Washington University in St. Louis

Official Study Title: Transcranial Magnetic stimulation and Cognitive training for treatment of cognitive decline in adults with schizophrenia: A Pilot Randomized Trial

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INFORMED CONSENT DOCUMENT

Project Title: Transcranial Magnetic Stimulation and cognitive training for treatment of cognitive decline in schizophrenia

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Co Investigator: Rita Haddad, MD

Research Team Contact: Rita Haddad, MD 314-333-2141

This consent form describes the research study and helps you decide if you want to participate. It provides important information about what you will be asked to do during the study, about the risks and benefits of the study, and about your rights and responsibilities as a research participant.

- You should read and understand the information in this document including the procedures, risks and potential benefits.
- If you have questions about anything in this form, you should ask the research team for more information before you agree to participate.
- You may also wish to talk to your family or friends about your participation in this study.
- Do not agree to participate in this study unless the research team has answered your questions and you decide that you want to be part of this study.

WHAT IS THE PURPOSE OF THIS STUDY?

This is a research study. We invite you to participate in this research study because you are an adult with schizophrenia or schizoaffective disorder.

The purpose of this research study is to examine the potential benefits of Transcranial Magnetic Stimulation in combination with computerized cognitive training program to improve cognition, such as memory, attention and concentration and functioning, such as self care. This study will compare the effectiveness of Trancranial Magnetic Stimulation plus cognitive training versus placebo, that is a non active transcranial magnetic stimulation plus cognitive training.

Transcranial Magnetic Stimulation is approved by the U.S. Food and Drug Administration to treat the symptoms of major depressive disorder (MDD) **.** However, the use of Transcranial Magnetic Stimulation is considered investigational in this study.

WHAT WILL HAPPEN DURING THIS STUDY?

During the study you will be scheduled to come for several visits.

Screening Visit: If you agree to participate, you will be asked to complete an approximately 2 and a half hour screening visit to determine if you are eligible to continue in the study. We will ask you questions about your medical history, mental health history, and medications you take. In the interview and questionnaires, you may skip questions you prefer not to answer. We will also perform a brief physical exam to evaluate your general health. If you are eligible to continue in the study and you choose to continue, all of the following will happen next.

Baseline Visit: After your screening visit, you will return for an in-person baseline visit lasting approximately 3 hours. During this visit, we will assess memory and problem-solving abilities using paper and pencil, computerized measures, and self-assessments of how you feel. These tests could include numbers, letters, symbols, words, or sentences. These tests will be repeated throughout the study.

Following testing, we will conduct an orientation and training session on the computerized cognitive training program, "Scientific Brain Training Pro" (www.scientificbraintrainingpro.com). We will educate you on the purpose of the cognitive training; create a profile of your personal cognitive strengths and weaknesses; and provide a manual to go over instructions, goals, and strategies for each exercise.

Motor Threshold (MT) determination: during your baseline visit, we also assess your motor threshold. Motor threshold is the lowest amount of magnetic stimulation needed to cause a muscle in your hand to react. This will help us determine the dose for the magnetic stimulation. We will check the MT by placing a magnetic coil over your scalp, on an area of the brain called motor strip. This area is responsible for movement of your body parts. We will apply magnetic pulses one at the time to induce a twitch on your thumb and/or fingers on the opposite hand of where we placed the coil on your scalp. This is not uncomfortable but you may feel a tingly sensation on your scalp. This takes about 30 min.

Transcranial Magnetic Stimulation: in this study, you will be randomly assigned (like flipping a coin) to receive transcranial magnetic stimulation or placebo (sham treatment) in a series of sessions. During the intervention sessions, you will be seated upright on a recliner while wearing earplugs. The magnet will be positioned on the left side of your brain over the area corresponding to the dorso-lateral pre frontal cortex, that is the area of the brain responsible for things like thinking and decision making. Magnetic pulses will be delivered on and off. You may feel a tingling or a tapping sensation on your scalp and a clicking sound. This stimulation takes about 12.5 min. Then the same procedure will be repeated on the right side of the head. If you are assigned to receive a sham intervention, stimulation will be delivered mimicking the pulse frequency, sound, sensation of the active stimulation but with no active magnetic pulse delivery.

Computerized cognitive training: In this study, everyone will receive a computerized cognitive training following the Transcranial Magnetic Stimulation or Sham treatment. We will use the computerized cognitive training program, "Scientific Brain Training Pro" (www.scientificbraintrainingpro.com). We will ask you to complete computerized exercises. This will take around 45 min.

The sessions will be done 3 times per week for 2 weeks. Each session will be identical to the one you received on day one. This means that you will receive either Transcranial Magnetic Stimulation or placebo and cognitive training in each visit. Each visit will take around one and a half hours.

At the end of the 6 sessions, you will be asked to complete thinking and functioning assessments. The last visit will take around two and a half hours to complete.

Should you fail to show up to scheduled appointments, we will attempt to contact you by phone and mail using the contact information you provided us during the initial visit.

Will you save my samples or research data to use in future research studies?

As part of this study, we are obtaining data from you. We would like to use this data for studies going on right now as well as studies that are conducted in the future. These studies may provide additional information that will be helpful in understanding cognitive impairment in individuals with schizophrenia or schizoaffective disorder, or other diseases or conditions, including research to develop investigational tests, treatments, drugs or devices that are not yet approved by the U.S. Food and Drug Administration. It is unlikely that what we learn from these studies will have a direct benefit to you. There are no plans to provide financial compensation to you should this occur. By allowing us to use your data you give up any property rights you may have in the data.

We will share your data with other researchers. They may be doing research in areas similar to this research or in other unrelated areas. These researchers may be at Washington University, at other research centers and institutions, or industry sponsors of research. We may also share your research data with large data repositories (a repository is a database of information) for broad sharing with the research community. If your individual research data is placed in one of these repositories only qualified researchers, who have received prior approval from individuals that monitor the use of the data, will be able to look at your information.

If you change your mind and do not want us to store and use your data for future research you should contact the research team member(s) identified at the top of this document. The data will no longer be used for research purposes. However, if some research with your data has already been completed, the information from that research may still be used. Also, if the data has been shared with other researchers it might not be possible to withdraw it to the extent it has been shared.

Please place your initials in the blank next to Yes or No for each of the questions below:

My data may be stored and used for future research as described above.

_____ Yes _____ No
Initials Initials

My data may be shared with other researchers and used by these researchers for the future research as described above.

_____ Yes _____ No

Initials Initials

HOW MANY PEOPLE WILL PARTICIPATE?

Approximately 35 people will take part in this study conducted by investigators at Washington University.

HOW LONG WILL I BE IN THIS STUDY?

If you agree to take part in this study, your involvement will last for up to 4 weeks.

- **The screening visit is about 2 hours and a half**
- **The baseline visit is about 3 hours**
- **Each intervention session will take about one hour and a half**
- **The last visit will take around 2 hours and a half**

WHAT ARE THE RISKS OF THIS STUDY?

You may experience one or more of the risks indicated below from being in this study. In addition to these, there may be other unknown risks, or risks that we did not anticipate, associated with being in this study.

Risks associated with Transcranial Magnetic Stimulation:
Likely/common:

- Mild headache
- Discomfort on the scalp at the stimulation site
- Tingling or pressure in the head
- Twitching in the scalp or face muscles during stimulation

Less likely/less common:

- Moderate intensity headache
- Nausea
- Vertigo (sensation of head spinning)
- Hearing loss (decreased by wearing earplugs)

Rare:
Life threatening:

- continuous seizure requiring emergency treatment

Serious:

- brief seizure

Mild:

- significant headache
- mania/hypomania (a period of excessive excitement, euphoria, over activity and possible delusions)

Rarely, the study intervention is associated with an increased risk of seizure. To decrease this risk, you will not be included in the study if you have a history of seizures. In the unlikely event that you experience a seizure, you will be asked to go to the emergency room for evaluation. If you experience a

seizure while receiving the study intervention, it will be unsafe for you to undergo more intervention sessions, therefore you will be withdrawn from the study.

Risks associated with computerized cognitive training:
While using the computerized cognitive training, you may feel frustrated, weary, have an inability to focus on tasks, or eye strain from looking at a computer screen.

Risks associated with questionnaires, study instruments and measures:
You may find some of the questions and procedures to be boring or difficult to answer and thus mildly distressing. You may experience some discomfort when answering some questions. Highly trained research staff will administer all assessments. Please let staff know if you feel any discomfort so they may discuss this with you.

Other risks:
Suicide risk: Because schizophrenia and schizoaffective disorder are associated with suicidal thoughts and behaviors, you may experience suicidal thoughts during your participation in the study. We ask that you please tell the study physician and or the study staff if you are experiencing suicidal thoughts or suicidal behaviors.

Breach of confidentiality: One risk of participating in this study is that confidential information about you may be accidentally disclosed. We will use our best efforts to keep the information about you secure. Please see the section in this consent form titled *"How will you keep my information confidential?"* for more information.

WHAT ARE THE BENEFITS OF THIS STUDY?

You may or may not benefit from being in this study.

However, we hope that, in the future, other people might benefit from this study because results of this research may lead to treatment or intervention that could improve cognitive functioning for adults with schizophrenia or schizoaffective disorder.

WILL IT COST ME ANYTHING TO BE IN THIS STUDY?

You will not have any costs for being in this research study. You and/or your medical/hospital insurance provider will remain responsible for your regular medical care expenses.

WILL I BE PAID FOR PARTICIPATING?

You will be paid for being in this research study. You will need to provide your social security number (SSN) in order for us to pay you. You may choose to participate without being paid if you do not wish to provide your social security number (SSN) for this purpose. You may also need to provide your address if a check will be mailed to you. Checks mailed to participants usually arrive with 4-6 weeks of the completed visit. If your social security number is obtained for payment purposes only, it will not be

retained for research purposes.

You will be paid up to $110 for your time and effort. If you do not complete all study visits, you will be paid for the visits you complete. For the following visits, you will receive: $15 for the screening visit, $10 for the baseline visit, $10 for each of the intervention visits and $25 for the last visit.

WHO IS FUNDING THIS STUDY?

The University and the research team are not receiving payment from other agencies, organizations, or companies to conduct this research study.

WHAT IF I AM INJURED AS A RESULT OF THIS STUDY?

Washington University investigators and staff will try to reduce, control, and treat any complications from this research. If you feel you are injured because of the study, please contact the investigator at 314-333-2141and/or the Human Research Protection Office at 1-(800)-438-0445.

Decisions about whether payment for medical treatment for injuries relating to your participation in research will be made by Washington University**.** If you need to seek medical care for a research-related injury, please notify the investigator as soon as possible.

HOW WILL YOU KEEP MY INFORMATION CONFIDENTIAL?

Other people such as those indicated below may become aware of your participation in this study and may inspect and copy records pertaining to this research. Some of these records could contain information that personally identifies you. We will keep your participation in this research study confidential to the extent permitted by law.

- Government representatives (including the Office for Human Research Protections) to complete federal or state responsibilities
- The U.S. Food and Drug Administration
- Your primary care physician if a medical condition that needs urgent attention is discovered.
- Hospital or University representatives, to complete Hospital or University responsibilities
- Information about your participation in this study may be documented in your health care records and be will be available to anyone with access to your health care record, including your health insurance company. This information may also be released as part of a release of information request.
- The last four digits of your social security number may be used in hospital or University systems to track billing information for research procedures.
- Washington University's Institutional Review Board (a committee that oversees the conduct of research involving human participants) and the Human Research Protection Office. The Institutional Review Board has reviewed and approved this study.

To help protect your confidentiality, we will store all data obtained from this research in a locked file cabinet and/or secured password database or computer. Your identity on these records will be indicated by an ID number rather than by your name. The study staff will maintain a document that links your ID number to your name, but this will be stored separately from the study data. All staff involved with this project have been thoroughly trained in the protection of research participants. Any report or article that we write will not include information that can directly identify you. The journals that publish these reports or articles require that we share your information that was collected for this study with others. Sharing this information will allow others to make sure the results of this study are correct and help develop new ideas for research. Your information will be shared in a way that cannot directly identify you.

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.

We will disclose to the proper authorities information shared with us or activities we observe concerning abuse, neglect or harm to others or yourself.

Are there additional protections for my health information

Protected Health Information (PHI) is health information that identifies you. PHI is protected by federal law under HIPAA (the Health Insurance Portability and Accountability Act). To take part in this research, you must give the research team permission to use and disclose (share) your PHI for the study as explained in this consent form. The research team will follow state and federal laws and may share your health information with the agencies and people listed under the previous section titled, "How will you keep my information confidential?"

Once your health information is shared with someone outside of the research team, it may no longer be protected by HIPAA.

The research team will only use and share your information as talked about in this form or as permitted or required by law. When possible, the research team will make sure information cannot be linked to you (de-identified). Once information is de-identified, it may be used and shared for other purposes not discussed in this consent form. If you have questions or concerns about your privacy and the use of your PHI, please contact the University's Privacy Officer at 866-747-4975.

Although you will not be allowed to see the study information, you may be given access to your health care records by contacting your health care provider.

If you decide not to sign this form, it will not affect

- your treatment or the care given by your health provider.
- your insurance payment or enrollment in any health plans.
- any benefits to which you are entitled.

However, it will not be possible for you to take part in the study.

If you sign this form:

- You authorize the use of your PHI for this research
- This authorization does not expire.
- You may later change your mind and not let the research team use or share your information (you may revoke your authorization).
    - To revoke your authorization, complete the withdrawal letter, found in the Participant section of the Human Research Protection Office website at https://hrpo.wustl.edu/participants/withdrawing-from-a-study/ or you may request that the investigator send you a copy of the letter.
        - **If you revoke your authorization:**
            - The research team may only use and share information already collected for the study.
            - Your information may still be used and shared as necessary to maintain the integrity of the research, for example, to account for a participant's withdrawal from the research study or for safety reasons.
            - You will not be allowed to continue to participate in the study.

Can we contact you by email?

We would like to contact you by email for the purposes listed below. Some of these emails may contain health information that identifies you.

- **Appointment scheduling**
- **Follow-up contact regarding your questions or report of a side effect**

Only the research team will have access to your email communications. We will only communicate by email to send you the information listed above. If you have any questions or need to contact us for an urgent or emergent situation, please contact the research team member identified at the top of this document.

You should be aware that there are risks associated with sending your health information via email.

- There is always a risk that the message could be intercepted or sent to the wrong email address. To avoid sending messages to the wrong email address, the first email we send you will be a test message to ensure we have the correct email address.
- When using any computer you should be careful to protect your username and password. Make sure you log-out before getting up from the computer.
- If you share a home computer with other family members, and do not want them to know you are participating in this study make sure you provide an email address that only you can access.
- Your employer will have access to any email communications sent or received on any electronic devices used for work or through a work server.

Do you agree to allow us to send your health information via email?

_____ **Yes** _____ **No**
Initials **Initials**

IS BEING IN THIS STUDY VOLUNTARY?

Taking part in this research study is completely voluntary. You may choose not to take part at all. If you decide to be in this study, you may stop participating at any time. Any data that was collected as part of your participation in the study will remain as part of the study records and cannot be removed.

If you decide not to be in this study, or if you stop participating at any time, you won't be penalized or lose any benefits for which you otherwise qualify.

What if I decide to withdraw from the study?

You may withdraw by telling the study team you are no longer interested in participating in the study or you may send in a withdrawal letter. A sample withdrawal letter can be found at https://hrpo.wustl.edu/participants/withdrawing-from-a-study/ under Withdrawing from a Research Study.

If you decide to leave the study early, we may ask you to complete a final study visit, potentially including memory and problem-solving assessments.

Will I receive new information about the study while participating?

If we obtain any new information during this study that might affect your willingness to continue participating in the study, we'll promptly provide you with that information.

Can someone else end my participation in this study?

Under certain circumstances, the investigator might decide to end your participation in this research study earlier than planned. This might happen for no reason or because in our judgment it would not be safe for you to continue.

WHAT IF I HAVE QUESTIONS?

We encourage you to ask questions. If you have any questions about the research study itself, please contact Dr. Rita Haddad, (314) 333- 2141. If you experience a research-related injury, please contact: Dr. Rita Haddad, (314) 333- 2141

If you have questions, concerns, or complaints about your rights as a research participant, please contact the Human Research Protection Office at 660 South Euclid Avenue, Campus Box 8089, St. Louis, MO 63110, 1-(800)-438-0445, or email hrpo@wustl.edu. General information about being a research participant can be found on the Human Research Protection Office web site, http://hrpo.wustl.edu. To offer input about your experiences as a research participant or to speak to someone other than the research staff, call the Human Research Protection Office at the number above.

This consent form is not a contract. It is a written explanation of what will happen during the study if you decide to participate. You are not waiving any legal rights by agreeing to participate in this study. As a participant you have rights and responsibilities as described in this document and including:

- To be given enough time before signing below to weigh the risks and potential benefits and decide if you want to participate without any pressure from the research team or others.
- To understand all of the information included in the document, have your questions answered, and receive an explanation of anything you do not understand.
- To follow the procedures described in this document and the instructions of the research team to the best of your ability unless you choose to stop your participation in the research study.
- To give the research team accurate and complete information.
- To tell the research team promptly about any problems you have related to your participation, or if you are unable to continue and wish to stop participating in the research study.

Your signature indicates that this research study has been explained to you, that your questions have been answered, and that you agree to take part in this study. You will receive a signed and dated copy of this form.

Do not sign this form if today's date is after EXPIRATION DATE: 09/06/22.

_____ _____
(Signature of Participant) (Date)

_____
(Participant's name – printed)

Statement of Person Who Obtained Consent

The information in this document has been discussed with the participant or, where appropriate, with the participant's legally authorized representative. The participant has indicated that they understand they risks, benefits, and procedures involved with participation in this research study.

_____ _____
(Signature of Person who Obtained Consent) (Date)

_____
(Name of Person who Obtained Consent - printed)