Neuromodulation for Exercise Adherence in Older Veterans

NCT03733041

January 12, 2022

Participant Name: _____ **Date:** _____

Title of Study: Neuromodulation for Exercise Adherence in Older Veterans

Principal Investigator: [redacted]

VAMC: Central Arkansas Veterans Healthcare System, 598 Version #6 Date: 12-7-2021

SUMMARY

You are being invited to participate in a research study. Your participation is voluntary, and you should only participate if you completely understand what the study requires and what the risks of participation are. You should ask the study team any questions you have related to participating before agreeing to join the study. If you have any questions about your rights as a human research participant at any time before, during, or after participation, please contact the Institutional Review Board (IRB) at [redacted] for assistance. If you have questions about this study, you may contact the Principal Investigator, Dr. [redacted] at [redacted].

The research is being done to see if stimulation of the brain using a magnet (repetitive transcranial magnetic stimulation (rTMS)) improves brain functions needed for planning and following-through (executive function). Planning and follow-through are important for adherence to a home-based exercise program. The study will also look at whether improved adherence to exercise improves walking and balance. Veterans aged 60 and older are eligible for the study.

If you agree to join the study, you will be asked to complete the following research procedures:

Study visits: You will be asked to come to the [redacted] clinic in [redacted] for study visits. During these visits, we will assess your health, executive function, and gait and balance. You may also be asked to attend Wii-Fit training and study treatment sessions.

The study will be done in three phases:

- Phase I (3 months): During Phase I, you will be asked to exercise using Wii-Fit at home for 60 minutes a day for five days each week.

- Phase II (2 weeks): After completing Phase I, you will be assigned to either the magnetic stimulation group or the observation group based on your adherence to the home exercises program. Participants in the magnetic stimulation group will be assigned randomly (like a flip of a coin) to receive rTMS or sham treatment. They will receive treatment for five days each week for two weeks. Participants in the observation group will continue to exercise at home.

- Phase III (6-months). During Phase III, you will be asked to exercise at home for 60 minutes a day for five days each week.

Home visits: The research coordinator will visit you at your home once a month during Phase I and Phase III.

Blood draws: Blood will be collected at the baseline, and at your 14-week, 16-week and 40-week visits.

APPROVED BY CAVHS IRB ON 1/12/2022

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Your part in the study will last for about 10 months. We can't promise that you will benefit from taking part in this research. However, you may learn more about your balance and executive function through study tests that are not part of standard care.

The most common risks related to treatment are discomfort or pain where they rTMS/sham coil touches your head, muscle twitching during treatment, and headache after treatment. There is a slight risk of seizures with rTMS. This risk is less than the risk of taking medicine for depression. There is a small risk of injury or falls during Wii-Fit exercises. We will take appropriate steps to reduce these risks.

The alternative to taking part in the study is not to participate in it. Currently, there are no FDA-approved treatments for improving executive function or adherence to an exercise program.

Please note that there are other factors to consider before agreeing to participate, such as additional procedures, use of your personal information, costs, and other possible risks not included here. If you are interested in participating, a member of the study team will review the full information with you. You are free to not participate or stop participating at any time during or after the consenting process.

INTRODUCTION
You are being invited to take part in a research study that is being carried out at the Central Arkansas Veterans Healthcare System. 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. The sponsor of the study is VA Office of Research and Development.

Read the information below closely and discuss it with family and friends if you wish. Ask one of the study staff if there is anything that is not clear or if you would like more details. Take your time to decide. If you do decide to take part in this study, your signature on this consent form will show that you received all of the information below, and that you were able to discuss any questions and concerns you had with a member of the study team.

BACKGROUND AND PURPOSE

- The purpose of this study is to see if repetitive Transcranial Magnetic Stimulation (rTMS) to the brain improves executive function (higher memory function) and adherence to a home-based exercise program in older Veterans. The study will also explore if improved adherence to exercise improves walking and balance.

- Exercising regularly is beneficial to health. Despite of knowing the importance of exercise, lot of people do not exercise. Not adhering to a home exercise program is a chronic problem. We will study if poor executive function is a marker of poor exercise adherence. We will also study if improving executive function would improve exercise adherence.

- rTMS is a non-invasive FDA-approved treatment for treatment resistant depression. rTMS stimulates specific parts of the brain by using electromagnetic fields with minimal discomfort.

- We will enroll about 106 Veterans at CAVHS.

DURATION OF THE RESEARCH

- This research study is expected to take approximately four years.
- Your individual participation in the project will take 10 months (40 weeks).
- You will come to the [redacted] clinic in [redacted] for anywhere between 10-20 visits. All clinic visits will last between 2-3 hours.

STUDY PROCEDURES

If you decide to take part in this study, this is what will happen:

ENROLLMENT VISIT: During this visit, the study team will talk about the study and go over this informed consent with you. If you decide to take part in this study, you will sign this informed consent document. The study team will ask you about your medical history and do a physical exam. You will be evaluated for your health, and memory. The exam will include taking your blood pressure and pulse. A blood sample will be drawn. Information will be collected from you, and your VA medical record. This visit will take 2-3 hours to complete. We will share the results of your visit with you. We will let you know if you are eligible to continue with this study.

BLOOD DRAWS: Your blood will be drawn at the baseline, 14-week, 16-week and 40-week visits. During each blood draw study staff will collect about 4 teaspoons (16 ml.) of blood. These blood samples will be used for:

- Biomarker testing.
- An extra blood draw could be ordered. This would be to follow-up on an abnormal laboratory result.

PHASE I: This phase will last for 14 weeks. This phase includes the two-weeks of exercise training sessions and the three-months of the home-based exercise program.

- **EXERCISE TRAINING SESSIONS**: The exercise training will include six visits. You will be taught all the exercises that you will be performing at home. You will be trained on the details of how to maintain the self-report diary at home. These visits will take approximately 1 hour.
- **HOME-BASED EXERCISE PROGRAM**: After completing the training sessions, a research coordinate will visit your home. He/she will set up the Wii equipment at your home. You will be asked to do the exercises at home for 60 minutes daily 5 days per week for 3-months. The research coordinator will visit you at your home every month. He will assess how the exercise program is coming along, and to check the Wii-console.

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PHASE II: This phase will last for 2 weeks. At the completion of the three-months of the home-based program, subjects will be divided into 2 groups. One group of participants will get the randomized (like a flip of a coin) into either rTMS or sham treatment and the other group will not be randomized.

- **GROUP THAT GETS RANDOMIZED**: If selected to get randomized, you will be randomly assigned, like the flipping of a coin, to get either rTMS treatment or sham treatment. Sham treatment is a procedure that will create the experience of the treatment without actually providing the treatment. So, neither you nor the research team will know if you are getting the rTMS treatment or sham treatment. Half of the participants in this group will get rTMS while the other half will get sham treatment.

- **TREATMENT SESSIONS**:
  - If you are randomized to receive rTMS or sham treatments. These will be given daily, five days per week, for two weeks (total of approximately 10 treatments).
  - Each treatment visit will last approximately 35 minutes.
  - Please plan an hour for each treatment.
  - During these visits you will sit in a comfortable chair. You will have the magnetic coil touching your head.
  - You will be fully awake. You will have the option of reading a book, watching TV or doing nothing.
  - You will be asked to wear ear plugs to soften the loud noise from the rTMS machine. If the ear plug falls off, the treatment will be paused. The ear plug will be re-inserted into your ear before the treatment resumes.
  - There will be a study team member in the room all through the treatment.
  - Please let him/her know if you experience any discomfort or your ear plugs fall.
  - If you experience any side effects, the treatment will be stopped. Consultation will be sought from the study physician before resuming the treatment.
  - After completing each session of rTMS treatment, subjects will exercise at the facility for the same time as they exercised at home.

- **GROUP THAT DOES NOT GET RANDOMIZED**: In this group, subjects will continue to do the home exercises for next 2 weeks.

PHASE III: This phase will last for 6-months. All subjects will be asked to do the exercises at home for 60 minutes daily, 5 days per for 6 months. The research coordinator will visit you at your home once a month. He/she will assess how the exercise program is coming along, to check the Wii-console, and to assess for any adverse events.

STUDY VISITS:
- Visits to assess outcome measures: Your health, executive function, and gait and balance will be assessed at baseline. Follow-up assessments will occur at 2 weeks, 14 weeks, 16 weeks, and 40 weeks.

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- Training session visits: You will be attending six training sessions in the first 2 weeks of the study after enrollment.
- rTMS/sham treatment visit: If you are in the group that gets randomized, you will get rTMS or sham treatment. The treatment visits will be daily, five days per week, for two weeks.

TELEPHONE CALLS: The study staff will contact you over the phone:
- Check to see that you are doing okay;
- Issues related to the study such as scheduling, and reminders

YOUR RESPONSIBILITY: We ask you to take responsibility for the following:
- Keep your study appointments. If it you miss an appointment, please contact the investigator or research staff to reschedule as soon as you know you will miss the appointment.
- Complete your questionnaires and testing as instructed.
- Ask questions as you think of them.
- Tell the investigator or research staff if you change your mind about staying in the study.
- While participating in this research study, do not take part in any other research project without approval from the investigators.

POSSIBLE RISKS OR DISCOMFORTS
Any procedure has possible risks and discomforts. The procedures in this study may cause all, some, or none of the risks or side effects listed. Rare, unknown, or unexpected risks also may occur. Participation may worsen pre-existing health conditions and unexpected risks may also exist. The study tries to exclude individuals at greater than normal risk from the study procedures. However, please report any unusual symptoms or problems to the study staff.

rTMS/SHAM TREATMENT RISK: rTMS has been demonstrated to be an extremely safe, well-tolerated treatment. We have taken extra precautions to ensure that no one at increased risk of side effects with the treatment gets into the study.

The most common side effects with rTMS are:
- Discomfort or 'application site pain'.
- Muscle twitching during treatment sessions
- Post treatment headache
- Transient hearing impairment (when hearing protection is not used)
- Fainting
- Symptoms of mania, including feelings of excessive happiness without a reason, increased energy, reduced need for sleep etc. in some patients.

Seizure risk: There is a slight risk of seizures with rTMS. This risk is less than the risk associated with use of medicines for depression. We have taken several steps to reduce seizure risk. We are using very conservative treatment parameters that have been tested in hundreds of studies before. We plan to use an adequate pretreatment clinical screening for potential seizure risk. Additionally, we will provide clinical

monitoring of the rTMS treatment sessions. We will also appropriately train all study team members regarding "first responder" seizure clinical skills.

You will be monitored for these conditions during this study. There also may be unknown or unexpected side effects. If any of these side effects develop and become hard to cope with, we will stop your study treatment. If the discomfort is due to the study treatment, it likely will go away after you stop the study treatment. If you stop the study treatment, you will still be asked to come for the regular study visits.

Wii-Fit Exercise Risks: Although no risks are likely for Wii-Fit use, a potential for injury cannot be ruled out. There is a small potential for injury or falls during exercise. Other possible injuries related to Wii-Fit use could include eyestrain, muscle sprain, and injuries related to repetitive use such as tendonitis, and bursitis. We have taken specific measures to avoid injuries such as appropriate placement and handling of the Wii equipment. You are instructed to stop and rest if you get tired, develop eyestrain or have symptoms of tingling, numbness, burning or stiffness while exercising.

RISKS OF TESTING & QUESTIONNAIRES: Testing may cause you to become upset, feel frustrated, or be tired. You have the right not to answer any questions you don't want to. You may ask to stop testing at any time for any reason.

RISKS ASSOCIATED WITH BLOOD DRAWS: Some people feel slight discomfort or pain when a blood sample is taken from the vein. Sometimes people feel faint for a few minutes or get a bruise after giving a blood sample. Any bruise should disappear in a few days.

Risks of the usual care you receive are not risks of the research. Those risks are not included in this consent form. You should talk with your health care providers if you have any questions about the risks of usual care. Participation in research may involve a loss of privacy. Your research records will be kept as confidential as possible.

CONFIDENTIALITY

This study will collect research data and personal information about you. This is required for participation but could result in a loss of privacy. However, your research data will be treated the same as any VA medical record and kept as confidential as possible.

This information will be protected in the following ways:

- Your data will be coded. The identification code will not be based on any information that could be used to identify you such as social security number, initials, birth date, etc. The master list linking your name to your code number will be kept separately from the research data. Only authorized individuals will have access to the master list and any other research documents.

- Paper research records will be stored in locked filing cabinets behind locked doors. Electronic data will be stored on VA computers protected with passwords and limited access folders on the

VA server. Records will be securely maintained for 6 years following the closure of the study, and will then be safely destroyed as required by the Record Control Schedule for research.

Information about you will be combined with information from other people taking part in the study. We will write about the combined data we have gathered. Any talks or papers about this study will not identify you.

The information collected for this study will be kept confidential. If you are a Veteran who is a patient at the VA Medical Center, a copy of your signed and dated consent and HIPAA forms will be placed in your medical record(s). If you are a Veteran but do not yet have an electronic medical record at CAVHS, you are required to provide a copy of your DD214 to the eligibility office so that one may be created for you before providing your informed consent to participate.

There are times when we might have to show your records to other people. Only authorized persons will have access to the information gathered in this study. Authorized persons may include regulatory agencies such as the Food and Drug Administration, (FDA), the Government Accounting Agency (GAO) or the Office for Human Research Protection (OHRP), Office of Research Oversight (ORO), as well as members of the Research Administration staff of CAVHS. The Department of Veterans Affairs (VA) requires some information to be recorded in the VA electronic medical record for all veteran and non-veteran research participants. By signing this document, you consent to such inspection.

Identifiers might be removed from the identifiable private information or identifiable biospecimens and that, after such removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from the subject or the LAR, if this might be a possibility.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov as required by U.S. Law under the clinical trials number NCT03733041. 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.

POTENTIAL BENEFITS
We can't promise that you will get any benefits from taking part in this research study. However, possible benefits may include

- You will learn more about your balance and executive function through tests which are not part of standard care.
- Others will benefit from the knowledge gained from this study.

ALTERNATIVES TO PARTICIPATING IN THIS RESEARCH
Currently, there are no FDA-approved treatments for improving executive function or adherence to an exercise program.

COSTS TO PARTICIPANTS AND PAYMENT
Costs to Participants*:* You will not be charged for any treatments or procedures that are part of this

study. If you usually pay co-payments for VA care and medications, you will still pay these co-payments for VA care and medications that are not part of this study.

Payment Offered for Participation:
Each participant will receive $20 for outcome assessment. Each participant will receive $10 for rTMS treatment. A bonus of $50 will be given to participants that complete all the visits. All payments will be made via electronic fund transfers or checks based on your preference.

Phase 1:
- Outcome assessment: $40 (2 visits)
- Training: $60 (6 visits)
- Total: $100

Phase 2 for those randomized:
- Outcome assessment: $20 (1 visit)
- rTMS sessions: $100 (10 visits)
- Total: $120

Phase 2 for those not randomized:
- Outcome assessment: $20 (1 visit)
- Total: $20

Phase 3:
- Outcome assessment: $20 (1 visit)
- Bonus for completion: $50
- Total: $70 with bonus

Additional compensation for travel will be available if you travel more than 60 miles round trip to study appointments. Travel reimbursement will be based on round-trip distance as detailed below:
- Less than 60 miles: $0
- 60-100 miles: $20
- 101-140 miles: $40
- More than 140 miles: $60

You can receive compensation after each visit, or as a one-time payment at the end of the study. Please let the study team know which option you prefer.

MEDICAL TREATMENT AND COMPENSATION FOR INJURY
According to federal regulations (Title 38 CFR17.85), the VA will provide necessary medical treatment to you as a research participant if you are injured by participation in this research project approved by the Research & Development Committee and conducted under the supervision of one or more VA employees. Except in limited circumstances, this care will be provided at this VA facility.

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This does not apply to treatment for injuries that result from non-compliance by you with study procedures.

If you should have a medical concern or get hurt or sick as a result of taking part in this study, call:

DURING THE DAY:
- [redacted] at [redacted], or
- [redacted] at [redacted]

AFTER HOURS: Study physician can be reached on her cell phone at [redacted]. Emergency and ongoing medical treatment will be provided as needed. However, the study has not made allowances for any compensation should an injury occur. If an injury does occur, you will be evaluated and possibly treated by the study physician or referred to your primary care physician for treatment.

You do not give up any of your legal rights and you do not release the VA from any liability by signing this form.

PARTICIPATION IS VOLUNTARY
It is up to you to decide whether or not to take part in this study. If you decide to take part you may still withdraw at any time. If you do not wish to be in this study or leave the study early, you will not lose any benefits to which you are entitled. If you don't take part, you can still receive all usual care that is available to you. Your decision not to take part will not affect the relationship you have with your doctors or other staff, and it will not affect the usual care that you receive as a patient.

If you decide to no longer do the rTMS treatment, we will still encourage you to remain in the study and continue with regular visits until the end of the study. If you choose to stop participating in the study completely for any reason, you will be asked to return to the research center to undergo a final evaluation. However, any data or lab samples collected from you prior to your decision to withdraw from the study will still be used by study staff.

You have the right to withdraw your permission to use or disclose personal information about your health. If you choose to withdraw your permission, you must notify [redacted] in writing: at [redacted].

SIGNIFICANT NEW FINDINGS
Sometimes during the course of a research study, new information becomes available about rTMS that is being studied that might change a person's decision to stay in the study. If this happens, your study doctor will tell you about it and discuss with you whether you want to continue in the study. If you decide to withdraw from the study, your study doctor will arrange for your medical care to continue. If you decide to continue in the study, you might be asked to sign an updated informed consent form. Your

study doctor could also decide it to be in your best interests to withdraw you from the study. If so, he or she will explain the reasons and arrange for your usual medical care to continue.

RIGHT OF INVESTIGATOR TO TERMINATE PARTICIPATION
Your participation might be terminated by the investigator without regard to your wishes to continue. This may happen under the following circumstances:

- If the study is cancelled or stopped by the sponsor.
- If staying in the study would be harmful.
- If you need treatment not allowed in the study.
- If you fail to follow instructions.
- There may be other reasons to take you out of the study that we do not know at this time.

This will be discussed with you in person or on the phone.

BIOMARKER RESEARCH
During this study, blood samples will be collected from you for biomarker testing. The testing's will be done at CAVHS.

- Biomarker Research: A biomarker is a chemical in your body that can be measured to give information about a disease or condition you have. We will look at biomarkers CRP and BDNF in your blood to learn how they may be related to exercise, and rTMS treatment.

The results of the biomarkers tests will be kept in scientific databases for this research study. These results are important only for research - not for helping care for you. For this reason, the results will not be released to you or your family. No information about your biomarker tests will be entered in your VA medical record.

RE-CONTACT
☐ *If you are willing to allow study staff to contact you regarding future studies within the VA, please check the box.*

If you've checked this box, one of the research team members may contact you by phone to discuss your interest in participating in another research study.

ADDITIONAL CONTACT INFORMATION
If at any time before, during or after your participation in this study you have questions or concerns, want to get additional information, lodge a complaint or offer your input with a person who is not part of the study team, you can contact the IRB Administrator at [redacted], the Research Compliance Officer at [redacted], or the Research and Development Coordinator at [redacted].

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AGREEMENT TO PARTICIPATE IN THE RESEARCH STUDY
A member of the study team 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.

_____ _____
Signature of Participant Date

_____ _____
Signature of Person Obtaining Consent Date