Permission to Take Part in a Human Research Study

Do not sign this consent if today's date is later than the stated expiration date above.

Title of Research Study: Locomotor function following transcutaneous electrical spinal cord stimulation in individuals with hemiplegic stroke

Investigator: ***Elliot J. Roth, MD***

Supported By: research is supported by the Shirley Ryan AbilityLab & Frankel Foundation

If your doctor is also the person responsible for this research study, please note that he is interested in both your clinical care and the conduct of this research study. You have the right to discuss this study with another person who is not part of the research team before deciding whether to participate in the research.

Why am I being asked to take part in this research study?

Key Information:
The first few pages of this document include a summary of this study to help you decide whether or not to participate. Detailed information is provided after the summary.

We are asking you to take part in this research study because you had a stroke that resulted in one-sided weakness.

What should I know about a research study?

- Someone will explain this research study to you.
- Whether or not you take part is up to you.
- You can choose not to take part.
- You can agree to take part and later change your mind.
- Your decision will not be held against you.
- You can ask all the questions you want before you decide.

Why is this research being done?

The purpose of this study is to determine whether non-invasive electrical stimulation of the spinal cord improves walking and balance for individuals with one sided weakness after a stroke. The data will be collected and analyzed for research. The stimulation devices are considered experimental because they are not currently approved by the U.S. Food and Drug Administration (FDA) for our purpose. The use of spinal stimulation is old technology being applied in a new way and depending on the outcome of this study, FDA approval may be pursued.

How long will the research last and what will I need to do?

We expect that you will be in this research study for 1 year**.**

You will be asked to participate in 38 visits total over the course of one year. You will be asked to perform different walking and balance activities while study equipment monitors your response to the activities. We will also use non-invasive magnetic brain stimulation called transcranial magnetic stimulation (TMS) to determine what effect the repeated spinal cord stimulation has on the excitability or responsiveness of circuits connecting the brain to your muscles.

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More detailed information about the study procedures can be found under the section **What happens if I say "Yes, I want to be in this research"?**

Is there any way being in this study could be bad for me?

There is a risk of skin irritation or reaction from the study equipement. There is also a risk of falling during the balance and walking activities. Participants may also feel discomfort from an increase in physical activity participation. Following TMS, a mild headache can occur. In rare cases the development of seizure activity has been reported during or immediately after magnetic brain stimulation. Individulas who have a history of seizures, have been diagnosed with epilepsy, or are on medications that increase the risk of seizure will be excluded from this research study.

More detailed information about the risks of this study can be found under **"Is there any way being in this study could be bad for me? (Detailed Risks)"**

Will being in this study help me any way?

We cannot promise any benefits to you or others from your taking part in this research. However, possible benefits include improved posture, balance and walking. Your participation in this study may also provide a better understanding of transcutaneous spinal cord stimulation and whether it improves rehabilitation for others.

What happens if I do not want to be in this research?

Participation in research is completely voluntary. You decide whether or not to participate. If you choose to not participate, there will be no penalty to you or loss of benefit to which you are entitled.

Your alternative to participating in this research study is to not participate.

Who can I talk to?

If you have questions, concerns, or complaints, or think the research has hurt you, talk to the research team at Dr. Elliot J. Roth at 312-238-4864.

This research has been reviewed and approved by an Institutional Review Board (IRB). You may talk to them at (312) 503-9338 or irb@northwestern.edu if:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You want to talk to someone besides the research team.
- You have questions about your rights as a research participant.
- You want to get information or provide input about this research.

How many people will be studied?

We expect about 36 people to complete this research study out of 36 people in the entire study nationally.

What happens if I say "Yes, I want to be in this research"?

If you decide to take part, this is what will happen:

You will participate in a total of 38 visits over one year. Each assessment and follow-up visit may last up to 4 hours and each treatment visit up to 2 hours and all visits will occur at the

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Shirley Ryan AbilityLab. The majority of the visits (24) occur during the 8 weeks of treatment/intervention visits. We have provided a breakdown of the type of visits followed by a detailed description of each visit type:

- 6 assessment visits (2 visits at each time point) at
  - Baseline (before study starts)
  - After 4 weeks of study intervention
  - After 8 weeks of study intervention
- 2 transcranial magnetic stimulation (TMS) visits at
  - Baseline (before study starts)
  - After 8 weeks of study intervention
- 24 treatment visits at a frequency of
  - 3 treatment sessions per week for 8 weeks
- 6 follow-up visits (2 visits at each time point)
  - After 3 months since last treatment session
  - After 6 months since last treatment session
  - After 12 months since last treatment session

Visits 1-2 (Baseline Assessment Visits): We will review your medical history and have you complete a standard evaluation of physical function to determine if you are eligible for this study. The standard evaluation of physical function includes:

- Assessment of your active range of motion. You will move your legs as directed by a trained researcher.
- Leg strength screen. A trained researcher will provide manual resistance against leg movements
- Assessment of passive range of motion. A trained researcher will move your legs through their range of motion.
- Assessment of spasticity using the Modified Ashworth Scale. A trained researcher will move your legs quickly at each joint.
- A trained researcher will assess the skin integrity of your legs through observation.
- Assessment of gait using the Functional Ambulation Category through observation.
- Assessment of arm and leg function. A trained researcher will complete the Action Research Arm Test, Fugl-Meyer Assessment of Motor Recovery after Stroke, Wolf Motor Function Test
  - Action Research Arm Test. Measures the ability to perform tasks that involve grasp, grip, pinch and general arm movements to handle objects of various sizes, weights and shapes
  - Fugl-Meyer Assessment of Motor Recovery after Stroke. Measures the patterns of movement and coordination in your arms and legs to determine severity of the stroke
  - Wolf Motor Function Test. Measures the ability of your arms through the completion of timed functional tasks, assessment of quality of movement and measures of strength
- Assessment for Depression using the Patient Health Questionnaire – 9 (PHQ-9)
- Assessment of the impact of the stroke on your health and life through completion of the Stroke Impact Scale-16
- Assessment of the integrity of motor pathways in the spinal cord by obtaining Spinal Motor Evoked Potentials (MEPs). The spinal cord will be stimulated in three locations using surface electrodes on your skin. The strength of muscle contractions in your legs in response to each pulse will be measured using sensors placed on your muscles

Next, we will ask you to complete different walking and balance tests to determine your baseline walking capability and standing balance. While you perform these tests, we will use equipment to help us understand how your body responds to different activities. We will place small sensors to various skin locations and place a mask over your nose and mouth.
The conditions include:

- Treadmill walking
    - You will be asked to walk on a treadmill for up to 10 minutes during the assessment visit in order us to measure the timing of your steps and how your legs move while walking on a treadmill
- Overground walking
    - Six minute walk test. You will be asked to walk for 6 minutes. You may request rest breaks as needed.
    - 10 meter walk test. We will record the amount of time it takes you to walk 10 meters (32 feet) at your normal walking pace and your fastest walking pace. You will perform this six times total (three at normal walking pace and three at fastest walking pace).
    - Electronic walkway. We will ask you to walk across a floor mat 3 times that is able to record the pressure of every step.
- Standing balance. We will ask you to stand on a force plate on the ground. This will record your body weight shifts while you perform different reaching tasks with your eyes open and closed.

Transcranial Magnetic Stimulation (TMS) Assessment Visits
You will also receive TMS before the first treatment session (baseline) and after 8 weeks of treatment. TMS is a non-invasive and painless method of brain stimulation. A trained researcher will apply short durations of magnetic impulses to stimulate the areas of the brain that control your legs. We will record the muscle activation from the stimulation through electrodes placed on your leg muscles. This will provide us information about the connectivity between the brain and leg muscles.

24 treatment visits: You will be randomly assigned to a treatment group. One treatment group will receive non-invasive electrical spinal cord stimulation while performing walking activities. The other group will complete the same walking activities, but will not receive the non-invasive electrical spinal cord stimulation.

If you are in the group that receives non--invasive electrical spinal cord stimulation, we will apply mild electrical stimulation through electrodes placed on your skin over the upper, mid and lower part of your back. The intensity of the stimulation at each site will be slowly increased until we observe consistent activity in your leg muscles. Stimulation intensity will not be increased beyond this point. The stimulation will not cause pain.

All study participants will have sensors applied to their legs to monitor your leg muscles and movements. You will perform stepping (walking) activities in up to three positions for up to 50 minutes. The first position is while lying on your non-impaired side. Your legs will be supported to reduce the effects of gravity while you perform sidelying stepping. In this position, we will also ask you to flex your ankles, point your toes down, bend your knees and straighten your knees to measure the strength of these muslces from the sensors placed on your muscles. The second position is upright on the treadmill with a harness worn for safety or to provide body weight support. The final position is upright over ground. During all

stepping conditions, the focus will be to improve your gait pattern and not the speed of walking.

Functional Assessment Visits (after week 4 and after week 8): During these four visits, we will repeat baseline assessmentsfrom visits 1 and 2 as described above. In addition, ALL participants will repeat the 10 meter walk test and walking on the electronic walkway while receiving non-invasive electrical spinal cord stimulation. This will help us determine if there are any immediate changes using non-invasive electrical spinal cord stimulation.

All visits will occur at the Shirley Ryan AbilityLab by a trained clinician and/or researcher from the hospital. Each visit will last up to 4 hours.

Some sessions may include video recordings of your leg movements during walking activities. Your upper body and head will not be included in any recordings.

Follow-up Visits: Once you have completed the treatment visits, we will have you return after 3 months, 6 months and 12 months to repeat the assessements from the functional assessment visits as outlined above over the course of 2 visits at each time point. You may resume physical therapy, as recommended by your physician, after completion of the functional assessment visit after week 8.

The treatment you get will be chosen by chance, like flipping a coin. Neither you nor the study doctor will choose what treatment you get. You will have a(n) equal chance of being given either treatment.

What are my responsibilities if I take part in this research?

If you take part in this research, you will be responsible to:

- Arrive to all scheduled sessions on time
- If you are not able to attend a session, please provide as much notice as possible. We will try to reschedule the session within the time frame described above.
- Update the team with any medical changes that occur during the study, including new medications.
- Do not participate in outside therapies until you have completed the treatment and after 8 week assessment visits.

What happens if I say "Yes", but I change my mind later?

You can leave the research at any time; it will not be held against you.

If you decide to leave the research, contact the investigator so that the investigator may cancel scheduled sessions. The investigator may ask your reasons for leaving the study.

Choosing not to be in this study or to stop being in this study will not result in any penalty to you or loss of benefit to which you are entitled. Specifically, your choice not to be in this study will not negatively affect your right to any present or future medical treatment.

If you agree, this data will be handled the same as research data.

Detailed Risks: Is there any way being in this study could be bad for me?

This research may hurt you in the following ways:

- Skin irritation. There is a minimal risk of skin irritation from the electrodes and/or wearable sensors. Please let us know if you have any known skin allergies or sensitivities. If you are not sure, we can apply a small test patch to monitor your sensitivity. We will also perform frequent skin checks to decrease this risk.
- Increase in respiration, shortness of breath, increased heart rate, lowering or elevation of blood pressure and/or dizziness from increased activity. We do not expect the increase in respiration and heart rate to be greater than what is normally experienced in an individual during regular exercise. This discomfort is reversible and you may stop the physical activity or rest at any time during the study.
- Muscle and/or joint soreness. These conditions are considered to be minimal risks and are reversible. It is also highly unlikely that you would suffer a muscle strain, joint sprain, or fracture. These conditions are considered moderate risks that very rarely or never occur and are treatable if they do. If these events should occur, you would immediately stop training and standard medical care will be provided.
- Thermal reaction (a burn) to the skin and surrounding tissue from the transcutaneous electrical stimulation. To prevent a burn from occurring there is a built in safety cut-off switch in the device to prevent delivering energy levels (electricity) beyond acceptable limits. There are also safety features in the software program that controls the device to limit the amount of time you are exposed to the stimulation.
- Increase in muscle spasms. If you have muscle spasms, the joint movements may trigger your spasms.
- Bruising. There is a risk of bruising from the gravity supporting harness equipment for your legs. We will monitor your skin and comfort level. We will adjust the harness fit, placement or provide additional padding. You should not be uncomfortable.
- Falling. There is a risk of falling during ambulation and balance activities. We will minimize this risk by having an experienced research personnel conduct each visit. They will provide verbal safety cues, physical assistance and use safety devices (harness or gait belt) to decrease this risk.

TMS:

- Hearing changes. There is a loud "click" produced by the TMS stimulator can cause temporary hearing changes following treatment, which is prevented by wearing soft foam earplugs during magnetic stimulation.
- Headache. A mild headache can occur following TMS that usually resolves soon after the procedure. The headaches may be from maintaining a fixed head position for the duration of TMS. We will try to reduce the risk of headache by assuring your comfort before and during the procedures.
- Seizures. Rare cases have reported the development of seizures during or immediately after magnetic brain stimulation. Individuals who have a history of seizures or have been diagnosed with epilepsy will be excluded from this research study.
- Muscle Twitching. You may feel twitches in the muscles of your arm, leg or face during the magnetic stimulation and/or if you receive electrical stimulation in the limbs.

We do not anticipate any long term or chronic harmful outcomes from participation in this study. All potential negative effects have been shown to reverse over time with proper care. It is highly unlikely that any act conducted within the outline of this study would lead to a worsening of your condition.

In addition to these risks, this research may hurt you in ways that are unknown. These may be a minor inconvenience or may be so severe as to cause death.

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What do I need to know about reproductive health and/or sexual activity if I am in this study?

The research may also hurt a pregnancy or fetus in ways that are unknown. These may be a minor inconvenience or may be so severe as to cause death.

You should not be or become pregnant while on this research study.

If you are sexually active, both men and women should use at least one effective means of birth control while participating in this research study. According to the World Health Organization and the United States Center for Disease Control and Prevention, the most effective forms of birth control include complete abstinence, surgical sterilization (both male and female), intrauterine devices (IUDs), and the contraceptive implant. The next most effective forms of birth control include injectables, oral contraceptive pills, the contraceptive ring, or the contraceptive patch. Acceptable but least effective methods of birth control include male condoms (with or without spermicide) and female condoms.
If you or your partner become pregnant while participating in this research study, it is important that you tell the study doctor or other research team member immediately. You may be required to stop participation in this study; however, other treatment options will be discussed with you at that time if necessary.

If you or your partner [are/is] considered to be postmenopausal, you are not required to use contraception while participating in this research study. Postmenopausal women rarely become pregnant. If you or your partner become pregnant while participating in this research study, it is important that you tell the study doctor or other research team member immediately. You may be required to stop participation in this study; however, other treatment options will be discussed with you at that time if necessary.

Will it cost me anything to participate in this research study?
Taking part in this research study may lead to added costs to you. This includes the cost of transportation to and from the study location.

Will being in this study help me in any way?
We cannot promise any benefits to you or others from your taking part in this research. However, possible benefits include: improved balance and walking ability. Your participation in this study may help us have a better understanding of transcutaneous spinal cord stimulation procedures and may help other people with their rehabilitation in the future.

What happens to the information collected for the research?
Efforts will be made to limit the use and disclosure of your personal information, including research study and medical records, to people who have a need to review this information. We cannot promise complete secrecy. Organizations that may inspect and copy your information include the IRB and other representatives of this institution. Our collaborating researchers at The Edgerton Neuromuscular Research Laboratory at the University of California, Los Angeles.

Data Sharing

De-identified data from this study may be shared with the research community at large to advance science and health. We will remove or code any personal information that could identify you before files are shared with other researchers to ensure that, by current scientific standards and known methods, no one will be able to identify you from the information we share. Despite these measures, we cannot guarantee anonymity of your personal data.

Can I be removed from the research without my OK?

The person in charge of the research study or the sponsor can remove you from the research study without your approval. Possible reasons for removal include inability to follow the investigator's instructions, your medical status changes per investigator discretion, or the study closes.

We will tell you about any new information that may affect your health, welfare, or choice to stay in the research.

What else do I need to know?

If you become ill or get injured as a result of this study (medications, devices or procedures), you should seek medical treatment through your doctor or treatment center of choice. You should promptly tell the study doctor about any illness or injury.

The hospital [university, researchers] will not pay for medical care required because of a bad outcome resulting from your participation in this research study. This does not keep you from seeking to be paid back for care required because of a bad outcome.

If you agree to take part in this research study, we will pay you $40 for each assessment and TMS visit and $25 per treatment visit (total of up to $1160). These funds are provided to help support you with time and travel associated with your participation.

The Shirley Ryan AbilityLab will issue you a ClinCard, which is a specially designed debit card for clinical research. Once a visit that qualifies for compensation is completed, funds will be approved and loaded onto your card. The funds will be available within 1 day after being loaded and can be used at your discretion.

You will be issued one card for the duration of your participation. If your card is lost or stolen, please call (866) 952-3795 or ask a coordinator for a replacement ClinCard.

Fees are incurred if used at an ATM (fees vary by location). However, if the card is used for in-store or online purchases via credit or debit, there are no associated fees and no expiration date.

Please be advised: Inactivity on the card for more than 3 months will incur a monthly fee. However, as long as there is activity on the card within 3 months (funds are added or a transaction is completed), the month period will reset and no monthly fee will be assessed.

If you do incur a monthly fee, please contact Greenphire Support at the number on the back of your card and they will reverse the fee. See "Tips for Using the Attached ClinCard" for more information.

The Finance Department at the Shirley Ryan AbilityLab will be provided with your information, including your Social Security Number, in order to issue payment for your study participation.

Study payments are considered taxable income and reportable to the Internal Revenue Service (IRS). An IRS Form 1099 will be sent to you if your total payments are $600 or more in a calendar year.

You may be given access to new inventions that are being developed by the investigator, the study sponsor, or other people involved in the study. Certain laws can make it harder to obtain legal protection for a new invention shared with a study participant, unless the study participant agrees to keep information about the invention confidential. You agree to keep confidential information you may receive about new inventions, such as new drugs, new devices, or new methods.

HIPAA Authorization

We are committed to respect your privacy and to keep your personal information confidential. When choosing to take part in this study, you are giving us the permission to use your personal health information that includes health information in your medical records and information that can identify you. For example, personal health information may include your name, address, phone number or social security number. Your health information we may collect and use for this research includes:

- All information in a medical record
- Results of physical examinations
- Medical history
- Lab tests, or certain health information indicating or relating to a particular condition as well diaries and questionnaires
- Records about study medication or drugs
- Records about study devices

This consent expires on February 1, 2022. After this date, Northwestern University may not gather new information about you, use or disclose your personal health information collected in this study for any purpose other than the research study described in this consent unless Northwestern University obtains permission to do so from you. Illinois State Law permits use and disclosure of your mental health information only to the extent specified in this document.

The following clinical providers may give the researchers information about you: all current and previous health care providers, including but not limited to the Shirley Ryan AbilityLab (SRALAB), Northwestern Medical Group (NMG), Northwestern Memorial Hospital (NMH), and Northwestern Lake Forest Hospital (NLFH).

Once we have the health information listed above, we may share some of this information with the following offices or entities outside of Northwestern University and its clinical partners (or affiliates): the Northwestern University Institutional Review Board Office and Office for Research Integrity; the US Office of Research Integrity; the US Office for Human Research Protections; the US Food and Drug Administration.

Any research information shared with outside entities will not contain your name, address, telephone or social security number or any other personal identifier unless disclosure of the identifier is necessary for review by such parties or is required by law or University policy [except that such information may be viewed by the Study sponsor and its partners or contractors at the Principal Investigator's office].

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- Authorized members of the Northwestern University and the Shirley Ryan AbilityLab workforce, who may need to see your information, such as administrative staff members from the Office for Research, Office for Research Integrity and members of the Institutional Review Board.
- Clinical affiliates, including but not limited to the Shirley Ryan AbilityLab (SRALAB), Northwestern Medical Group (NMG), Northwestern Memorial Hospital (NMH), Northwestern Lake Forest Hospital (NLFH), and the Ann & Robert H. Lurie Children's Hospital of Chicago (Lurie Children's). Your participation in this clinical trial may be tracked in an electronic database and may be seen by investigators running other trials that you are enrolled in and by your healthcare providers.
- Government agencies and public health authorities, such as the Food and Drug Administration (FDA) and the Department of Health and Human Services (DHHS).
- Others: The following individuals or organizations may also access, receive, or use your personal health information: The Edgerton Neuromuscular Research Laboratory at the University of California, Los Angeles.

Those persons who get your health information may not be required by Federal privacy laws (such as the Privacy Rule) to protect it. Some of those persons may be able to share your information with others without your separate permission.

However, Illinois law does not allow the re-release of HIV/AIDS, genetic testing, mental health and developmental disabilities information by the recievers of the information except in precise situations allowed by law.

Also, Federal Confidentiality Rules, 42 CFR Part 2, prohibit making any further disclosure of substance use disorder information unless further disclosure of this information is expressly permitted by written consent of the person to whom it pertains or as otherwise permitted by 42 CFR Part 2.

The results of this study may also be used for teaching, publications, or for presentation at scientific meetings.

Unless you revoke your consent, it will expire at the end of the research study.

Although you may revoke consent to participation in this research at any time and in any format, you must revoke authorization for use or disclosure of your health information in writing. To revoke your authorization, write to:

PI's Name: Dr. Elliot J. Roth, MD
Institution: Shirley Ryan AbilityLab
Department: Co-Medical Director, Brain Innovation Center
Address:355 E. Erie Street, Chicago, IL 60611

You do not have to authorize the use or disclosure of your health information; however, you will not be allowed to take part in this research study. If you do not authorize the use or disclosure of your health information, it will not affect your treatment by health care providers, or the payment or enrollment in any health plans, or affect your eligibility for benefits.

A copy of this signed consent document, information about this study, and the results of any test or procedure done may be included in your medical records and may be seen by your insurance company.

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Optional Elements:

The following research activities are optional, meaning that you do not have to agree to them in order to participate in the research study. Please indicate your willingness to participate in these optional activities by placing your initials next to each activity.

I agree	I disagree	
_____	_____	The researcher may audio or video record me to aid with data analysis. The researcher will not share these recordings with anyone outside of the immediate study team.
_____	_____	The researcher may audio or video record me for use in scholarly presentations or publications. My identity may be shared as part of this activity, although the researcher will attempt to limit such identification by avoiding inclusion of my face from recordings. If this occurs, the researcher will black block my face.
_____	_____	The researcher may contact me in the future to see whether I am interested in participating in other research studies by the Principal Investigator of this study.

Your signature documents your permission to take part in this research. You will be provided a copy of this signed document.

_____ _____
Signature of Participant Date

_____
Printed Name of Participant

_____ _____
Signature of Person Obtaining Consent Date

_____
Printed Name of Person Obtaining Consent

My signature below documents that the information in the consent document and any other written and information was accurately explained to, and apparently understood by, the participant, and that consent was freely given by the participant.

_____ _____
Signature of Witness to Consent Process Date

_____
Printed Name of Person Witnessing Consent Process