Official title:

Cervical and Lumbosacral Transspinal Stimulation to Reconnect the Injured Human Spinal Cord

NCT number: Not assigned yet

Document Date: 5/14/2025

THE CITY UNIVERSITY OF NEW YORK
College of Staten Island
Department of Physical Therapy

CONSENT TO PARTICIPATE IN A RESEARCH STUDY

Title of Research Study: Cervical and Lumbosacral Transspinal Stimulation to Reconnect the Injured Human Spinal Cord

Principal Investigator: Maria Knikou, PT, MBA, PhD
Professor

You are being asked to participate in a research study because you are an adult with a diagnosis of spinal cord injury (SCI), and there are no medical or health reasons that do not allow you to receive stimulation over your back and/or robotic gait training.

This is a clinical study/trial performed at the Klab4Recovery; a research lab directed by Dr. Maria Knikou located at the College of Staten Island campus.

Purpose:
The purpose of this research study is to establish:

1) The neuromodulation effects on spinal and brain excitability of arms and legs following stimulation over the neck and low back at rest (single recordings),
2) The muscle synergies following stimulation over the neck and low back during robotic assisted stepping (single recordings),
3) Recovery of sensation, motor function, walking function, and spasticity following multiple sessions (N=20) of stimulation over the neck and low back while at rest or during robotic gait training (recordings at baseline and after intervention). Robotic gait training means that you will be walking on a moving treadmill with body weight support while the movement of your legs will be assisted by motor-driven leg braces.

Key Information:

- The consent is being sought for research purposes only, and participation is voluntary.
- The purpose of the research is to provide clinical and scientific evidence on the potential benefits of stimulation over the neck and low back when delivered at rest or during robotic gait training in individuals with SCI.
- The expected duration of each prospective subject's participation is either 2 single visits for single recordings or 24 consecutive visits (if you want to participate in the intervention), excluding weekends and holidays.
- The foreseeable risks or discomforts include discomfort by the stimulation over the neck and low back or nerve behind the knee, sensation of pressure on the abdominal area by the upper body harness, and sensation of pressure in the legs by the motor-driven leg braces.

- There might be no direct benefit to you or to others. However, stimulation and gait training have been shown to improve standing and walking performance as well as being beneficial for maintenance of bone and muscle integrity after SCI.
- This research study is NOT a treatment.
- The alternative is not to participate in the research study.

Procedures:

If you volunteer to participate in this research study, we will ask you to do the following: You will come to the Klab4Recovery research lab located at 2800 Victory Blvd, Building 5N, Room 218, College of Staten Island.

If you enroll in the single session study, you will come twice to the lab and you will stay in the lab for 3 hours.

If you enroll in the clinical trial, you will come 24 times to the lab. The first 2 visits in the beginning and at the end you will stay in the lab for 3 hours. On the other days you will stay for 1 hour. You will come at times previously arranged for you based on your schedule.

In this study, we will use a constant current stimulator (DS7A or DS8R, Digitimer Ltd., United Kingdom) to stimulate your neck and back during your daily sessions of stimulation. You may receive stimulation during robotic gait training. We will use the same stimulator to stimulate a nerve in the back of your knee at the beginning and at the end of the study to describe changes in the nervous system. These responses will detect changes in your nervous system after the intervention. If you have present responses following brain stimulation, we will use a transcranial magnetic stimulator to evoke and record these responses from your arm and leg muscles.

INTERVENTION VISITS

PRE-TRAINING TESTING VISITS 1 and 2 (3 hours each):

At the first and last two days you will need to bring or wear shorts that are loose in the legs in order for us to place pads on your legs to record the twitches of your muscles following stimulation.

Initially, we will measure your blood pressure while you are seated and will assess your sensation, movement of your legs and ability to walk via standard clinical tests. This will be repeated also after you complete all training sessions.

Then, the skin on the front and back of your legs and arms will be dry shaved (if needed) and cleaned with alcohol pads. Next, we will place pads (known as surface electrodes) on the front and back parts of your arms and legs. These pads will be secured with non-allergenic sterilized tape. These pads will record 1) the twitches from your arm muscles when the skin at your neck is stimulated, 2) the twitches from your leg muscles when the skin of your back at your waist level and the nerve in the back of your knee are stimulated separately, 3) the twitches of your arm or leg muscles following brain stimulation.

For this, stimulating pads will be placed on the neck and back and in front of your shoulders and waist. These pads will deliver stimulation to the spinal cord, and you will feel twitches in your leg and arm muscles. None of the stimulation is painful, but if you feel discomfort we will decrease the intensity or stop altogether. At that point, you can decide to take a break and continue when you are ready or you can end participation in the study if you wish. The nerves or the skin over your back ,

arms and legs will be stimulated with a single pulse and 20 stimulations will be delivered. This will be repeated no more than 10 times.

The second day, we will place again pads on the skin of your legs, and you will transfer to the treadmill of the robotic device known as Lokomat®. Full body weight support will be provided to you based on your ability to stand. Similarly, the leg braces will assist you to step based on your ability to move your legs. Then, you will start walking with body weight support and your legs movement will be assisted by the motor-driven leg braces. You will walk for a few minutes to get used to the treadmill. When you will be walking on the treadmill, we will deliver low-intensity stimulation to the nerve behind the knee in your right leg every 5 steps. We will also deliver low-intensity stimulation to your back when you will be walking on the treadmill, and at the skin of your lower leg. Stimulations will produce twitches in your leg muscles that you will not be able to stop them.

Stimulation may be uncomfortable and may produce some discomfort but the intensity will be low in amplitude, similar to that utilized during standard clinical electrophysiological tests used for diagnosis. Treadmill speed will be set at a value that you feel most comfortable to step.

SPINAL STIMULATION
VISITS 3 THROUGH 22 (1 hour each):
During these visits, you will receive non-invasive spinal stimulation over your neck and low back for 1 hour while at rest or during robotic assisted stepping. Transspinal tonic stimulation will be delivered either as 1 ms single pulses every 3 seconds or at 30 Hz (charge-balanced, symmetric, biphasic rectangular pulses of a 1-ms width per phase) at bouts of 10 minutes of subthreshold and suprathreshold intensity. Stimulation may be uncomfortable, but the intensity will be lowered, if necessary, based on your comfort level.
When the stimulation is delivered during assisted step training on the robotic device (Lokomat®), the robotic device will provide, as needed, leg guidance and body weight support via an upper body harness. The robotic-assisted treadmill walking will be similar to the procedure described above in the Testing Visits. Each training session will last 1 hour. Treadmill speed, body weight support and leg guidance force by the robotic device will be set when you feel most comfortable to step.

POST-TRAINING TESTING: VISITS 23-24 (3 hours each)
Using similar techniques as described above in the Testing Visits 1-2, we will record your muscle twitches in response to stimulation of your nerves while seated, and the muscles twitches of your legs during walking with the robotic device. We will also repeat the clinical assessment of your leg muscle tone, leg muscle strength, and your walking capacity (if applicable) during the testing visit.

Audio Recording/Video Recording/Photographs:
We will record you via video during clinical assessments of spasticity and during overground walking (if you can) and following stimulation over the spine to document recovery of movement by the intervention. You can still participate in this study if you do not consent to video recording.

Time Commitment:
Your participation in this research study is expected to last for a total of 5 consecutive weeks. You will not have to come during weekends and holidays.

Potential Risks or Discomforts:

There is a small risk of feeling uncomfortable with stimulation delivered either to your low back or to the nerve behind your knee.

- The study team members are trained and experienced in stimulation of nerves found in the legs, and recording responses from your leg muscles upon stimulation. If you feel discomfort, we will decrease the stimulation intensity and will give you breaks.

There is a small risk of falling during transfers between wheelchairs and treadmills; with the risk of falling is the risk of bone fracture.

- The study team members are trained and experienced in the care and rehabilitation of participants with limited mobility, including extensive safety experience in preventing falls. You will never be left unattended during a test or training session.

There is a possible risk that electrical stimulation or treadmill walking may cause an "autonomic response" – this could include symptoms such as nausea, light-headedness, and sweating. It may even cause you to faint. If this happens, we will immediately stop the procedure. The symptoms should resolve within seconds of stopping electrical stimulation.

- The investigators will be monitoring your blood pressure, heart rate, and symptoms during all visits. If there are significant symptoms with changes in vital signs, they will halt the procedure immediately.

There is a possible risk for blood pressure variation with stimulation or orthostatic hypotension because some participants are immobile.

- To counteract this potential risk, we will monitor your blood pressure at every training and testing session.

There is a small risk of headaches from magnetic stimulation.

- This risk is small and has only been reported for participants undergoing repetitive magnetic stimulation – you will only be receiving one magnetic pulse at a time, so the risk is even smaller.
- Before you begin participation in the Study, we will screen you for migraine and seizure risk, such as history of prior brain injury, or taking certain medications that raise the risk of seizure. If your seizure risk is too high, you will not be able to participate in the Study.

The investigator conducting magnetic stimulation, Dr. Maria Knikou, is a neurophysiologist with extensive experience in this type of stimulation.

There is a risk of tinnitus from magnetic stimulation.

- The possibility of mild tinnitus is sometimes reported after magnetic stimulation. This risk will be minimized by taking breaks during the stimulation part of the protocol.
- The magnet makes a clicking noise that can irritate the ears. This will be minimized by using earplugs during magnetic stimulation.

Potential Benefits:

There might be direct benefits to you by participating in this study. By participating in the study, you may have improvements in your bladder control, and spasticity of your leg/abdominal spasms may

decrease. If you receive transspinal stimulation during stepping improvements in posture and walking ability may be possible.

Alternatives to Participation:
The alternative is not to participate. All participants with SCI in this study will get physical exercise by robotic gait training. During study participation, you will be asked to not undergo any *new* physical treatments or other clinical research outside of this study. No routine clinical care or medications that you are scheduled for will be withheld from you. You have the option not to participate in this study.

Participation in other rehabilitation treatments or research studies:
During the duration of the clinical trial study, you will continue your daily routine as usual. You will continue stretching or standing, if that's what your daily routine involves. You will not participate concomitantly in another research clinical trial. Also, you should not receive regular rehab treatment for the duration of the study. Since it is more than 6 months from the time you had the spinal cord injury, participation in this study will not affect your current recovery status. Stimulation of skin, nerves, and brain are used in many patients, but we do not know in advance how the stimulation will affect your recovery.

Payment for Participation:
You will receive $100 for each testing session, and $50 for each training session. The total amount of stipend will not exceed $2,000 if you complete all testing and training sessions. You will receive the stipends from the Research Foundation of CUNY that handles the stipends to subjects for all funded research projects.

Research Related Injury
If you become ill or injured because of the study (devices or procedures), seek medical treatment through your doctor or treatment center of choice. You will not be reimbursed for these expenses. Promptly tell Dr. Knikou about any illness or injury.

New Information:
You will be notified of any new information regarding this study that may affect your willingness to participate in a timely manner.

Confidentiality:
We will make our best efforts to maintain confidentiality of any information that is collected during this research study, and that can identify you. We will disclose this information only with your permission or as required by law.

We will protect your confidentiality by giving you a subject code. We will not use your name or other identifying information. The recordings and the results of your tests will be stored by a subject code on a personal computer at Dr. Maria Knikou's office located on the second floor of building 5-North, room 218 at the College of Staten Island that is password protected. Any paper records, including health information and medical records, will be kept in a locked file cabinet at the Principal Investigator's office. Only researchers involved with this study will have access to this information.

Results of this study may be used for teaching, research, publications, or presentations at scientific meetings. If your individual results are discussed, your identity will be protected and not disclosed.

The only people who know that you are a research subject are members of the research team and, if appropriate, your physicians and nurses. No information about you, or provided by you during the research, will be disclosed to others without your written permission, except if necessary to protect your rights or welfare (for example, if you are injured and need emergency care), or if required by law.

The research team and authorized CUNY staff may have access to research data and records to monitor the research. Research records provided to authorized CUNY and non-CUNY individuals will not contain identifiable information about you. Publications and/or presentations that result from this study will not identify you by name.

The information we collect from you as part of this study will not be used or distributed for future research.

Participants' Rights:

- Your participation in this research study is entirely **voluntary**. If you decide not to participate, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled.

- You can decide to withdraw your consent and stop participating in the research at any time, without any penalty.

Questions, Comments or Concerns:

If you have any questions, comments or concerns about the research, you can talk to one of the following researchers:

- Dr. Maria Knikou at 718-687-2893, Monday through Friday, during or after office hours.

If you have questions about your rights as a research participant, or you have comments or concerns that you would like to discuss with someone other than the researchers, please call the CUNY Research Compliance Administrator at 646-664-8918 or email HRPP@cuny.edu.

Alternately, you can write to:
CUNY Office of the Vice Chancellor for Research
Attn: Research Compliance Administrator
205 East 42nd Street
New York, NY 10017

Participant Signature for Audio/Video Recording:

If you agree to audio recording/video recording, please indicate this below.

_____ I agree to audio recording/video recording.

_____ I do **NOT** agree to audio recording/ video recording.

Signature of Participant:

If you agree to participate in this research study, please sign and date below. You will be given a copy of this consent form to keep.

_____

Printed Name of Participant

_____ _____

Signature of Participant Date

Signature of Individual Obtaining Consent:

_____

Printed Name of Individual Obtaining Consent

_____ _____

Signature of Individual Obtaining Consent Date