New York State Psychiatric Institute - Columbia University Department of Psychiatry
INFORMED CONSENT TO PARTICIPATE IN A RESEARCH STUDY

RESEARCH SUMMARY COVER SHEET

- The goal of this research is to assess safety and efficacy of magnetic seizure therapy (MST) in the treatment of depression in the elderly.
- MST will be compared to a well known, standard of care treatment, called electroconvulsive therapy (ECT).
- Participants will be assigned randomly (like flipping a coin), to either MST or ECT treatment arms.
- Both groups, MST or ECT, will receive convulsive therapy; there is no placebo group.
- Participants will have intravenous (IV) line placed on the morning of the treatment. Through this line they will receive two kinds of medications at the beginning of the treatment. First medication will make them fall asleep (for a brief period of time, lasting a few minutes); second one will relax their muscles.
- During the treatment, participants will remain under the care of two doctors. The first one is an anesthesiologist – a doctor who puts the patient to sleep and monitors patient's vital signs and the second one is the treating psychiatrist.
- Participants will be asked to wear earplugs because of the brief noise generated during the treatment, while under anesthesia.
- Treatments are performed 3 times a week: on Monday, Wednesday and Friday mornings.
- In order to evaluate study progress, standard tests will be given before, after and in-between treatments.

New York State Psychiatric Institute - Columbia University Department of Psychiatry
INFORMED CONSENT TO PARTICIPATE IN A RESEARCH STUDY

The purpose of this Consent Form is to provide you with information you need to consider before you decide whether to participate in this research study.

STUDY TITLE: IMPROVING OUTCOMES IN GERIATRIC DEPRESSION: MAGNETIC SEIZURE THERAPY

PRINCIPAL INVESTIGATOR: STEFAN ROWNY, M.D.

AFFILIATION OF PRINCIPAL INVESTIGATOR:
NEW YORK STATE PSYCHIATRIC INSTITUTE / COLUMBIA UNIVERSITY

Purpose of Study and Overview

You are eligible to participate in this study because you have severe depression and it has been recommended that you receive treatment for your depression that uses electricity to cause a seizure (convulsive therapy). You have been invited to participate in a research study using a new type of convulsive therapy, called magnetic seizure therapy (MST), which will be compared to an existing standard of care treatment, electroconvulsive therapy (ECT). Like ECT, MST causes a seizure. Unlike ECT, which uses electricity, MST uses magnetic fields that create a small amount of electricity in the brain to trigger the seizure. MST is experimental and is not approved by the Food and Drug Administration (FDA). MST has only been used previously to treat depression in about 150 patients. Two investigational devices are available worldwide, with which magnetic seizure therapy treatments have been performed to date. At the time of writing this consent form, 57 individuals have received acute series of treatments with the device that we use currently. Limited published data exist at this time, but early reports suggest promising results in treating depression with fewer side effects from this new convulsive treatment. However, because of the small number of published reports and limited number of patients who received this treatment under research conditions so far, it is not known if MST is effective in treating depression, particularly depression in the elderly. Its safety has not been fully evaluated yet. The most commonly reported side effects will be discussed elsewhere. In general, those who received MST treatment have a few minutes of confusion after treatment, not different from that of general anesthesia. The risk of short-term and long-term memory loss, appears to be minimal, temporary and only in the setting of receiving the acute treatment. This study will compare the effects of MST and ECT in the elderly. We will also compare the safety of MST with ECT. This information will teach us more about whether MST may someday be a useful alternative to ECT in the treatment of depression. The investigators plan to include 30 participants in this research. This study is funded by a grant from the National Institute of Mental Health.

Voluntary

Participation in this research study is voluntary. If you decide not to participate, or if you later decide to stop participating, you will not lose any of the benefits to which you are otherwise entitled. A decision not to participate or withdraw of your participation will not affect your current or future treatment at the New York State Psychiatric Institute or Columbia University.

You will be notified of significant new findings that may relate to your willingness to participate.

Alternatives to Participation

You do not have to participate in this study to receive treatment for your depression. The alternative to participating in this study would be to receive other treatments for depression like ECT, antidepressant medication, and psychotherapy. These alternative treatments have their own benefits and risks. The question of whether convulsive therapy or an alternative treatment is best for you depends on your prior experience with these treatments, your psychiatric and medical condition and other considerations that you should discuss with your doctor.

Procedures

Clinical and Study Evaluations: Before starting treatment, you will be asked about your past and current physical and mental health. During the time that you are receiving convulsive treatments and during the week after you finish treatment, you will be interviewed about changes in your symptoms and side effects. You will be interviewed about your depression and side effects two and six months after the last treatment.

To test the effects of treatment on your thinking and memory, you will receive a set of tests before and after each session. This will take about 45 minutes. In addition, a longer session with similar tests will be given within three days before the start of treatment, within three days after the last session, and again 6 months after the last treatment.

Schedule of testing: This study is performed in a psychiatric hospital. On the first testing day, you will be admitted to the hospital. Even if you are accepted for outpatient treatment, you will still need to be admitted to the inpatient unit for the first week of treatment and will receive the same study procedures. You will be interviewed, have a physical exam, hearing test, and an interview about your psychiatric condition. You will also have your blood drawn, give a urine sample, and have a chest X-Ray. If you are taking medications to treat your depression, these medications will be gradually stopped. You will be off of these medications for at least five days before you start receiving treatments. Therefore, your actual delay to treatment may be as short as 5 and possibly as long as 7 days or even longer, depending on how you tolerate the medication washout and when the actual washout begins. Treatments are given only on Mondays, Wednesdays and Fridays. You will be assigned to receive either MST (with magnetic coil placed at the surface of your head) or right unilateral ECT (a standard method of ECT with two electrodes touching the scalp). If you decide to participate in the study, you will have a fifty percent chance (or 1 out of 2) of receiving MST. You will then receive your assigned treatment three times a week. Neither you nor the clinician who evaluates the level of your depression will know which treatment you are receiving. The study assignment is made in advance by a procedure similar to drawing straws. Treatments will continue usually for two to six weeks, depending on your doctor's judgment of how you are responding. Your participation in the study will be stopped after eight treatments if your depression does not improve by at least 25% as measured by a test we use (Hamilton Depression Rating Scale). There is no maximum number of treatments. However, if you need more than 25 treatments, a new consent form will need to be signed. At the first and last treatment sessions, you will receive several stimulations until the smallest amount of MST or ECT needed to cause a seizure is reached. At the other sessions, you will be treated at a dosage

above that threshold. Before and after each session, you will complete tests of your memory and thinking. You will also complete a questionnaire about side effects and be asked questions about your depression. After your first, sixth, and last session, your hearing will also be tested. If the test shows that your hearing has worsened during the study, the doctor will discuss treatment options with you and carefully assess whether to continue with treatment. If the hearing tests show that you have experienced hearing loss, your hearing will be tested again periodically until either it returns to the level where it was before treatment or the doctor determines that it will not improve any more. At the end of the treatment course, one of the study investigators will provide you with a letter stating that the seizure(s) you experienced were produced as part of an experiment.

Blood tests: A blood sample will be taken to carry out recommended tests before convulsive therapy. Further blood tests will be drawn at your second, sixth, and next to last session to look at hormonal effects of the treatment. The total amount of blood taken for all research procedures will be less than one cup. This is about half the amount of a typical donation to a blood bank.

Studies of the nervous system function (Neurophysiology): A set of tests will be done to examine the effects of the MST and ECT on brain activity. These tests include electroencephalography (referred to as EEG, or looking at "brain waves") and tests of your brain's responses to magnetic pulses (referred to as motor cortex excitability studies). For the EEG, your scalp will be cleaned and sensors placed on your head and near your eyes. The sensors are used to measure the brain waves that naturally occur in your brain, while you lie quietly. The EEG will be measured before treatment, during two of the MST/ECT sessions, and during the week following the last treatment.

The test of your brain's responses to magnetic pulses will be done before your first session and in the week following your last session. During this procedure, small sensors will be attached to the skin of your hands and/or legs to measure muscle twitching. A technician will hold a magnetic coil over your head or on the back of your neck. This coil will give a number of quick magnetic pulses. Some of these pulses will cause your fingers or foot to twitch. Earplugs will be worn throughout the testing because the stimulator makes a clicking noise.

MST/ECT: At each treatment, you will be under the care of an anesthesiologist, a psychiatrist, and a nurse. To receive each treatment you will be brought to a special room containing all the appropriate equipment that is needed for your treatment. The treatments are given in the morning, before breakfast. Because the treatments are done under general anesthesia (while you are asleep), you will not be allowed to drink or eat for at least eight hours before each treatment. During the treatment, medications will be given to you through a thin plastic tube (an "IV line" or catheter) placed in your arm. You will be given medicine that will quickly put you to sleep. You will be given a second drug that will relax your muscles. Because you will be asleep, you will not feel pain or discomfort during the procedure.

To prepare for the treatments, monitoring sensors will be put on your head and other parts of your body. This is done to monitor your brain, your heart, and your blood pressure. These recordings involve no pain or discomfort. A blood pressure cuff will be put on one of your legs. Before starting the MST/ECT procedure, you will be asked to remove any metal or

magnetized objects (such as keys, jewelry, hair pins, and credit cards). MST makes a loud clicking sound, so you will be given earplugs for your comfort and safety.

If you are assigned to MST, after you are asleep the MST coil will be placed on your head. MST is given using a magnetic stimulator. A magnetic stimulator is a device that makes a magnetic field. The magnetic field is made by passing current through a coil of wire. The magnetic field passes through the skull to the brain. The magnetic field creates a small amount of electricity in the brain. That electricity triggers a seizure (convulsion).

If you are assigned to ECT, after you are asleep, electrodes used to stimulate the brain will be placed on your head. ECT is given using an electrical stimulator, which is a device that can pass an electrical current between two stimulating electrodes. When the current is passed, a seizure is produced in the brain.

Because you will have received a medication to relax your muscles, body movements that would ordinarily happen during a seizure will be much weaker. The seizure will last for about one minute. Within a few minutes, the medicine that put you to sleep will wear off and you will wake up. You will be given oxygen to help you breathe. After waking up, you will be taken to a recovery room, where you will be watched for about 45 minutes (the time varies for different people) until you are ready to leave the recovery area.

You will be monitored very closely while the seizure is going on. There will be sensors on your forehead that will allow the psychiatrist to track the progress of the seizure in your brain. The psychiatrist and nurse will also monitor your seizure by inflating a blood pressure cuff around one of your ankles. This cuff decreases the amount of muscle relaxant that can reach your foot, so that the psychiatrist and nurse will be able to see your foot moving even though the rest of your body is relaxed. Your motor seizure (seizure visible in your foot) will also be timed.

If MST fails to cause a seizure, you will be allowed to wake up and your treatment options will be discussed with you. At any point in the study, you are free to switch to ECT if MST fails to cause a seizure or to improve your depression. If you do not respond to treatment, you will be provided other treatment options that are best for you. As a clinical inpatient at NYSPI other psychiatric treatment options would be provided at no cost.

Risks and Inconveniences

Experimental Nature of the Treatment: MST is experimental and it may have unknown side effects. MST may not help your depression get better and it is possible that your depression will get worse; receiving MST may delay your ability to receive effective treatment. Delay in treatment of depression may also result in making your symptoms worse.

Medication Withdrawal: Stopping your medications that you are taking to treat your depression, if any, may cause your depression to get worse. There may also be side effects from stopping some medications. Your medications will be stopped on a schedule that is best for you so that these effects can be minimized. The length of time of your withdrawal from medication will depend on the type of medication you are currently taking.

Risk due to general anesthesia: Both MST and ECT require general anesthesia. As

with any procedure where you are put to sleep (general anesthesia), there is a remote risk of death. The risk of death attributable to the management of general anesthesia with convulsive treatment is estimated to be one out of 10,000 patients treated.

Risks common to outpatient Treatment for both MST and ECT: If you participate as an outpatient, there is an increased risk of falling and thus injuring yourself after each treatment, risk of injury from operating dangerous machinery (such as driving or using the stove). If you eat or drink after midnight, serious risk of aspirating the content of your stomach exists during anesthesia. This can lead to pneumonia and other serious medical complications, including in rare cases, death. To reduce these risks, we require that in order to participate as an outpatient, you remain under the supervision of another responsible adult who will oversee the treatment regimen. We also require that a minimum of 3 treatments be administered on the inpatient unit.

MST: Although it is expected that the side effects of MST will be similar or less intense than the side effects of electroconvulsive therapy (ECT), the risks and benefits are not known. The risks may include memory loss, confusion, headache, muscle soreness, nausea, and dental pain. It is possible that, if you experience dental pain, it could last beyond when your MST treatment ends. Both ECT and MST put electricity into the brain and cause a seizure. Magnetic fields do not enter into the brain as deeply as the electric fields used in ECT. This might mean that the memory side effects from the stimulation of deeper parts of the brain may be less with MST than ECT, but this is not known. In the cases of healthy volunteers who had accidental seizures with magnetic stimulation, there have been no signs of any long-term side effects.

The clicking noise made by the stimulator may affect hearing for a short time. Earplugs reduce this risk, so you will be asked to wear earplugs during MST. As with all antidepressant treatments, including ECT, there is a possible risk of inducing mania.

ECT: Like other medical procedures, ECT involves some risks. Serious medical complications with ECT are rare. With introduction of modern anesthesia, bone fractures and dislocations are exceedingly rare and none such occurred in the last 25 years of our experience with treatments in this institution. Each patient receives a dental exam by the anesthesiologist prior to treatment to address any potential problems and to reduce the risk of dental complications like teeth or caps cracking. While also rare, the most common medical complications with ECT are changes in heart rate and rhythm, which can be effectively treated in most cases. To reduce the risk of medical complications, you will receive a careful medical evaluation before starting ECT. But, even with precautions there is a small chance that you may have a medical complication. If this happens, medical care and treatment will be started immediately. Facilities to handle emergencies are available.

A common side effect of ECT is memory loss. How much memory is lost is likely to be related to the number and type of treatments given. A smaller number of treatments is likely to cause less memory loss than a larger number of treatments. The memory problems with ECT follow a certain pattern. Shortly after a treatment, the problems with memory are most noticeable. As more time goes by, memory improves. Shortly after the last ECT treatment, you may have trouble remembering things that happened before and while you received ECT. Problems with memories for the past may go back to several months before you

had ECT, and rarely, to one, two, or more years. Many of these memories will return during the first few months after ECT. However, you may be left with permanent gaps in memory, especially for things that happened around the time of the ECT treatments. In addition, for a short period following ECT, you may have trouble learning and remembering new events. This difficulty in making new memories should be short and will most likely go away within several weeks after the last ECT treatment.

The amount of confusion and memory problems during and shortly following ECT varies among people. However, depression itself worsens learning and memory. A small percentage of patients report severe problems in memory that last for months or even years. The reasons for these reports of long-lasting memory problems are not fully understood. However, as with any medical treatment, people who receive ECT differ in the way they experience side effects. Rarely, ECT may cause permanent and large gaps in memory.

When you wake up after each treatment, you may feel confused. The confusion usually goes away within an hour. Shortly after the treatment, you may have a headache, muscle soreness, or feel sick to your stomach. These side effects usually respond to simple treatment.

Because of the possible problems with confusion and memory in both ECT and MST, it is important that you not make important personal or business decisions during treatment or immediately following treatment. This may mean postponing decisions about financial or family matters. After the treatment, you will begin a "convalescence (recovery) period." This usually lasts one to three weeks, but this varies from patient to patient. During this period you should not drive, do business, or other activities for which poor concentration or memory may be a problem, until your doctor tells you to do so.

Neurophysiological Studies involving EEG: There are no anticipated risks of the EEG procedure. EEG electrodes will be slotted or made from plastic to reduce electrode heating, as recommended by the literature.

Neurophysiological Studies to determine Motor Threshold:

The tests of muscle twitching use magnetic pulses given at low frequency (less than one per second). Low frequency magnetic pulses pose no significant health risk. Electrical current is produced in the brain from magnetic pulses. This current is well below harmful levels. The most serious known risk of low frequency magnetic stimulation is seizure, although low frequency magnetic stimulation has not been known to cause seizure in properly selected individuals. In spite of these precautions, there is a chance that you will experience a seizure or other medical complication from low frequency magnetic stimulation during this test. If you have a seizure, you may have to be admitted to the hospital and follow-up neurological evaluation. Having had a seizure may adversely affect your medical insurance, your future employment, and your ability to drive. It is not known whether having had one seizure will make a person more likely to have future seizures.

The most commonly reported side effect of low frequency magnetic stimulation is a "muscle-tension" type headache. About 17 out of every 100 people will experience a mild headache with this type of magnetic stimulation. If a headache occurs, it usually starts during or immediately after the low frequency magnetic stimulation and lasts from minutes to hours later. The headache usually goes away with standard over the counter pain medications

(acetaminophen, ibuprofen, Toradol (ketorolac tromethamine)). Neck pain may also occur, and it is also usually managed easily with the same standard over the counter painkillers. You may also experience some discomfort on your head where the coil is held. This is due to contraction of scalp muscles. The clicking noise produced during the stimulation may temporarily affect hearing. The earplugs will reduce this risk.

***Blood tests*:** A blood sample will be taken to carry out typically recommended studies before convulsive therapy. For most people, drawing blood does not cause any serious problems. However, there is a risk of bleeding, bruising, discomfort, dizziness, infections and pain at the needle site. These side effects usually go away in a few days.

Clinical Evaluation, Neuropsychological Procedures and Physical Examination: There are no known or expected risks to you from the interview about your history. There are no known risks of the physical and neurological examination. The interviews are time consuming and they are about personal matters. It is possible that you will feel upset, tired or anxious. If this happens, you can choose not to answer specific questions or ask to have the interview stopped at any time.

Unforeseen risks: A previously unknown problem could result from your participation in this research. There could be an interaction between MST/ECT/anesthesia medication, and other medications you take (prescribed or over the counter). It is not possible to estimate the chances of such problems or how serious the problems could be.

Benefits

You may or may not benefit from this study. Whether you are assigned to receive ECT or MST, your depression may improve, although there is no guarantee that this will happen. Information obtained from this study may add to knowledge about safer treatments for severe depression.

Confidentiality

Your right to privacy and the confidentiality of your participation in this project, should you choose to participate, will be safeguarded and, if research papers are written, you will not be mentioned by name. Research records, like other medical and clinical records, will be kept confidential to the extent permitted by law. Any information obtained during this study and identified with you will remain confidential. Records will be available to the research staff, and Federal, State and Institutional regulatory personnel, who may review records as part of the routine audits. There are legal advocacy organizations that have the authority under state law to access otherwise confidential research records, though they cannot re-disclose this information without your consent. All information will be stored in locked files and will not have your name or any other identifying information associated with it.

All data (written and electronic) will be coded. A master list matching the subject with codes will be kept under lock and key, separate from any research records or the computer database, with access restricted to research staff, to the extent permitted by law. Only staff directly involved in this project will have access to the master list linking your name to code numbers. Your name and other personal identifying information will be stored in an electronically secure database at the New York State Psychiatric Institute.

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.

You should know that if we learn that you or someone else is threatened with serious harm, such as a child or an elderly person being abused, the investigators would take actions to protect you and others, including reporting these situations to proper authorities.

Study Compensation

There is no cost for participation in this study. You will not be paid to participate in this study.

In Case of Injury

Federal regulations require that we inform you about our institution's policy with regard to compensation and payment for treatment of research-related injuries. Short term emergency medical treatment, which has been determined to be necessary by New York State Psychiatric Institute's doctors, and which is within the capability of New York State Psychiatric Institute will be provided. In addition, we will provide assistance in arranging follow up care in such instances.

New York State Psychiatric Institute or Research Foundation for Mental Hygiene does not provide compensation or payment for treatment of research related injuries. However, you should be aware that participation in this research does not waive any of your legal rights to seek such compensation through the courts.

Your participation in this research study is completely voluntary. You may refuse to participate or withdraw at any time, without loss of benefits to which you are otherwise entitled. The Investigator may also end your participation in this study if it is no longer in your best interests to participate, if you do not keep appointments or follow instructions, or if the study is ended prematurely. Such a decision will not affect your medical care at the New York State Psychiatric Institute, now or in the future. The doctors conducting this research study are also responsible for your clinical care.

Questions

The principal investigator, Dr. Rowny, will answer to the best of his ability any questions **you** may have now or in the future about this study and research procedures. If you have any questions about the study procedures or about your response to the procedures, you may contact **Dr. Rowny at (646) 774-5417**. You will be given the opportunity to discuss in confidence any questions you may have. You will be given a copy of this consent form for you to keep.

If you have any questions about your rights as a research participant, want to provide feedback, or have a complaint, you may call the NYSPI Institutional Review Board (IRB).(An IRB is a committee that protects the rights of **participants** in research studies). You may call the **IRB Main Office** at (646)774-7155 during regular office hours.

Statement of Consent

I voluntarily agree to participate in the research study described above.

Signature of participant_____ Date_____

Printed name of participant_____

I have discussed the proposed research with this patient including the risks, benefits, and alternatives to participation (including the alternative of not participating in the research). The participant has had an opportunity to ask questions and in my opinion, this patient is capable of freely consenting to participate in this research.

Signed: _____

Print name: _____ Date_____
Person Designated to Obtain Consent

Project Director: Stefan B Rowny, M.D.
Division of Brain Stimulation and Therapeutic Modulation
New York State Psychiatric Institute
(646) 774-5417

Capacity to Consent Addendum Protocol # 6427

I have examined _____ on _____ for the purpose of determining whether he/she is capable of understanding the purpose, nature, risks, benefits and alternatives (including non-participation) of the research, making a decision about participation, and understanding that the decision about participation in the research will involve no penalty or loss of benefits to which the patient is otherwise entitled, for Dr. Stefan Rowny's research project "Improving Outcomes in Geriatric Depression: Magnetic Seizure Therapy". On the basis of this examination I have arrived at the conclusion that:

_____ A. This patient has this capacity at this time.

_____ B. There is a question about this patient's capacity at this time.

_____ C. This patient clearly lacks this capacity.

Signature _____ Date _____

Printed Name _____
Member of Treatment Team MD or PhD (not a co-Investigator)