New York State Psychiatric Institute

Institutional Review Board

July 11, 2017

To: Dr. Stefan Rowny

From: Dr. Edward Nunes, Co-Chairman, IRB
Dr. Laurence Greenhill, Co-Chairman, IRB

Subject: **APPROVAL NOTICE**: **CONTINUATION APPROVAL**
EXPEDITED PER 45CFR46.110(b)(1)(f)(8)(c)

Your protocol **#6427** entitled: **IMPROVING OUTCOMES IN GERIATRIC DEPRESSION: MAGNETIC SEIZURE THERAPY** ACAR/PSF version date 7/5/17 and consent forms (version) have been approved by the New York State Psychiatric Institute - Columbia University Department of Psychiatry Institutional Review Board from **JULY 25, 2017 TO JULY 24, 2018.**

Consent requirements:

X Not applicable: (RECRUITMENT COMPLETED. DATA BEING ANALYZED)

☐ 45CFR46.116(d) waiver or alteration of consent for the telephone screen.

☐ Signature by the person(s) obtaining consent is required to document the consent process.

☐ Documentation of an independent assessment of the participant's capacity to consent is also required.

Approved for recruitment of subjects who lack capacity to consent: ☐ No ☐ Yes

Field Monitoring Requirements: ☐ Routine ☐ Special: _____

✓ Only copies of consent documents that are currently approved by the IRB may be used to obtain consent for participation in this study.
✓ A progress report and application for continuing review is required 2 months prior to the expiration date of IRB approval.
✓ Changes to this research may not be initiated without the review and approval of the IRB except when necessary to eliminate immediate hazards to participants.
✓ All serious and/or unanticipated problems or events involving risks to subjects or others must be reported immediately to the IRB. Please refer to the PI-IRB website at http://irb.nyspi.org for Adverse Event Reporting Procedures and additional reporting requirements.

CC: RFMH

EN/LG/ls

Signed copy on file at IRB

Protocol Title:
Improving Outcomes in Geriatric Depression: Magnetic Seizure Therapy

Version Date:
07/11/2017

Protocol Number:
6427

First Approval:
12/27/2011

Clinic:
Brain and Behavior Clinic

Expiration Date:
07/24/2017

Contact Principal Investigator:
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Joan Prudic, MD
Peter Bulow, MD
Daniel Javitt, MD, PHD

Cover Sheet

Choose ONE option from the following that is applicable to your study
If you are creating a new protocol, select "I am submitting a new protocol." As 5 Year Renewals are no longer required, this option remains for historical purposes.
I am submitting an annual continuation without modifications

Division & Personnel

Division

What Division/Department does the PI belong to?
Experimental Therapeutics
Within the division/department, what Center or group are you affiliated with, if any?
Brain Stimulation

Unaffiliated Personnel

List investigators, if any, who will be participating in this protocol but are not affiliated with New York State Psychiatric Institute or Columbia University. Provide: Full Name, Degrees and Affiliation.

n/a

Application for Continuation of Research

Status

Current Status of Study:
All research interventions were completed. Only data analysis is ongoing.

Summary of Experiences to Date

Please provide a summary of scientific progress of the study and the experience of research participants, to date. This requirement is designed to allow for the investigator and the IRB to reassess the study's risks and benefits in terms of developments in the field, changing practice patterns, and new IRB policies and procedures.

We have completed all research procedures for subjects enrolled in this study and are just beginning data analysis.

In conclusion, eighteen medication resistant patients with MDE have completed convulsive treatment (ECT or MST) following medication washout. From baseline, the mean drop in HRSD24 was 19.3 points. Fifteen patients met remission criteria (reduction of 60% in HRSD24 scores from baseline or a HRSD24 score less than or equal to 10). One patient was randomized into treatment but after discussion of risks and benefits within the anesthesiology team chose to seek a traditional medication treatment and therefore withdrew from the study. One patient demonstrated a 45.16% reduction in depressive symptoms, and two other patients were terminated from the study to a clinical treatment modality because their response did not meed the study's criteria for progress.

Across the board, participants experienced minimal side effects from their treatment and all had fully recovered, completing the standard post-treatment reorientation battery. Patients' Mini-Mental State Exam scores remained stable from baseline to assessment immediately following the treatment course and six months post-treatment, indicating a lack of significant impairment in cognition on this measure.

In this reporting period there were no anticipated or unanticipated adverse effects to report, and there were no deviations from the protocol.

Funding

Have there been any changes in funding status since the prior approval?
No
Have the principal investigator and other investigators made all required disclosures of financial interest in the study sponsor/product?

Yes

Summary

Have there been any study findings, recent literature, or untoward events occuring here or at other sites in the past year which might affect the analysis of the safety, risks or benefits of study participation?
No
Have there been any serious adverse events (serious and/or unanticipated problems involving risks to subjects or others at this site which occured in the past year)?
No
Have all study staff with a significant role in the design or implementation of the human subject components of this study received required training in human research subject protections?
Yes
Is the study covered by a certificate of confidentiality?
No

Overall Progress

Approved sample size
20
Total number of participants enrolled to date
18
Number of participants who have completed the study to date
18
Have there been any significant deviations from the anticipated study recruitment, retention or completion estimates?
No
Comments / additional information

Sample Demographics

Specify population
Older adults aged 55-90 years
Total number of participants enrolled from this population to date
18
Gender, Racial and Ethnic Breakdown

58.8% Female
42.2% Male

88.8% Caucasian
5.6% African-American
5.6% Asian

Summary of Current Year's Enrollment and Drop-out

Number of participants who signed consent in the past year
1
Did the investigator withdraw participants from the study?
No
Did participants decide to discontinue study involvement?
No

Procedures

To create the protocol summary form, first indicate if this research will include any of the following procedures

✓ Psychiatric Assessment
✓ Neuropsychological Evaluation
✓ Collection of Biological Specimens
✓ Medication-Free Period or Treatment Washout
✓ Device Trial
✓ Use of Investigational Drug or Device

Population

Indicate which of the following populations will be included in this research

✓ Adults over 50
✓ Inpatients

Research Support/Funding

Will an existing internal account be used to support the project?
Yes
Describe internal account
RFMH (K23)
Is the project externally funded or is external funding planned?
No

Study Location

Indicate if the research is/will be conducted at any of the following

✓ NYSPI

This protocol describes research conducted by the PI at other facilities/locations
No

Lay Summary of Proposed Research

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Unlike any other treatment, electroconvulsive therapy (ECT) is highly effective for severe depression and both, the depressed and manic phases of bipolar disorder. This is noteworthy since effective treatment of bipolar depression remains an unsolved clinical problem. Why, then, does a treatment that is based in its ability to elicit a seizure, like ECT, not play a more prominent role in the treatment of mood disorder? ECT is underutilized in large part because of its adverse cognitive effects, some of which can be persistent. Magnetic seizure therapy (MST) is under development as a means of improving the side effect profile of ECT so that more patients may benefit without suffering significant detrimental effects on cognition. Magnetic fields offer markedly better control over the spatial distribution and the extent of stimulation, factors that largely determine the efficacy and side effects of ECT. Our preliminary studies demonstrated that MST can induce seizures with substantially fewer cognitive side effects than ECT, and provided the first open-label evidence of antidepressant efficacy. This new protocol is a 5-year randomized controlled trial of 30 patients to test the efficacy of MST in severe depression (additional 8 open treatments will be performed as necessary outside of the randomized controlled trial, to integrate new devices into the protocol). The results of this study will help elucidate neurobiological mechanisms of treatment response to two types of convulsive treatment and help to determine whether MST will proceed to the next phase of clinical development leading to eventual FDA-approval of this novel therapeutic intervention. If our hypotheses are supported, MST will provide a well-tolerated, effective treatment for patients with the most disabling and life-threatening mood disorders.

Background, Significance and Rationale

Background, Significance and Rationale

This is a randomized controlled trial of Magnetic Seizure Therapy (MST) in the treatment of depression. In addition to the randomized, controlled trial recruitment with a sample target of 30 volunteers, the treatment and data collection may be expanded by up to 4 patients in each arm to allow for new equipment integration into the protocol. Phase 1 is a double-masked, randomized, controlled trial that contrasts the efficacy and safety of MST and ECT. Eligible patients will be randomized 1:1 to each. Safety and adverse events will be assessed using standardized scales as well as pre- and post-treatment testing of cognition (see Table 1 for list of measures). Phase 1 provides a randomized comparison of MST versus ECT. Since MST involves general anesthesia (which carries risk of its own), a true placebo condition would not have been ethically permissible. Phase 2, the follow up, will provide a descriptive within-subject characterization of longer-term outcomes (i.e., long-term durability of benefit and/or persistence of side effects).

We have been testing the safety of MST in the nonhuman primate over the past 15 years. This work has demonstrated the safety of MST in comparison to electroconvulsive shock (ECS) using cognitive, physiological, neuroanatomical, neuropathological, and stereological assessments. Our results show that the electric field induced by MST is less intense and more confined to superficial cortex than ECS. MST-induced seizures show less robust ictal expression, less postictal suppression. Most importantly to this protocol, there is less generalization to hippocampus and deeper brain structures. There was less robust serum prolactin surge and less immediate post-stimulus bradycardia. These marked physiological differences are consistent with MST having less of an impact than ECS on temporal lobe and diencephalic structures, as hypothesized, and with less impact on parasympathetic outflow that should lower the risk of cardiac complications. We found that ECS, but not MST, induces the sprouting of mossy fiber in aberrant locations of the dentate gyrus. Lack of physiological and structural changes in the hippocampus with MST may relate to its superior cognitive profile. Indeed, our nonhuman primate model of the amnestic side effects of ECT revealed that monkeys were more accurate and faster following MST as compared to ECS.

We now have 12 years of experience performing MST in human patients with depression. To date, approximately 160 patients have received MST worldwide (about 1/3 of these were treated at NYSPI). This work has shown that human MST is feasible, well-tolerated, has fewer acute cognitive side effects than ECT, and shows evidence of antidepressant activity in an open trial. Our clinical work guided the development of a higher output device (maximal frequency 100 Hz) that was needed to keep pace with treatment-induced increases in seizure threshold and to broaden the available dosage range of the device. Our prior human work with the original MST device mostly involved triggering seizures from the motor strip, since this area has a lower seizure threshold than prefrontal cortex. Even so, there was evidence of antidepressant activity in an open setting, with an average drop in Hamilton scores by 49% after an average of 9 treatments. Our most recent study yielded preliminary data suggesting that MST is safe and effective in the geriatric population. In this most recent, two-center study comparing ECT with MST at Columbia University and University of Texas South Western (the former now transferred to Duke University), 15 patients over 55 years-old, received MST and tolerated it well. There were no serious adverse events to date in this geriatric (or any other) sample and the study is now over 75% complete. Device and coil performance during the seizure induction sessions have been within the expected parameters, with no cases of excessive heating. Seizure threshold titrations have been successfully performed. The speed of reorientation immediately following the MST session was recorded. The average time to regain full orientation following the MST session was 385 ± 162 seconds. All of these patients also received ECT in the past. We therefore selected the ECT treatment closest in time to the MST session and compared recovery time with this matched ECT session. The average recovery time with ECT in these patients was 1148 ± 97 seconds, which is nearly 4-fold longer than recovery following MST. Paired t-test revealed that recovery time post ECT was significantly longer than with MST ($t(5)=7.4$, $p<0.0007$). Results from these first cases were accepted for presentation at the 2007 annual meeting of the Society of Biological Psychiatry.This protocol is essentially the same as that of Dr. Lisanby's MST-3 (2007-2010 funded by Stanley Foundation) study mentioned above at NYSPI, but with a narrowed focus to population over 55 years-old.

Outside of the United States, at least twenty patients with depression have now been treated with the same devices that the PI of this proposed study had gained expertise during the last 4 years of his work with Dr. Lisanby, before her NYSPI IRB-approved studies were moved to Duke University. The foreign academic centers involved in the development of MST as a novel therapy for depression, exist in UK, Germany, and Australia, where this treatment was given as part of IRB-approved protocols in Cardiff and Edinburgh, UK, as well as in Bonn and Berlin, Germany, and Melbourne, Australia.Treatments were well tolerated. Anesthesia was identical to the standard used at these centers for clinical ECT.

Specific Aims and Hypotheses

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The goal of this project is to develop MST as a treatment for severe mood disorder for the elderly with fewer cognitive side effects than ECT, the most effective treatment for severe depression. Unlike ECT, MST can initiate seizures in superficial cortex, while limiting impact on deeper medial temporal structures and thereby resulting in less cognitive side effects. Results from previous trials in the general population sample, support the safety of MST and provide open-label evidence of antidepressant action. The specific aims and hypotheses are:

AIM 1.

To evaluate the feasibility, tolerability, and efficacy of MST in elderly patients with a major depressive episode, who are randomly assigned to receive an acute course of MST or ECT. We hypothesize:

1a. MST will elicit seizures of at least 20 second duration recorded via electroencephalography (EEG) and motor expression in a cuffed limb.

1b. MST will show less cognitive side effects, less tachycardia and less post-stimulus bradycardia than ECT.

1c. MST will show antidepressant efficacy as indicated by a significant drop in depression scores as measured by Hamilton Depression Rating Scale (HRSD). This primary outcome will be compared between the MST and ECT groups with respect to response and remission.

AIM 2.

To contrast the neurophysiological effects of MST and ECT in geriatric depression. We hypothesize:

2a. MST will show lower total ictal power and less post-ictal suppression than ECT as measured by quantitative scalp EEG.

2b. MST will show a differential topographical pattern relative to ECT as measured by 64-channel scalp EEG, with less generalization to the temporal lobe.

Description of Subject Population

Sample #1

Specify subject population
geriatric volunteers with depression
Number of completers required to accomplish study aims
20
Projected number of subjects who will be enrolled to obtain required number of completers
30
Age range of subject population
55-90

Gender, Racial and Ethnic Breakdown
Gender: 53% Female, 46% Male.
Racial and Ethinic: 87.5% Caucasian, 6.3% African-America, and 6.3% Asian
Description of subject population

Adults 55-90 with severe depression.

Recruitment Procedures

Describe settings where recruitment will occur

Patients are referred by private physicians and by clinical services at NYSPI and other psychiatric facilities. Capacity to consent will be assessed by a member of the treatment team who is not an investigator on this study (such as the inpatient attending psychiatrist or the unit director). The individual obtaining informed consent will fully disclose and explain the risks and benefits of the study procedures, and answer the patient's questions about the study and the material presented in the informed consent form. Alternatives to study participation will be discussed, and the voluntary nature of participation in the study will be emphasized. This consent discussion will be documented in a consent note placed in the patient's chart.

How and by whom will subjects be approached and/or recruited?

In addition to the previously implemented strategies, we intend to accelerate our recruitment in the final stages of the project through the following ways.

First, Dr. Prudic's expiring study #6599—"Cognitive Training for Memory Deficits Associated With Electroconvulsive Therapy" will end recruitment in July 2015. Dr. Prudic is a co-investigator on this #6427 protocol and her robust referrals will significantly augment our enrollment.

Second, a new RA is assigned to weekly checking and reposting of flyers and clinic brochures in the NYSPI building; this activity has already yielded positive results as the currently treated study volunteer was referred to us by the Geriatric Division clinic.

Third, this RA together with the PI of the study will conduct daily phone calls to the acquainted attending colleagues at the Presbyterian Hospital's CPEP, as needed, for potential study candidates who may be interested in clinical research of depression. It is also important to note that in discussions with the current mentor to the PI of this training K23 grant, Dr. Javitt, as well as the program official at NIMH, it was concluded that the sample size may be reduced without adversely affecting the study goals. Additionally, the PI is going to apply for a no-cost extension for the project. The latter extension was discussed and welcomed by the program official.

How will the study be advertised/publicized?

We have a flyer posted within NYSPI. In addition, we have contacted most of Manhattan based senior citizen's community centers and discussed leaving flyers to be regularly posted after their institutional approval, once we obtain our ACAR stamp for the flyer used in this continuation submission.

Do you have ads/recruitment material requiring review at this time?
Yes
Does this study involve a clinical trial?
Yes
Please provide the NCT Registration Number
NCT01869374

Concurrent Research Studies

Will subjects in this study participate in or be recruited from other studies?
Yes
Describe concurrent research involvement

Participants from this study may also volunteer to participate in Protocol #6942 - Functional Connectivity and Resting State Changes Following Brain Stimulation: Effects Of Convulsive Therapy.

Concurrent involvement in study #6942 will require participants to undergo approximately 1.5 hours baseline MRI scanning session prior to undergoing a series of acute convulsive therapy treatments and again, post-treatment MRI scan within one week of his/her last convulsive therapy treatment. During these two scan sessions standard anatomical and resting state functional MRI data will be collected as fully described in the Specific Aims and Hypotheses of that protocol.

Inclusion/Exclusion Criteria

Name the subject group/sub sample
Adults 55-90 with severe depression
Create or insert table to describe the inclusion criteria and methods to ascertain them

INCLUSION CRITERIA:	METHOD OF ASCERTAINMENT
1. Age 55-90	Self-report
2. Clinical diagnosis of major depressive episode, in the context of unipolar or bipolar disorder	Structured Clinical Interview for Diagnosis (SCID-IV)
3. Willing and capable to provide informed consent	Physician evaluation
4. Convulsive therapy clinically indicated	Physician evaluation
5. Hamilton Rating Scale for Depression ($HRSD_{24}$) $\geq$20	$HRSD_{24}$
6. Mini Mental State Exam (MMSE) $\geq$24	MMSE
7. For outpatients: responsible adult living with patient	Self-report

Create or insert table to describe the exclusion criteria and methods to ascertain them

EXCLUSION CRITERIA:	METHOD OF ASCERTAINMENT

1. Current unstable or serious medical condition, or any comorbid medical condition that substantially increases the risks of ECT (such as acute myocardial infarction, space occupying brain lesion or other cause of increased intracranial pressure, unstable aneurysm or vascular malformation, poorly controlled diabetes mellitus, carcinoma, renal failure, hepatic failure)	Physical evaluation (physical and neurological examination, EKG, blood and urine analysis)
2. History of neurological disorder, epilepsy, stroke, brain surgery, metal in the head, history of known structural brain lesion	Physician evaluation (TASS, medical history, and neurological examination)
3. Presence of devices that may be affected by MST (pacemaker, medication pump, cochlear implant, implanted brain stimulator, or vagus nerve stimulator implanted)	Physician evaluation (TASS, medical history)
4. History of head trauma with loss of consciousness for greater than 5 minutes	Physician evaluation (medical history)
5. History of schizophrenia, schizoaffective disorder, or rapid cycling bipolar disorder	Structured Clinical Interview for Diagnosis (SCID-IV)
6. History of substance abuse or dependence in past 3 months	SCID-IV, urine toxicology screen
7. History of ECT in the past 6 months and/or failure to respond to an adequate trial of ECT lifetime	Physician evaluation (history) and ATHF
8. Presence of intracardiac lines	Physician evaluation (TASS, medical history)

Waiver of Consent/Authorization

Indicate if you are requesting any of the following consent waivers
Waiver of consent for use of records that include protected health information (a HIPAA waiver of Authorization)
No
Waiver or alteration of consent

No
Waiver of documentation of consent
No
Waiver of parental consent
No

Consent Procedures

Is eligibility screening for this study conducted under a different IRB protocol?
No
Describe procedures used to obtain consent during the screening process

Potential patients referred to protocol #6427 are screened in the Brain Behavior Clinic under the umbrella protocol for our division's stimulation research screenings, protocol #6987 Evaluation for Brain Stimulation Treatment Research in the Brain Behavior Clinic.

Once admitted to 5S inpatient unit, the prospective volunteers will have a choice of signing the consent or not, after they have had an opportunity to have their questions about the study answered, and prior to any research evaluations or procedures. Should they choose not to participate in the study, they will receive clinical treatment only and no research procedures will be performed.

Describe Study Consent Procedures
The individual obtaining informed consent will fully disclose and explain the risks and benefits of the study procedures, and answer the patient's questions about the study and the material presented in the informed consent form. Alternatives to study participation will be discussed, and the voluntary nature of participation in the study will be emphasized. This consent discussion will be documented in a consent note placed in the patient's chart.
Indicate which of the following are employed as a part of screening or main study consent procedures
✓ Consent Form

Persons designated to discuss and document consent

Select the names of persons designated to obtain consent/assent
Berman, Joshua, MD
Prudic, Joan, MD
Rowny, Stefan, MD
Type in the name(s) not found in the above list
n/a

Independent Assessment of Capacity

You have indicated that your study involves subjects who MAY LACK capacity to consent.
Does this study require an independent assessment of capacity?
Yes
Methods/procedures for capacity assessment

An attending psychiatrist on the inpatient unit at NYSPI will perform an independent capacity assessment and appropriately document in "Capacity to Consent Addendum" at the end of the ICF as quoted below.

"Capacity to Consent Addendum Protocol # _____

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 "Magnetic Seizure Therapy for the Treatment of Major Severe Mood Disorder". 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 _____
Member of Treatment Team (M.D. or Ph.D.)

Print Name _____
Member of Treatment Team (not a co-Investigator) "

Study Procedures

Describe the procedures required for this study

Informed Consent, Screening, and Medical Management

Patients referred for convulsive therapy will be asked to sign a written informed consent. Standard pre-ECT workup will be performed, including medical history, physical exam, blood work, urine analysis/toxicology, chest x-ray, and medical clearance in accordance with the NYSPI Policy and Procedure Manual for ECT. Also, in accordance with the Policy and Procedure Manual

for ECT, patients may be admitted to the study as outpatients, on the condition that they have responsible adult available to provide direct support and to oversee treatment adherence. Patients desiring outpatient treatment and qualified for such under inclusion/exclusion criteria will be admitted and undergo at least 3 treatments as inpatients. They will be cleared by the clinical team before they are discharged to outpatient therapy.

Psychotropic Medication Washout

To determine efficacy in the absence of ancillary treatment, all patients will be washed out from psychotropic medications (except for PRN lorazepam up to 3 mg/day) for 5 days prior to treatment following admission to the inpatient unit at NYSPI. There will be no outpatient taper of medications by the research team. Patients may, if clinically indicated, make changes to their medication regimen prior to hospitalization only under their outpatient provider's orders and that provider's subsequent supervision. While the half-life of some medications will be longer, the severity of depression of patients referred for ECT necessitates a shorter washout period for clinical reasons. Patients will be monitored on the inpatient unit during the washout period via clinical interviews. The taper schedule will be tailored to each patient according to their individual medications and clinical status. Medications for medical conditions will be administered as clinically indicated and as ordered by the patient's treatment team or the research team. As is standard practice in the NYSPI ECT service, and as recommended by the APA Task Force Report on ECT, benzodiazepines are withheld for 10 hours prior to the treatment.

Motor Threshold (MT)

MT is defined as the minimum magnetic flux needed to elicit a threshold EMG response (50 μV in peak to peak amplitude) in a target muscle in 5 out of 10 trials using single pulse TMS administered to the contralateral primary motor cortex. MT is the standard in the field for determining the intensity of subconvulsive repetitive transcranial magnetic stimulation (rTMS) for each individual to reduce seizure risk. However, data on its relationship with magnetic seizure threshold are limited. MT will be determined in each subject at his/her first and last treatment sessions. EMG responses will be displayed on a portable digital oscilloscope for rapid MT determination (approximately 5 minutes).

Anesthesia and Monitoring

MST will be performed under general anesthesia of the type used in standard clinical ECT. Anesthesia will be administered by anesthesiologists with specific training and experience in ECT. Atropine (0.4 mg i.v.) will be given two minutes prior to anesthesia induction. Standard anesthetic will be used as determined most appropriate by the anesthesiology team, as used in clinical ECT practice and succinylcholine (0.75-1.0 mg/kg) will be used as the intravenous muscle relaxant agent. Patients will be oxygenated from the time of anesthetic administration until return of spontaneous respirations. Seizure duration will be monitored with two frontal-mastoid EEG channels, as well as motor manifestations using the cuff technique. The cuff technique entails the placement of a blood pressure cuff on a limb. The cuff is then inflated above the systolic blood pressure immediately prior to the infusion of succinylcholine. This maneuver prevents the limb from being exposed to the paralytic effects of succinylcholine so that a motor seizure will be

observed in that limb, and can be timed. The succinylcholine will block the expression of a motor seizure in the rest of the body, thereby reducing risk of injury to the extremities that can result from an unmodified tonic-clonic seizure. Using conservative criteria (≥20 seconds), generalized seizures of adequate duration will be elicited at each treatment.

MST/ECT

MST will be performed under general anesthesia (as outlined above) in the NYSPI ECT suite using a custom MST device with which the PI has 5 years of experimental experience in a similar MST protocol, under an Investigational Device Exemption from FDA. The ECT suite is staffed by personnel trained in the acute care of patients undergoing convulsive therapy, and in the prompt recognition and treatment of potential post-ictal complications. The ECT suite is fully equipped to manage potential medical emergencies. This emergency equipment includes oxygen supply, IV line supplies, emergency medications, and a crash cart.

During MT determination and MST, patients and experimenters will wear earplugs to protect inner and middle ear structures from the potential acoustic trauma of the magnetic coil stimulation artifact and thus prevent the risk of transient auditory threshold shifts.

On the first and last session, seizure threshold (ST) will be determined by the ascending method of limits procedure. Threshold determination entails the repeated application of increasingly powerful stimuli until a seizure is obtained. At least 20 seconds will be allowed between successive stimuli, as is standard practice with ECT, to monitor for delayed onset seizures. For those patients assigned to MST, subsequent treatments will be given at maximal stimulator output or up to 6x ST as is standard in unilateral ECT treatments. For those patients assigned to ECT, right unilateral ECT will be administered at 6xST using an ultrabrief stimulus (0.25-0.3 ms). Our work has shown that this form of ECT provides the best cognitive profile without sacrificing efficacy.

Treatment will be administered three times per week. There will be no maximum number of sessions; the number of treatments will be based on the treating physician's clinical assessment. It is expected that most patients will receive treatment for two to six weeks (six to 18 sessions).

If MST fails to induce a seizure: To date, we have been successful in inducing seizures in all humans and animals that have undergone the procedure. Therefore, we do not expect it to be a common occurrence for MST not to induce a seizure. However, if a patient fails to have a seizure during any MST session the patient will be offered to repeat the treatment with different frequency and amplitude settings or will be dropped from the randomized portion of the study and offered routine clinical care. Ultimately, the decision as to what is the best next treatment is a clinical one to be made by the patient in consultation with the treatment team.

Electroencephalography

Quantitative, Regional Brain Electrical Activity (qEEG) will involve recording multi-lead topographical EEG during eyes closed and eyes open conditions. EEG will be conducted at pretreatment and during the first week post-treatment. In addition, multi-lead EEG will be

conducted during the convulsive treatment course at the second and penultimate treatments. These acute studies involve EEG measurement for a 10 minute period prior to treatment, throughout the treatment period, and for 10 minutes in the immediate postictal period. EEG electrodes will be slotted (or made from plastic) to reduce electrode heating.

Neuropsychological Testing and Audiometry

The neuropsychological testing was modeled after that used in our IRB protocols 5097, 4371, 4087, and 3482 to enable comparisons across studies. A technician masked to the treatment condition will administer neuropsychological tests at various time-points to assess the acute, short-term, and long-term memory effects of the treatments (see Table 1). A short version of the battery will be administered before and after each treatment session, while a longer version will be administered at baseline, within 72 hrs post-Phase 1, and 2-month and 6-month follow ups. This battery was designed to be brief to enhance completion rates, and to quantifiably sample a sufficient range of functions to have clinical relevance and scientific value. The short- and long-term batteries were designed to sample those aspects of cognition (a) most vulnerable to ECT (e.g., retrograde and anterograde amnesia), and (b) most reliant on prefrontal lobe function (e.g., executive function tasks) which is the target site of MST stimulation. Psychomotor tasks are included as controls. The battery includes measures to contrast actual performance with the patient's subjective experience. At baseline, after the sixth treatment, and after the final treatment, patients will undergo pure tone audiometry testing for safety screening. If a change in auditory threshold is discovered, the treating physician will inform the patient and discuss whether or not to continue with treatment. Furthermore, if a change is discovered, the patient's hearing will be tested again periodically until either it returns baseline or the clinician determines that the change is permanent.

Clinical Ratings

Ratings will be conducted at baseline, twice a week during acute course of MST/ECT treatments, within 7 days after the last MST/ECT session, and at 2 and 6 month follow up. For remitters, ratings will continue bimonthly for two months, then monthly during Phase 2 through the 6-month "follow-up". The primary clinical outcome measure is the $HRSD_{24}$ since this is the primary outcome measure in the ECT literature. The Inventory of Depressive Symptomatology – Clinician-Rated ($IDS\text{-}C_{30}$) will serve as a secondary outcome measure. Other clinical ratings will include the IDS-self report ($IDS\text{-}SR_{30}$), the Clinical Global Impression - Improvement (CGI-I), the Global Assessment of Functioning (GAF), and the Medical Outcomes Study Short-Form Health Survey. The $IDS\text{-}C_{30}$ and the $IDS\text{-}SR_{30}$ provide objective and subjective ratings of antidepressant response using comparable items. The Columbia University ECT Side Effects Scale will be administered after every treatment. This scale was sensitive in detecting differences between MST and ECT in acute somatic side effects. Subjective memory complaints will be assessed with the Squire Memory Complaint Questionnaire and the Cognitive Failures Questionnaire. The YMRS will be utilized to screen for treatment emergent hypomania or mania, which can be observed with ECT, but which has not been reported with MST.

Consistent with the standard of practice in ECT, there is no predetermined minimum or maximum number of treatments. Treatments will be continued until maximal improvement is achieved. During initial taper and washout, patients who test 6 or higher on a weekly CGI-I will be dropped from the study and referred for clinical treatment. If significant clinical improvement is not achieved by the 8^{th} session ($\geq$25% drop in $HRSD_{24}$), treatment will be stopped. Otherwise, treatment will be continued until there has been a plateau (defined as drop in $HRSD_{24}$ of equal or less than 3 points as measured on week-to-week basis on non-treatment days, i.e. Tuesdays and Thursdays). Should we have a lesser improvement than indicated by this week to week benchmark, provoked by an unusual and/or unanticipated stressful event, then we may appeal to IRB for exemption of the 3- point drop rule. In addition, If the patient receives 15 treatments, the Director of the ECT Service will review the case with the clinical staff and document the clinical decision about continuing treatment. If more than 25 treatments need to be given, the Clinical Director is consulted and consent will be re-obtained.

Clinical response is defined as ≥50% drop in $HRSD_{24}$. Remission is defined as ≥60% drop or $HRSD_{24}$ ≤10. The HRSD remission number is informed by our experience with the elderly population receiving convulsive therapy and is consistent with other comparable protocols previously approved by NYSPI (as in PRIDE study).

Treatment options following acute study treatment

For the responders to Phase-1 study treatment, the acute phase treatments will be terminated upon achieving maximum therapeutic benefit as previously described. These patients will be then started on maintenance medication prior to discharge, in coordination with their existing outpatient provider. Upon discharge, treatment will be transferred back to the existing primary care doctor or psychiatrist. Should patients wish to transfer their care to a different primary provider, appropriate referral will be made with an appointment scheduled typically within one week from the day of discharge. Maintenance medications will be provided to patients at no cost to last until their first appointment with their primary provider. There will be no other outpatient treatment offered following discharge from this study.

Patients, who fail to improve as part of study treatment, will be offered standard-of-care inpatient clinical treatment at no cost to the patient, which may include medications or open ECT, to be determined by the clinicians responsible for patients' care in consultation with the ECT MD and PI of the study. To protect blinding of the study, previous ECT/MST treatment will be discussed only with the inpatient clinician-attending prior to determining the best post-study treatment option, on the condition that this attending not reveal the randomization to the patient or other personnel.

Patients, who were receiving study treatment as outpatients and failed to respond, will be given a choice of returning to their physician for ongoing treatment or being re-admitted for inpatient ECT, following discussion of the study treatment with their provider in the same manner as described above for inpatient non-responders. ECT as a clinical inpatient is available at no cost to the patient.

TMS motor cortex excitability studies

A battery of TMS motor cortex excitability studies will be performed in the week prior to and the week following the course of MST, to explore the neurophysiological responses to the treatment. This is the same battery as used in protocols # 5097, 3482 and 4371, and consists of motor threshold, central motor conduction time, paired pulse curve, and input/output curve. All of these assays are performed with single pulse magnetic stimulators (low frequency).

Biochemical Studies

At the second, sixth, and penultimate treatments, blood will be drawn immediately before and at 3 time-points following the seizure (5, 15, and 30 minutes). This blood will be assayed for prolactin, and cortisol levels to explore the neuroendocrine response to the treatment. If a viable venous draw is unsuccessful, an attempt to draw blood will be made on the subsequent treatment/s.

Naturalistic Follow-Up (Phase 2).

Patients will be followed for 6 months to monitor persistence of clinical benefit and of side effects. To be classified as a relapse during the follow-up phase, patients must have a $HRSD_{24}$≥20 and a ≥10 point increase in $HRSD_{24}$ maintained across 2 visits at least a week apart, or experience emergence of psychosis or suicidal ideation, or require hospitalization. This definition should capture sufficient worsening that would necessitate a change in clinical management. To characterize the nature of the naturalistic treatment received during Phase 2, information on treatment type, dosage, and duration of exposure will be collected at each assessment. We will follow nonremitters who subsequently receive ECT with pre and post $HRSD_{24}$ scores to determine whether ECT following MST results in a significant rate of response.

You can upload charts or diagrams if any

Criteria for Early Discontinuation

Criteria for Early Discontinuation

Failing to respond to treatment is defined as not having achieved a ≥ 25% drop in HRSD after completing treatment #8. In such case, the treatment team will be free to recommend whatever treatment is judged best for the patient, based upon his/her clinical status and medication history. Treatment as a clinical inpatient at NYSPI will be provided at no cost.

Blood and other Biological Samples

Please create or insert a table describing the proposed collection of blood or other biological specimens

Baseline lab work: approximately 25 ml of blood, which include routine preECT labs (blood and urine) workup to screen for medical conditions that may affect the ECT course and a toxicology screen for substance use.

Biochemical studies: approximately 25 ml at each of 3 assessments during the second, sixth, and penultimate treatments, analyzed for serum Prolactin and Cortisol.

Assessment Instruments

Create a table or give a brief description of the instruments that will be used for assessment

Table 1. Schedule of Research Procedures

Assessments*	Baseline	Treatment #1	Every Tx	Post Tx #6	Last Tx	Post Phase 1	2-Month	6-Month
Clinical Ratings								
Structured Clinical Interview for Diagnosis (SCID) – 1 hr	x							
Transcranial magnetic stimulation Adult Safety Screen (TASS) – 5 min	x							
Antidepressant Treatment History Form (ATHF) – 30 min	x							
Hamilton Rating Scale for Depression ($HRSD_{24}$) – 30 min	x	x	x*	x	x	x	x	x
Inventory of Depressive Symptomatology ($-SR_{30}$, $-C_{30}$) – 10 min	x			x		x	x	x
Medical Outcomes Study Health Survey (SF-36) - 15 min	x					x	x	x
Clinical Global Improvement (CGI) – 5 min	x					x	x	x
Global Assessment of Functioning (GAF) – 5 min	x					x	x	x
Young Mania Rating Scale (YMRS) – 10 min	x					x	x	x
Columbia ECT Subjective Side Effects Scale - 5 min	x	x	x	x	x	x		
Neuropsychological Battery - Acute Effects								
Treatment Effects Battery – 45 min	x	x	x	x	x			

Neuropsychological Battery - Short and Long-Term Effects **1 ½ days**								
Global Cognitive Function								
Modified Mini Mental Status Exam (mMMS) and Wide Range Achievement Test	x					x		x
Anterograde Learning and Memory								
Buschke Selective Reminding Test, WRAT3	x					x		x
Complex Figure Copying (with 20 min delay)	x					x		x
Retrograde Memory								
Autobiographical Memory Interview - Short Form	x					x		x
Goldberg Remote Memory Questionnaire	x					x		x
Psychomotor								
Simple Reaction Time	x					x		x
Choice Reaction Task, Grooved Pegboard, Trail Making A	x					x		x
Executive Function								
N-Back Working Memory, Trail Making B, Sorting, Stroop	x					x		x
Digit Span, Controlled Oral Word Assoc, Fluency, Go-No Go	x					x		x
Subjective Cognitive Evaluation								
Cognitive Failures Questionnaire	x					x		x
Neurophysiological Studies								
MST Seizure Threshold Titration		x			x			
TMS Motor Threshold Studies	x					x		

* HRSD24 testing will be performed twice weekly, on non-treatment days.

Please attach copies, unless standard instruments are used

Off label and investigational use of drugs/devices

Choose from the following that will be applicable to your study
✓ Device

Off label and investigational use of devices

Device #1

Name of the device

MagVenture MagPro MST Device
Manufacturer and other information

MagVenture, Inc.

Approval Status
IDE is approved
IDE#
G090145-R002
Who holds the IDE/IDE sponsor?
IDE is held by PI/CU Investigator
Rowny, Stefan, MD

Device #2

Name of the device
Magstim MST Device
Manufacturer and other information
Magstim Company Limited
Approval Status
IDE application is pending
Who holds the IDE/IDE sponsor?
IDE is held by PI/CU Investigator
Rowny, Stefan, MD

Research Related Delay to Treatment

Will research procedures result in a delay to treatment?
Yes
Maximum duration of delay to any treatment

Patients will undergo a taper followed by a 5-day psychotropic medication washout prior to the start of MST. The duration of the taper depends upon the particular medications the patient is taking. Some of these medications would need to be tapered and washed out or reduced for clinical reasons prior to receiving convulsive therapy (e.g., lithium, benzodiazepines) and are not strictly related to research procedures. Although this taper varies in each individual, in most cases it can be accomplished in 3 to 5 days and is also required in approved convulsive treatment (ECT). Therefore, the maximum expected delay to treatment is 8 to 10 days and in cases of no medication washout the maximum delay to treatment is usually no more 3 days, considering that treatments are offered 3 times a week and allowing for the first day to be dedicated to inpatient intake procedures.

Maximum duration of delay to standard care or treatment of known efficacy

There is no sham or placebo in this study, but MST is experimental and therefore does not have known efficacy. For those patients randomized to MST, the delay to receiving a known active treatment is the duration of Phase 1 plus the washout period. The duration of Phase 1 depends upon clinical response (see above), but patients will be withdrawn from the study and given routine clinical care with a treatment of known efficacy if they do not achieve improvement by the 8th treatment (treatments are given x3/wk, so 8 treatments would take 2 ½ weeks plus medication washout period). For those patients randomized to ECT, they will begin receiving a treatment with known efficacy immediately after the 5-day washout.

Treatment to be provided at the end of the study

Patients who fail to respond to MST or RUL ECT will be offered standard treatment as clinically indicated by the inpatient or outpatient treatment team, which may include another form of ECT (e.g. bilateral) if clinically appropriate or antidepressant medication. The treatment team will be free to recommend whatever treatment is judged best for the patient, based upon his/her clinical status and medication history. For patients who have responded to MST or ECT, it is recommended that they be started on antidepressant medication to maintain that response and prevent relapse.

Clinical Treatment Alternatives

Clinical treatment alternatives
Depending on severity of depression and adequacy of previous treatment trials, a different class of medication or therapy may be suggested prior to acceptance of a patient to a study.

Risks/Discomforts/Inconveniences

Risks that could be encountered during the study period

We expect that the side effects of MST should be equal to or less than the side effects of ECT (discussed in detail below). Both treatments entail the induction of electricity in the brain and the initiation of a seizure. Magnetic fields do not penetrate as deeply as electric fields, suggesting that the cognitive side effects resulting from the stimulation of deeper brain structures should be less with MST than ECT. In the first case in which MST was conducted in humans, the only reported side effect was headache. In the first trial of 10 patients conducted at NYSPI, we found that MST had fewer acute cognitive side effects than ECT. In our second trial of MST (10 at

NYSPI and 10 at UTSW), we found MST was well tolerated with substantially fewer cognitive side effects than patients receiving ECT in other studies simultaneously conducted. Now a series of 10 patients have been treated with MST in Bern, Switzerland, with comparable results and 20 more in Germany also with the same results. In none of these cases has there been a significant or unexpected adverse event. There has been one mention in the literature of dental pain that may persist after the MST treatment course has ended. The cases of inadvertent seizure induction with rTMS in unanesthetized subjects have indicated no evidence of any long-term adverse medical or neurological consequences of rTMS-elicited seizures. Since MST is investigational, MST may not be effective, thus receiving MST may delay effective treatment. Delay in treatment of depression may result in worsening of the clinical condition (e.g., intensified symptoms, suicidal ideation). As with all antidepressant treatments, including ECT, there is a theoretical risk of inducing mania. Patients participating as outpatients also have risk of falling, risk of noncompliance with treatment instructions, and risk of danger from operating dangerous machinery, such as driving or using the stove.

ECT:

Immediately following ECT, patients are typically disoriented or confused. Following ECT sessions, some patients report headache, muscle soreness, or nausea. These side effects usually respond to simple treatment. Serious medical complications are rare. Dislocations, bone fractures, and dental complications have been reported with ECT, but have not been observed at NYSPI for the last 25 years. Cardiac complications are more common and constitute the leading cause of morbidity and mortality with ECT. The likelihood of these complications is reduced by (1) careful medical workup and the use of cardiology consultants in patients with significant preexisting cardiac disease; (2) careful monitoring of cardiac status during ECT; (3) modification of anesthetic procedures for prophylactic purposes (e.g., use of pharmacological agents to block hemodynamic changes). The availability of senior neuroanesthesiologists, who average several years of experience in conducting anesthesia for ECT, limits the development or sequelae of cardiac complications. Fatality associated with ECT is estimated to occur in 1/10,000 patients, and to our knowledge has never occurred at NYSPI.

ECT commonly results in memory deficits. These memory deficits are of two types: anterograde and retrograde amnesia. The anterograde amnesia involves a deficit in the capacity to retain newly formed information over delays (i.e. rapid forgetting). It is most intense immediately following a treatment, and displays rapid recovery. There is little objective evidence that anterograde amnestic deficits persist more than two weeks following an ECT course. In group data, studies at NYSPI have failed to observe persistent anterograde deficits. Retrograde amnesia pertains to a retrieval (and in some cases recognition) deficit for memory of events that occurred before and during the ECT course. This deficit also appears to be most marked immediately following a treatment and is less likely to occur, with respect to memory events temporally further away from the treatment. Thus the descriptor ‘grade’ in the name. In an overwhelming majority of cases the deficit pertains to recent memories, for example those during the patient’s hospitalization, with more remote memories spared. While subject to rapid recovery, this deficit may never totally recede. Objective testing and subjective patient reports suggest that some

patients will have permanent spottiness in memory for events that occurred close in time to the ECT course.

The magnitude of both memory deficits is sensitive to the parameters used in the conduct of ECT. In general, these deficits are more severe with bilateral versus right unilateral electrode placement, sine wave versus brief pulse stimulation, higher versus lower electrical intensity, closer spacing of the treatments, and larger number of treatments. Precautions that are taken in this protocol include the use of brief pulse, constant current stimulation and the titration of electrical dosage relative to seizure threshold. Further, the number of treatments is limited to that necessary to achieve clinical response or to ensure an adequate ECT trial. During the treatment course, there is careful monitoring of acute (post-ictal) and short-term (inter-ictal) cognitive side effects. Spacing of treatments may be increased or the treatment course terminated in the context of unacceptable side effects. Patients participating as outpatients also have risk of falling, risk of noncompliance with treatment instructions, and risk of danger from operating dangerous machinery, such as driving or using the stove.

Evaluation Procedures:

The medical evaluations present no risks beyond what is expected for routine clinical care of a patient undergoing a course of ECT. The procedures involve collection of blood through venipuncture for the initial screening blood work-up (25 ml).

Neuropsychological Testing:

There may be a risk of fatigue from participation in the neuropsychological testing, but there are no other known risks from these procedures.

Medication Washout:

Withdrawing antidepressant medication carries a risk of worsening the underlying depression. However, our ECT protocols require 5 days. Washout also carries a risk of withdrawal side effects, depending upon the specific medications.

Motor Cortex Excitability Studies:

The methods used to evaluate motor threshold and other measures of motor cortex excitability involve the administration of single or paired pulse TMS given at long inter-pulse intervals. The most serious known risk of low frequency TMS is seizure. Low-frequency TMS has not been associated with seizure in appropriately screened individuals. If a patient has a seizure, he/she may require admission to a medical service and follow-up neurological evaluation. Having had a seizure may adversely affect medical insurability, future employment, and ability to drive. It is not known whether having had one seizure will make a person more prone to have future seizures. If a seizure occurs, the patient will be given a letter documenting that it was experimentally induced. The most commonly reported side effect of low frequency TMS is a “muscle-tension” type headache. About 17 out of every 100 people will experience a mild headache with this type of TMS. If a headache occurs, it usually starts during or immediately after the TMS and lasts from

minutes to hours later. The headache usually goes away with standard, non-narcotic, pain medications (aspirin, acetaminophen or Ketorolac). Neck pain may also occur, and it is also usually managed easily with standard over the counter painkillers. There may also be scalp discomfort due to contraction of scalp muscles. The clicking noise produced during the stimulation may temporarily affect hearing. The earplugs will reduce this risk. Patients participating as outpatients also have risk of falling, risk of noncompliance with treatment instructions, and risk of danger from operating dangerous machinery, such as driving or using the stove.

Describe procedures for minimizing risks

Procedures for Minimizing Risks:

The safety measures recommended by the manufacturer regarding not operating the magnetic stimulation device in the context of cardiac pacemakers, metallic implants, and loose paramagnetic objects will be followed. These exclusions prevent the risk of pacemaker malfunction and the torque that may be exerted on metallic implants by the magnetic field. Metallic objects are removed from the vicinity of the device (≤ 10 cm). This includes removing jewelry, scissors, needles, and other paramagnetic objects. Magnetic sensitive materials (e.g., watches, credit cards, computer disks) are also removed to avoid the possibility of damage. When not in use, the Magnetic Stimulator is disabled and the cart housing it is locked.

Screening of Subjects Prior to Stimulation:

As described above, the screening assessment of potential subjects will identify and exclude from participation individuals with current or past medical conditions that may place them at increased risk for adverse effects from magnetic stimulation. Screening will include administration of the Transcranial magnetic stimulation Adult Safety Screen (TASS), which assesses medical history, neurological history (seizure, stroke, and brain lesion), head trauma, metallic implants, and implanted devices. Screening will be performed by physician evaluation, physical examination, and blood/urine analysis.

Screening to allow outpatient participation after initial 3 inpatient treatments will also include an evaluation of a responsible adult, who will assist the patient during the time of the acute treatments. The function of the “Responsible Adult” is to provide direct support to the research participant receiving convulsive treatment on the outpatient basis, and to facilitate safety by enhancing communication between the treating team and the patient. The responsible adult does not need to be domiciled together with the participant, but needs to be with the patient for 24 hours after each treatment, as per NYSPI policy. The responsible adult will be given a checklist to use in discharging his/her responsibilities.

Protection From Excessive Noise:

Earplugs will be worn by staff and patients prior to any magnetic stimulation to prevent exposure to excessive noise.

Protection From Excessive Temperatures:

The stimulation coil is insulated to retard heating. The coils contain temperature sensors, providing continuous readouts. The controller software disables the device if coil temperature exceeds safe levels. Plastic or slotted EEG electrodes that have been shown on testing to avoid electrode heating with MST will be used in this study.

Supervision of Subjects During Stimulation Sessions:

Stimulation sessions will be conducted by a physician team (psychiatrist and anesthesiologist) with the participation of other trained personnel, including a licensed RN. These personnel will be in visual and auditory contact with the patients at all times. Health status will be monitored continuously as described above.

Emergency Power Interruption:

In the event of an emergency, stimulation will be discontinued immediately by removing the coil from the head and then disabling the device.

Controller Unit Safety Features:

The dedicated computer controller software for the Magnetic Stimulator has internal limits on stimulation parameters. These limits prevent the device from being programmed to deliver pulses that exceed predetermined limits. The software logs all pulses administered, as well as parameter values.

Emergency Medical Procedures:

If at any moment during the stimulation session, there is a clinical suspicion of a possible serious adverse health effect, the coil will be immediately removed from the patient's head and the stimulator will be disabled. The ECT suite is staffed by medical personnel with extensive experience in ECT and has access to emergency equipment (oxygen, IV medications, crash cart) to handle potential adverse events.

Methods to Protect Confidentiality

Describe methods to protect confidentiality

All data (written and electronic) will be coded by number. A master list identifying subjects 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 subject names to code numbers. In the informed consent form, subjects are told that the information they provide and all

findings of testing will be kept strictly confidential, with access limited to the research staff, and possibly state or federal regulatory personnel. Information about the patients' condition and treatment will be kept in a computer but the patients' names will not appear in this database. The information will only be linked to a code number assigned for the purposed of maintaining privacy. Only members of the research team will have access to the computer.

Will the study be conducted under a certificate of confidentiality?
No

Direct Benefits to Subjects

Direct Benefits to Subjects

Patients with major depression will receive a course of convulsive therapy. ECT is an approved and effective treatment for major depression, but the therapeutic effects of MST are not yet known.

Compensation and/or Reimbursement

Will compensation or reimbursement for expenses be offered to subjects?
No

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Uploads

Upload copy(ies) of unbolded Consent Form(s)
#6427_CF_Unbolded.pdf
Upload copy(ies) of bolded Consent Form(s)
Upload copy(ies) of recruitment materials/ads to be reviewed
Upload evidence of FDA IDE approval(s)
Upload copy(ies) of the HIPAA form
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Upload any additional documents that may be related to this study

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)

New York State Psychiatric Institute (NYSPI)
Authorization to Use or Disclose Health Information during a Research Study

Protocol Number: IRB#6427 **Principal Investigator:** Stefan Rowny, MD

Name of Study: Improving Outcomes in Geriatric Depression: Magnetic Seizure Therapy

Before researchers can use or share any identifiable health information ("Health Information") about you as part of the above study (the "Research"), the New York State Psychiatric Institute (NYSPI) is required to obtain your authorization. You agree to allow the following individuals and entities to use and disclose Health Information about you as described below:

- New York State Psychiatric Institute (NYSPI), your doctors and other health care providers, if any, and
- The Principal Investigator and his/her staff (together "Researchers"). Researchers may include staff of NYSPI, the New York State Office of Mental Health (OMH), Research Foundation for Mental Hygiene, Inc. (RFMH), and Columbia University (CU), provided such staff is a part of the study, and
- Providers of services for the Research at CU, NYSPI and/or RFMH, such as MRI or PET, or Central Reference Laboratories (NKI), if indicated in the consent form**.**

1. The Health Information that may be used and/or disclosed for this Research includes:

☑ All information collected during the Research as told to you in the Informed Consent Form.
☑ Health Information in your clinical research record which includes the results of physical exams, medical and psychiatric history, laboratory or diagnostic tests, or Health Information relating to a particular condition that is related to the Research.
☐ Additional information may include:

2. **The Health Information listed above may be disclosed to:**

☑ Researchers and their staff at the following organizations involved with this Research:
Stefan Rowny, MD; Daniel Javitt, MD, PhD; Joan Prudic, MD

☑ The Sponsor of the Research,
RFMH(K23)
and its agents and contractors (together, "Sponsor"); and
☑ Representatives of regulatory and government agencies, institutional review boards, representatives of the Researchers and their institutions to the level needed to carry out their responsibilities related to the conduct of the research.
☑ Private laboratories and other persons and organizations that analyze your health information in connection with this study
Bioreference Laboratory, Elmwood Park, NJ 07407

☐ Other (family members or significant others, study buddies, outside agencies etc.) Specify:

3. By giving permission to release your Health Information as described above, you understand that your Health Information may be disclosed to individuals or entities which are not required to comply with the federal and state privacy laws which govern the use and disclosure of personal Health Information by NYSPI. This means that once your Health

Information has been disclosed to a third party which does not have to follow these laws (e.g., a drug company or the Sponsor of the Research), it may no longer be protected under the HIPAA or NYS Mental Hygiene Law requirements but is subject to the terms of the consent form and may be subject to other state or federal privacy laws or regulations.

4. Please note that:

- You do not have to sign this Authorization form, but if you do not, you may not be able to participate in the study or receive study related care. You may change your mind at any time and for any reason. If you do so, you may no longer be allowed to participate in the study. If you withdraw this Authorization the research staff and the Sponsor, if this is sponsored research, may still use or disclose Health Information containing identifying information they already have collected about you as needed to maintain the reliability of the research. Any request to withdraw this Authorization must be made in writing to (enter name and contact information below):

  Daniel Javitt, MD, PhD
  New York State Psychiatric Institute
  1051 Riverside Drive, Unit 21
  New York, NY 10032

- While the Research is going on, you may not be allowed to review the Health Information in your clinical research record that has been created or collected by NYSPI. When this research has been completed you may be allowed to see this information. If it is needed for your care, your Health Information will be given to you or your Doctor.

5. This Authorization does not have an end date.

6. You will be given a copy of this form after you have signed it.

I agree to the use and disclosure of Health Information about me as described above:

_____ _____

Signature of Participant/ Legal Representative Date

_____

Printed Name of Participant

_____

Relationship of Legal Representative to Participant (if applicable)

We also ask you or your legal representative to initial the statements below:

☐ **I have received a copy of the NYSPI/OMH Notice of Privacy Practices.**