TITLE: Short-term Genital Nerve Stimulation in Individuals Living with Spinal Cord Injury

Introduction

You are being asked to participate in this research study of a therapy for reducing bowel accidents after spinal cord injury. Before you can decide whether to volunteer for this study, you must be informed of the purpose of the research study, how this study may help you, any risks to you, and what is expected of you. This process is called informed consent.

You do not have to participate in this study. You may stop your participation in this study at any time without changing your current or future relations with MetroHealth Medical Center or its doctors.

If you decide to participate in this study, you will be told about any new information learned during the study that might cause you to change your mind about staying in the study. If you withdraw, we will still provide you with information regarding possible impacts to your health status or future health care decisions.

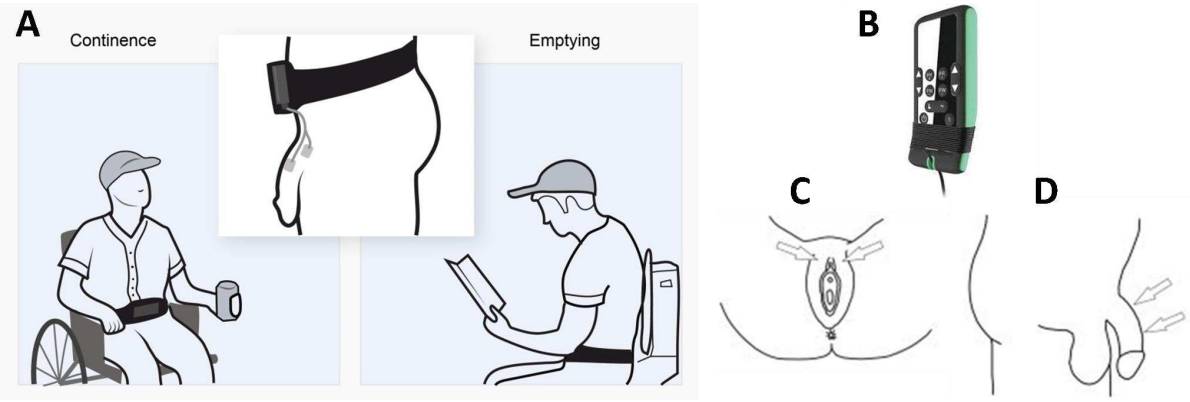
Individuals with spinal cord injury are being asked to be involved in research about a non-invasive electrical stimulation method to reduce bowel problems.

Why is this study being done?

The purpose of this study is to test whether electrical stimulation of the skin in the pelvic area (near the genitals) can reduce the reflexes that cause bowel accidents.

A total of 52 people will complete this study. To reach that number, up to 200 people will be asked to participate in this study.

The picture on the next page shows an overview of how this study will use electrical stimulation in the pelvic area (the genital nerve) to try to reduce bowel accidents.



Genital nerve stimulation. (A) We are testing a non-invasive surface stimulation approach to reducing bowel accidents with minimal inconvenience to the wearer. (B) For this study, a commercially available FDA-approved device will be used without making any changes. (C) Women will apply electrodes (sticky pads for delivering electrical stimulation) on the skin surrounding the pubic area to target the genital nerve. (D) Men will place electrodes on the top surface of the penis.

What is involved in the study?

Frequency of Visits –

In this study, you will be asked to come to the MetroHealth Rehabilitation Institute 1-2 times over the next 1 month. The first visit will last between 2 ½ hours and the second visit will last 4 hours. You can choose to do both visits on the same day.

Screening – The Screening visit will be done to find out if you are eligible for the study. You will answer some questions about yourself, your spinal cord injury, and your medical history. The study doctor will then perform the following 3 clinical tests:

1. Spinal cord exam – This will test your arm and leg muscles and your ability to feel light touch and pinprick. This gives us information about your spinal cord injury.
2. Bowel and genital exam – This will test for whether you have reflexes in the genital area and whether you can feel or move your anal sphincter. This gives us more information about your spinal cord injury and how it alters your bowel control.
3. Genital nerve stimulation – This will determine whether your genital nerve responds to electrical stimulation.

The Screening visit should not take longer than 2 ½ hours. If you are eligible and choose to continue with the study, your Manometry visit will be done that same day or be scheduled within 1-2 weeks.

Manometry – The Manometry visit involves having a clinical test during the nerve stimulation. The clinical test is called Anorectal Manometry (also called ARM). This test will tell us a lot about how your

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bowels are working or not working on the inside (in your rectum). During this test you will lay on your side on an exam table. A small tube will be inserted into your rectum. This tube is called a catheter and it can measure the pressures in your rectum. Trained study staff will give you instructions about when to relax, when to try to squeeze, and when to try to push. Measurements will be recorded by the catheter during all these activities. Your blood pressure will be monitored during this ARM test. You will also receive stimulation of the genital nerve at various times during this test so that we can measure the response in your rectum.

The entire Manometry visit should last no longer than 4 hours.

What happens if I discontinue or withdraw from the study?
You may withdraw from the study before its completion.

Your participation in this study may be stopped if the Investigator determines that you are not performing the study requirements or if you are experiencing side effects that put you at risk.

What are the risks of this study?
We cannot predict all risks or potential side effects. There may be unknown and/or delayed risks that may occur months or years after treatment. The risks we know of are:

- *Uncomfortable Sensation (common)* – Participants that have sensation in the genital area, may feel the electrical stimulation. This sensation may feel like a slight buzzing, tickling, tingling, or could be painful. During the screening test for genital nerve stimulation, lower levels of stimulation will be used first to see if you feel anything, then higher levels of stimulation will be tested. If you cannot tolerate sensations you experience with this testing, you will not continue with the study.
- *Skin Irritation (common)* – There is a risk of skin irritation from the sticky electrodes applied to the skin for stimulation or from the gel adhesive used to secure them. This is a common risk. This will be minimized by using electrodes that are not known to be allergenic and by using gel that is commonly used for other types of electrical stimulation. Additionally, if open wounds in the genital region are discovered during screening, you will not be invited to participate until any such wounds are healed.
- *Tissue burn (rare)* – There is a very small risk that the skin electrodes for stimulation could cause a tissue burn. This risk is very low because of the level of electrical stimulation and safety testing of the device as well as the low levels of stimulation being used in this study.
- *Autonomic Dysreflexia (rare)* – There is a very low risk that genital nerve or sham stimulation may trigger autonomic dysreflexia (AD) in individuals with SCI (risk< 1%). There is the possibility that the ARM procedure may trigger AD in some participants. This condition may be characterized by excessively high blood pressure, headache, sweating, flushing, and goose bumps. AD is easily recognized and treated immediately. In the unlikely event that you develop AD during the ARM test, you will be promptly treated. Most times treatment consists of the

removal of the triggering element like draining of a full bladder, relieving pressure over an area under constant pressure, or removal of painful stimuli like stimulation.

- *Emotional and Psychological Risks (rare)* – Some of the questions we ask may be upsetting, or you may feel uncomfortable answering them. If you do not wish to answer a question, you may skip it and go to the next question.
- *Breach of Confidentiality (rare)* – As part of study participation, information about you will be collected and then kept on paper and in computer files. There is a risk that this information could be stolen. Great care will be taken to safeguard all forms of such information, for example using locks for files with paperwork, using passwords for computer files, and by following HIPAA regulations.
- *Unknown Risks (unknown)* – There may be unknown or unforeseen risks associated with study participation.

Reproductive Health/Sexual Activity – The effects on the developing child of using genital nerve stimulation during pregnancy and the risk of birth defects are unknown. Therefore, women who are pregnant may not participate in this study. Women should not become pregnant while participating in this study. If sexually active, women should use an effective method of birth control while performing the study treatment. Barrier contraceptives (such as a condom or diaphragm), Depo-Provera, Norplant, oral contraceptive pills and complete abstinence are examples of effective methods. If you become pregnant before the end of the study, it is important that you notify your study nurse/doctor immediately. You may be required to stop the study treatment at which time other treatment options will be discussed with you.

Your condition may not improve or may worsen while you are taking part in this study.

Are there benefits to taking part in the study?

It is possible that electrical stimulation to the genital nerve will improve your bowel function, but this cannot be guaranteed nor any other benefit. The knowledge gained from this trial will help us better understand the risk-benefit profile of short-term stimulation on bowel activity in people living with spinal cord injury.

What other options are there?

This is a research study. You may decide not to participate.

If you do not wish to participate in this study, the following alternative treatments are available:

- Usual bowel care strategies suggested by your doctor such as diet, fluids, laxatives, suppositories, digital stimulation, antegrade enema, or colostomy.

What are the costs?

There is no cost to you or your insurance company for participation in this study

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What happens if I am injured while participating in this study?
All research involves a chance that something bad might happen to you. This may include the risk of personal injury. In spite of all safety measures, you might develop a reaction or injury from being in this study. If such problems occur during the course of the study, you must contact your study doctor, Dr. James Wilson at (216) 778-4414. Necessary medical care will be provided to you by The MetroHealth System. The MetroHealth System has not set aside funds to pay you for any such reactions or injuries or for the related medical care. This medical care is not free. You and/or your insurance company will be responsible for the costs. However, you can still try to collect compensation for injury related to malpractice, fault, or blame on the part of those involved in the research, including the hospital.

Will I be paid for participating in this study?
You will receive up to $130 for your participation in this research study and it will be divided into the following amounts after each visit:

Screening visit – $50.
Manometry visit – $80.

It will be paid using a ClinCard which is a re-loadable debit card after each visit. If you withdraw from the study, you will be paid for the portions of the study that you have completed.

The Accounting Department at MetroHealth will be given your name, address, and Social Security Number in order to process payment for your study participation. Study payments are considered taxable income and reportable to the IRS. A Form 1099 will be sent to you if your total payments are $600 or more in a calendar year.

If you live in the region (Cuyahoga, Lorain, Medina, Lake, or Geauga counties) and need assistance with transportation to get to and from the research site for a visit, the study team will make these arrangements at no cost to you. If you live outside of the region, the study team will reimburse your transportation expenses up to a maximum of $556 per visit.

If you live a distance away from the research site for which it would be easier for you to spend the night closer for a research visit, accessible lodging is available at the Zubizarreta House. This house is right next door to the MetroHealth Rehabilitation Institute and is designed for people with spinal cord injuries. The overnight stay will be provided at no cost to you, but if you need a caregiver to stay with you that is your responsibility.

HIPAA:
As part of this study, we are collecting PHI such as: date of birth, date of spinal injury, name, medical record number (social security number), address, email, and phone number. This information is being collected for research purposes and to pay for your participation. All information will be kept private on a password protected secure network computer drive and/or in a locked office or a locked file in a

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locked office. Only research staff will have access to these files. The following individuals, departments, or agencies will have access to your PHI, i.e., IRB (Institutional Review Board), FDA (Food & Drug Administration), or DoD (Department of Defense) for the purpose of data analysis and research study protocol requirements. The Investigator will have access to your PHI collected until all study requirements are complete and data analysis is complete. At that time, the PHI will be destroyed. The study file will be kept for 4 years after study completion, at which time it too will be destroyed. You will have access to the PHI that is related to this study. You have the right to withdraw your permission/authorization for us to access your PHI at any time except to the extent the PHI already collected by the investigators before your withdrawal has already been acted upon based on your signed Authorization. No new PHI about you will be collected for study purposes unless required by law.

What about Confidentiality?

We will make every effort to keep your research records private, but confidentiality cannot be assured. The MetroHealth System has no control over the use of this information once it is released. The Department of Defense (DoD) is funding this study. The information about you that is collected in this study will be shared with the DoD as part of its human subjects protection oversight activities and may be combined with information gathered from public sources or other research studies. This information may be used for purposes unrelated to this research and could potentially be used to identify you.

Records that identify you and this consent form may be looked at by a regulatory agency such as:

The Food and Drug Administration (FDA)
Department of Health and Human Services agencies
MetroHealth Institutional Review Board
National Committee for Quality Assurance
Department of Defense (DoD)

If the results of the study are published or presented in public, your name will not be used. At the end of the study, all participants' de-identified data will be shared through the Interuniversity Consortium for Political and Social Research. No PHI will be included.

What are my rights as a study participant?

Taking part in this study is voluntary. You have the right to choose not to take part in this study. If you do not take part in the study, your doctor will still take care of you. You will not lose any benefits or medical care to which you are entitled. If you withdraw from the study, with your written permission, clinical data will continue to be collected from your medical records.

A Medical Monitor (an expert in anorectal manometry and gastrointestinal medicine) will be reviewing the data from this research throughout the study to ensure participant safety.

If you chose to take part, you have the right to stop at any time. You will be told of any new findings from this or other studies that may affect your health, welfare, or willingness to stay in this study.

If you are an employee or student, whether or not you take part in this study will not affect your job, current or future medical care, or studies.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Website will not include information that can identify you. At most, the Website will include a summary of the results. You can search this Web site at any time.

Does MetroHealth or any member of the research team have a financial conflict of interest in this study?

This study is being sponsored by a grant from the Department of Defense (DoD). Portions of Dr. Hoey's, Dr. Anderson's, and the research team's salaries are being paid by this grant.

Whom do I call if I have questions or problems?

If you have questions about any part of the study now or in the future, or if you wish to communicate concerns or a complaint you should contact Dr. Robert Hoey, who may be reached at (216) 957-3665. If you experience any side effects or injuries while participating in this study, please contact Dr. James Wilson, who may be reached at (216) 778-4414. If you have any questions about your rights as a research participant, or if you wish to express any concerns or complaints, please contact the MetroHealth Medical Center's Institutional Review Board (which is a group of people who review the research to protect your rights) at (216) 778-2021.

Participant Acknowledgement:

The procedures, purposes, known discomforts and risks, possible benefits to me and to others, and the availability of alternative procedures regarding this research study have been explained to me. I have read this consent form, or it has been read to me, and I have been given the opportunity to ask questions or request clarifications for anything I do not understand. I voluntarily agree to participate in this study. I have been given a copy of this consent form.

_____	_____	_____
Participant Signature	Date	Time
_____	_____	_____
Signature of Person Obtaining Informed Consent	Date	Time

If the participant is unable to sign due to their SCI, ask:
Do you agree to participate? (Circle One): Yes No

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Participant Name Date