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**Approved by the Beth Israel Deaconess Medical Center
Committee on Clinical Investigations:**Consent Approval Date: 12/3/2021Protocol Number: 2021P000749

INFORMED CONSENT FORM TO TAKE PART IN A RESEARCH STUDY

SUBJECT'S NAME:
TITLE OF RESEARCH PROTOCOL: Behavioral impact and neural correlates of network-based brain stimulation in schizophrenia
PRINCIPAL INVESTIGATOR: Roscoe Brady, MD, PhD
PROTOCOL NUMBER: 2021P000749

KEY INFORMATION

The following is a short summary of this study to help you decide whether or not to be a part of this study. More detailed information is listed later on in this form.

Why am I being invited to take part in a research study?

You are invited to take part in a research study about the use of a technique of brain stimulation to improve mental functioning in schizophrenia and schizoaffective disorder, diseases that may affect the way you think. The method of brain stimulation is called transcranial magnetic stimulation (TMS).

You are being asked to take part in this study because you are an adult with schizophrenia or schizoaffective disorder who smokes cigarettes. This is NOT a smoking cessation study.

What should I know about a research study?

- Someone will explain this research study to you.
- Whether or not you take part is up to you.
- Your participation is completely voluntary.
- You can choose not to take part.
- You can agree to take part and later change your mind.
- Your decision will not be held against you.
- Your refusal to participate will not result in any consequences or any loss of benefits that you are otherwise entitled to receive.
- You can ask all the questions you want before you decide.
- If you choose not to take part, or if you leave the study, your decision will in no way harm your relationship with any member of the research team or any other individuals at Beth Israel Deaconess Medical Center or your ability to access services at the Department of Mental Health and Massachusetts Mental Health Center.

Why is this research being done?



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The main purpose of this study is to learn how stimulating parts of your brain that are related to cognition (how you think and solve problems) influences your brain activity. We will stimulate your brain using transcranial magnetic stimulation (**TMS**). **TMS** is a noninvasive way of stimulating the brain. TMS uses a magnetic field to cause changes in activity in the brain. The magnetic field is produced by a coil that is held next to your scalp.

Functional magnetic resonance imaging (**fMRI**) will be used to identify areas in your brain that we will stimulate and to examine the networks related to cognition. **fMRI** allows investigators to look at changes in blood flow to areas of the brain and to visualize brain networks. This information can be used to determine which networks we are stimulating with TMS.

How long will the research last and what will I need to do?

We expect that you will be in this research study for about 1 month.

You will be asked to attend 5 study visits. The first study visit is a Screening Visit, where we will determine if you are eligible to participate in this research study. At this visit, we will ask you questions, ask you to fill out questionnaires, complete neuropsychology testing that will measure your thinking, and to provide a urine sample for drug use and pregnancy testing. We will also ask you to do a breath test to measure how much you smoke. The 2nd study visit is a Baseline MRI visit, where you will undergo an MRI, answer questionnaires, and do another smoking breath test. At the 3rd, 4th, and 5th study visits, you will answer some questionnaires, perform tests of your thinking, do a smoking breath test, undergo 1 session of TMS and have an fMRI before and after TMS.

More detailed information about the study procedures can be found under **“DESCRIPTION OF STUDY DETAILS”**.

Is there any way being in this study could be harmful to me?

You may experience mild pain or headache during or after receiving TMS. You may also experience frustration or emotional distress resulting from a series of questions in a survey or questionnaire.

More detailed information about the risks can be found under **“RISKS AND DISCOMFORTS”**.

Will being in this study help me in any way?

There is no direct benefit to you from being in this study. However, your participation may help others in the future as a result of knowledge gained from the research.

What happens if I do not want to be in this research?

Participation in research is completely voluntary. You can decide to participate or not to participate.

Your alternative to participating in this research study is to not participate.

DETAILED INFORMATION SECTION

Please read this consent form carefully and ask the investigators or study staff to explain any words or



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information that you do not clearly understand. Once you read this consent form and understand what your participation in this study will involve, you will be asked to sign this form if you wish to take part. You will be given a signed copy of the form to keep for your records.

If you decide to withdraw from this study, this will not affect your access to services at the Department of Mental Health or Massachusetts Mental Health Center.

DISCLOSURE OF SPECIAL INTERESTS OF BIDMC AND INVESTIGATORS

This study is being conducted by Roscoe Brady, MD, PhD and is funded by the Sidney R. Baer, Jr. Foundation Fellowship. The funding agency in this study (Baer Foundation) is paying Beth Israel Deaconess Medical Center (BIDMC) and Dr. Brady to perform this research. Neither BIDMC nor Dr. Brady have any additional interests in this research project.

WHOM TO CONTACT IF YOU HAVE QUESTIONS OR PROBLEMS

If you have any questions, concerns or complaints about this research or experience any problems, you should contact Dr. Roscoe Brady at 617-754-1261.

PURPOSE

The main purpose of this study is to learn how stimulating networks in your brain that are related to cognition (how you think and solve problems) and cigarette smoking influences those networks. In previous research, we have observed that there are changes in brain network function that are related to cigarette smoking and to cognition. We will stimulate your brain networks using transcranial magnetic stimulation (**TMS**). Functional magnetic resonance imaging (**fMRI**) will be used to identify areas in your brain that we will stimulate and to examine the networks related to cognition and cigarette smoking. In this study, we will test if TMS can be used to change brain networks in a way that also changes cognition and cigarette smoking.

TMS is a noninvasive way of stimulating the brain. TMS uses a magnetic field to cause changes in activity in the brain. The magnetic field is produced by a coil that is held next to your scalp. In this study we will be stimulating your brain to learn more about how TMS may affect the way you think and solve problems.

The device involved in this study, TMS, is investigational. This means that the study device is still being tested in research studies and is not approved by the Food and Drug Administration [FDA] for the way that it is being used in this study. This particular device, TMS, has been approved by the FDA for use in other diseases or conditions, but the FDA has not reviewed its use in schizophrenia or schizoaffective disorder.

fMRI allows investigators to look at changes in blood flow to areas of the brain and to visualize brain networks. This information can be used to determine which networks we are stimulating with TMS.

STUDY PARTICIPANTS



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You have been asked to be in the study because you are an adult with schizophrenia or schizoaffective disorder who smokes cigarettes.

Approximately 50 people will take part in this study at Beth Israel Deaconess Medical Center.

DESCRIPTION OF STUDY DETAILS

If you agree to be in this study, you will be in this research study for about 1 month.

After you sign the consent form, the following things will happen:

1. **Screening Procedures:** Screening procedures are tests and procedures that will be done to determine if you are eligible to take part in the research study. This process should take approximately 4 hours and will take place at BIDMC.

For this research study, the screening procedures include:

- Answering questions to learn:
 - if it is safe for you to have transcranial magnetic stimulation (TMS) and an MRI – for example, you will be asked if you have any metal in your body.
 - about your demographics, for example your age, education history.
- You will review with the study team:
 - your medical and medication history
 - your psychiatric history
 - your nicotine and substance use history
 - You will be asked to sign an authorization form that will allow us to contact your psychiatric provider in order to verify your diagnosis
- You will be asked to do a breath test to measure how much you smoke
- You will participate in an interview with the study doctor that will include:
 - An interview about your psychiatric history
 - Questions about symptoms that you experience
- You will complete neuropsychology testing that will assess your cognitive functioning (thinking). This testing will take about 1-2 hours.
- You will be asked to provide the following samples:
 - A urine sample for a urine drug screen
 - A urine sample to do a pregnancy test if you are a women of childbearing potential. If the test finds that you are pregnant, you will not be able to participate in the study

If you receive services from the Department of Mental Health (DMH) you will also be asked to sign a separate DMH authorization form permitting the research investigators to contact your psychiatric provider in order to verify your diagnosis. This authorization form will have an expiration date that will indicate how long we can contact your provider.



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Please note that if we develop concerns about your mental health during any part of this study (e.g., if we are concerned that you may harm yourself or others), we will reach out to your healthcare providers. We may also arrange for you to be evaluated at the Beth Israel Deaconess Medical Center emergency room if needed.

2. TMS Procedures:

In this study, you will receive 3 different types of TMS, 1 type at each of the TMS/MRI visits: 1) intermittent theta burst TMS (iTBS), 2) continuous theta burst (cTBS), and 3) sham TMS. iTBS and cTBS use different frequencies to affect brain activity. It is thought that iTBS can facilitate change in brain activity, while cTBS is thought to prevent change in brain activity. Sham means that you will receive stimulation that feels like "real" TMS but is not. Sham TMS contains no real stimulation. We use sham to learn whether the results of the study are from the TMS or not from the TMS. The order in which you receive each type of TMS will be randomly assigned (like the flip of a coin). All TMS will take place at the Harvard University Center for Brain Science.

You will not know which type of TMS you are receiving at each visit. However, this information can be learned in case of an emergency.

3. Research Procedures: If you qualify to take part in this research study, you will undergo these research procedures:

We will do our best to schedule our testing to accommodate you. The TMS visits will occur at least 2 days apart.

Baseline MRI Visit:

The following will happen during your baseline visit:

- The Baseline MRI Visit will take place at the Harvard University Center for Brain Science.
- You will participate in clinical symptom interviews where we assess your mood and your signs and symptoms of schizophrenia or schizoaffective disorder.
- You will complete questionnaires about your smoking behavior and any drug use
- We will measure your smoking using a breath test
- Magnetic Resonance Imaging (MRI)

The MRI will take around 1 – 1 ½ hours to complete.

MRI is a method of taking pictures of the brain and of the blood flow in the brain, using a large magnet and radio signals. You will be asked to lie down on a platform that can



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slide into the magnet. An MRI imaging coil, which is made from special wires that are covered in plastic, will be placed around your head. Foam pads will be placed around your head to limit head movement during the scan. During the scan, you will be asked to lie still on your back for about 20 to 30 minutes. You will hear a loud knocking or hammering noise while the MRI is taking pictures, but the process itself will be painless. You will be given disposable earplugs to use to help make the noise less noticeable. During the procedure, you will be in constant contact with the MRI technician through an intercom. If at any time during the scan you feel too uncomfortable to continue, no matter what the reason, the procedure will be immediately stopped and you will be removed from the magnet. (MRI scanner)

This is not an MRI to be used to diagnose problems; it is used for research purposes only. This means that the pictures will not be looked at by a radiologist. A radiologist is a doctor that looks at pictures taken by an MRI for potential diseases and damage. In the event that an incidental finding is noticed by the study staff, the scan will be looked at by Dr. Brady, who will then determine whether to send it to a radiologist to be reviewed. Any results will be given to you and you will be referred to a neurologist if a follow up is recommended.

During each MRI, you will complete a computer game called the Gradual Continuous Performance Task (gradCPT). The gradCPT is a behavioral task done on a computer that measures how closely you pay attention.

- This visit should take about 2 hours. The study staff will arrange transportation to and from study visits.

TMS/MRI Visits #1-3:

At each TMS/MRI visit, you will receive 1 of 3 types of TMS: 1) intermittent theta burst TMS (iTBS), 2) continuous theta burst (cTBS), or 3) sham TMS.

The following will happen during each TMS/MRI visit:

- If you are capable of getting pregnant and your last negative pregnancy test was more than 30 days ago, you will be asked to provide a sample for repeat urine pregnancy testing before receiving TMS. If the test finds that you are pregnant, you will not be able to participate in the study
- You will complete cognitive assessments, which test your thinking
- You will complete questionnaires about your smoking behavior and substance use
- We will measure your smoking using a breath test
- You will have 1 session of TMS, which will take about 15 minutes.
- You will have an MRI before and after the TMS session. The MRI will take 1-1 ½ hours.

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- During each MRI, you will complete a computer game called the Gradual Continuous Performance Task (gradCPT). The gradCPT is a behavioral task done on a computer that measures how closely you pay attention.

For each TMS session, the following will happen:

- You will be seated in a chair
- You will have Electromyography (EMG) electrodes – small metal plates - placed onto your hands which will be used to monitor muscle movements. The electrodes will not hurt at all.
- The research team will place a coil that is about the size of a telephone receiver against your head.
 - The coil is made up of wires that are covered in plastic.
 - A researcher will hold the coil firmly, but comfortably against your scalp.
 - The coil produces a magnetic field about the size of the tip of your finger on the targeted part of your head that will briefly affect your brain
- You will hear a clicking noise when the magnetic stimulation or pulse is delivered, and you might feel a twitch of your scalp muscle. This will feel like a tap or a pinch on your scalp.
- When the magnetic pulse is delivered, your fingers may twitch.
- The TMS coil will be placed on your scalp for the stimulation. You will be asked to wear earplugs during the TMS session.

After *the treatment*, the following will happen:

- You will answer questions about any possible side effects

The study staff will arrange transportation to and from study visits.

Study Visit	Screening	Baseline MRI	TMS #1	TMS #2	TMS #3
Consent	X				
Capacity	X				
Demographics	X				
Medical History	X				
Safety Screening	X				
Smoking and Drug Questionnaires	X	X	X	X	X
Pregnancy Test (for women of childbearing potential)	X				
Urine Drug Test	X				



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Personalizing TMS to you			X		
Symptom Questionnaires		X			
MRI		X	X	X	X
TMS			X	X	X
Computer Game		X	X	X	X
Cognitive Testing	X		X	X	X
TMS Side Effects			X	X	X
Visit Duration	4h	2h	2h	2h	2h
Compensation		\$100	\$100	\$100	\$200

Individual Research Results

Your study doctor will disclose any clinically relevant research results to you, including a urine pregnancy test and urine drug test.

Most tests done on samples in research studies are only for research and have no clear meaning for health care. The research testing done in this study is just a stepping stone to learning more about schizophrenia.

While you should not expect to receive any results from the research testing, if we find that research results from your sample are of high medical importance, we may attempt to contact your medical provider to discuss the results. In some situations, follow up testing might be needed in a Clinical Laboratory Improvement Amendments (CLIA) certified clinical lab. You and your medical insurer may be responsible for the costs of these tests and any follow up care, including deductibles and co-payments. It is possible that you will never be contacted with individual research findings. This does not mean that you don't have or won't develop an important health problem.

Information and Biological Samples

Your information and biological samples will be used and shared with the researchers involved in this study to conduct the research. The consent form provides information on who will have access to identifiable information and identifiable biological samples during the study. We also want you to know that your information or biological samples may be stripped of any identifiers (for example your name, medical record number or date of birth) and used for future research studies or distributed to another researcher for future research studies without additional informed consent. BIDMC researchers or other third party researchers may use your information and samples in other scientific research, product testing or commercial development. It is unknown whether a product will ultimately be developed from the research described in this consent form or from any such work that may be performed by BIDMC or other third parties receiving your information or biological samples. In signing this consent form, you are acknowledging and voluntarily consenting to the possibility that your information and biological samples may be used for commercial purposes. For example, your samples



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and information may be used to develop a new product or medical test to be sold. BIDMC and other researchers may benefit if this happens. There are no plans to pay you if your samples and information are used for this purpose.

If your identifiers are removed, we will not be able to destroy or remove your information or biological samples from distributed information or samples. As part of this research program and as further explained in this form, samples of your tissue and/or information about your medical history may be provided to other researchers and/or outside collaborators.

RISKS AND DISCOMFORTS

As a result of your participation in this study, you are at risk for side effects listed in this section. You should discuss these with the investigator and with your regular doctor if you choose.

TMS

More Common

Pain:

As many as 20-40% of people having TMS experiences headaches – that is 4 in 10 participants. You may have a pain – such as a headache, pain in your face or neck pain during or after TMS.

Rare:

Hearing Problems

The TMS procedure includes a loud clicking noise throughout. It is possible that you could experience a temporary change in your hearing. There is one report of someone whose hearing protection fell out who experienced permanent hearing loss from TMS. You will wear earplugs during the TMS to reduce the noise to prevent the risk of hearing problems. We will ask you to let us know immediately if your ear plug loosen, becomes detached or falls out.

You will be promptly referred for hearing tests if you experience hearing loss, ringing in the ear, or ear fullness following completion of the TMS.

Seizures:

TMS may sometimes cause a seizure. This is rare and occurs in less than 1 in 1000 participants. A seizure may be thought of as a convulsion where a person's body shakes. Many seizures are not like this. Some have very mild symptoms. If you have a seizure, you will receive immediate medical care. You may be transferred to the emergency room.

Experiencing a seizure caused by TMS does not mean that you will have another seizure. Participants who had seizures from TMS have not had any continued seizure related health problems.



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Syncope (Fainting):

It is possible that you could faint during TMS. This does not happen often, but can happen if you are anxious, nervous, or have not eaten. You could immediately tell the study staff if you feel dizzy, lightheaded or that you might pass out.

If you have any of the above symptoms, the TMS will be stopped immediately. You will be monitored until you are feeling better.

Concentration:

TMS could cause changes in your attention and concentration. It could be related to some of the study procedures like wearing a tight cap or headband and positioning. This could also be related to other side effects like headache or sleepiness. These changes would be very mild. If this occurs you will experience these changes for less than 1 hour. These changes happen very rarely.

Mood:

If you have depression or mood disorder, you may experience an episode of mania (an abnormally high mood that can be dangerous) when treated with TMS, although the risk is low. There have been rare reports of psychiatric problems such as psychotic symptoms (personality changes, acting irrationally and losing sense of reality), anxiety, agitation, suicidal thoughts (thoughts of killing or harming yourself) and insomnia (trouble sleeping). These problems have not been found to be more common in people with schizophrenia or schizoaffective disorder.

In every case, these side effects from TMS did not last long, resolved after TMS was stopped or when medication was given.

In a rare circumstance in which you experience suicidal thoughts, Dr. Brady or a covering physician will be contacted to provide care and, if necessary, arrange transportation to an emergency room for further care.

Dental Pain:

The possibility of dental pain during TMS has been reported. If this happens to you, alert the study investigator. The TMS will be immediately stopped. This may mean that you have a cavity and that you need dental care. This dental pain should not lead to any lasting problems or complications.

Hallucinations:

The possibility that hallucinations may increase in frequency as a result of TMS has been reported. If this happens to you, alert the study investigator. The TMS will be immediately stopped. You will be monitored until you are feeling better.

Although TMS has been used worldwide since 1984, there may be complications that are not yet known.



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Pregnancy

Because of the effects of TMS on the developing fetus are not known, you may not participate in this study if you are pregnant. You will be required to take a pregnancy test to verify that you are not pregnant before TMS will be given.

For the duration of the study, if you are engaged in sexual activity that could cause you or your partner(s) to become pregnant, you and your partner(s) must agree to use a highly effective method of birth control or abstain from sexual activity that could cause you or your partner(s) to become pregnant.

The methods of highly effective birth control for this study are below:

1. Contraceptive implant, such as Nexplanon or Implanon
2. Levonorgestrel or copper intrauterine device (IUD), such as Mirena, Skyla, ParaGard or Liletta
3. Permanent female sterilization, such as tubal ligation or Essure with confirmed tubal occlusion
4. Male partner(s) has had a vasectomy more than three months before study enrollment
5. Oral contraceptives pill, patch or ring
6. Injectable contraception, such as Depo Provera
7. Consistent use of a barrier method, such as diaphragm with spermicide or condoms

If you believe you have become pregnant while participating in this study, you must inform your study doctor immediately. In this case, the study doctor may order a pregnancy test, and you will be withdrawn from the study if you are pregnant.

Electromyography (EMG)

The sticky pads used for EMG may cause skin irritation or redness. Taking the sticky pads off causes discomfort similar to when taking off a band-aid.

MRI

MRI is a safe and painless procedure for most people. However, it is not safe for people who have pacemakers, ear implants, shrapnel injuries, or other types of metal or electric devices in their body, such persons will not be allowed participate in the study. You must tell your doctor and the investigator about any operations you have had and any metal you may have in your body, so it can be decided if it is safe for you to proceed with the scan. We will also require that all people involved with the study remove all metal from their clothing and all metal objects from their pockets. No metal objects will be allowed into the magnet room at any time.

You may also experience mild psychological stress as a result of being in an MRI machine for the following reasons:

- Some people get a feeling of claustrophobia (fear of small places) while lying in the MRI. The sides and top of the scanner are very close to your face and body. If you suffer from claustrophobia, we ask that you do not participate in the study. The examiner and the



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technologist performing the scan will have voice contact with you constantly while you are in the MRI. If you feel the need to be removed from the MRI at any time, the scan will be stopped immediately.

- Lying in the MRI for an extended period of time may cause temporary discomfort. However, the investigators will make every effort to make you as comfortable as possible.
- The MRI makes loud banging noises as it takes pictures. Earplugs will be offered to you to reduce this noise.

Cognitive Testing

You may feel frustrated or fatigued during the cognitive tasks. Breaks are built in to help avoid fatigue.

Psychological Stress:

There may be questions or moments during study interviews or assessments and tasks that make you feel uncomfortable, frustrated, or tired. You may refuse to answer any of the questions, and you may take a break at any time. If you do grow tired, a rest period can be given so you can complete the interview later. The interview can also be broken up into short sessions. You may stop your participation in the study at any time.

Participation in this study may be stressful. Due to the nature of these questions, you may find that this increased stress may make your symptoms worse, such as paranoia. You may become paranoid about technology. If you feel worse at any time, you should inform study staff. We will be checking on your symptoms during the research study. You may stop participation in the study at any time.

Loss of confidentiality

There is the potential for loss of confidentiality by participating in this study. Every effort will be made to protect the confidentiality of your identifiable information. However, if your participation becomes known, it could create a problem or hardship for you depending upon the type of information disclosed.

CONFIDENTIALITY

Information learned about you during this research program will be maintained confidentially by the research staff as described in this form.

Information learned from your participation in this study and from your medical record may be reviewed and photocopied by the Food and Drug Administration (FDA) and/or other federal and state regulatory agencies, including the Department of Mental Health and Massachusetts Mental Health Center, and by the transcranial magnetic stimulation device manufacturer, accreditation agencies, the Committee on Clinical Investigations, the Human Subjects Protection Office and others involved in research administration of the Beth Israel Deaconess Medical Center. Information resulting from this study and from your medical record may be used for research purposes and may be published;



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however, you will not be identified by name in such publications.

Massachusetts law requires that certain trained individuals (mandated reporters) disclose to the proper authorities any information shared with them about abuse of the elderly, abuse of mentally ill or developmentally disabled persons, child abuse, or child sexual abuse. The investigators on this study are mandated reporters. The investigators may also be required by law to report threats of harm that you make, either to yourself or to others.

MEDICAL RECORD

A copy of this consent form and information collected during this research may become part of your medical record, if the information is relevant to the care you receive at Beth Israel Deaconess Medical Center. Medical records are considered permanent records; therefore, information cannot be deleted from the record. Medical records are available to health care professionals at Beth Israel Deaconess Medical Center and may be reviewed by staff when carrying out their responsibilities, as well as by external parties such as health care insurers and others in certain circumstances. If you are not currently a patient at Beth Israel Deaconess Medical Center and do not have a medical record at Beth Israel Deaconess Medical Center, one may be created for you for your participation in this research. You may also be required to register as a patient of Beth Israel Deaconess Medical Center in order to participate in this research.

Information collected during this research will not be added to your medical records with the Massachusetts Mental Health Center.

POSSIBLE BENEFITS

There is no direct benefit to you from being in this study. However, your participation may help others in the future as a result of knowledge gained from the research.

OTHER AVAILABLE OPTIONS

Taking part in this study is voluntary. Instead of being in this study, you have the following options: to not participate in the study. Deciding not to participate in this study will not affect your access to services at the Department of Mental Health and Massachusetts Mental Health Center.

This research study is not meant to diagnose or treat medical problems. Participation in this research study does not take the place of routine physical examinations or visits to your regular doctor.

We recommend that you discuss these and other options with the investigator and your regular doctor so that you can make a well-informed decision about participating in this study.

IF YOU DECIDE NOT TO TAKE PART IN THE STUDY

Participation in this study is voluntary. You have the right to decide not to take part in this study. If you choose to participate, you have the right to leave the study at any time. Your decision to not participate will not result in any penalties or loss of benefits to you. The investigators will tell you



SUBJECT'S NAME:
TITLE OF RESEARCH PROTOCOL: Behavioral impact and neural correlates of network-based brain stimulation in schizophrenia
PRINCIPAL INVESTIGATOR'S NAME: ROSCOE BRADY, MD, PhD
PROTOCOL #: 2021P000749

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about new information that may affect your willingness to stay in this study.

If you decide not to participate in the study or decide to leave the study early, your decision will not affect your relationship with the research team or any other individual at Beth Israel Deaconess Medical Center, the Department of Mental Health, or Massachusetts Mental Health Center. A decision to withdraw from the study will not affect your access to services at the Department of Mental Health and Massachusetts Mental Health Center.

INVESTIGATORS RIGHT TO STOP THE STUDY

The investigators have the right to end your participation in this study if they determine that you no longer qualify to take part, or if it would be dangerous for you to continue, or if you do not follow study procedures as directed by the investigators. Beth Israel Deaconess Medical Center or the funding source may stop the study at any time.

COSTS AND/OR PAYMENTS TO YOU

COSTS COVERED BY STUDY

You will not be charged for the TMS nor for the MRI that are part of this research study.

PAYMENTS TO YOU:

For your participation in this study, you may receive up to \$500 paid by check. You will be paid for each study visit you attend. You will receive \$100 after completing the Screening and Baseline MRI Visits. You will receive \$100 for completing each of the TMS/MRI Visit #1 and #2. You will receive \$200 for completing TMS/MRI Visit #3. It may take up to 8 weeks for you to receive payment by check.

Any payments made to you may be taxable income to you. This does not include any payments you may receive to reimburse (pay you back) you for certain expenses like parking fees or travel. We are required to obtain your name and social security number for preparation and submission of Internal Revenue Service (IRS) Form 1099-Misc. You may receive an Internal Revenue Service Form 1099 from BIDMC if you receive more than \$600 or more in one calendar year for taking part in one or more research studies at BIDMC. Questions about your own tax status should be referred to your personal tax advisor.

COST OF RESEARCH RELATED INJURY:

If you are injured as a direct result of your participation in this study, you should contact the Investigator at the number provided under the section "Who to Call if You Have Questions" in this form. You will be offered the necessary care to treat your injury. We reserve the right to bill your insurance company or the sponsor, if appropriate, for the care you get for the injury. We will try to get these costs paid for, but you may be responsible for some of them. You may be responsible for



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all co-payments and deductibles required under your insurance. At this time there is no plan to reimburse you for items such as lost wages or lost time from work. By signing this consent form you have not given up any legal rights.

AUTHORIZATION FOR USE AND DISCLOSURE OF YOUR PROTECTED HEALTH INFORMATION

As part of this study, we will be collecting, using and sharing with others information about you. Please review this section carefully as it contains information about the federal privacy rules and the use and disclosure of your information.

DESCRIPTION OF PROTECTED HEALTH INFORMATION [PHI]

By signing this informed consent document, you are allowing the investigators and other authorized personnel to use and disclose health information about you. This may include information about you that already exists (for example: your medical records and other sources of health information, demographic information, the results of any laboratory tests, and mental health records if applicable, such as past diagnosis or case notes describing symptoms, as well as any new information generated as part of this study. This is your Protected Health Information.

PEOPLE/GROUPS AT BIDMC WHO WILL SHARE AND USE YOUR PROTECTED HEALTH INFORMATION

Your Protected Health Information may be shared with and used by investigators working on this study, including the supporting research team (such as research assistants and coordinators, statisticians, data managers, laboratory personnel, pharmacy personnel, and administrative assistants), and may also be shared with and used by other health care providers at BIDMC who have treated you in the past and have information relevant to the research, or who provide services to you in connection with the research. Your Protected Health Information may also be shared with the members and staff of the Committee on Clinical Investigations of Beth Israel Deaconess Medical Center, which is responsible for reviewing studies for the protection of the research subjects, so that it can carry out its oversight responsibilities with respect to the study.

PEOPLE/GROUPS OUTSIDE OF BIDMC TO WHOM YOUR PROTECTED HEALTH INFORMATION WILL BE DISCLOSED (SHARED) AND WHO MAY USE YOUR PROTECTED HEALTH INFORMATION

We will take care to maintain confidentiality and privacy about you and your Protected Health Information. We may share your Protected Health Information with the following groups so that they may carry out their duties related to this research study:

- The funding source and/or sponsor of this study Baer Foundation and, where applicable, the people and companies that the funding source and/or sponsor use to oversee, administer, or conduct the research (for example, clinical research organizations are companies that are sometimes hired by research sponsors to help manage and run a clinical research study)
- The other hospitals and medical centers taking part in this study and research collaborators at those institutions.
- Other research collaborators and supporting research team members taking part in this study

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- Any external health care providers who provide services to you in connection with this research
- Laboratories not affiliated with BIDMC that are involved in conducting tests related to the research
- Statisticians and other data monitors not affiliated with BIDMC
- The members and staff of any other IRBs (beyond the BIDMC Committee on Clinical Investigations) that oversee the research
- Centralized data collectors
- Your health insurance company
- The Food and Drug Administration [FDA], the Department of Health and Human Services [DHHS], the National Institute of Health [NIH], the Office for Human Research Protections [OHRP], the Massachusetts Department of Mental Health, the Massachusetts Department of Mental Health Institutional Review Board, Massachusetts Mental Health Center, and other federal and state agencies that may have jurisdiction over the research
- Hospital and Clinical Research Accrediting Agencies

Those who receive your Protected Health Information during the course of the research may not be required by the federal privacy regulations to protect it, and they may make further disclosures to others and use your information without being subject to penalties under those laws.

PURPOSE: WHY WE ARE USING AND SHARING YOUR PROTECTED HEALTH INFORMATION

The reason for using and sharing your Protected Health Information is to conduct and oversee the current, secondary, and future research described in this Informed Consent Document. There are many other reasons beyond the research for which BIDMC may use or disclose your Protected Health Information. Not all of these reasons require your express written authorization. For example, we will use and share your Protected Health Information to ensure that the research meets legal, institutional and accreditation requirements and to conduct public health activities. The various ways in which BIDMC may use and disclose your protected health information without your authorization are explained in a document called the Notice of Privacy Practices. If you have not received a copy of BIDMC's Notice of Privacy Practices, please ask us for one and review it before signing this form. In addition to signing this document, you may also be asked to sign a BIDMC General Agreement form acknowledging that you have received the BIDMC Notice of Privacy Practices.

NO EXPIRATION DATE – RIGHT TO WITHDRAW AUTHORIZATION

Your authorization for the use and disclosure of your Protected Health Information in this Study shall never expire. However, you may withdraw your authorization for the use and disclosure of your Protected Health Information at any time provided you notify the Principal Investigator in writing. If you would like to take back your authorization so that your Protected Health Information can no longer be used in this study, please send a letter notifying the Principal Investigator of your withdrawal of your authorization to Roscoe Brady, MD, PhD at 375 Longwood Ave., Suite 367, Boston, MA 02215. Please be aware that the investigators in this study will not be required to



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destroy or retrieve any of your Protected Health Information that has already been used or disclosed before the Principal Investigator receives your letter, and they are permitted to continue to use and disclose your previously collected information as necessary to complete the research.

REFUSAL TO SIGN

Your clinical treatment may not be conditioned upon whether you sign the Authorization for Research. However, if you choose not to sign this informed consent document and authorization for the use and disclosure of your Protected Health Information, you will not be allowed to take part in the research study.

RIGHT TO ACCESS AND COPY YOUR PHI

If you wish to review or copy your Protected Health Information as it is made part of your medical record, you may do so after the completion or termination of the study by sending a letter to the Principal Investigator requesting a copy of your Protected Health Information. You may not be allowed to inspect or copy your Protected Health Information until this study is completed or terminated.

ADDITIONAL CONTACT FOR QUESTIONS OR CONCERNS

You may contact the Human Subjects Protection Office at [617] 975-8500 in the event that you would like to obtain information or to offer input about the research study. This office is independent of the investigator or investigator's research staff and can also assist with questions relating to your rights as a participant in research, which may include questions, concerns or complaints about your participation in the study.

THE FOLLOWING PARAGRAPHS CONTAIN SOME STANDARD INFORMATION WHICH



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GENERALLY APPLIES TO INDIVIDUALS PARTICIPATING IN A RESEARCH STUDY.**CONSENT FORM FOR CLINICAL RESEARCH**

I have read the previous page[s] of the consent form and the investigator has explained the details of the study. I understand that I am free to ask additional questions.

If I wish additional information regarding this research and my rights as a research subject, or if I believe I have been harmed by this study, I may contact the Human Subjects Protection Office (HSPO).

I am aware that this is a research project and that unforeseen side effects may occur.

I understand that the Beth Israel Deaconess Medical Center has no formal program for compensating patients for medical injuries arising from this research. Medical treatment will be provided for injuries at the usual charge to me or to my insurer unless payment is otherwise provided for in this consent form.

I understand that participation in this study is voluntary and I may refuse to participate or may discontinue participation at any time without penalty, loss of benefits, or prejudice to the quality of care which I will receive.

I acknowledge that no guarantees have been made to me regarding the results of the treatment involved in this study, and I consent to participate in the study and have been given a copy of this form.

Signature of Subject or
Legally Authorized Representative
(Parent if the subject is a minor)

Date

Relationship of Legally Authorized Representative to Subject

The subject has been given the opportunity to read this consent form and to ask questions before signing, and has been given a copy.

SIGNATURE OF INVESTIGATOR/Co-Investigator

DATE

PRINT INVESTIGATOR'S/Co-Investigator's

NAME

A signing co-investigator must be listed on the study's approved Research Staffing Form at the time of consent.



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THE FOLLOWING SECTIONS ARE NOT NEEDED FOR ALL STUDIES AND SHOULD BE UTILIZED AS INDICATED:

If the subject is able to speak and understand English but is not able to read or write

I was present during the entire oral presentation of the informed consent and witnessed the subject's agreement to participate in the study. Signature of Witness: _____ Printed Name of Witness: _____ Date: _____

If the subject is able to understand English but is not physically able to read or write or see

I was present during the entire oral presentation of the informed consent and witnessed the subject's agreement to participate in the study. Signature of Witness: _____ Printed Name of Witness: _____ Date: _____

If the subject is not English speaking and signed the translated Short Form in lieu of the English consent document.

As someone who understands both English and the language spoken by the subject, I interpreted, in the subject's language, the researcher's presentation of the English consent form. The subject was given the opportunity to ask questions. Signature of Interpreter: _____ Printed name of Interpreter: _____ Date: _____
