Operant Conditioning of Sensory Evoked Potentials to Reduce Phantom Limb Pain

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NCT05880251

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Participant Name: _____ Date:_____

Title of Study: Operant Conditioning of Evoked Potentials to Reduce Phantom Limb Pain

Principal Investigator: Jodi A. Brangaccio, DPT VA Facility: Stratton VA Medical Center, Albany, NY

KEY SUMMARY INFORMATION ABOUT THIS STUDY

You are being invited to take part in a research study that is being funded by the Department of Veterans Affairs. Before you decide to take part, it is important for you to know why the research is being done and what it will involve. This includes any potential risks to you, as well as any potential benefits you might receive. Taking part in this study is completely voluntary.

WHAT IS THE STUDY ABOUT AND HOW LONG WILL IT LAST?

By doing this study, we hope to learn if we can improve the sensory processing and sensation in the arm or leg after a traumatic amputation which may help reduce pain in the residual limb. Your participation in this research will last about 10-12 weeks (3 one-hour sessions per week), with 2 follow-up sessions at 3- and 6- months after the last session.

WHAT ARE KEY REASONS YOU MIGHT CHOOSE TO VOLUNTEER FOR THIS STUDY?

There will normally be no direct benefits to you as a result of being in this study. However, it is expected that the results from the proposed research will help to develop these therapeutic treatments to non-invasively and non-pharmacologically restore sensory processing and reduce pain for Veterans after an amputation. These may potentially reduce dependency on medication and improve quality of life for people with amputation and pain. It may also guide us in developing similar pain treatment for other disorders, such as stroke. In addition, it is possible that some participants may show some pain reduction from taking part in the intervention.

WHAT ARE KEY REASONS YOU MIGHT CHOOSE NOT TO VOLUNTEER FOR THIS STUDY?

The risks in the study are no greater than minimal risk, please see the section on Detailed Information of this consent. However, the study requests your time commitment to the protocol for 8-9 weeks (3 one-hour sessions per week).

Alternative therapies: We are exploring the basic science and developing the clinical applications of novel approaches to enhancing recovery for people with pain after an amputation which may be applicable to other devastating disorders with pain as well. These approaches are fundamentally new. Thus, equivalent alternatives to them do not exist.

DO YOU HAVE TO TAKE PART IN THE STUDY?

If you decide to take part in the study, it should be because you really want to volunteer. You will not lose any services, benefits or rights you would normally have if you choose not to volunteer.

WHAT IF YOU HAVE QUESTIONS, SUGGESTIONS OR CONCERNS?

The persons in charge of the study are Dr. Jodi A. Brangaccio, DPT at the Stratton VA Medical Center, Albany. If you have questions, suggestions, or concerns regarding this study or you want to withdraw from the study the contact information is: Jodi.Brangaccio@va.gov, 518-626-5636

DETAILED INFORMATION ABOUT THE STUDY

WHAT IS THE PURPOSE OF THIS STUDY?

The purpose of this study is to investigate how new, noninvasive rehabilitation methods (e.g., operant conditioning or training with feedback and cutaneous reflex conditioning) cause changes in the brain, and to develop and test clinical applications using these noninvasive procedures that may help Veterans with pain. You are being asked to take part because you

1) You qualify as a healthy participant without a history of neurological disease, chronic pain, or other major medical disorder or
2) You have had an amputation at least 6 months ago, your health is stable, but you are experiencing phantom limb pain,
3) You are able and willing to participate in up to three 1-hr sessions/wk. for about 8-9 wks. and up to two subsequent follow-up sessions (3 and 6 months later).
4) You expect that your medications will not change during the study.
5) You have met all exclusion criteria

The Stratton VA Medical Center will enroll 10-12 people per study group for three groups. This study at the Stratton VA Medical Center is funded by a grant from Veterans Affairs Office of Research and Development.

HOW LONG WILL I BE IN THE STUDY?

This research study is expected to take approximately 2 years and will involve the participation of 30 people. Your individual participation in the project will take 8-9 weeks (3 one-hour sessions per week), and 2 follow up sessions at 3- and 6- months after the last intervention session.

WHAT WILL HAPPEN IF I TAKE PART IN THE STUDY?

After consenting to be in the study, you will be asked to come to the Stratton VA Medical Center (VAMC) for a screening session. At the screening, you will be asked to fill questionnaires and

be assessed for pain, and sensory-motor processing, by our study clinical research physician and research investigator.

At the screening session, you may complete the following questionnaires: a Demographic and Health History questionnaire (e.g., age, gender, health history, current medications etc.), an inventory to help determine your dominant hand (if applicable), IDMC screening, and pain level. It will take you under 30 minutes to complete these questionnaires. All information you provide is confidential. You are free to skip questions that you may not wish to answer. If some of those questions are important for assessing inclusion/exclusion criteria, the study team will let you know. If you have a neurological disorder, you will meet with a VA physician and/or physical therapist to evaluate your ability to participate safely in the study and to review your current medical condition.

After enrollment in the study, you will come for an assessment session at the VAMC, Wing A 6th floor. Research staff will perform more extensive pre-intervention evaluations of pain, hand/arm (or foot/leg if applicable) sensation and movement, attention and quality-of-life, with standard tests like West-Haven Yale Multidimensional pain inventory. This will be followed by sensory-motor assessments performed with EEG and EMG with simple non-invasive, #non-painful tactile and motor tasks, such as finger tapping or foot tapping. If required, a picture of the electrode placement on your arm or leg will be taken. This picture will not have any identifying information on it, just your study code. Staff will use it as a reference to place the electrodes in the same locations each time you come in for a session. You will sign a separate consent form giving the research staff permission to photograph your arm or leg. The screening and first pre-assessment session may be combined as a single session.

You will then be assigned to an intervention group: either the Control group or the Conditioning group by chance or like the flip of a coin. The session protocol for both the groups is similar. The only difference is that the Conditioning group will receive immediate conditioning feedback during the session, while the Control group will not. You will not be told about your group, till the end of your study participation.

Next, for the intervention sessions, you will come to the VAMC for up to three study visits per week (about 1 hour each visit) for about 8-9 weeks and then up to 2 follow-up visits at 3- and 6-month after the last intervention session.

During the study, you will mainly interact with the Principal Investigator (Dr. Jodi A. Brangaccio, Co-investigator (Dr. Disha Gupta) and Clinical Research Physician (Dr. Donald S. Higgins).

All procedures will be overseen by the research team. Your usual care providers at the VA are not involved in this study. If you see any non-VA health care providers for your usual care, tell them you are in this study, and give them the name and phone number of the Principal

Investigator (Dr. Jodi A. Brangaccio 1-518-626-5636). A copy of this consent form will be placed in your medical records.

If you agree, you will participate only in the activities next to the checked boxes below.

Please read the descriptions next to any checked box. Place your initials next to that box to indicate your understanding and approval. If any box is left unchecked, it does not apply to you, and you can ignore it.

☐ **Evoked Potential Testing/Training** – about three sessions per week for 8-9 weeks with follow-up sessions at three and six months.

1. At the beginning of each session, you will be seated in a chair or on a table. Research the skin on your limb with alcohol and place surface electrodes (small sticky pads) over your arm (or leg) muscles and nerve to measure their activity.
2. You will then be asked to maintain a moderate level of muscle activity within a defined range. You will see the muscle activity level displayed on the screen in front of you. While you maintain this muscle activity, you will feel a weak stimulus (vibrotactile or electrical) on your intact hand (or leg) that will generate a sensory response. *On stimulation you may feel a momentary, non-painful sensation (e.g., tingling). Staff will adjust the electrode location to prevent any discomfort.* You may be asked to go through three sets of multi-trial blocks with
3. At the start and end of a session, the research staff will gather information on pain level with a standard four-question Defense and Veterans Pain Rating Scale.
4. Before, after, or during the evoked potential training sessions, an investigator will measure your arm muscle activity, sensation and movement with simple standard sensory-motor tasks.

☐ **Electroencephalography (EEG):** In some sessions, you may be asked to wear a cloth cap or a plastic headset containing small metal disks for recording brain activity (i.e., electroencephalographic (EEG) activity). A small amount of gel used daily in clinical practice will be placed on each disk in the cloth cap. The gel will wash out of your hair with soap and water. The plastic headset does not require gel. You will see the EEG activity displayed on the screen in front of you. There is no sensation associated with this recording.

☐ **Electromyography (EMG):** We may monitor the activity of muscles in your arms, legs, during different tasks. This is done by placing small sticky pads with electrodes (metal disks) on the surface of your skin. The electrodes are connected to a computer system that records the electrical activity in your muscles. There is no sensation associated with this recording.

☐ **Videography:** In some sessions, your movement will be recorded with a video camera. These videos will not include any identifying information about you.

☐ **Motion Capture:** You may be asked to perform simple motor tasks, such as hand movements/grasping, with small round reflective markers or motion sensors placed on the surface of your skin or clothing using two-sided tape. Special cameras will record the movement of the reflective markers while you move.

☐ **Behavioral Tasks:** You may be asked to perform simple sensation and motor behavioral tasks that evaluate your sensory-motor performance (e.g., finger tapping task).

☐ **Methods Refinement:** You will participate in sessions intended to refine methods for study that use one or more of the procedures described in the boxes that are checked above.

WHAT IS EXPECTED OF ME IF I TAKE PART IN THIS STUDY?

- Please follow the instructions provided in the assessment and intervention sessions. If anything is unclear, please feel free to ask questions.
- Keep your study appointments. If you miss an appointment, please contact the investigator or research staff to reschedule as soon as you know you will miss the appointment.
- While participating in this research study, please do not take part in any other research project without approval from the investigators. There is no safety issue in taking part in another study, but depending on the nature of the study, it may invalidate the results of this study, as well as that of the other studies. We request to discuss with the investigators of this study prior to participating in another study.

WHAT POSSIBLE RISKS OR DISCOMFORTS MIGHT I HAVE IF I TAKE PART IN THIS STUDY?

For your safety, you must follow all instructions given to you by the study doctor and research staff while you are in this study. If you see any non-VA health care providers for your usual care, tell them you are in this study, and give them the name and phone number of the Principal Investigator (Dr. Jodi A. Brangaccio 1-518-626-5636).

Being in this study may involve some added risks. These include:

1. **EMG:** There is a very small possibility that the recording electrodes may produce minor skin irritation (e.g., itchiness). However, this is extremely unlikely in the typically short session periods (≤ 90 min). If itchiness does occur, an over-the-counter topical anesthetic will be applied

to the skin over which the electrodes were placed. Careful electrode placement minimizes any discomfort. Occasionally, stimulated digit or muscle may feel fatigued after the session; such fatigue typically resolves quickly. To prevent this problem, we allow participants to take breaks between trials as needed.

2. **EEG:** EEG is recorded with clinical-grade equipment. Thus, the risk is no greater than the extremely small risk associated with routine clinical EEG recording.
3. Since electrical equipment is being used, there is a theoretical possibility of an unwanted shock. This risk is minimized using clinical-grade equipment, and by ongoing careful monitoring of the experimental apparatus, cable connections, and stimulus isolation. Extremely safe operation is thereby achieved.
4. **Fatigue:** To avoid fatigue we will keep the data collection part of the session <60 min and allow for short breaks.
5. **Pain:** The participants in this study would already be experiencing pain. The goal of the study is to reduce pain and we will monitor pain at each session with the DVPRS 2.0. It may be possible that initially pain is felt to increase slightly. If pain increases significantly, we will re-evaluate collectively as a team, with guidance from Dr. Higgins and the participant, to decide whether to pause the sessions, to end participation, or to continue, for that Veteran. This is applicable to participants with limb amputation who already have chronic pain. Healthy volunteers will not experience pain as they do not have pain at baseline.
6. As with all studies involving motor performance, there is a small risk of minor musculoskeletal strain or injury.
7. There is a slight chance that someone outside of the study staff may see your confidential health information due to human error. However, the investigators of this study are committed to protecting your privacy and the confidentiality of information related to research and your health care. You will be assigned a study code. That code will be the only identifier on your completed questionnaires and data sheets.

You will be told if any new information is learned that might affect you or that might change how you feel about being in this study. The information in this form is just for this study. The list given above does not include any risks or discomforts that may come from the care you receive outside this study. Please speak with your regular health care provider(s) if you have any questions about your usual care. For your safety, please tell the study doctor or research staff about any care you receive that is not part of this study.

WHAT ARE THE POSSIBLE BENEFITS OF THIS STUDY?

There will normally be no direct benefits to you as a result of being in this study. However, it is expected that the results from the proposed research will help to develop these methods for a

non-invasive non-pharmacological therapeutic treatment to reduce phantom limb pain after an amputation. These may potentially reduce dependency on medication and improve quality of life for people with amputation and pain. In addition, it is possible that some of the participants with amputation and pain may show some pain reduction because of changes in sensory processing.

WHAT OTHER CHOICES DO I HAVE IF I DO NOT WANT TO JOIN THIS STUDY?

You do not have to be in this study. If you decide now that you want to be in this study, and you change your mind later, you can stop at any time. Whatever you decide, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled. If you decide not to be in this study, you may decide to pursue other therapies for your condition. Please tell the study doctor or a member of the research staff if you decide you want to stop. They will explain what you need to do to withdraw from the study. You may be asked to come in for a final study visit. Sometimes, people need to be taken out of a study even if they do not want to stop. This could happen if you do not follow instructions, or the study is no longer safe for you, or the study is stopped. If this happens, you will be told, and the reason will be explained to you.

HOW WILL MY PRIVATE INFORMATION BE PROTECTED?

All information will be held confidential (or private) except when the Institutional Review Board or study sponsors require reporting. Your name, any other identifying information, questionnaires, and consent forms will be kept on password protected folders and computers and in locked file cabinets only accessible to the research team associated with this study at the local VA site.

If you agree to be in this study, the following people or groups may need to review your records: The study doctor and research staff

- Your regular health care provider(s)
- The Stratton VA Medical Center Institutional Review Board (IRB), a group that reviews research studies to make sure the participant's rights, safety and welfare are protected. • Other officials of the Stratton VA Medical Center or the Department of Veterans Affairs Federal agencies including, but not limited to, the Office of Human Research Protections (OHRP), the VA Office of Research Oversight (ORO) and the VA Office of the Inspector General (OIG).

If you agree to be in this study, your name will be added to a master list of all participants who are in the study. The master list will be kept with the other records from the study on a VA secure server, with restricted access. A copy of this consent form will also be placed in your VA

medical record, if you are a patient at the Stratton VAMC. If you do not have a VA medical record, one may be created for you.

We may share your *de-identified* data with researchers from other hospitals, universities, or institutions. There will be no way to connect the data to you personally. If the results of this study are reported in medical journals or at meetings, the authors will not share personal details about you specifically. You will not be identified by name, recognizable photo, or any other means, unless you give us specific permission to do so.

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 website at any time.

WHAT ARE THE COSTS TO ME IF I TAKE PART IN THIS STUDY?

There will be no costs to you (or your insurance company, if you have insurance) for any of the treatment or testing that is required by the study protocol. This includes treatment of any injury caused by the research. Some Veterans are required to pay copayments for medical care and services that are provided by the VA. If this applies to you, you will need to continue making these copayments for VA medical care and services that are not part of this study.

WHAT WILL BE THE COMPENSATION FOR BEING IN THIS STUDY?

Being in this study may lead to added costs for travel. You will be compensated $40 per session to cover these expenses. Additional funds may be available for special transportation services. You will receive this payment even if you do not complete the entire session. You will be paid via direct debit. We will make sure that you receive payments for the sessions you have attended, even if you decide to withdraw.

WHAT WILL HAPPEN IF I AM INJURED BECAUSE OF MY BEING IN THE STUDY?

As a VA study participant, the VA (not you or your insurance) will provide necessary medical treatment should you be injured by being in this study. You will be treated for the injury at no cost to you. This care may be provided by the Albany Stratton VAMC or arrangements maybe be made for contracted care at another facility. You have not released the institution from liability for negligence. In the case of a research related injury resulting from this study, you should contact your study team. If you have questions about medical treatment for any study related injuries, you can call the Administrative Officer for Research at this VA Medical Center at 518-626-5621.If you should have a medical concern or get hurt or sick because of taking part in this study, call:

DURING THE DAY:
Dr. Jodi Brangaccio @ 518-626-5636
AFTER HOURS: @ 518-626-5636
Dr. Jodi Brangaccio

DO I HAVE TO TAKE PART IN THE STUDY?

Your participation in this study is voluntary. Refusal to take part in the study will involve no penalty or loss of benefits to which you are otherwise entitled.

You may decide to discontinue taking part at any time without any consequences, penalty or loss of benefits. If you decide to withdraw from the study, you will still receive the same standard of care you would otherwise have received. We may request an extra follow-up session to appropriately terminate the study participation.

The research team may continue to review the data already collected for the study, prior to the withdrawal, but cannot collect further information, except from public records, such as survival data. Any electronic or behavioral data already used, cannot be withdrawn.

RIGHT OF INVESTIGATOR TO TERMINATE MY PARTICIPATION

The research team also holds the right to withdraw a participant from the study under specific circumstances such as non-compliance with the requested research methods. We may request an extra follow-up session to appropriately terminate the study participation. Such a withdrawal will also have no penalty, or loss of benefits that you would otherwise have received.

WHO DO I CONTACT ABOUT THIS STUDY IF I HAVE QUESTIONS?

Please contact your study doctor or the research staff if you have any questions about the research, or if you think you have been injured by this study.

Study Contact: Jodi A. Brangaccio, DPT. **Phone Number:** 518-626-5636. If you cannot reach the study doctor or research staff at the number above, please contact the Stratton VA Medical Center operator at 518-626-5000 and request to be connected with on-call neurology staff.

If you have questions about your rights as a study participant, or you want to make sure this is a valid VA study, you may contact the Stratton VA Institutional Review Board at 518-626-5624. This is the Board that is responsible for overseeing the safety of human participants in this study. You may call the Stratton VA Institutional Review Board if you have questions, complaints or concerns about the study or if you would like to obtain information or offer input.

Participant Name: _____ Date:_____

Title of Study: Operant Conditioning of Evoked Potentials to Reduce Phantom Limb Pain.

Principal Investigator: Jodi A. Brangaccio, DPT VA Facility: Stratton VA Medical Center, Albany, NY _

FUTURE USE OF DATA AND RE-CONTACT

At the end of the study, all data will be stored on a secure VA server. All records from this study will be kept indefinitely by the VA, as required by the VA Records Control Schedule. Some of the above groups may need to review your records even after the study is finished. Identifiers will be removed from all identifiable private information, after such removal, the information could then be used for future research studies or distributed to another investigator for future research studies, without additional informed consent from the subject or the legally authorized representative. You can withdraw your consent for future use of collected data at any time during the study until the closure.

AGREEMENT TO PARTICIPATE IN THE RESEARCH STUDY

Dr./Mr./Ms._____has explained the research study to you. You have been told of the risks or discomforts and possible benefits of the study. You have been told of other choices of treatment available to you. You have been given the chance to ask questions and obtain answers.

By signing this document below, you voluntarily consent to participate in this study You also confirm that you have read this consent, or it has been read to you. You will receive a copy of this consent after you sign it. A copy of this signed consent will also be put in your medical record.

Please initial the line if a copy of this consent was offered to you: _____
Please initial the line if you declined to accept a copy of this consent form: _____
Please initial the line if we may contact you for future studies: _____

#I agree to participate in this research study as has been explained in this form.		
_____ Participant's Name	_____ Participant's Signature	_____ Date
_____ Consenter's Name	_____ Consenter's Signature	_____ Date

FOR IRB USE ONLY

PI/SC Approval Date:

Stratton VA Medical Center Institutional Review Board (IRB)
Effective Date: May 29, 2025