study Title:
The Neural Mechanisms of Split-Belt Treadmill Adaptation in People with Multiple Sclerosis
NCT05878873

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Consent to Participate in a Research Study
Colorado State University

TITLE OF STUDY: Neural Underpinnings and Sensory Feedback Augmentation During Split-belt Treadmill Training in People with Multiple Sclerosis

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SPONSOR: National Multiple Sclerosis Society (NMSS)

WHAT IF I HAVE QUESTIONS?
Before you decide whether to accept this invitation to take part in the study, please ask any questions that might come to mind now. Later, if you have questions about the study, you can contact the student investigator, Andrew Hagen at (970) 491-6160 or the principal investigator, Dr. Brett Fling at (970) 491-3451. If you have any questions about your rights as a volunteer in this research, contact the CSU IRB at: CSU_IRB@colostate.edu; 970-491-1553. We will give you a copy of this consent form to take with you.

CONCISE STATEMENT OF STUDY:
Majority of people with multiple sclerosis experience difficulty with balance and mobility, leading to an increased risk of falls. The goal of this study is to learn about brain activity during walking adaptation in people with multiple sclerosis. Also, this study will test a form of nerve stimulation to see if it can improve walking performance.
The main questions it aims to answer are:

- What areas of the brain are the most active during walking adaptation?
- Can nerve stimulation make walking adaptation more effective?

Participants will walk on a treadmill where each leg will go a different speed which will create walking adaptation. At the same time, brain scans will occur. There will be two sessions of walking adaptation, one with nerve stimulation, and one without nerve stimulation. Researchers will compare people with multiple sclerosis to healthy young adults to see if there are differences in brain activity.

This study is registered at ClinicalTrials.gov. The registration identification number is NCT05878873

WHAT IS THE PURPOSE OF THIS STUDY?
People with multiple sclerosis commonly experience challenges with walking, resulting in a higher risk of falls and a significant impact on their daily lives. This project aims to

identify brain activity patterns during walking adaptation to better understand the way the brain can adapt walking. Also, this study will assess the impact of nerve stimulation on the ability to adapt walking in people with multiple sclerosis. This study will provide further information about how people may adapt their walking which may lead to better rehabilitation strategies for people with multiple sclerosis.

WHY AM I BEING INVITED TO TAKE PART IN THIS RESEARCH?
You are being invited to participate in this study because you have a diagnosis of relapsing-remitting multiple sclerosis (MS) or are a healthy adult 18 - 86 years of age and are able to stand and walk without the use of an assistive device.

WHO IS DOING THE STUDY?
This study is being designed and executed by the investigators of the Sensorimotor Neuroimaging Laboratory at Colorado State University. Investigators of this laboratory are interested in neurological disorders/problems and their impacts on balance and gait (mobility).

WHERE IS THE STUDY GOING TO TAKE PLACE AND HOW LONG WILL IT LAST?
The study will take place in the Sensorimotor Neuroimaging Laboratory, located within the Human Performance Clinical Research Laboratory at Colorado State University. Participants in this research study will be participating in two testing session each lasting roughly 2 hours. The total commitment for each participant will be 4 hours of participation over the course of two testing sessions performed on separate days four weeks apart. Participants are required to provide their own transportation to and from testing for both study visits. Testing time does not include travel time to Colorado State University.

WHAT WILL I BE ASKED TO DO?
Before visiting the lab, you will complete a phone interview. This interview will take 15 minutes and consist of screening questions including disability status, medical history, and mobility. In the following section, the reasons you may not be eligible to participate are listed. Once you are deemed eligible, we will schedule your first visit to Colorado State University.

For the first testing session at Colorado State University, you will undergo:

- Signing of the Consent Form with research staff
- Questionnaires: Your demographic, body characteristics including leg length, height and weight and self-reported physical fitness including exercise frequency, duration, and self-reported exercise intensity will be recorded. Additionally, we will have you answer questionnaires related to your balance, cognition, depression, and activities of daily living.
- Clinical tests of balance and of multiple sclerosis symptoms: We will have you stand on a balance board to test your balance with your eyes open, eyes closed, and standing on a foam pad. Additionally, we will ask you questions and have you perform small tests of your sensation to better understand your symptoms. These tests will take around five minutes to complete.
- Split-belt treadmill walk testing.
    - For this you will come into the laboratory and will be fitted with a number of small reflective balls taped to your clothing. These small reflective balls

are used to measure how you are walking on the split-belt treadmill. For safety, you will be fitted with a harness which will be attached to a suspended beam in case you lose your balance while walking. Prior to data collection, you will walk on the treadmill with the speed of the two belts moving at the same speed.

- For these small reflective balls to be in the correct position, we will need you to wear tight fitting shorts and an athletic shirt. If you do not have suitable clothing, we have clothing that you can change into.
- The testing session will last a total of 20 minutes, during the testing periods on the split-belt treadmill, you will walk with the 2 belts moving at the same speed and at different speeds. When the belts are moving at the same speed the treadmill belt speeds will be set at a calculated and predetermined slow speed. In the split-belt configuration, one treadmill belt will be set at your slow speed whereas the other will be set at a predetermined fast speed.
- While walking on the split-belt treadmill we will place a cap on your head that has 32 sensors that allow us to measure your brain activity. This cap is flexible and feels like wearing a stocking cap with little beads inside of it. We have multiple cap sizes and tension settings that allow for you to be as comfortable as possible. Additionally, you will wear a rectangular box on your back attached with backpack-like straps. This box collects the brain activity information and sends it to our computer.
- Additionally, during the split-belt treadmill training we will use transcutaneous electrical nerve stimulation (TENS). This is a popular and readily available form of stimulation. We will place sticky pads on your thighs and on your lower legs that will be attached to a small device that will clip onto your pants. This device will send nerve stimulation to the sticky pads. This is not painful, and it simply feels like slight tingling under the sticky pads. During each visit, the TENS device may or may not be turned on. Additionally, we may need to shave a small region of your legs in order to get the pads to stick well.

For the second testing session at Colorado State University participants will undergo the same split-belt treadmill training as in session one. In this session you will have the opposite treatment of TENS. For example, if your TENS was turned on for the first visit, your TENS will be turned off for the second visit and vice versa.

ARE THERE REASONS WHY I SHOULD NOT TAKE PART IN THIS STUDY?

The researchers may discontinue you from the study if you become unable or no longer want to participate in the requested assessments. You will not be allowed to participate in this study if you are unable to walk three tenths of a mile without stopping to rest, are pregnant, have an inner ear injury that affects balance, have a history of illicit drug use, have a history or traumatic brain injury, or cannot abstain from medications that can impair balance, such as narcotics and antihistamines, for the 24 hours prior to testing. Additionally, if you have a musculoskeletal injury (i.e. broken leg, sprained ankle, etc.), have incurred a lower extremity surgical operation in the last 6 months you will be asked not to participate. Inability to meet any of this screening and inclusion criteria from questionnaires will result in disqualification from the study.

At any time during the visit, if you are unable to walk either on your own within the hallway, or on our treadmill in a safe manner, your participation would be halted immediately. Triggers that would identify unsafe walking include repeated stumbling, tripping, or falls where our body weight support harness catches you.

ARE THERE ANY BENEFITS FROM TAKING PART IN THIS STUDY?
You will not benefit from being in this study. However, by serving as a participant you may contribute new information that may benefit patients in the future.
Upon completion of the study, all enrolled participants will receive a page summarizing group results. This will not mention any identifiable data and only group results will be present. This page will also include the meaning of the results, the clinical application, and the future directions of our work.

WHAT ARE THE POSSIBLE RISKS AND DISCOMFORTS?
Falls. The walking tasks may cause you to lose your balance or fall. However, our trained research staff will fit you with a harness to catch you if you fall while on the treadmill and during the over ground will research staff will walk alongside you at all times; if you happen to lose your balance, our research staff will be there to assist and prevent a fall. All safety measures will be taken to ensure a secure and comfortable environment. You will be allowed to take a break from the balance and walking tasks whenever necessary. It is not likely that you will fall.

Musculoskeletal injury. There is a low risk of joint, tendon, or muscle pain, inflammation, or swelling during or after a testing session of your gait, and balance. This risk is reduced through the use of well-trained assistants, the harness you will be wearing on the treadmill, and also by the mild nature of the gait testing.

Headache. Although rare, a potential side effect of our brain measurement is headache due to pressure on your scalp. However, we have many adjustments available in our cap to make you as comfortable as possible and mitigate this risk.

Skin Irritation. The electrical impulses that a TENS unit produces may cause a buzzing, tingling, or prickling sensation, which some people may find uncomfortable. Some people may be allergic to the adhesive pads. In rare cases, patients have reported burns at the sites where the electrodes are placed. However, we use a very mild level of stimulation which greatly reduces this risk.

A TENS unit consists of a battery-powered device that delivers electrical impulses through electrodes (or sticky pads) placed on the surface of your skin. Overall, for the vast majority of people, TENS is believed to be safe and well-tolerated with little to no side effects. However, manufacturers of TENS units universally warn individuals with pacemakers, epilepsy, or are pregnant that these conditions are contraindications to use as they can lead to potential complications. We are only placing TENS on the legs, so these warnings will not be relevant to this study.

Breach of confidentiality: Although robust protocols and procedures are in place to keep your information private and secure, there is a chance of a breach of confidentiality which could lead to your data being accessed. Through data storage on our own private servers, this risk is minimized. If anything were to be accessed, we would inform you immediately. The research team works to ensure confidentiality to the degree permitted

by technology. It is possible, although unlikely, that unauthorized individuals could gain access to your responses. However, your participation involves risks similar to a person's everyday use of the internet.

Emotional distress. Some of the questions asked may be personal or embarrassing. You may refuse to answer them if you don't want to. Also, you may learn information about your balance and walking and that could be upsetting to you.

It is not possible to identify all potential risks in research procedures, but the researcher(s) have taken reasonable safeguards to minimize any known and potential, but unknown, risks.

WILL I RECEIVE ANY COMPENSATION FOR TAKING PART IN THIS STUDY?
Individuals participating in this study will receive $50.00 for each session completed with the potential of earning a total of $100.00 for the competition of both testing sessions. If a participant drops out or withdrawals from the study partway through a session that participant will still be compensated $50.00. You will not receive compensation for the screening phone interview.

WHO WILL SEE THE INFORMATION THAT I GIVE?
We will keep private all research records that identify you, to the extent allowed by law. Your information will be combined with information from other people taking part in the study. When we write about the study to share with other researchers, we will write about the combined information we have gathered. You will not be identified in these written materials. We may publish the results of this study; however, your identifying information will not be included. A description of this clinical trial will be available on http://www.ClincialTrials.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.

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. For example, your name will be kept separate from your research records and these two things will be stored in different places under lock and key. You should know, however, that there are some circumstances in which we may have to show your information to other people. We may be asked to share the research files with the CSU Institutional Review Board ethics committee for auditing purposes, if necessary. In addition, for funded studies, the CSU financial management team may also request an audit of research expenditures. For financial audits, only the fact that you participated would be shared, not any research data. When we write about the study to share with other researchers, we will write about the combined information we have gathered.

WILL MY DATA BE USED FOR FUTURE RESEARCH?
If you choose to take part in this study, your private information will be collected. Any identifiers linking you to your private information will be removed. After we remove those identifiers, the information could be used for future studies or distributed to another research for future research studies without your permission.

DO I HAVE TO TAKE PART IN THE STUDY?

Your participation in this research is voluntary. If you decide to participate in the study, you may withdraw your consent and stop participating at any time without penalty or loss of benefits to which you are otherwise entitled. Reasons an individual may be removed from the study include an inability or refusal by the participant to complete the requested assessments.

WHAT HAPPENS IF I AM INJURED BECAUSE OF THE RESEARCH?
If you are injured because of participation in this study, please contact the Principal Investigator at the number listed at the top of this form. The Colorado Governmental Immunity Act determines and may limit Colorado State University's legal responsibility if an injury happens because of this study. Should you need medical aid, you or your health insurance will be responsible for the costs.

WHAT ELSE DO I NEED TO KNOW?

- During the duration of the gait testing portions of this study, you will be videotaped enable investigators to review walking trials.

- As a participant in this study, the data obtained from this study could be applied and used for control data in future research studies.

WILL VIDEOS OR PHOTOS BE TAKEN?

For analysis purposes the research team would like to request your permission to video the duration of testing in this study. These videos will be stored on our private server with password protected access only available to the research team.

Video/Photo Release Terms

I am 18 – 86 years of age and hereby give my permission to use any photos or videotape material taken of myself during research on]. The photos and videotape material will only be used for research purposes and for the presentation of the research. My name will not be used in any publication. I will make no monetary or other claim against CSU for the use of the photograph(s)/video. As with all research consent, I may at any time withdraw permission for photos or video footage of me to be used in this research project.

- Check [Yes] if you accept the permission of video/photo use for this study.
- Check [No] if you deny the permission of any video/photo use for this study.

Yes **No**

- Check [Yes] if you accept the permission to be contacted for future studies conducted by the Somatosensory Neuroimaging Laboratory.
- Check [No] if you deny the permission to be contacted for future studies conducted by the Somatosensory Neuroimaging Laboratory.

Yes **No**

Your signature acknowledges that you have read the information stated and willingly sign this consent form. Your signature also acknowledges that you have received, on the date signed, a copy of this document containing _7_ pages.

_____ _____
Signature of person agreeing to take part in the study Date

_____
Printed name of person agreeing to take part in the study

_____ _____
Name of person providing information to participant Date

_____
Signature of person providing information to participant