Spinal Cord Stimulation to Restore Cough
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METROHEALTH MEDICAL CENTER

Human Investigation Consent Form

SPINAL CORD STIMULATION TO RESTORE COUGH

Introduction

You are being asked to participate in a research study entitled "Spinal Cord Stimulation to Restore Cough." 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 course of 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 and impaired ability to cough are being asked to be involved in this research study to investigate the efficacy of a device to produce cough.

Why is this study being done?

The purpose of this study is to attempt to provide an artificial cough by stimulating your expiratory muscles (muscles responsible for coughing). These include the intercostal muscles (muscles in between the ribs) of the lower rib cage and the abdominal muscles. We plan to place small electrodes (small metal discs) over the surface of the spinal cord on the lower back to stimulate the expiratory muscles and restore your cough. If successful, this technique should provide you with a means of removing airway secretions and help prevent respiratory tract infections. We plan to study 18 adults with different levels of spinal cord injury. No pregnant women will be studied. Active participation in this study should take approximately 12 months. However, as long as the device remains implanted, its integrity and function may be assessed periodically thereafter.

What is involved in the study?

Screening:

After an evaluation of your medical history and brief physical examination, we will perform some initial testing. Routine breathing tests will be done to measure the amount and speed of air movement which you can achieve voluntarily. We will also measure the strength of your

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respiratory muscles by having you make maximal efforts during inhalation and exhalation while your airway is blocked for brief periods (3-4 sec). It will be necessary for you to breathe through a mouthpiece and wear nose clips for us to obtain accurate measurements.

Within two weeks before surgery, you will have routine tests performed. You may need to be admitted to the Clinical Research Unit (CRU), a unit here at MHMC to complete these procedures. These include an electrocardiogram (ECG), which measures the electrical activity of your heart, a chest X-ray, an x-ray of the thoracic and lumbar spine, an MRI, and blood and urine samples.

Surgical:

The surgeon will make a small incision (about 2 inches) over the spinal cord and place electrodes. A receiver (about the size of a half dollar) will be implanted just under the skin over the chest or abdominal wall and connected to the electrodes. Since you have a spinal cord injury, you should have no pain in this area. However, some patients may have asymmetric injures resulting in some residual sensation below the level of injury. For this reason, general anesthesia will be provided during this procedure. Stimulation will be applied in the operating room, and measurements of airway pressure and volume and airflow changes will be made.

After surgery, you will stay at the CRU for approximately 4 - 7 days. On the last day of your stay or at a subsequent visit, stimulation will be applied for brief periods at low settings while monitoring your heart rate and rhythm, blood pressure and oxygen saturation. During stimulation, we will measure airway pressure and volume and airflow changes at your mouth or tracheal opening (if you have a tracheostomy). Following your discharge, several visits will take place at the CRU to collect data. In addition to these scheduled visits (outlined below), more frequent assessments may be necessary. Although unlikely, it is possible that a surgical revision may be necessary to obtain optimal results.

Initial Response:

You will be asked to return to the CRU approximately three weeks following your surgery. At this visit, stimulation will be applied for brief periods while measuring airway pressure and volume and airflow changes at your mouth or tracheal opening. During stimulation, we will monitor your heart rate and rhythm, blood pressure and oxygen saturation. In order to measure degree of muscle activity, an electromyogram (EMG) will be performed; we
will place small needles into the abdominal muscles to record their activity during stimulation. Due to your spinal cord injury, you will not feel this. Also, we will measure pressure changes

occurring in the chest and abdomen during stimulation. In order to do so, 2 small latex balloons (1 inch x 1/8 inch) connected to 2 small diameter catheters (0.075 inch) will be passed through your nose or mouth and positioned in your esophagus and stomach. This procedure takes about an hour, and although associated with minor discomfort, it is not painful.

Conditioning:

It is anticipated that the expiratory muscles have atrophied (decreased in size and strength) due to your spinal cord injury. In order to strengthen these muscles, you and your caregiver will be trained on how to stimulate them for short periods at a time, approximately 5 minutes, 3 times a day until optimal strength has been achieved.

You will be asked to return to the CRU on three occasions during this phase of the study to obtain Expiratory Muscle Assessments. These assessments include measuring changes of pressure occurring in your chest and abdomen as well as changes in airway pressure and volume and airflow at your mouth or tracheal opening. Throughout stimulation, heart rate, blood pressure and oxygen saturation will be monitored.

The conditioning phase will end when airway pressure does not increase further and remains stable over a 2-3-week period. It is expected that this phase will last 6-8 weeks.

Post-Conditioning:

When the conditioning phase has ended, you will move to the post-conditioning phase. During this phase, a caregiver will apply stimulation as needed for cough production. However, in order to maintain expiratory muscle strength, stimulation should be applied at least twice a day.

You will be asked to return to the CRU five times during this period to obtain Expiratory Muscle Assessments. A chest x-ray will be obtained during two of these visits (weeks 24 & 52).

What happens if I discontinue or withdraw from the study?

If you withdraw from the study before its completion, you will be asked to return the external components of the investigational device, and for your safety, to come in for a final study visit in order to assess that the implanted components are not damaged. If you chose to withdraw from the study and to end all contact with the study team, we will not be available should you have any complaints regarding the implanted components. If you agree to stay in contact with the study team, we will be available to address any future concerns with the implanted components of the investigational device.

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Your participation in this project may be terminated if you are not compliant with the research performed or if you are not benefiting from this research.

What are the risks of this study?

Pre-surgical:

When blood is drawn from a vein, there will be some temporary discomfort and the minimal risk of local bruising, infection or blockage of the vein. Rarely, fainting occurs. Suitable precautions will be taken to minimize these risks.

Because the MRI machine acts like a large magnet, it could move iron-containing objects in the MRI room during your examination that could possibly harm you. Precautions have been taken to minimize such an event from happening. Loose metal objects, like pocketknives or key chains, are not allowed in the MRI room. If you have a piece of metal in your body, such as a fragment in your eye, aneurysms clips, ear implants, spinal nerve stimulators, or a pacemaker, you will not be allowed into the MRI room and cannot have a MRI.

Having a MRI may mean some added discomfort for you. In particular, you may be bothered by feelings of claustrophobia (being closed in a small space) and by the loud banging noise during the test. Temporary hearing loss has been reported from this loud noise. This is why you will be asked to wear earplugs. At times during the test, you may be asked to not swallow for a while, which can be uncomfortable.

Surgical:

Any surgical procedure carries a risk of infection and bleeding. Every effort to minimize this risk will be taken before, during, and after the procedure. Although unlikely, there is also a chance that your body will reject the implanted materials, which will require their removal. It is possible to develop a pocket of fluid (seroma) around the receiver, and, if infected, the receiver will have to be removed. There is also the possibility that the electrodes will become infected and need to be removed. There is a rare possibility that the stitches holding the electrode and receiver in place will break causing these to shift in position. There is a rare possibility that the receiver will erode through the skin increasing the risk of infection. Your skin should be inspected daily for redness and/or irritation. Immediately report any abnormalities to the study team.

Spinal Cord Stimulation:

The possible side effects of spinal cord stimulation are elevated blood pressure and pulse, which should subside quickly with discontinuation of stimulation. There is a remote possibility that bowel or bladder discharge will occur due to contraction of the abdominal

muscles during stimulation. The placement of the esophageal and stomach catheters may cause some minor discomfort of the nasal passages and throat. Topical anesthesia will be used to minimize this discomfort.

There is the rare possibility of bleeding and/or infection associated with placement of abdominal recording electrodes. Very small needles will be used to place the electrodes under sterile conditions minimizing the risk of this occurrence. There is the rare possibility of spasm of the expiratory muscles during stimulation, which may restrict your breathing. Spasm can be terminated by removing the transmitter coil from the skin. Use of sedatives or other drugs which interfere with muscular activity could reduce the effectiveness of this technique. We will attempt to avoid these medications and reduce the dose if you are currently taking them. The implanted components may obscure the view of anatomical structures during X-rays or scans. If you should need to have an MRI, the study team should assure proper functioning of each of the spinal cord disc electrodes prior to scanning, and the external components (antenna and control box) should not be taken into the MRI room. There is the rare possibility of scarring around the electrodes or other device malfunction which could reduce the effectiveness of this technique.

There may be unknown, delayed risks which may occur months or years after treatment. If this procedure is unsuccessful, you may either leave the implanted materials alone or have them removed at no cost to you, within 2 years of the procedure.

You will be told of any new information learned during the course of the study that might cause you to change your mind about staying in the study.

Are there benefits to taking part in the study?

This study may benefit you if this technique is successful in restoring your cough mechanism. This would allow you to clear airway secretions more easily. Lung infections are a significant cause of hospitalizations and death in spinal cord injured patients. Restoration of cough may allow you to clear secretions more normally, hopefully improve your level of comfort and prevent respiratory complications. Benefit however is not guaranteed.

What other options are there?

There are currently a number of ways to clear your secretions: suctioning, assisted cough, gravity, pneumo-belt, insufflator-exsufflator, surface stimulation, and magnetic stimulation. Unfortunately, all of these have limitations that reduce their effectiveness. We will explain each technique to you in detail if you are not familiar with them.

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What are the costs?

The investigational device and all related medical services, including the rehabilitation and follow-up testing that are routine parts of this study, will be provided at no cost to you while you are participating in this study. The cost of all services that result from your participation in this study including costs of treatment due to medical complications that might arise as a result of participating in the study will be billed, wherever allowable, to your health plan (Medicare, Medicaid, Bureau of Worker's Compensation, etc) and/or your insurance company, if you have one. If you do not have insurance, or your insurance company will not cover the costs associated with research studies, the cost will be covered by the funding source of this study. Some health plans and insurance companies may not cover costs associated with studies. If this is the case, the costs will be covered by the funding source of this study. Any deductible, co-insurance, or co-pays for those services, and any non-covered or out-of-network services will be covered by the funding source of this study, as permitted by law. If you receive a bill related to this study, please contact the study coordinator. The study team will continue to be available for maintaining the implanted system in good working order as long as research funding is available.

All other medical services that you would have received if you were not in this study will be billed to you or your health plan/insurance company. You will be responsible for paying any deductible, co-insurance, or co-pays, for those services, and for any non-covered or out-of-network services.

What happens if I am injured while participating in this study?

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 the study coordinator or the study doctor immediately. You and/or your health plan or insurance company will be billed for expenses that result from the treatment of such injury.

Will I be paid for participating in this study?

You will be reimbursed for your transportation and parking expenses. You will be reimbursed at the IRS standard mileage rate for transportation in your private vehicle. Reimbursement will be paid in the form of a check issued to you. Parking in MHMC visitors parking lots/garages will be covered by validating your parking pass for each study visit. If you do not have a private vehicle, transportation will be provided to you at the discretion of the study team. If you live in a health care facility which provides transportation, that service may

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be used. If transportation to the hospital for research visits would result in any direct cost to you, the cost will be covered by the funding source of this study.

You will receive no special compensation for participating in the regularly scheduled aspects of this research project required to install, maintain or monitor the performance of the device. You will only be reimbursed for legitimate travel expenses up to a maximum of $2,000.

When you participate in follow-up testing, experiments, teaching sessions or demonstrations other than what is required to install, maintain or monitor the performance of the system, you will receive either $50.00 per session or reimbursement for legitimate travel expenses. You can expect this to be less than $1,000 per year.

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.

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, the MetroHealth Institutional Review Board, the Data Safety Monitoring Board and the National Committee for Quality Assurance.

If the results of the study are published or presented in public, your name will not be used.

What will happen to video or audio records upon completion of the study?

We may publish or present photographs, audio recordings, and videos of you, including your face. No other personal information about you will be included in the presentation.

All videotapes, audio tapes, and photographs will be maintained for future use in advertising material, presentations at professional meetings or publications. Prior to obtaining this material, you will need to sign a consent form which will detail to how the material will be used.

What are my rights as a study participant?

You are under no obligation to participate in this study. 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

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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. If you are an employee or student, participation or non-participation in this study will not affect current or future medical care at MetroHealth Medical Center (MHMC) and/or position of employment or course of studies with MHMC or Case Western Reserve University.

A Data Safety and Monitoring Board (an independent group of experts) will be reviewing the data from this research throughout the study.

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.

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

The principal investigator of this study is a Founder of and has a significant financial interest in Synapse BioMedical, Inc, a manufacturer of diaphragm pacing systems. Dr. DiMarco has the potential to realize a financial gain should this entity market the technology related to this research study.

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. Anthony F. DiMarco, who may be reached at (216) 778-3906, Monday through Friday. If you experience any side effects or injuries while participating in this study, please contact Dr. DiMarco at (216) 778-3906 during the week. If these occur at night or on the weekend, Dr. DiMarco can be reached at (440) 248-3125. 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) 778-2077.

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Patient/Subject 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 understand it. I agree to participate in this study. I have been given a copy of this consent form."

_____ _____

Patient/Subject Signature Date

OR

_____ _____

Legal Guardian/Representative Signature Date

_____

Relationship to subject

AND

_____ _____

Signature of Person Obtaining Consent Date

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