Cost-effectiveness and Efficacy of a Combined Intervention to Facilitate Motor Recovery Following Stroke

NCT Number: NCT03819764

Informed Consent

Date of approval: July 6, 2022

Cleveland Clinic
Consent to Participate in a Research Study

Study Title: Cost-effectiveness and efficacy of a combined intervention to facilitate motor recovery following stroke

Principal Investigator: Susan Linder, PT, DPT, NCS (216-445-9815). If you are unable to reach Dr. Linder, please call Dr. Anson Rosenfeldt at 216-445-3277. If you are calling after hours, please call 216-704-6372.

Sponsor: National Institutes of Health

Carefully review this consent document. The purpose of a consent document is to provide you with information to help you decide whether you wish to participate in research. Your decision is completely voluntary and will not affect your medical care if you choose not to participate. It is important for you to ask questions and understand the research risks, benefits and alternatives.

Please note:

- **You are being asked to participate in a research study (a research study is designed to answer specific questions about new ways to prevent, detect, and treat disease).**
- **Ask as many questions as needed so you can make an informed decision**
- **Carefully consider the risks, benefits and alternatives of the research**
- **Your decision to participate is completely voluntary and will have no effect on the quality of your medical care if you choose not to participate. You can also withdraw from the study at any time.**
- **You will be provided a copy of this consent form.**

1. INFORMATION ON THE RESEARCH

You are being asked to participate in the research entitled, "Cost-effectiveness and efficacy of a combined intervention to facilitate motor recovery following stroke" because you have previously experienced a stroke. The purpose of this study is to gain a better understanding of how exercise training affects stroke recovery. We want to investigate whether aerobic exercise improves your ability to recover function in the arm and leg affected by your stroke. We are also investigating the cost effectiveness of the rehabilitation interventions. Your participation in this study will be placed in your medical record; however, your data will not be placed in your medical record. 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 at any time.

How Many People Will Take Part In The Study?

About 60 people will take part in this study at the main campus of the Cleveland Clinic. If you decide to participate in this study, you will be randomized into one of two groups: assisted exercise and upper extremity repetitive task practice or time-matched upper extremity repetitive task practice only. The groups will be chosen by chance by a computer system that uses your demographic information to randomly place you in a group. This process is called randomization. Neither you nor study staff can select the group to which you will be assigned. If for some reason you are unable to participate in a group, you will be randomized to the other group. Participants will complete a battery of tests before, during the middle, and after the 8-week intervention period, as well as 4 weeks after the study

completion. Additionally, participants will be asked to return to complete testing at 6 months and 1 year following the end of the intervention. The intervention will take place three times per week for eight weeks. During the course of this study, you will be asked to visit the Cleveland Clinic main campus a total of 31 times.

Progression of Study Activities:

1. Screening
2. Baseline exercise testing and clinical evaluations
3. *Optional: Gait and cognitive baseline testing and/or Electroencephalogram (EEG) testing
4. Randomization (assignment to your therapy group)
5. Intervention period (3 times per week for a total of 8 weeks)
6. Mid-intervention evaluation with optional Electroencephalogram (EEG) testing
7. Post-intervention exercise testing and clinical evaluations
8. *Optional: Gait and cognitive post-intervention testing and/or Electroencephalogram (EEG) testing
9. 4 weeks post-intervention clinical evaluation
10. 6 month post-intervention clinical evaluation
11. 1 year post-intervention clinical evaluation

*All participants consenting to participate in this study can choose whether or not they would like to undergo the optional gait, cognitive, or EEG evaluations. If you choose to complete these additional tests, you will be asked to visit the Cleveland Clinic main campus 2 additional times.

Screening

At this time, you will be asked questions to assess the safety of your participation in this study. The study coordinator will ask you questions primarily regarding your medical history as it relates to your cardiac health and your recent stroke. In addition, the study coordinator will assess your arm function to determine your eligibility to participate in the study. If you meet eligibility requirements and agree to participate, exercise testing will be scheduled. Your doctor will be notified of your interest in participating before you undergo the exercise testing.

Exercise Testing

Two exercise testing sessions will be completed: baseline (before exercise intervention begins) and post-exercise (after 8 weeks of the exercise program). Exercise testing will be completed at the Cardiac Rehabilitation Center (CRC) at the Cleveland Clinic under the supervision of the director of the CRC. You will be asked to refrain from consuming anything with caffeine for 12 hours prior to the test. You should plan to consume only clear liquids for 4 hours before the test and take all medications as prescribed. You should report to the CRC in clothing conducive to exercise testing, such as shorts and a t-shirt. During exercise testing you will pedal a stationary bicycle while your heart rate and breathing are monitored. Your heart rate will be monitored with electrodes worn under your t-shirt, and your breathing will be monitored through a specially designed mask. As the exercise test progresses the resistance to pedaling will increase (i.e.: pedaling will become more difficult). You will continue to pedal until you feel tired and feel you can no longer continue. After you finish the exercise test you will be asked to remain in the CRC for approximately 30 minutes to let you rest before you leave. During this time your heart rate will be monitored. If during exercise testing an abnormality in heart function is detected you will not be allowed to participate in the study. You will be informed of any abnormalities that may be detected.

During this test we may see something that should be checked by your doctor. If that happens, we will call you within a week of the test to let you know. We will then send the test results to your doctor. If you do not have a primary care doctor, we will refer you to one within the Cleveland Clinic system. Please note that we are not specifically looking for any medical problems so it is very unlikely that we will find any underlying issues. This test is not the same as regular medical care.

Clinical Evaluations (Pre, mid, post-intervention, and 4 weeks, 6 months, and 1 year post-intervention)

For your clinical evaluations you will come to the Neural Control Lab at the Main Campus of the Cleveland Clinic. These evaluations are simply methods of measuring your motor function and quality of life both before and after therapy. You may be asked to complete the following clinical evaluations: Wolf Motor Function Test (WMFT), Fugl-Meyer Motor Assessment Test (FMA), Action Research Arm Test (ARAT), 6-minute walk test, Centers for Epidemiologic Studies Depression Scale, Processing Speed Test (PST), Stroke Impact Scale, PROMIS 29, and manual dexterity tasks. These evaluations are comprised of questionnaires, tasks performed by your hands and arms, and a measure of the distance you can walk in 6 minutes. A combination of these tests will be performed before the intervention begins, during week 4 of the intervention, at the end of the 8 week intervention, and 4 weeks, 6 months, and 1 year after the study has been completed.

Optional Testing

All participants meeting inclusion/exclusion criteria will have the option to complete testing that examines gait function, cognitive function, and brain activity. Your decision to participate in these optional tests does not in any way affect your eligibility to participate in the study. Participants opting to participate in the gait testing will come to the Mellen Center at the main campus of the Cleveland Clinic to examine aspects of walking using a device called the CAREN (Computer Assisted Rehabilitation Environment) system. The CAREN system is a high-tech medical and research system that allows for experts to view and analyze balance, walking, and coordination in a controlled and safe environment. The gait assessment will take approximately one hour. If you choose to undergo this additional testing, it will be administered before the intervention begins and at the end of the 8 week intervention

Assessments that measure various aspects of cognitive function such as memory, attention, and executive function will be administered by a trained therapist. The cognitive assessment will take approximately one-half hour. If you choose to undergo this additional testing, it will be administered before the intervention begins and at the end of the 8 week intervention

You may also elect to undergo Electroencephalograms (EEGs) testing. EEG allows us to non-invasively measure changes in brain activity associated with cycling exercise. Measuring brain activity during cycling may provide useful information on how different cycling rates impact the way various parts of the brain communicate with each other during exercise. Measuring brain activity before and after participation in the study in will provide additional information about any long-term changes in brain function associated with the different assigned exercise programs. This information will be useful for understanding which brain areas are beneficially changed by the exercise and if one's brain needs to have certain characteristics in order for that person to benefit from various exercise routines.

Up to 64 EEG sensors will be placed on the scalp using a conductive jell or paste to measure general brain activity before, during, and after the study. This may entail cleaning the skin first with an alcohol wipe and/or mild exfoliant to remove any oils and dead skin. You should refrain from using any hair products that are left in the hair on the days EEGs will be collected (e.g. mousse, gels, hairspray). An

elastic cap or net will be used to ensure that the sensors maintain contact with the scalp during the tests. Additional adhesive electrodes may be placed over nerves and muscles on the arms, legs, and neck to help us determine how well sensory information from the periphery is being conveyed to the brain and how well movement commands from the brain are activating the peripheral muscles. You may be asked to participate in two different types of EEG testing. One EEG test is designed to record brain signals during cycling. For that test, recording electrodes will just be attached to your head and you will wear the electrodes throughout your regular exercise session (warmup, exercise, and cool down) as well as during some additional cycling where you simply relax while the bike moves your legs for you. The second set of EEG tests will be performed over multiple days. Specifically EEGs may be collected before you start the exercise program, once partway through your 8-week long program, immediately after you have completed the program, and then again 4 weeks after you have stopped your assigned exercise program. In the second set of tests, the EEG electrodes will be placed on the head and additional electrodes will be placed on your arms and legs over nerves and muscles. While you are sitting comfortably in a chair, brain signals will be recorded first while the experimenter moves each arm and leg joint while you simply relax. Then you will be asked to try to repeat those movements on your own. Finally, electrodes over sensory nerves in each arm and leg will be used to deliver brief pulses of mild electrical current to activate the sensory nerves. This stimulation enables us to measure the somatosensory evoked potential—the brains response to sensory input. For this test, stimulation levels will be kept as low as possible while still activating the nerve. You may tell us to stop at any time if you find the sensation uncomfortable.

The EEG test is optional. If you choose to undergo this additional testing, it will be administered up to 4 times during the program.

Exercise Intervention

Regardless of the group you are assigned to, you will be asked to attend training sessions three times per week for eight weeks (a total of 24 exercise sessions). You should report to these sessions wearing appropriate attire for exercise, such as shorts and a t-shirt. All exercise training will be conducted within Dr. Alberts' lab at the Walker Center at the Cleveland Clinic. Each exercise training session requires approximately one hour and forty-five minutes of your time. Participants in the assisted exercise group will complete a 45-minute exercise session on a semi-recumbent stationary exercise cycle followed by 45 minutes of exercises aimed at recovering function in the arm affected by your stroke. Participants in this assisted exercise group will be on a stationary bike that increases their pedaling speed. Participants assigned to the upper extremity repetitive task practice group will complete two back-to-back 45-minute sessions of exercises aimed at recovering function in the arm affected by your stroke. A brief 5-10 minute break will be provided between the two sessions.

Each exercise session on the stationary bike will consist of a 5 minute warm up period (easy pedaling on stationary cycle), followed by 35 minutes of exercise and then a 5 minute cool down period (easy pedaling). During the 35 minute main exercise set you will exercise at a moderately intense level. The intensity of exercise will be determined by calculating your age-determined target heart rate zone. We will monitor your heart rate, blood pressure, and oxygen level during all exercise testing and training.

Should anything occur that would prevent you from completing the therapy (vacation, hospitalization, equipment malfunction), you will be able to reschedule in order to complete the 8 week program over a 12 week period of time. If you are hospitalized, you will be re-evaluated once discharged to determine whether or not you still meet criteria to safely participate in the study and to determine if you are able to complete the study.

Photos, Videos and Audio Recordings

Videos may be taken during initial and follow-up tests to compare movements observed with data collected. We will store the videos on Cleveland Clinic network drives that are password protected and behind the institutional firewalls. Video recording is optional for participants, and declining will not affect your ability to participate in the study.

2. RISKS AND DISCOMFORTS

Loss of Confidentiality: There is a potential loss of confidentiality of your data. Every effort will be made to keep your information confidential through the use of the following safeguards: study codes are used instead of your name; all computers are password protected; electronic data are stored in a secure RedCap database accessible only to the research team; and paper documents are stored in a locked storage cabinet accessible only to research lab personnel.

Questionnaires: Some of the questions we will ask you as part of this study may make you feel uncomfortable. You may refuse to answer any of the questions and you may take a break at any time during the study. You may stop participation in this study at any time.

Skin irritation or inflammation*:* The conductive gels used with surface electrodes for the heart monitors and the tapes or adhesives used to secure sensors to your body can irritate your skin. You may experience a temporary redness under the dressings in contact with your skin. Skin may also become irritated during exercise sessions. Appropriate exercise clothing will help to minimize this risk.

Sprains, falls or mechanical trauma*:* There is a small risk of losing your balance while performing these assessments that could lead to a stumble or fall. Sprains or other injuries to your joints or lower extremities are also possible. This risk is minimized however, by having the therapists standing beside you to steady you.

Exercise*:* The intensity of the exercise may be slightly uncomfortable at times but you will be allowed to rest at any time during each 45-minute session, if needed. The appropriate intensity level will be personalized to your age and general activity level.

To minimize potential risks associated with exercise all research staff that will be supervising your exercise sessions will be trained in Basic Cardiac Life Support including emergency resuscitation and life sustaining techniques. A cardiac arrest and resuscitation team is also available 24 hours a day within the hospital and can respond immediately to any emergency. Although the exercise bicycle you will be exercising on is very stable, there is a risk of injury while getting on or off the cycle. To minimize risk, the therapist or exercise physiologist will assist you when getting on or off the cycle.

EEG: Risks are minimal and consist of the potential to develop a sensitivity to the conductive gel or adhesive material in the electrodes. Participants are verbally screened for known allergies and they are instructed on how to wash the gel/paste from the hair completely after testing to minimize the chance of irritation. Any resulting irritation is treated by stopping participation in the EEG portion of the study. All recording/stimulation equipment is optically isolated and will be safety tested by the Cleveland Clinic engineering staff prior to use. To minimize risk, participants will be excluded from EEG testing if they have: 1) Known allergy to the conductive gel/paste used for EEG collection or the adhesive conductive

electrode material used to attach recording/stimulating electrodes on the limbs. 2) Open/active wounds on the scalp. 3) History of seizures. 4) Current implants in the brain or body such as shunts, a pacemaker, deep brain stimulator, etc.

3. BENEFITS

Your cardiovascular fitness may improve over the course of the study for those randomized to the exercise group, and upper extremity function may improve for both groups. Improvements in cardiovascular fitness post-stroke often lead to increases in ambulatory efficiency and decreased risk for future cardiovascular events or recurrent stroke. Although you may or may not benefit from this study, society may benefit from a clearer understanding of the role of aerobic exercise, and particularly, assisted aerobic exercise in the recovery of function post-stroke. This could lead to improved rehabilitation outcomes for patients after stroke.

4. ALTERNATIVES

The alternative to participation is to simply NOT participate in this study. Your decision to participate or not will not affect treatment you are receiving now or in the future.

5. PRIVACY AND CONFIDENTIALITY

Cleveland Clinic has rules and procedures to protect information about you. Federal and State laws also protect your privacy.

The research team working on the study will collect information about you. Protected health information such as phone number, email, street address with zip code, date of birth, emergency contact name and phone number, and dates of visits will be stored in RedCap, a secure electronic database. Your social security number is only required for compensation and will also be stored in RedCap. You may choose to participate in the study without compensation if you chose not to disclose your social security number. Generally, only people on the research team will know your identity and that you are in the research study. Sometimes other people at Cleveland Clinic may see or give out your information. These include people who review research studies including the Institutional Review Board and Research Compliance, their staff, lawyers, or other Cleveland Clinic staff.

People outside Cleveland Clinic may need to see your information for this study. Examples include government groups (such as the Food and Drug Administration), safety monitors, other hospitals in the study and the sponsor of the research and their agents. Cleveland Clinic will do our best to ensure your information is kept confidential and that only the health information which is minimally required to conduct the study is used or disclosed to people outside Cleveland Clinic; however, people outside Cleveland Clinic who receive your information may not be covered by this promise.

You do not have to give this permission to use and give out your information; however you will not be able to participate in this research study without providing this permission by signing this consent form. The use and disclosure of your information has no expiration date.

You may cancel your permission to use and disclose your information at any time by notifying the Principal Investigator in writing**, Susan Linder, 9500 Euclid Avenue ND-20, Cleveland, Ohio 44195.** If you do cancel your permission to use and disclose your information, your participation in this study

will end and no further information about you will be collected. Your cancellation would not affect information already collected in the study.

OPTIONAL PHOTO, VIDEO, AND AUDIO RECORDING USE RELATED TO THE RESEARCH

As previously indicated, we will take video recordings of your participation in this study for … By initialing below to "Opt in", you give permission for us to use your video recordings internally to compare movements observed with data collected. If you do not agree to allow us to videotape the test sessions, your study status will not be affected. Please initial below if you agree (Opt in) or if you disagree (Opt out).

Check one and initial:

☐ Opt in: _____
Participant Initials

☐ Opt out: _____
Participant Initials

6. RESEARCH RELATED INJURIES

In the event you are injured as a result of participation in this research, medical care is available to you. The costs of such medical care will be billed to you or your insurance company. There are no plans to provide compensation for lost wages, direct or indirect losses. The Cleveland Clinic will not voluntarily provide compensation for research related injury. You are not waiving any legal rights by signing this form. Further information about research related injury is available by contacting the Institutional Review Board at 216-444-2924.

7. COSTS

The study intervention or other study related tests/procedures/visits will be provided at no cost to you. These include the both exercise stress tests (at the beginning and end of the study), clinical testing of your arm function, and 24 intervention sessions. The cost for routine tests and services that would normally be performed even if you don't participate in the study will be billed to you or your insurance provider. For example, if you visit your doctor on your own and have lab tests done at your doctor's request, the cost of the exam and tests would be billed to you or your insurance.

8. COMPENSATION

Parking vouchers will be provided for the 2 visits to Preventive Cardiology that are required when you undergo exercise stress tests at the beginning and end of the study. Parking vouchers will also be provided for the 2 optional visits to the Mellen Center.

For your visits that take place at the W.O. Walker Center, you will have the choice of being provided with a daily parking voucher to cover the cost of your parking during clinical testing and exercise sessions (value equivalent to ~$100), or you have the option of receiving a total of $100 in checks to offset the cost of travel (provided in two $50 increments after completion of mid-point testing and following 4 weeks post-testing).

The IRS requires Cleveland Clinic Foundation to report payments to an individual of $600.00 or greater (in a calendar year) on a Form 1099-MISC. Your name, address, and social security number will be collected to track the payments made to you and, if you receive $600.00 or greater, will be used to process a Form 1099-MISC.

9. VOLUNTARY PARTICIPATION

Taking part in this study is voluntary. You will be told of any new relevant information from the research that may affect your health, welfare, or willingness to continue in this study. You may choose not to take part or may leave the study at any time. Withdrawing from the study will not result in any penalty or loss of benefits to which you are entitled.

10. QUESTIONS

If you have any questions, concerns or complaints about the research, or develop a research-related problem, contact Dr. Susan Linder at 216-445-9815. If you are unable to reach Dr. Linder, please call Dr. Anson Rosenfeldt at 216-445-3277. If you are calling after hours, please call 216-704-6372. If you have questions about your rights as a research subject, you should contact the Institutional Review Board at (216) 444-2924.

11. SIGNATURE

I have read and have had verbally explained to me the above information and have had all my questions answered to my satisfaction. I understand that my participation is voluntary and that I may stop my participation in the study at any time. Signing this form does not waive any of my legal rights. I understand that a copy of this consent will be provided to me. By signing below, I agree to take part in this research study.

_____
Printed name of Participant

_____ _____
Participant Signature Date

Statement of Person Conducting Informed Consent Discussion

I have discussed the information contained in this document with the participant and it is my opinion that the participant understands the risks, benefits, alternatives and procedures involved with this research study.

_____
Printed name of person obtaining consent

_____ _____
Signature of person obtaining consent Date