Title: *Improving Spinal Cord Injury Rehabilitation Interventions by Retraining the Brain*

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Consent to Participate in a Research Study

Sponsor: **U.S. Department of Defense**

Study Title: **Improving Spinal Cord Injury Rehabilitation Interventions by Retraining the Brain**

Principal Investigator: **Ela B. Plow, PhD, PT**

Study Sites: Cleveland Clinic Foundation (main site), Kessler Rehabilitation Institute (partnering site), Louis B. Stokes Cleveland VA (partnering site), MetroHealth Hospital

Cleveland Clinic Foundation Consent Form for Subjects with Spinal Cord Injury

Carefully review this consent document. The purpose of a consent document is to provide you with information to help you decide if you wish to participate in this research study at one of our three sites: Cleveland Clinic's Main Campus, Kessler Rehabilitation Institute, the Cleveland VA, or MetroHealth Hospital. 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 to understand the research risks, benefits, and alternatives.

Please note:

- **You are being asked to participate in a research study**
- **Carefully consider the risks, benefits, and alternatives of the research**
- **Your decision to participate is completely voluntary**

PURPOSE OF THE STUDY

Why Are You Being Asked To Take Part In This Research?

You are being asked to participate in this research study because you have an incomplete spinal cord injury (SCI)/lesion that occurred at least 1 year ago, you are 18 years or older, and you have difficulties/complaints about using your affected upper limbs (shoulders/arms/hands) in your daily activities.

Why Is This Study Being Done?

The purpose of this study is to investigate whether combining training of the affected upper limbs in patients with SCI with a noninvasive technique of brain stimulation called transcranial direct current stimulation (tDCS) can improve training outcomes. tDCS is a painless and noninvasive method (that is, does not involve surgery) of activating the brain with the use of low-level direct electrical current. It is considered a safe technique and has been used in treatment of a variety of neurological diseases for research study purposes only. In our study, the side of the brain opposite to the hand that was more greatly affected by the injury (the "weaker" hand) will be stimulated (left brain/right hand, right brain/left hand).

How Many People Will Take Part In The Study?

In all, atleast 49 (up to 53) people with SCI will ultimately participate in the study 21(up to 25) at the Cleveland Clinic, 14 at the Kessler Foundation/Kessler Institute for Rehabilitation, 6 at the Louis B. Stokes Cleveland VA Medical Center, and 8 at MetroHealth Hospital).

RESEARCH PROCEDURES

Participation in this study involves screening for eligibility, 15 upper limb training sessions, and testing at the beginning and end of the study. To study whether tDCS benefits people with SCI, there will be two groups of patients in the study: upper limb training + active stimulation and upper limb training + sham stimulation. Participants are chosen randomly to be part of one of these two groups. Regardless of the group, all participants will receive 15 upper limb training sessions. In total there are about 22 visits you will be asked to come to at the Cleveland Clinic main campus.

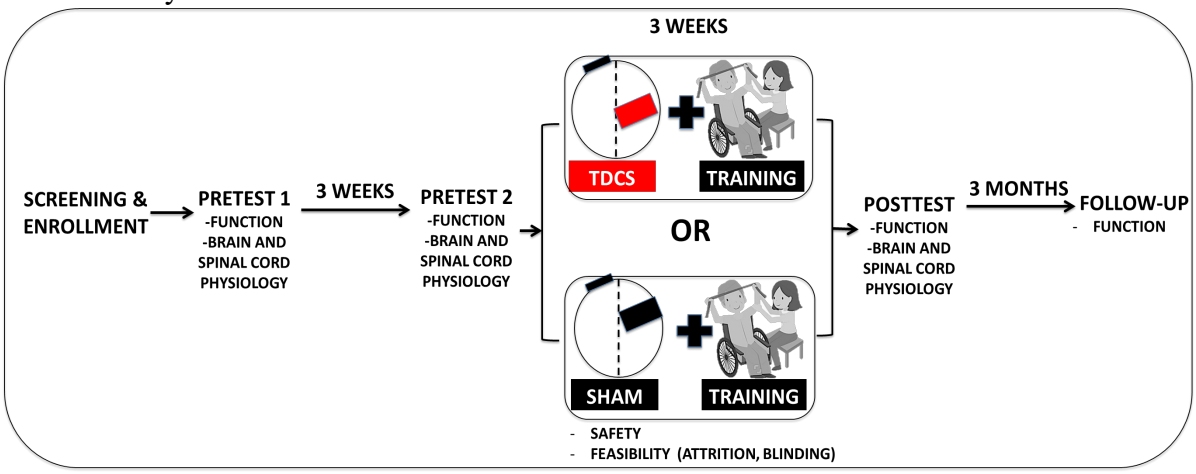
All participants will be asked to complete the ideal study design. This consists of first completing a screening and enrollment visit. After screening and enrollment has been completed, participants will complete two pre-testing visits. These two pre-testing visits will be scheduled 3 weeks apart, during which participants will perform only normal activities of daily living. After pre-test #1 (2 visits) and pre-test #2 (2 visits) are completed the intervention phase will be scheduled: upper limb training sessions 5 times a week for 3 weeks. After completion of the intervention phase the post-testing (2 visits) visit will be scheduled to happen as soon as possible after the final upper limb training sessions, preferably within one week. Upon completion of the post-testing visit, participants will enter the 3 months of home exercises until the 3 month follow-up visit. During this time the participant will perform exercises given by study personnel, and complete bi-weekly phone calls with the site coordinator. After completion of the 3 month follow-up visit the participant will exit the study.

It is ideal to complete procedures as listed above, however this may not work for all participants. The number of upper limb training sessions during the intervention phase may be changed to suit your personal needs. If any change occurs to the intervention phase, the length of time between pre-test#1 and pre-test#2 would be changed to match the extended length of the intervention phase.

1. **Screening procedures:** Potential candidates will be determined by a few methods: physician referrals, finding clinicaltrials.gov entry, and from EPIC chart review. We will find subjects for EPIC chart review from EPIC HEAT requests and KP query requests which provide us patient MRNs based on filtered criteria. Potential subject's physician will be contacted to get permission to send a letter to the subject. Letters will be sent to the subjects which will provide our phone number to call if interested. Screening procedures will be conducted over the phone by the study coordinator to determine if you are eligible to take part in the research study. When we first speak we will give you a brief description of the study and go through a preliminary phone screen with you. The preliminary phone screen will help us determine your basic eligibility for participating in the study. If it is determined that you are eligible for the study, we will make an appointment for you to visit to the Cleveland Clinic Main Campus. However, if it is not reasonable for you to come to the Cleveland Clinic for your eligibility screen, we can conduct a video screening with the treating physician and/or therapist.This visit will involve discussing the details of the study and obtaining your informed consent to participate. If you provide consent, you will be seen by physician and study staff, who will confirm your eligibility for the study. Note: If you are a woman of childbearing age, there

may be unforeseen risks to an unborn child associated with research procedures done as part of this study. Therefore, you will be asked to undergo a pregnancy test. If it is found that you are pregnant, you will be deemed ineligible for participation in this study. If you are unwilling to undergo pregnancy testing, we will ask you to not participate in this study.

If deemed eligible to participate in the study, you will join the study. We advise that you keep your current medications at the prescribed dose unless advised otherwise by your doctor, in which case, we ask that you inform us of the changes. The diagram illustrates the steps in this research study.



2. **<u>Pre-Test #1 (8-11 hours occurring over two days):</u>** You will undergo upper-limb function tests (strength, activities, and impairments), spinal excitability test (H-Reflex), and brain function tests at the Cleveland Clinic.

Functional testing day (4-5 hours)

- **Functional testing (3-4 hours):** Your upper-limb function will be evaluated using specialized tests, including ones that measure the time required to pick up objects, your ability to make a pinch and grasp and release objects, and others that test the strength of your upper-limb muscles. You will also answer questions, which will assess how the injury has impacted your activities of daily living and your participation in life's roles.

- **Spinal Excitability studied with Hoffman-Reflex (H-Reflex) (1 hour):** During the functional testing visit we will collect a measure of spinal excitability called H-Reflex. This test is commonly performed in the clinical setting and will be performed using a clinical grade stimulation device. This test involves stimulating one of the nerves in your arm to test the integrity of nerve connections at the level of the spinal cord. During this test we will place EMG stickers on a flexor muscle of the forearm and then stimulate the median nerve under the biceps muscles.

Brain function studied with transcranial magnetic stimulation (TMS) day (4-6 hours)
Following tests of upper-limb function, you will undergo testing with TMS. TMS is an

investigational device that provides a way to test the function of a specific part of the brain that is devoted to moving your affected upper limbs by directing a low electrical current to that part of the brain through the scalp. The investigator will hold an enclosed coil of copper wire atop your head. This device looks like the number eight with a handle and is covered with thick plastic so that no part of the copper wire will ever be in contact with you. A current is passed through the coil; it creates a magnetic field that will cross your skin and bone and enter your brain. You will hear a snapping sound when the current passes through the coil. To protect your hearing, foam earplugs will be available. Using removable skin (electromyography, EMG) sensors, the activity of the muscles of your hands will also be recorded while TMS is delivered. All electronic devices and hearing aids will have to be removed prior to TMS procedure. If you wear prescribed hearing aids, safety hand gestures, cards and cues will be instated after the hearing aids are removed.

3. **Pre-Test #2 (8-11 hours occurring over two days):** Pre-test #2 will take place 3 weeks after the completion of pre-test #1. During this 3 week period between pre-test #1 and pre-test #2 you will be asked to maintain your normal daily activities. For pre-test #2 you will repeat the tests performed at pre-test #1: upper-limb function, spinal excitability (H-Reflex), and brain function (TMS). For these tests again, you will visit the Cleveland Clinic's Main Campus.

4. **Intervention phase:**

   Randomization procedures: You will be randomly assigned to receive either upper limb training combined with active stimulation *or* upper limb training combined with sham stimulation, a decision that will be based on chance (like the flip of a coin). The difference between the two groups is that the sham group will not receive intended type and level of current to the brain. You will not know whether you will be receiving the active stimulation or the sham stimulation. However, this information can be learned in case of an emergency. There will be 22 participants in each treatment group. You will not be able to choose which group you become assigned to.

   Training for the affected hand: Regardless of the group you are assigned to, you will receive physical training, called Massed Practice-based upper-limb training, for 2 hours per day, 5 times a week, for 3 weeks at the Cleveland Clinic's Main Campus. The times in which the sessions occur can be changed to suit your needs. The total number of sessions will remain the same but the sessions can be spread out to 3 times a week for 5 weeks if that becomes necessary based on your personal needs. We recommend that you at least participate in 3 sessions a week to help gain or maintain any benefit. Training will involve repeated practice of tasks used in daily life, such as large arm-hand motions, grip, grip with rotation of forearm, pinch, and pinch with rotation of the hand/arm. These training sessions will be conducted in Clinical research labs with oversight from clinical and research personnel.

   Training will be specific to your impairments: Ten different variations of each task will be practiced for 25 min each. Each task will be performed in a set of 10 trials. At the end of each set of 10 trials, the task will typically be changed. The level of difficulty of each task will be slightly beyond what you can accomplish easily, to encourage you to do a little better than on the previous trial. Tasks will be made progressively more difficult as you improve. If you feel tasks are excessively difficult, then a simpler task involving similar movements will be substituted. Rest intervals will be allowed during each session. Positive feedback or reward will be provided visually, such as graphs of your daily performance. We will have 3 summary feedback sessions in total; after visits 5, 10, and 15 to update participants on progress and achievements made.

Transcranial direct current stimulation (tDCS): The stimulation procedure involves directing a weak amount of electric current from a 9-volt battery-operated device to stimulate your brain, without any invasive procedure. Electrodes, covered in small sponges soaked in a salt solution (saline), will be placed over certain parts of your head and secured to your scalp while you receive training. The direct current will flow through the electrodes, penetrate your scalp, and create a flow of electrical current in your brain. You may feel slight itching on your scalp initially and at the end of the tDCS session. The itching sensation is not related to whether you are receiving active tDCS or not. Although the tDCS set-up will be applied as described above regardless of what group you are assigned to, current will only be delivered if you are in the "training-plus-stimulation group. You will not be able to sense the difference to realize whether you are receiving real or sham tDCS. There will be two sessions of tDCS applied during physical training. tDCS will be applied for the first 30 minutes of each hour of physical training, which allows a rest interval between the two tDCS training sessions. A safety questionnaire will be completed at the end of each visit of the therapy-plus-tDCS (active or sham) sessions to assure your safety with the stimulation you are receiving.

Vital sign recordings: During each visit vital signs will be recorded twice; once upon arrival to the lab before starting any research procedures and second at the end of all research procedures for that day before your depart from the lab. Vital signs recorded will include blood pressure, heart rate, respiration, and blood oxygen saturation.

Virtual Visits: For this study, all visits will take place at the Cleveland Clinic Main campus. At the PI's discretion, we may ask you to perform virtual visits during times you do not have access to the Cleveland Clinic. Virtual visits will be conducted with you over a video sharing application such as "Skype" or "Zoom" by study personnel using a Cleveland Clinic encrypted device.

5. **Post-Test (8-11 hours occurring over two days):** After completion of the intervention phase (3 weeks), you will repeat the tests and procedures done at baseline; upper-limb function, H-reflex, and brain function (TMS).

6. **3-Month Follow-Up (1-2 hours):** At 3 months following the post-test, you will be tested on upper-limb function.

OPTIONAL: The study team may determine that we would like to perform additional up to 5 visits. The first visit will be for tests on H-reflex and Brain stimulation (TMS) at 3 month-follow up, and 2 visits each will be at 6 months and/or 12 months (see below 7 and 8). Given that these additional tests are optional and that we only plan to include 4 participants due to limitations in funds and time resources, the addition of optional follow-up visits will be determined by the study team at the time after post-testing. If we determine that we would like to bring you back into the clinic to perform testing there will be up to 5 additional visits.

7. 3 Month Follow-Up (6-8 hours) (OPTIONAL): If you opt into this additional testing we will perform the neurophysiology testing visit (TMS and H-Reflex) as performed at Baseline

8. 6 Month Follow-Up (8-11 hours occurring over two days) (OPTIONAL): If you opt into this additional testing, we will repeat the tests and procedures done at baseline; upper-limb

function, H-reflex, and brain function (TMS) at 6 months following the post-test.

9. 12 Month Follow-Up (8-11 hours occurring over two days) (OPTIONAL): If you opt into this additional testing, we will repeat the tests and procedures done at baseline; upper-limb function, H-reflex, and brain function (TMS) at 12 months following the post-test.

How Long Will You Be In The Study?

You will visit your study site 23 times. Total involvement in the study from the first visit to the follow-up will be 5 months. The amount of time spent in the study could change if the frequency of upper limb training sessions changes. If you agree to be in the OPTIONAL follow up testing you will visit the study site up to 28 times and the total involvement in the study will be up to 15 months.

RISKS AND DISCOMFORT

Listed below are the risks and the measures taken to minimize them.

tDCS:

Many different researchers have studied the safety of tDCS. They have all concluded that tDCS is a safe and painless technique for electrically stimulating the brain with almost no risk of harm. The only adverse (negative) effects that have been reported were:

- Temporary itchiness and/or a redness of the skin in the area of stimulation. The reddening lasts for only a short time, given the levels of stimulation proposed in this study. However, skin will be inspected regularly at the site of stimulation to ensure redness is relieved.
- Transient and mild headache, tingling, and a burning sensation in the area of stimulation, but these effects occur at doses higher than the low levels used in the study.
- Although the risks of tDCS are considered to be minimal, tDCS might result in temporary brain- or movement-related side effects such as dizziness, disorientation, or confusion; if they do appear, these symptoms usually disappear shortly. All subjects will be constantly supervised by study staff.

TMS:

Transcranial magnetic stimulation (TMS) has been used in a growing number of laboratories worldwide since 1984, and safety guidelines have been developed. In the present study, the investigators will use all recommended safety precautions for TMS. Although unlikely, given the relatively low stimulation levels applied in the present study, the following side effects are still possible:

COMMON SIDE-EFFECTS:

- Headache: Subjects may have a headache following TMS. This is believed to be due to muscle tension. In the case of headache, subjects will be offered acetaminophen or aspirin, which in all prior cases of headaches induced by TMS have promptly resolved the discomfort. The risk of headache is estimated to be approximately 10%-25%.

- Hearing: TMS produces a loud clicking sound when a current is passed through the stimulation coil. This loud clicking can result in ringing in the ear and temporary shifts in the subject's ability to determine the pitch and loudness of sounds, if no protection is used. To prevent this possible side effect, we will ask subjects to wear earplugs that block the noise of the TMS. Hearing damage is possible; one person is known to have suffered permanent hearing damage when the hearing protection fell out of the ear. Animal and human studies have shown that earplugs or headphones can effectively prevent the risk of hearing disturbance due to TMS.

RARE SIDE-EFFECTS:

- Seizure: There have been reports that subjects had a seizure induced by TMS. If a seizure were to occur, it would occur during the TMS application itself, not after. If you are currently taking a prescription medication that has the potential to lower the seizure threshold, you may be at increased risk for seizure from the procedures in this study. As a patient with SCI, you must maintain your current medications at the prescribed dose for the whole length of time you are involved in this study. Seizures are a very rare complication. First, the TMS levels that we propose to use are low and have never been reported to cause a seizure. Second, during the TMS session, subjects will undergo continuous monitoring of muscle activity (via electromyography, EMG) to allow investigators to detect the earliest warning signs of a seizure and be able to prevent it. Nevertheless, a seizure could occur. For this reason, TMS will be applied by investigators properly trained in the prompt recognition and treatment of a seizure and certified in basic life support. Clinical research nursing support, physicians, and resources (such as "crash cart" medications related to seizure protocol) will be available. Should a seizure occur, subjects will receive prompt treatment by a physician. Experiencing a seizure induced by TMS does not mean that subjects will have another seizure again; it does not make the subject an epileptic person and will not mean that subjects will have to take medications to prevent seizures in the future. A letter approved by the U.S. Food and Drug Administration (FDA) documenting these facts will be offered to any subject who may experience a seizure induced by TMS. Nevertheless, seizure occurrence with single-pulse TMS is rare. Less than five persons have had seizures induced by the type of TMS we are using (single-stimulus/pulse TMS) among the many thousands of subjects who have undergone TMS worldwide. Furthermore, the investigators will use precautions to further reduce the risk.

- Memory/ability to concentrate: After receiving TMS, memory or attention may be affected for a short period of time (a few minutes). The TMS levels used in this study have never been shown to cause such problems.

- Unknown issues: Finally, even though TMS has been used in many laboratories worldwide since 1984, there could be some unforeseen complications.

- Pregnancy considerations: As stated above, there may be unforeseen risks to an unborn child associated with the mother's undergoing TMS. To address this risk, women will be

excluded from the study if they are found to be pregnant during our prior testing procedures.

Discomfort associated with H-Reflex:

During the H-Reflex test, you may or may not experience discomfort from brief electrical shocks to your arm. The investigator will use the lowest needed shock strength for the tests. The Investigator performing the testing will assure that you can tolerate the testing and will stop if you request. These tests are routinely used in clinical settings and usually are well tolerated.

SCI patient population:

Many patients with tetraplegia have reported severe difficulties with neuropathic pain, sensation, walking, bladder and bowel function, trunk stability, sexual function, and arm/hand function. Some of SCI patient population present with co-morbidities such as autonomic emergencies, spasticity, and depression. Even though the co-morbidities may be unrelated to the study procedures, this patient population can still experience the following:

- *Autonomic dysreflexia:* This syndrome occurs in individuals with spinal cord lesions above the T6 level. Since the study plans to enroll patients with levels of injury between C2 and C6, patients may be at risk for autonomic dysreflexia. The syndrome is caused by overstimulation of the involuntary nervous system, which is usually a result of improper emptying of the bowels or bladder or a urinary tract infection. Study staff is aware of the symptoms of autonomic dysreflexia (severe hypertension, headaches, sweating, flushing of skin, and slow heart rate). If a participant develops the syndrome during a study session, the participant will immediately inform the responsible treating physician. Clinical Research Unit nurses will be on-site during all sessions and will help identify signs early on. They will help initiate preventive measures, such as ensuring catheter bags are not full or there is no obstruction to catheter tubing. If an event occurs, study staff will initiate the emergency code for paging the emergency response team; the on-call physician will be paged, and nursing staff will implement the medical orders. With such precautionary measures, no autonomic emergencies have occurred in Dr. Plow's previous clinical trial in patients with tetraplegia.

- *Exacerbated spasticity:* Some SCI patients experience spasticity, which is described as involuntary stiffness of the muscles. Depending on the severity, spasticity could affect the patient's comfort level as well as ability to perform tasks during the intervention phase of the study. During the intervention, breaks will be provided to minimize fatigue and allow passive movements and stretching. Participants will be asked to maintain their dose of anti-spasticity medications.

- *Neuropathic pain:* Patients with SCI could have damaged nerve fibers, which transmit incorrect signals and cause pain. This neuropathic pain could affect the participant's comfort level as well as ability to perform tasks during the intervention phase of the study. The level of neuropathic pain will be taken into consideration when designing the specific intervention for a participant to minimize any exacerbation of the pain.

Risks Associated with COVID-19 Virus:

The Cleveland Clinic is taking the necessary precautions to reduce the risk of patients and caregivers being infected. The study team will also take additional precautions by reducing the number of personnel you are in contact with at study visits, and they may ask you sanitize/wash your hands upon arrival to those visits.

Even with the necessary precautions put in place, there is a possibility that you may still contract COVID-19. If you are experiencing any respiratory symptoms please contact your primary care physician. These symptoms may include fever, cough, and/or shortness of breath. If you have any of these symptoms, please do not come to your scheduled study visits and contact the research team to let them know. We will continue to update you on Cleveland Clinic COVID-19 policies as they arise.

COVID-19 Virus Risk Mitigation:

- In response to the COVID-19 Pandemic, the Cleveland Clinic has been continuing to update and provide guidance for conducting clinical and research procedures in the safest manner possible at the Cleveland Clinic
- Keeping the well-being of our subjects and colleagues in mind we will implement safety measures for subject visits to the Cleveland Clinic and ask that you comply with the following:
    - Clinical screening at the COVID checkpoint upon arriving at the Cleveland Clinic
    - Wearing a mask while at the Cleveland Clinic.
        - At this time wearing of a mask is a sensitive topic across the country. We realize this and have asked you wear a mask per CCF guidance which has been provided so that we may best protect our participants.
    - Social distancing while at the Cleveland Clinic
    - Visitors at the Cleveland Clinic are limited, so we will ask that you do not enter the building with a caregiver until further notice. We will work with you on how to best manage your care when attending research visits.
    - Opportunities for hand washing and sanitization will be given to you frequently.
    - We will call you the day before your visit to ask about COVID-19 symptoms
    - Possible additional virtual screening visits with physicians may occur. We will inform you ahead of time of these if they are to occur.
    - Any visits that we have the ability to, we will make virtual.
    - If you have tested positive for COVID-19, we request that you provide a letter from your primary care physician that you have recovered from the virus and no longer have any of the symptoms.
    - If you have knowledge of having come into contact with someone who was diagnosed with COVID-19 or had COVID-19 like symptoms you will be referred

to follow-up with your PCP and follow CDC guidelines before resuming any study procedures.

- If you have travelled out of state, we request you disclose:
    - Where you travelled to
    - The dates of your trip
    - Summary of trip details so we may understand the COVID-19 exposure risk

      If you have self-quarantined since returning from your trip

Risks Associated Transportation:

If you require transportation to study visits and receive transportation assistance from the Cleveland Clinic study team you should be aware of the risks involved. These risks are no different from those you undertake when you leave home for a medical or personal visit, yet these should be known. During transportation to and from the Cleveland Clinic one may suffer automobile- related, roadway-related, weather-related or other unexpected risks. These risks can include automobile accident, slip/fall within the vehicle or while getting on or off, bodily injury or other unforeseen risks which may even cause serious/critical illness or death. Some of these risks are preventable with proper restraint application and adhering to safety protocols, but some other risks such as auto accident or sudden braking to prevent an accident or inclement weather may be hard to foresee or predict and thereby protect against. To mitigate the risks involved with transportation the following measures will be taken by transportation companies: harnessing the power wheelchair to the vehicle floor, placing a strap across the person and/or their chair, checking to make sure all of your wheelchair straps are secured, any other measure that the transportation company utilizes for safe transport of their clients. The transportation companies we have selected are in the business for transporting for medical reasons and have safety guidelines that we recommend you adhere to be safe.

Cleveland Clinic personnel will be present upon your arrival to study visits. Cleveland Clinic personnel will also be with you as you board the vehicle. We recommend adhering to all transportation guidelines explained by the transport company to ensure your safety during transport and getting in and off a vehicle.

If physical injury occurs during your transportation Cleveland Clinic shall not pay for the medical care costs required. Compensation for lost wages and/or direct or indirect losses are not available. Cleveland Clinic will not provide compensation for medical expenses or any other compensation for transportation-related injuries.

BENEFITS

Are There Benefits To Taking Part In The Study?

Although you will be receiving upper limb training in the study, you may or may not directly benefit from participation in the study. However, your participation may help others in the future as a result of knowledge gained from the research.

ALTERNATIVES

What Other Options Are There?

You do not have to enroll in this study to receive upper-limb training. You should discuss other options with the investigator and your regular doctor so that you can make a well-informed decision about participating in this study.

PRIVACY AND CONFIDENTIALITY

The medical and research information recorded about you for this research study will be used within Cleveland Clinic and/or may be disclosed outside Cleveland Clinic.

Representatives of the U.S. Army Medical Research and Materiel Command (USAMRMC, a unit of the Department of Defense, which is funding this study) are authorized to review research records as part of their responsibility to protect human research volunteers. Accurate and complete study records will be maintained and made available to USAMRMC representatives. Research records will be stored in a confidential manner so as to protect the confidentiality of subject information.

Federal regulations require that you authorize the release of any health information that may reveal your identity. The persons and entities that you are authorizing to use or disclose your individually identifiable health information may include the study staff, Cleveland Clinic monitors/auditors and Institutional Review Board (IRB, which monitors all studies done in people), the FDA, the Department of Health and Human Services (DHHS), and USAMRMC representatives. Because of the need to release information to these parties, absolute confidentiality cannot be guaranteed. Cleveland Clinic also may use and disclose this information for treatment and reimbursement reasons. In unusual situations, Cleveland Clinic will comply with legal requirements that mandate disclosure of identifiable information. Once your personal health information is released, there is a possibility that it may be re-disclosed and no longer protected by federal privacy laws.

Before sharing data with other sites, we will remove all participant identifiers to protect your privacy. Identifiers that are removed include name, address, date of birth, or date of spinal cord injury. Your identifiable information will remain at the site that you enroll into the study with.

Per guidelines of the Congressionally Directed Medical Research Programs (CDMRP, an office within the Department of Defense), CDMRP-funded studies should make their “final research data” as freely and widely available as possible. To meet this specification, we are planning to share “raw data” that is completely de-identified. That way, your privacy and confidentiality will not be affected. Since our partner institutions, MetroHealth Rehabilitation Institute and Kessler Foundation/Kessler Institute for Rehabilitation, are two of the 14 Spinal Cord Injury Model Systems in the U.S., we plan to allow them to enter the de-identified data collected in this study into their national database. This process would allow all spinal cord injury Model Systems across the country to have access to our raw (de-identified) values and compare those with values from their patients and study participant pool. The results of this research may also be presented at meetings or in publications; however, the results will be de-identified and your identity will not be disclosed in those presentations.

The Research Monitor of this clinical trial is authorized to review research records, including identifiable protected health information, as part of their responsibility. The Research Monitor is responsible to oversee the safety of research subjects and report observations/findings to the IRB.

As the TMS tests are not used to diagnose an injury, no clinical report will be generated. The information recorded about you as part of this research will be maintained in a confidential manner.

Photos and Video Recording:
We will request to take photos and video recordings of your participation in this study for CCF study team research purposes. You may choose not to allow us to take photo/video for research purposes and it would not affect participation. The photos and videos for research purposes will be taken with Cleveland Clinic equipment and not shared outside of Cleveland Clinic. If you agree to allow us to take photo/video for CCF internal team research purposes we will ask you to opt in below.

We may additionally request you to allow us to use the photos and videos of you outside of the Cleveland Clinic for scientific research presentations, seminars, community outreach presentations, etc. If you agree to allow us to use your videos outside of the Cleveland Clinic we will ask that you sign two forms: "HIPPA Research Release" and "Photo/Video Release". Signing these forms will allow us to use the full photo and videos without editing out your features or the sound. Not allowing us to use your photo/video outside of the Cleveland Clinic and not signing the two release forms will not affect your participation in the study.

Upon completion of the study, you may have access to the research information. While the study is going on, however, your access to research information about you will be limited. Preventing this access during the study keeps the knowledge of study results from affecting the reliability of the study. This information will be available should an emergency arise that would require your treating physician to know this information to assist in treating you.

Your research information may be used and disclosed indefinitely. However, you may stop these uses and disclosures at any time by writing to the Lead PI of the site you have enrolled into the study with. If you do so, your participation in the research will stop, but any information previously recorded about you cannot be removed from the records and will continue to be used as part of the research. Also, information already disclosed outside of the site you enrolled into the study with cannot be retrieved. Even is you ask us to stop outside disclosures, information collected about you will be disclosed as required by state and federal law. You may also contact either of the other two sites other than the site you enrolled with to discuss any concerns about data that may have been shared with their sites. Below are the list of sites and their contacts.

- Ela B. Plow, PhD, PT: (216) 445-4589
  Cleveland Clinic, 9500 Euclid Avenue, ND20; Cleveland, OH 44195
- Gail Forrest, MD: (973) 324-3518
  Kessler Foundation, 1199 Pleasant Valley Way; West Orange, NJ 07052
- Svetlana Pundik, MD: (216) 791-3800 ext 3732
  Cleveland VA Medical Center & Case Western Reserve University School of Medicine, 10701 East Blvd; Cleveland, OH 44106

- Anne Bryden, PhD: (216) 957-3594
  MetroHealth Old Brooklyn Health Center, 4229 Pearl Road; Cleveland, OH 44109
- David Cunningham, PhD: (216) 957-3349
  MetroHealth Old Brooklyn Health Center, 4229 Pearl Road; Cleveland, OH 44109

Cleveland Clinic will not use or disclose the information collected in this study for another research purpose without your written permission unless Cleveland Clinic's Institutional Review Board (IRB) gives permission after ensuring that appropriate privacy safeguards are in place. The IRB is a committee whose job is to protect the safety and welfare of research subjects.

By signing this informed consent form, you are authorizing access to your medical records and the sharing of your de-identified data with our partner sites. If you choose not to sign this consent form, you will not be permitted to participate in this research study.

RESEARCH-RELATED INJURIES:

If physical injury occurs due to involvement in this research, medical treatment is available, but you or your medical insurance must pay the cost of treatment. Such medical treatments that are not covered by your medical insurance shall not be paid by Cleveland Clinic. Compensation for lost wages and/or direct or indirect losses are not available. Cleveland Clinic will not provide compensation for medical expenses or any other compensation for research-related injuries. Further information about research-related injuries is available by contacting the Institutional Review Board at (216) 444-2924.

COSTS

What Are The Costs?

The study related tests/procedures/visits will be provided at no cost to you.

In the event you are affected by COVID-19, the study will not be able to provide compensation for treatment, loss in wages, pain and suffering, or other direct or indirect losses related to the virus.

You will be compensated $150.00 for your participation and completion of the study. Partial completion of study procedures, but not completing the study, will result in pro-rated amount of the $150.00 compensation for total study completion. Compensation will be mailed to you by check at the end of the study. Parking will be available to you at no cost.

VOLUNTARY PARTICIPATION

What Are Your Rights As A Participant?

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.

In the event that a severe adverse reaction occurs, such as seizure during TMS, you will be withdrawn from the study, even without your approval. As no ongoing risks are associated once these procedures are completed, ending the procedure at any time can be considered safe.

VIDEO AND PHOTO USE IN RESEARCH PRESENTATIONS

By initialing below to "Opt in," you give permission for us to use your video recordings and photographs for research purposes. If you do not agree to allow us to use these photos and video recordings for research purposes your participation in the study will not be affected. Please initial below if you agree (Opt in) or if you disagree (Opt out).

Check one and initial for video and photo use:

☐ ☐

Opt in: _____ Opt out: _____
Participant Initials Participant Initials

VIRTUAL VISTS

By initialing below to "Opt in," you give permission for us to perform virtual visits with you for study visits at the PI's discretion. If you do not agree to allow us to perform virtual visits when access to the Cleveland Clinic is not allowed for research subjects your participation in the study will not be affected. Please initial below if you agree (Opt in) or if you disagree (Opt out).

Check one and initial for the option to have virtual visits at the PI's discretion:

☐ ☐

Opt in: _____ Opt out: _____
Participant Initials Participant Initials

ADDITIONAL EXTENDED FOLLOW-UP VISITS (OPTIONAL)

If the study team determines that we would like to bring you in for additional follow-up testing at 6 and/or 12 months as described on page 6 of this consent, we will let you know verbally after completing the post-testing visits. If you agree and are determined to be brought back in by the study team you will receive up to 4 more visits of testing after completing the 3 month follow-up.

By initialing below to "Opt in," you agree to come in for up to 4 visits of testing at 6 and/or 12 months. If you do not agree to participate in the optional 6 and/or 12 month follow-up your participation in the study will not be affected. Please initial below if you agree (Opt in) or if you disagree (Opt out).

Check one and initial for the option to participate in the 6 and/or 12 month follow-up testing visits at the PI's discretion:

☐ ☐

Opt in: _____ Opt out: _____

QUESTIONS

Whom Do You Call With Questions Or Problems?

If you have any questions, concerns or complaints about the research, or develop a research-related problem, contact Ela B. Plow, PhD, PT, at (216) 445-4589 or (216) 445-6728. If you have questions about your rights as a research subject, contact the Institutional Review Board at (216) 444-2924.

Cleveland Clinic Clinical Research Unit (CRU) study participants may also contact the CRU Research Subject Advocate (RSA) at (216) 636-1077 or (216) 444-2200 and ask the operator to page beeper # 28152 with regard to questions about study participation and research subject protections.

SIGNATURE

Statement of Participant

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 form 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

Statement of Witness

My signature as witness certifies that the subject signed this consent form in my presence as his/her voluntary act and deed.

_____
Printed Name of Witness

_____ _____
Signature of Witness Date

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