2023

Consent Document

Repeated Transcranial Magnetic Stimulation and Rehabilitation for Individuals with Complex Regional Pain Syndrome Type 1

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RESEARCH SUBJECT CONSENT & AUTHORIZATION FORM

Title: Repeated Transcranial Magnetic Stimulation and Rehabilitation for Individuals with Complex Regional Pain Syndrome Type 1.

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RESEARCH CONSENT SUMMARY

You are being asked for your consent to take part in a research study. This document provides a concise summary of this research. It describes the key information that we believe most people need to decide whether to take part in this research. Later sections of this document will provide all relevant details.

What should you know about this research?

- Someone will explain this research to you.
- This form sums up that explanation.
- Taking part in this research is voluntary. Whether you take part is up to you.
- If you don't take part, it won't be held against you.
- You can take part now and later drop out, and it won't be held against you
- If you don't understand, ask questions.
- Ask all the questions you want before you decide.

How long will you be in this research?

We expect that your taking part in the first part of this research project will last 4 weeks. During this time, you will be asked to attend 10 treatment sessions at The Institute of Human Performance (505 Irving Ave, Syracuse NY). Each session will last between 1 and 2 hours. After the 4-week treatment period, you will receive a short survey via e-mail at 4-weeks, 3 months, 6 months, and 1 year after your last session. These surveys will take 15-20 minutes to complete. Participants in the project must be 18 years old or older.

Why is this research being done?

The purpose of this research is to see if patients with Complex Regional Pain Syndrome (CRPS) have reduced pain and improved function with repeated Transcranial Magnetic Stimulation (rTMS) combined with rehabilitation.

What happens to you if you agree to take part in this research?

If you decide to take part in this research study, the general procedures include treatment with magnetic stimulation and rehabilitation treatments performed by a physical therapist. Participants will be screened for eligibility using a questionnaire, be asked to fill out surveys about the disorder and how it impacts their lives, and undergo the treatment as described below.

Magnetic Stimulation: rTMS stimulates the brain using a magnetic field that is produced by an FDA-approved device that is being used off-label. Participants will be seated in a chair wearing a swimming-style cap. Sticky electrodes will be placed on the participant's hand to measure muscle activation. The stimulation device will rest against the participant's head and a magnet pulse will be delivered. The researcher will make marks on the swim cap and stimulate in different areas to determine where to apply the treatment stimulation. Several single-pulse stimulations will be delivered to locate the optimal stimulation location and to determine the correct stimulation intensity. Once localization is completed repeated magnetic stimulations will be administered for approximately 20 minutes. The goal of this treatment is to calm the nerves in the brain resulting in less pain and discomfort. Participants will either get real rTMS or sham rTMS. Sham rTMS will include the same process as described above but the intensity of the magnetic field will be below therapeutic levels.

Rehabilitation: Subjects in both groups will receive rehabilitation treatments from a physical therapist. This will include education, exercises, and other activities that have been shown to help people with CRPS. This will include in-person sessions and activities for you to do at home.

Sessions: The first week you will include 4 rTMS (real or sham) treatments and 2 rehabilitation sessions (4 in-person sessions). For weeks 2-4 participants will attend sessions 2 times a week and receive rTMS or sham rTMS followed by a rehabilitation session. Sessions will last approximately 1 hour and 30 minutes.

Could being in this research hurt you?

The most important risks or discomforts that you may expect from taking part in this research include local discomfort, headaches, and worsening of your CRPS symptoms. In rare cases, individuals receiving rTMS may have seizures or a seizure-like response. The protocol in this study is designed to reduce the risk of seizures, but the risk is still present. Seizures related to rTMS have not been found to have any lasting negative effects. If a seizure does occur during the study, participants are responsible for all associated medical care. Finally, there is a risk of COVID-19 exposure while visiting the laboratory where the study is being conducted. We feel this risk is small as the following precautions to limit possible exposure or transmission of covid-19 will be followed; everyone is screened before entering the facility and required to wear a mask at all times.

Will being in this research benefit you?

The most important benefits that you may expect from taking part in this research include reduced pain, greater function, and improved quality of life.

Possible benefits to others include a better understanding about the effectiveness of rTMS and rehabilitation for the treatment of CRPS.

What other choices do you have besides taking part in this research?

Instead of being in this research, your choices may include various treatments provided by healthcare providers including oral, topical, or injected medication, exercise, de-sensitization activities, meditation, cognitive behavioral therapy, spinal cord stimulators, and various other treatments.

What else should you know about this research?

Other information that may be important for you to consider so you can decide whether to take part in this research is the need for transportation, the cost of parking, and the cost of a phone application. The visits will include interviews, physical exam, and exercise.

DETAILED RESEARCH CONSENT

You are being invited to take part in a research study. A person who takes part in a research study is called a research subject, or research participant.

Why is this research being done?

Complex Regional Pain Syndrome (CRPS) can cause long lasting pain and disability. There are several treatment options for CRPS, but they are not always effective. Recent studies have found that repeated Transcranial Magnetic Stimulation (rTMS) can significantly reduce pain in patients with CRPS who have failed to respond to other treatments. Specific rehabilitation techniques have also been found to be helpful for some patients with CRPS. No studies have investigated the effectiveness of combining rTMS and rehabilitation for the treatment of CRPS. This study aims to determine if rTMS combined with rehabilitation reduces pain and improves the function of individuals with CRPS.

About 20 subjects will take part in this research.

What happens to you if you agree to take part in this research?

You will be put into a study group by chance (like a coin toss/ like drawing straws). You have a 1 out of 2 chance of being placed in each group. You cannot choose your study group. You and the physical therapist providing your rehabilitation will not know what group you have been placed in.

Group 1 will receive rTMS and rehabilitation provided by a physical therapist.

Group 2 will receive sham (fake) rTMS and real rehabilitation provided by a physical therapist.

Treatments:

Repeated Transcranial Magnetic Stimulation (rTMS) will be delivered by an FDA approved device, Rapid^2, Magstim Inc, Eden Prairie, MN, FDA 510(K)# K162935. This device has been approved for treating depression and its use for Complex Regional Pain Syndrome (CRPS) is experimental. Electromyography (EMG) monitors muscle activity and will be used to assist with rTMS targeting and intensity settings, Motion Lab System Inc, Baton Rouge, LA. EMG will be collected using sticky electrodes on the participants hand and it will read the electrical activity of the muscle. Subjects in this study will receive 10 treatments with rTMS or sham rTMS. rTMS will deliver magnetic stimulation to the brain and sham rTMS will use the same device but deliver minimal to no magnetic stimulation. Treatment with rTMS for CRPS is not currently available outside of this study. Further studies may occur with this device and subjects who do or do not participate in this study may be eligible to participate in future studies. The following treatment procedures will be performed.

- Subjects will be seated comfortably with their back supported.
- A lycra cap (similar to a swimming cap) will be placed on the subject's head to assist with targeting and electromyography electrodes will be placed on the subject's thumb and wrist.
- The researcher will then begin to deliver single magnetic pulses at 10 Hz with the Rapid^2 rTMS device at various locations on the subject's head opposite the involved side. EMG readings will be monitored to find the location that causes the most EMG activity in the abductor pollicis brevis (thumb muscle). When the optimal location is located a mark will be placed on the lycra cap to note the stimulation location. The stimulation intensity will then be adjusted to find the motor threshold (lowest stimulation that will produce the desired muscle contraction). During this time the subject will feel twitching in some muscles and may feel some local discomfort.
- Once the stimulation location is identified and the motor threshold intensity is found treatment will begin. To increase safety the stimulation intensity will be set at 20% less than the motor threshold intensity from the step above. Treatment pulses will be delivered at 10Hz for 10 seconds, with a 30-second rest for 20 repetitions. This will result in a total of 2,000 pulses of magnetic stimulation.
- During the treatment subjects will be monitored by the research personnel for increasing reactivity to the stimulation. Elevated thumb EMG readings, excessive or increasing contraction of other muscles (assessed visually), or subjective symptoms that are not tolerable will result in the researcher reducing the stimulation intensity.

Sham Repeated Transcranial Magnetic Stimulation (rTMS) will be delivered by an FDA approved device, Rapid^2, Magstim Inc, Eden Prairie, MN, FDA 510(K)# K162935. This device has been approved for treating depression and is not approved for treating pain or Complex Regional Pain Syndrome (CRPS). The Rapid^2 magnetic stimulation device is investigational for

the treatment of CRPS, which means that it is not approved by the Food and Drug Administration (FDA) for the treatment of CRPS.

Electromyography will be used to target the stimulation and monitor response, Motion Lab System Inc, Baton Rouge, LA. Subjects in this study will receive 10 treatments with rTMS or sham rTMS. The following treatment procedures will be performed.

- Subjects will be seated comfortably with their feet on the ground and back supported.
- A lycra cap (similar to a swimming cap) will be placed on the subject's head to assist with targeting and electromyography electrodes will be placed on the subject's thumb and wrist.
- The researcher will then begin to deliver single magnetic pulses at 10 Hz with the Rapid^2 rTMS device at various locations on the subject's head opposite the involved side. EMG readings will be monitored to find the location that causes the most EMG activity in the abductor pollicis brevis (thumb muscle). When the optimal location is located a mark will be placed on the lycra cap to note the stimulation location. The stimulation intensity will then be adjusted to find the motor threshold (lowest stimulation that will produce the desired muscle contraction). During this time the subject will feel twitching in some muscles and may feel some local discomfort.
- Once the stimulation location is identified and the motor threshold intensity is found treatment will begin. Treatment delivered to this group will be given at a subclinical intensity over a location that is not likely to benefit subjects with CRPS. Subjects may still feel local sensations and side-effects are still possible. Treatment pulses will be delivered at 10Hz for 10 seconds, with a 30-second rest for 20 repetitions. This will result in a total of 2,000 sham pulses of magnetic stimulation.
- During the treatment subjects will be monitored by the research personnel for increasing reactivity to the stimulation. Excessive or increasing contraction of muscles (assessed visually), or subjective symptoms that are not tolerable will result in the researcher reducing the stimulation intensity.

Rehabilitation Delivered by a Physical Therapist

Subjects in both groups will receive the same physical therapy.

- The first physical therapy session will start with a basic exam. This will include an interview about the condition, a discussion of the subject's goals, and a short physical exam assessing things like motion, pressure tolerance, and strength. This will be adjusted based on the subject's condition and tolerance. Subsequent visits will include a re-assessment of the physical exam (as needed). The following interventions will be included in the rehabilitation.

  Interventions will be performed in the lab during sessions and at home.

  - Shared goal setting based on the subject's functional needs

- Education about pain and the condition

- Left-right discrimination training. A phone application will be used for this treatment (Recognize, NOI Group). The application will show pictures of either arms or hands, or feet and legs (based on the involved area). Subjects will attempt to identify if the picture is a left or right extremity. If a subject does not have an electronic device to run the Recognize app, flash card pictures will be provided for this training.

- Graded imagery. Subjects will be asked to perform visualization exercises of extremity motion and function.

- Mirror therapy. Subjects will be asked to perform exercises while looking at the reflection of their extremity in a mirror.

- Graded activity. Exercises that target the subject's functional goals will be prescribed. These exercises will start as tolerated and will be slowly progressed.

- Meditation. Subjects will be asked to participate in guided meditation activities. These will be done in the clinic and with recordings at home. The meditation will focus on imagery that will promote relaxation and pain relief.

- Home activity log. Subjects will be asked to keep a record of the rehabilitation activities and exercises they perform at home.

Testing

To assess the effectiveness of the interventions several outcome measures will be used. These measures will consist of questions about pain levels, physical, social and emotional functioning, the subject's perception of status change, and the subject's satisfaction with the treatment. Subjects will complete the questionnaires at baseline, weekly during treatment sessions, and 4 weeks, 3 months, 6 months, and 1 year after completion of the sessions. These instruments will be completed on a computer or other electronic device. The questions will take 15-20 minutes to complete and will include:

1. Numeric pain rating scales (1-3 minutes). These scales will ask subjects to measure their pain on a 0 to 10 scale.

2. Patient-Reported Outcomes Measurement Information System (PROMIS) (10-15 minutes). These are standardized questions about the impact of pain on the subject's life, physical function, social activity, fatigue, and psychological status.

3. Global Rating of Change Scale (1 minute). This scale measures the amount of change in the subject's condition using a -7 to 7 scale.

4. Patient Acceptable Symptoms State (1 minute). Rating scale measuring the subject's satisfaction with their current condition

Sessions

The times provided are estimates and the actual time will vary based on the subject.

1. Telephone screening (20 minutes)
    a. A brief phone call to describe the study and determine the subject's eligibility.
2. Initial Visit (2 hours)
    a. In-person screening for eligibility
    b. Review of study and consent documents
    c. Baseline testing
    d. rTMS/sham rTMS session
    e. PT session
3. Standalone rTMS/sham rTMS (30-40 minutes): During the first-week subjects will receive 4 rTMS sessions, over 4 days. 2 of those sessions will include rehabilitation sessions on the same day and 2 of the rTMS sessions will be stand-alone.
    a. rTMS screening questions
    b. rTMS/sham rTMS session
4. Treatment sessions (1-1.5 hours):8 sessions over 4 weeks
    a. rTMS screening questions
    b. rTMS/sham rTMS session
    c. PT session
    d. Follow-up testing (1 time per week)
5. Testing (15-20 minutes): After the 4-week treatment session an e-mail questionnaire will be sent that will include the testing measures used during the study and questions about the continuation of rehabilitation activity and initiation of other new interventions. The e-mail survey will be sent at 4 time points.
    a. 4-weeks after the last session
    b. 3 months after the last session
    c. 6 months after the last session
    d. 1 year after the last session

At the end of the study testing period (1-year after the last session), if desired, subjects will be told if they received real or sham rTMS. Those subjects in sham rTMS will **not be** given the opportunity to have real rTMS as part of this study. They may be eligible to participate in follow-up studies. Subjects, if interested, can also request information on the results of the study after the 1-year follow-up.

What are your responsibilities if you take part in this research?

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

- Attend the 10 treatment sessions (4 sessions week 1 and 2 times a week for 3-weeks)
- Complete the rTMS screening documents before each rTMS session
- Perform rehabilitation activities at home and complete the activity log
- Not start any new treatments for CRPS over the 4-week treatment phase of the study
- Complete the testing questionnaires weekly and at the 4 time points after the treatment sessions
- Inform the research team of any negative effects of the treatment
- Not discuss their experience with the rTMS treatments with other study subjects
- Immediately seek medical attention if a serious side-effect occurs.

Could being in this research hurt you?

It is possible that subjects could experience harm from participating in this study. The most common symptoms are short-term and mild, and include:

- Short-term aggravation of symptoms
- Muscle soreness from doing new exercises
- Local scalp pain at the site of rTMS
- Headache
- Nausea
- Psychological distress
- Discomfort from the rTMS sound

It is possible for subjects to experience more serious harm from participating in this study. These harms are rare and have not been found to be long-lasting.

- Significant aggravation of symptoms
- Seizure (less than .02/1000 sessions or 1 seizure per 60,000 sessions)

Other potential harms include:

- The cost of transportation, parking, and Recognize phone application
- Medical expenses that may occur as a result of treatment side effects

In addition to these risks, taking part in this research may harm you in unknown ways.

The impact of rTMS on pregnancy or a fetus is unknown. We are excluding individuals who are pregnant. If you are pregnant or expect that you have become pregnant during the 4-week treatment sessions please inform the research team and stop participating in the treatment. Pregnancy that occurs after the 4-week treatment phase of the study is not a concern.

Will it cost you money to take part in this research?

Taking part in this research may lead to added costs to you, such as:

- Transportation costs
- Parking costs
- Recognize application (6$) (phone application)

Will being in this research benefit you?

We cannot promise any benefits to you or others from your taking part in this research. However, possible benefits to you include reduced pain, reduction in other symptoms, improved function, and improve psychological wellbeing.

Possible benefits to others include improved treatments for CRPS.

What other choices do you have besides taking part in this research?

Instead of being in this research, your choices may include:

- Medications provided by a healthcare professional
- Counseling services provided by a healthcare professional
- Invasive procedures provided by a healthcare professional, including injections and spinal cord stimulators
- Rehabilitation provided by physical therapists or other healthcare providers

This research is not designed to diagnose, treat or prevent any disease. Your alternative is to not take part in the research.

What happens to the information collected for this research?

Data collected in this research might be de-identified and used for future research or distributed to another investigator for future research without your consent.

Who can answer your questions about this research?

If you have questions, concerns, or complaints, or think this research has hurt you or made you sick, talk to the research team at the phone number listed above on the first page.

This research is being overseen by an Institutional Review Board ("IRB"). An IRB is a group of people who perform independent review of research studies. You may talk to them at (315) 464-4317 if:

- You have questions, concerns, or complaints that are not being answered by the research team.
- You are not getting answers from the research team.
- You cannot reach the research team.
- You want to talk to someone else about the research.
- You have questions about your rights as a research subject.

What if you are injured because of taking part in this research?

In the event of a research related injury, treatment is available at University Hospital but is not free of charge. The costs will be billed to you or your insurance company in the usual fashion. SUNY Upstate Medical University has no funds set aside to compensate you for injuries. You have not waived any of your legal rights by signing this form.

Can you be removed from this research without your approval?

The person in charge of this research can remove you from this research without your approval. Possible reasons for removal include:

- Not attending treatment sessions
- A negative response to the treatment
- A change in medical status that impacts your eligibility for the study
- Inappropriate behavior that places the research team or other subjects at risk
- If you become pregnant

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

What happens if you agree to be in this research, but you change your mind later?

If you decide to leave this research, contact the research team so that the investigator can cancel your further sessions or follow-up testing. Researchers will ask you why you have decided to leave the study. This question is for scientific purposes only. Subjects can refuse to provide a reason for withdrawing from the study.

Will you be paid for taking part in this research?

You will not be paid for taking part in this research.

Confidentiality of records and authorization to use/share protected health information for research:

If you agree to participate in this research, identifiable health information about you will be used and shared with others involved in this research. For you to be in this research we need your permission to collect and share this information. Federal law protects your right to privacy concerning this information.

When you sign this consent form at the end, it means that you have read this section and authorize the use and/or sharing of your protected health information as explained below. Your signature also means you have received a copy of Upstate's Notice of Privacy Practices.

Individually identifiable health information under the federal privacy law is considered to be any information from your medical record, or obtained from this study, that can be associated with you, and relates to your past, present, or future physical or mental health or condition. This is referred to as protected health information.

Your protected health information will be kept confidential. Your identity will not be revealed in any publication or presentation of the results of this research.

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

Why is it necessary to use/share your protected health information with others?
The main reason to use and share your health information is to conduct the research as described in this consent form. Your information may also be shared with people and organizations that make sure the research is being done correctly, and to report unexpected or bad side effects you may have.

In addition, we may be required by law to release protected health information about you; for example, if a judge requires such release in a lawsuit, or if you tell us of your intent to harm yourself or others.

What protected health information about you will be used or shared with others as part of this research?
We may use and share the results of tests, questionnaires, and interviews. We may also use and share information from your medical and research records. We will only collect information that is needed for the research.

Who will be authorized to use and/or share your protected health information?
The researchers, their staff and the staff of Upstate Medical University participating in the research will use your protected health information for this research study. In addition, the Upstate Institutional Review Board (IRB), a committee responsible for protecting the rights of research subjects, and other Upstate Medical University or University Hospital staff who supervise the way the research is done may have access to your protected health information.

The researchers and their staff will determine if your protected health information will be used or shared with others outside of Upstate Medical University for purposes directly related to the conduct of the research.

With whom would the protected health information be shared?
Your protected health information may be shared with:

- Federal agencies that supervise the way the research is conducted, such as the Department of Health and Human Services' Office for Human Research Protections, the Food and Drug Administration (FDA), the National Institutes of Health, or other governmental offices in the US or other countries, as required by law.
- The Institutional Review Board Office (IRB)
- Your insurance company

All reasonable efforts will be used to protect the confidentiality of your protected health information. However, not all individuals or groups have to comply with the Federal privacy law. Therefore, once your protected health information is disclosed (leaves Upstate Medical University), the Federal privacy law may not protect it.

For how long will your protected health information be used or shared with others?
There is no scheduled date at which this information will be destroyed or no longer used. This is because information that is collected for research purposes continues to be used and analyzed for many years and it is not possible to determine when this will be complete.

Can you withdraw your authorization to collect/use/share your protected health information?
You always have the right to withdraw your permission (revoke authorization) for us to use and share your health information, by putting your request in writing to the investigator in charge of the study. This means that no further private health information will be collected. Once authorization is revoked, you may no longer participate in this research activity, but standard medical care and any other benefits to which you are entitled will not be affected. Revoking your authorization only affects uses and sharing of information obtained after your written request has been received, but not information obtained prior to that time.

Even after you withdraw your permission, Upstate Medical University may continue to use and share information needed for the integrity of the study; for example, information about an unexpected or bad side effect you experienced related to the study.

Can you have access to your health information?
At the end of the study, you have the right to see and copy health information about you in accordance with the SUNY Upstate Medical University policies; however, your access may be limited while the study is in progress.

Statement of Consent to Participate in Research & Authorization to use and share personal health information

- Participation in this study is entirely voluntary. You can choose not to take part. There will be no penalty or loss of benefits to which you are otherwise entitled.
- If you agree to take part and later change your mind. There will be no penalty or loss of benefits to which you are otherwise entitled.
- I have read this information and this study has been explained to me.
- It has been written in a language that I understand.
- All my questions about the study have been answered to my satisfaction.

****Consent Signatures Will Be Collected Electronically on REDCap****

For Subjects 18 Years Of Age And Older

I hereby give my consent to participate in this research study and agree that my personal health information can be collected, used and shared by the researchers and staff for the research study described in this form. I will receive a signed copy of this consent form.

_____ _____
Signature of subject Date

_____
Print name of subject

_____ _____
Signature of Person Obtaining Consent/Authorization Date

_____
Name of Person Obtaining Consent/Authorization