Antidepressant Response in Older Adults with Comorbid PTSD and MDD

Protocol ID 8111
NCT04697693

Protocol Summary Form and Consent Form

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Protocol Title:
Antidepressant Response in Older Adults with Comorbid PTSD and MDD

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Research Chief:
Bret Rutherford, MD

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 proposing an amendment only to an existing protocol

Department & Unaffiliated Personnel

Department

What Department does the PI belong to?
Neurobiology and Therapeutics of Aging
Within the department, what Center or group are you affiliated with, if any?
Clinic on Aging, Anxiety, and Mood Disorders

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.
none

Amendment

Describe the change(s) being made
One research staff member, Nurse Practitioner Denise McClellan, was added to the list of persons designated to discuss and document consent. Additionally, one research staff member, Nurse Practitioner Galit Marcus, was removed from the list of persons designated to discuss and document consent, as the staff member has resigned from her position in our clinic.
Provide the rationale for the change(s)
To maintain clinic capacity for visits and recruitment for the study and update the list of personnel who are able to discuss and document consent.
Comment on the extent to which the proposed change(s) alter or affect risks/benefits to subjects
The proposed change will not alter the risks or benefits to subjects.
Comment on if the proposed change(s) require a modification to the Consent Form (CF)
No modifications were made to the consent form.

Procedures

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

✓ Psychiatric Assessment
✓ Neuropsychological Evaluation
✓ Medication Trial
✓ Internet-based Data Collection or Transmission

Population

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

✓ Adults over 50

Research Support/Funding

Will an existing internal account be used to support the project?
Yes
Describe internal account
Dr. Rutherford's Columbia University Irving Scholar account
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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In our ongoing studies of Posttraumatic Stress Disorder (PTSD) in older adults, we have found that older adults with PTSD frequently meet criteria for comorbid Major Depressive Disorder (MDD). Moreover, relative to trauma-exposed healthy controls (TEHCs), elders with PTSD manifest executive function deficits, fatiagability, and mobility and physical function deficits that are consistent with what we have observed in depressed older adults. Yet, we have found that very few older adults with combined PTSD/MDD have received appropriate antidepressant treatment for their condition.
These findings give rise to the questions of (1) how effective is antidepressant treatment for depressive symptoms in the context of PTSD/MDD and (2) are cognitive and physical function deficits in PTSD/MDD patients reversible with effective antidepressant treatment?
Participants who recently completed IRB 7489 and who sign consent to participate in this open treatment study will be treated for 8-weeks with antidepressant medication. Participants will be seen in person for the week 0 (baseline) visit, where they will complete baseline testing. Participants will meet with research assistants and clinicians every two weeks virtually, via a HIPAA compliant video platform, Webex. They will then come in person for the final study visit, week 8. Week 8 will be conducted in person and will consist of repeat baseline testing. This will be the second study visit conducted in person, unless a significant clinical worsening occurs and/or the participant wishes to be seen in person for a visit. Following the 8 weeks, participants will be eligible for 3 months post protocol open treatment and will continue to receive referrals for PTSD treatment.

Background, Significance and Rationale

Background, Significance and Rationale

Chronic PTSD in older adults leads to increased risk of mortality from cardiovascular disease, metabolic syndrome, diabetes mellitus, and ulcerative gastrointestinal disease. PTSD appears to promote aging-associated syndromes such as frailty, and older patients with PTSD exhibit faster cognitive decline and have twice the risk of dementia compared to individuals without PTSD. In addition, laboratory studies report accelerated biological signatures of aging in PTSD patients, including shortened leukocyte telomere length,

increases in pro-inflammatory cytokines, and increased oxidative stress. PTSD is associated with similar anatomical brain changes to those occurring with cognitive aging, including bilateral hippocampal volume reductions, specifically affecting the dentate gyrus (DG) and CA3 subregion, and increased microvascular lesions (white matter hyperintensities [WMH]). These observations suggest that the adverse health and functional outcomes associated with chronic PTSD in older patients may be explained by a deleterious interaction between pathophysiologic changes underlying PTSD and the biology of aging, the end result of which is to accelerate senescence throughout the body and particularly in the brain. However, no prior study has explicitly tested this hypothesis by examining indices of aging in older adults with and without PTSD.

In our ongoing IRB #7489, we hypothesize that chronic PTSD, over and above other contributing factors, accelerates biological aging in the brain and body, leading to adverse behavioral consequences such as frailty and cognitive decline. To test these hypotheses, 150 individuals are being recruited who are aged ≥50 and diagnosed with PTSD. A control group of 150 age-, sex-, and trauma exposure-matched subjects without PTSD are being recruited and assessed. Included subjects undergo comprehensive neuropsychological assessment and cerebral blood volume functional magnetic resonance imaging (CBV-fMRI) to assess regional hippocampal metabolic activity and function. Structural MRI is performed to quantify WMH, regional brain volume, and cortical thickness, while resting state fMRI measures functional connectivity within hippocampal networks. PTSD subjects and controls are compared on measures of aging within the following domains: neural (DG CBV, WMH, morphology), cognitive (processing speed, memory, executive function, pattern separation), somatic (peripheral inflammatory markers, leukocyte telomere length, and measures of oxidative stress), and behavioral (grip strength, gait speed, fatigue levels). By elucidating the interaction of chronic PTSD with aging processes, data from this project may contribute to the development of rationally designed, personalized, and age-appropriate novel treatments.

Interim analyses of PTSD subjects in this study demonstrate a high degree of comorbidity with MDD. Among participants with PTSD enrolled to date, 67.1% meet criteria for MDD and mean Hamilton Rating Scale for Depression (HRSD) is 18.1. The most prominent cognitive differences observed to date in our study between PTSD and TEHC subjects is executive dysfunction, which is common in late life depression. PTSD subjects have dramatically increased fatigability and prevalence of frailty criteria compared to TEHCs, abnormalities which are also frequently seen in our older MDD samples. Yet, we have found that less than 25% of these individuals are currently receiving an adequate dose and duration of first-line pharmacotherapy for MDD, while only one third report any past medication treatment. These data raise the question of whether patients with combined PTSD/MDD could benefit from adequate antidepressant medication treatment and to what degree their cognitive and physical function deficits would be reversible with this therapy.

Specific Aims and Hypotheses

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Aim 1. To study the effectiveness of antidepressant medications to treat depressive symptoms in older adults with PTSD/MDD.

Hyp 1: A significant improvement in depressive symptoms will be observed, and response rates to open antidepressant medication treatment in this population will be greater than 50%.

Aim 2: To evaluate change in cognition and physical function following antidepressant medication treatment.

Hyp 2: As compared to non-responders, responders to antidepressant treatment will demonstrate significantly greater improvement in executive function (NIH Toolbox) and gait speed.

Description of Subject Population

Sample #1

Specify subject population
Participants in IRB 7489 with combined PTSD and MDD
Number of completers required to accomplish study aims
20
Projected number of subjects who will be enrolled to obtain required number of completers
25
Age range of subject population
50 years and older

Gender, Racial and Ethnic Breakdown

We anticipate the sample will be composed of approximately 60% women and 40% men.

Racial/ethnic group: On the basis of previous depression studies conducted in the Clinic for Aging, Anxiety, and Mood Disorders, it is anticipated that the sample will be composed of approximately 75% Caucasian, 15% African American, and 10% Hispanic subjects.
Description of subject population
The proposed study will enroll 25 outpatients who are (1) participants in IRB 7489, (2) diagnosed with DSM 5 MDD, (3) have HRSD >=18, and (4) are willing to and capable of providing informed consent and complying with study procedures. Participants will be excluded for (1) history of allergic or adverse reaction to escitalopram and duloxetine, (2) non-response to adequate trial of escitalopram (at least 4 weeks at dose of 20mg) and duloxetine (at least 4 weeks at dose of 60mg) during the current episode, or (3) current treatment with psychotherapy, antidepressants, or other psychotropic medications.

Recruitment Procedures

Describe settings where recruitment will occur
Subjects will be recruited from participation in IRB 7489.

How and by whom will subjects be approached and/or recruited?
The research assistant will notify a study clinician once a participant completing IRB 7489 is known to meet the selection criteria. The clinician will then approach the participant and discuss potential treatment in this protocol, with its attendant risks, benefits, and alternatives.
How will the study be advertised/publicized?
There is no advertisement for this study other than what is undertaken in IRB 7489.
Do you have ads/recruitment material requiring review at this time?
No
Does this study involve a clinical trial?
Yes
Please provide the NCT Registration Number
04697693

Concurrent Research Studies

Will subjects in this study participate in or be recruited from other studies?
Yes
Describe concurrent research involvement
Potential participants in this open treatment study will have recently completed IRB 7489.

Inclusion/Exclusion Criteria

Name the subject group/sub sample
Depressed irb 7489 participants
Create or insert table to describe the inclusion criteria and methods to ascertain them

Inclusion criteria:	Method of ascertainment:
1. Individual has completed IRB 7489	1. Study records
2. Diagnosed with DSM 5 MDD	2. SCID, data from IRB 7489
3. HRSD >=18	3. Data from IRB 7489
4. Willing to and capable of providing informed consent and complying with study procedures.	4. Clinical interview

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

Exclusion criteria:	Method of ascertainment:
1. History of allergic or adverse reaction to escitalopram and duloxetine	1. Clinical interview, data from IRB 7489

2. Non-response to adequate trial of escitalopram (at least 4 weeks at dose of 20mg) and duloxetine (at least 4 weeks at dose of 60mg) during the current episode	2. Clinical interview, data from IRB 7489
3. Current treatment with psychotherapy, antidepressants, or other psychotropic medications.	3. Clinical interview, data from IRB 7489

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
Yes
Waiver of parental consent
No

Consent Procedures

Is eligibility screening for this study conducted under a different IRB protocol?
Yes
Indicate NYSPI IRB #
7489
Describe Study Consent Procedures
Participants who complete IRB 7489, meet the study selection criteria and agreed to be contacted in the future will be approached by a study clinician, Psychiatrist (MD), or a Psychiatric Nurse Practitioner (NP) authorized to obtain patient consent. Study clinicians who obtain consent for this study are licensed Doctors of Medicine (MD) and/or Psychiatric Nurse practitioners (NP) in the State of New York. Participants may be approached on the day of their final study visit for protocol IRB 7489 or may be contacted by phone. Participants who have a computer/smartphone/tablet access will be asked to provide verbal consent to participate in the interviews, and verbal consent will be documented. The participant will receive a consent form and HIPAA form via REDCap for e-consent, if a participant has access to a computer and email. The Clinician (MD or NP) will explain to the participants their diagnosis with MDD, symptom level, and the options for treating this will be discussed (including not treating it). The clinician (MD or NP) will discuss the risks, benefits, and alternatives to treatment with escitalopram or duloxetine and allow the participant the opportunity to ask questions. This will take place via a HIPAA compliant video conferencing platform,

Webex. The consent process will also include a discussion and explanation of Webex and will address any concerns the participant may have, such as access to private space in which to take calls, or accessibility at home to adequate devices, cell signal, or WIFI. If a participant does not have the appropriate technology in order to complete e-consent through REDCap, than a research staff member will verbally consent the participant and it will be documented. These participants will be mailed a copy of the consent form and HIPAA form. A consent procedure note will include all information discussed with the participants regarding the remote consent process, procedures and also the risk involved in traveling for in-person visits during the COVID-19 pandemic.
Indicate which of the following are employed as a part of screening or main study consent procedures
✓ Consent Form

Waiver of Documentation of Consent

Would the consent form signature be the only link between the subject's identity and the research data?
No
Is breach of confidentiality the main study risk?
No
Is consent for this research procedure ordinarily not required outside of the research context? Explain
We plan to consent potential participants on the last study visit for protocol #7489. Participants who have already completed their last study visit will be contacted by a study clinician (MD/NP), authorized to obtain consent, who will explain the study procedures and answer any questions that the participant may have via a HIPAA compliant Video conferencing platform, Webex. If the subject agrees to participate, they will be sent an online link using REDCap to access the consent form. We are requesting a waiver of documentation of consent for participants who do not have the technology to sign the consent via REDCap. Participants will be asked to sign a paper consent form when they arrive to clinic for the in person visit.

Persons designated to discuss and document consent

Select the names of persons designated to obtain consent/assent
Brewster, Katharine
Broft, Allegra, MD
McClellan, Denise
Roose, Steven, MD
Rutherford, Bret, MD
Type in the name(s) not found in the above list

Study Procedures

Describe the procedures required for this study

I attest to follow the COVID-19 Safety Guidelines for Columbia Psychiatry and NYSPI Re-Entry outlined in the NYSPI Director's June 1stmemo, which include but are not limited to:

- Infection Control/PPE –Guidelines
- Research participants will only come on-site if absolutely necessary for study procedures.
- No volunteers/externs on-site during Stage 1.
- Clinical research teams will screen their participants for COVID symptoms (night before and day of onsite visit, documenting this in the chart), and escort them in and out of the building.
- COVID/COVID-like symptoms in participants will be reported to the IRB via PRISMas an SAE.

1. Following consent, the participant will be begun on either escitalopram 10mg or duloxetine 30mg. The default medication will be escitalopram. Subjects will begin escitalopram 10mg, continue this dosage for 4 weeks, then if the HRSD >7 at Week 4, he/she will have their dosage increased to 20mg for the remainder of the 8 week study. Participants who have not responded to or not tolerated escitalopram in the current depressive episode will be started on duloxetine. They will take 30mg **of duloxetine for the first 2 weeks**, then, **contingent on clinical assessment that the 30mg dose is sufficiently well tolerated,** be increased to 60mg for the **remaining 6 weeks** of the study. Participants will be provided with the study medication during the Week 0 (baseline) in person visit. During the week 4 (virtual) visit**,** participants **taking escitalopram** will be sent the study medication directly to their home via Fedex. **This will be done during the week 2 (virtual) visit for participants taking duloxetine.** If significant worsening occurs and/or the participant wishes to be seen in person for the week 4 **or week 2** visit, they will be provided with the study medication onsite.

Study Visits will occur in person/virtually as outlined below:

- Week 0: In-person
- Week 2: Virtual
- Week 4: Virtual
- Week 6: Virtual
- Week 8: In-person

2. Subjects unable to tolerate the higher dose of study medication will have their dose reduced to the previously tolerated dose. Subjects unable to tolerate the beginning dose of study medication will be tried (if possible given their history) on the other study medication. Participants unable to tolerate the beginning dose of either study medication will be dropped from the study and enter post protocol open treatment.

3. Subjects will have telephone/video-conference visits via a telephone and/or a HIPAA compliant video conferencing platform, Webex with the research assistant and study clinician every two weeks. The RA will check Hamilton Rating Scale for Depression (HRSD) and Hamilton Anxiety Rating Scale (HARS) at each call. The study clinician will then evaluate the participant and complete the Clinical Global Impressions (CGI) Severity and Improvement. If the participant requests or significant clinical worsening in the

judgement of the study clinician occurs, then the participant will be brought to NYSPI for in person evaluation.

4. At Week 8 study endpoint, participants will return to the Clinic on Aging, Anxiety, and Mood Disorders (CAAM) **and the Anxiety Disorders Clinic (ADC)** for HRSD, HARS, CGI Severity and Improvement, **PCL-5, and CAPS-5**. In addition, repeat neuropsychological testing and physical function assessment (the same tests from baseline in IRB 7489) will be performed. These include frailty characteristics assessed from the Fried model: unintentional weight loss (10 lbs or 5% of body weight in the past year), self-reported exhaustion, weakness (grip strength), slow walking speed, and low physical activity. Exhaustion will be dichotomized as yes/no using a physical fatigability cutoff score of >10 on the Pittsburgh Fatigability Scale (PFS). Grip Strength is measured using a Jamar dynamometer with maximum grip strength measured over 3 trials. Gait will be assessed as walking speed in m/s on a GaitRITE walkway. Physical activity is assessed via a measure of weekly kilocalories (kcal) derived from the 18-item Minnesota Leisure Time Physical Activity Questionnaire. Function will be assessed using the Short Physical Performance Battery (SPPB), the 36-item self-report World Health Organization Disability Assessment Schedule 2.0 (WHODAS2), and the self- report Measure of Everyday Cognition (ECog). Cognitive scales will include Coding from WAIS-III, Trail Making Test Part A, Pattern and Letter Comparison Tests, Rey AVLT, in addition to testing with the NIH Toolbox for cognition supplemented by NIH EXAMINER.

5. As in IRB 7489, throughout all assessment procedures, the following safety plan will be in place to mitigate the risk that subjects will become frustrated or upset. First, a discussion will be had with participants as to the schedule of assessments. Flexibility will be maintained insofar as possible, such that assessments will be scheduled according to subjects' preferences (e.g., all at one time vs. breaking up over multiple sessions). Second, subjects will be offered a 15 minute break after each hour of assessments. Third, subjects will be informed that a study clinician is available should they become frustrated or upset. Upon the subject's request or if the subject appears upset, the research staff member conducting the assessment will stop the assessment and contact the study clinician. The study clinician will come assess the subject and make a determination of whether or not assessment may proceed or whether clinical treatment is indicated.

6. Following the 8 weeks of open treatment, participants will be eligible for 3 months of post protocol open antidepressant treatment. They will continue to receive referrals for PTSD treatment as specified in IRB 7489.

You can upload charts or diagrams if any

Criteria for Early Discontinuation

Criteria for Early Discontinuation
If a patient discontinues medication due to tolerability problems, ineffectiveness, patient preference, or other reasons, the patient will be dropped out of the study and enter the 3 month long open treatment phase. Appropriate medication options will be discussed with the patient based on their symptoms and history. If the patient wishes, they will be provided referrals for psychotherapy or treatment options outside of our research clinic. No further research measures will be conducted once a patient enters the open treatment phase.

Patients in all treatment cells will be discontinued from the acute treatment phase if there is there is a rating of 6 (much worse) or 7 (very much worse) on the CGI—I for 2 consecutive weeks. Patients may also be discontinued from the study if this is indicated in the clinical judgement of the study physician and/or principal investigator. Patients receiving escitalopram/duloxetine may continue receiving the same medication if clinically indicated after being dropped from the study. No further research measures will be performed on patient dropped from the study.

Patients will be informed that should they experience a crisis or acute symptom worsening between scheduled weekly appointments, they should call their study clinician via the clinic office/research coordinator or the 24 hr doctor on call pager for CAAM. The study physician will evaluate the patient and make appropriate follow up arrangements, which may include activating EMS, calling the relevant mobile crisis team, or scheduling pt for immediate outpatient appointment in the CAAM. Patients in crisis will be assessed immediately and appropriate clinical action taken as above (i.e., those meeting criteria for early discontinuation will be dropped from the study and treated openly).

Blood and other Biological Samples

Please create or insert a table describing the proposed collection of blood or other biological specimens
No additional blood will be drawn over and above what was already drawn for IRB 7489.

Assessment Instruments

Create a table or give a brief description of the instruments that will be used for assessment
Hamilton Anxiety Rating Scale (HARS) 14-item scale: standard measure of anxiety severity in pharmacotherapy studies and has been shown to have good reliability and validity.
--15 minutes

24-item Hamilton Rating Scale for Depression (HRSD): standard measure of depression severity used across diverse patient samples, including PTSD.
--15 minutes

CGI Severity and Improvement: scales measuring the clinician's view of subjects' global functioning.
--1 minute

Digit Symbol test from the WAIS-III: measure of processing speed.
--2 minutes

Pattern and Letter Comparison tests: reliable measures of processing speed.
--4 minutes

Trail Making Test Part A: reliable test of motor speed.
--3 minutes

Selective Reminding Test: test of episodic memory functioning will allow us to identify deficits in episodic memory functioning consistent with a classification of amnestic mild cognitive impairment (aMCI).
--10-15 minutes

NIH-EXAMINER battery: designed to assess executive functions reliably, comprehensively, and efficiently. This battery examines working memory, inhibition, set shifting, fluency, insight, planning, social cognition and behavior.
--1 hour

NIH Toolbox Cognition Battery: brief, diverse, accessible, and psychometrically sound set of 7 computerized instruments that measure 6 ability subdomains important for cognitive health.
--45 minutes

Frailty characteristics: unintentional weight loss (10 lbs or 5% of body weight in the past year), selfreported exhaustion, weakness (grip strength), slow walking speed, and low physical activity.
--10 minutes

Pittsburgh Fatigability Scale (PFS): the only self-report measure of fatigability associated with performance and perceived exertion.
--5 minutes

Minnesota Leisure Time Physical Activity Questionnaire: measure of physical activities, with activity levels < 383 kcal considered frail.
--5 minutes

Posttraumatic Stress Disorder Checklist (PCL-5): 20-item self-report PTSD symptom screening instrument that has been shown to have good internal consistency, strong correlations with other PTSD scales, and high diagnostic efficiency.
--5-10 minutes

Clinician-Administered PTSD Scale for DSM-5 (CAPS-5): The CAPS is a 30-item instrument containing 0- 4 Likert-style item frequency and intensity scales for PTSD symptoms, with subscales for intrusion, avoidance, and hyperarousal symptom clusters, and associated affective features.
--45 minutes

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

Research Related Delay to Treatment

Will research procedures result in a delay to treatment?
No
Treatment to be provided at the end of the study
Post-protocol open treatment for 3 months as described above. Following that, patients will receive appropriate referrals, which may include further research studies.

Clinical Treatment Alternatives

Clinical treatment alternatives
Patients could opt to be treated for their depression with other antidepressant medications or psychotherapy. They could also opt not to undergo treatment.

Risks/Discomforts/Inconveniences

Risks that could be encountered during the study period

Patients may experience:

1. Interview, emergencies, and possible suicidal ideation: Subjects may experience discomfort during the clinical interview and evaluations when discussing symptoms and current life events.

2. Antidepressant Side Effects: Side effects will be assessed at each planned visit and if needed through additional or unscheduled contacts. Side effects of these medications include somnolence, diarrhea, nausea, impaired ejaculation, impotence, dry mouth, tremor, and sweating. Escitalopram and duloxetine have black box warnings regarding an increased risk for suicidal thinking and behavior in adolescents and young adults (less than 24 years old) given the drug. Both drugs are of unknown risk to a fetus.

3. Breach of confidentiality: There is the potential risk of breach of confidentiality of clinical information.

4. Due to the COVID-19 pandemic, the additional risk of contracting the virus with any human interaction is present, due to the method of how the virus is transmitted.

Describe procedures for minimizing risks

1. Interview, emergencies, and possible suicidal ideation: The study coordinators are experienced and skilled in interviewing depressed subjects. Half-way through the initial assessment, the coordinator will ask the subject if they would like to take a break, and this will be provided if desired. A study clinician will be

available during all aspects of the assessment if there are any questions or problems. In addition, should the subject express suicidal ideation at any time during the interview, the study clinician will be contacted immediately to assess the subject and to determine the appropriate course of action. Options for addressing suicidal ideation will include contacting the individual's mental health caregiver, referring for urgent (same day) evaluation and treatment in an outpatient clinic, or emergency room evaluation and hospitalization. Similar practices will be used for other emergencies, including but not limited to psychosis, homicidal or violent thoughts, or an acute change in a subject's physical status.

2. Antidepressant Side Effects: We will attempt to minimize side effects by slow dosage titration and allowance for dose reduction if needed. We will withdraw subjects from the study if they cannot tolerate the lowest dose of escitalopram or duloxetine. Since the proposed study will enroll subjects aged 50 and older, the particular risks mentioned above are not expected to be applicable. Regardless, all subjects will be asked to tell their doctors immediately if they experience suicidal thoughts, and menopausal status and date of last menstrual period will be documented in all female participants.

3. Breach of confidentiality: Dr. Rutherford has extensive experience as a clinical investigator in dealing with sensitive information and assuring that data is adequately protected. Safeguards to protect confidentiality include locked records and firewalls around password-protected electronic data, and all study data being coded, with the key linking the code with a subject's identity being kept in a separate, locked file. Of note, any and all videoconferencing sessions will be hosted via WebEx-- secure, HIPAA-compliant video conferencing. For participants with email access, self-report measures will be sent via encrypted email.

4. Specifically, for in-person visits to NYSPI, individuals are at increased risk for exposure to COVID-19 both in transit to NYSPI as well as during their time at NYSPI. Procedures are in place to minimize this risk. We plan to offer car transportation subject to a maximum of $50 each way, which minimizes exposure to public transportation for those participants. At NYSPI, personal protective equipment such as masks will be utilized at all times both by staff and participants, and social distancing will be adhered to when possible. Screen shields between patient and staff will be used during neuropsychological testing to further minimize exposure risk.

Methods to Protect Confidentiality

Describe methods to protect confidentiality
All records of the participating subjects will be kept in a locked room with access provided only to staff members. Records will be available to research staff, and to Federal, State and Institutional regulatory personnel (who may review as part of routine audits). Patients' names will be linked with code numbers in a password protected file to which only the research assistant has access. Only these code numbers will appear on all pill bottles and paper measures collected during study. All data collected will be kept confidential and used for professional purposes only. Publications using these data will be done in a manner that protects the subjects' anonymity. All electronically stored data will be accessible by password known only to the principal investigator and research assistants for the study. Due to the implementation of virtual visits, additional measures to protect patient confidentiality will be employed. These include using only

secure platforms for virtual calls (WebEx, etc.), the use of headphones during virtual calls, and not including any PHI on assessment forms that are to be scanned and sent to research coordinators after patient completion for weekly visits.
Will the study be conducted under a certificate of confidentiality?
No

Direct Benefits to Subjects

Direct Benefits to Subjects
No direct benefit to subjects are guaranteed, but patients who are not currently in treatment and are experiencing depressive symptoms will receive a medication proven effective for their condition and may achieve remission from the depression as a result of participating in the study.

Compensation and/or Reimbursement

Will compensation or reimbursement for expenses be offered to subjects?
Yes
Please describe and indicate total amount and schedule of payment(s).
Include justification for compensation amounts and indicate if there are bonus payments.

Subjects will receive reasonable compensation for the time and effort associated with the completion of study visits. Participants will receive $25 for each biweekly visit (Week 0, 2, 4, 6) for a total of $100. Participants will receive $100 for completion of the end of treatment assessments (Week 8).

Thus, the maximum compensation that a participant may receive for completion of all study visits will be $200. This money will be paid by gift card or check at the conclusion of each study visit.

References

References

Uploads

Upload copy(ies) of unbolded Consent Form(s)
Upload copy(ies) of bolded Consent Form(s)
Upload copy(ies) of the HIPAA form

PTSD Treatment_HIPAA_Authorization_1.8.21.pdf
Upload any additional documents that may be related to this study

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

Protocol Number: 8111 **Principal Investigator:** Bret R. Rutherford, MD

Name of Study: Antidepressant Response in Older Adultswith Comorbid PTSD and MDD

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:
The New York State Psychiatric Institute; Columbia University Irving Medical Center

☑ The Sponsor of the Research,
Columbia University Irving Medical Center
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

☐ 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):

  Bret R. Rutherford, MD
  1051 Riverside Drive, Box 98
  New York, New York 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.**

NEW YORK STATE PSYCHIATRIC INSTITUTE

ANTIDEPRESSANT RESPONSE IN OLDER ADULTS WITH COMORBID PTSD

Overview

Below is a summary of the study in which you are asked to take part in. This outline is meant to be a guide for you to use while considering the study and reading the consent form. It is not meant to replace the consent form, which you will have to sign if you decide to participate in the study. The study described is a treatment study in which you would receive treatment with a Food and Drug Administration (FDA) approved medication for depression. The purpose of this 8 Week research study is to understand whether antidepressant medication is effective treatment for depressive symptoms in older adults who have chronic Posttraumatic Stress Disorder (PTSD).

Participation is 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 benefits to which you are otherwise entitled. A decision not to participate or withdraw your participation will not affect your current or future treatment at the New York State Psychiatric Institute (NYSPI) or Columbia University Irving Medical Center (CUIMC).

Alternatives

You do not have to participate in this study to receive treatment for depression. Other FDA-approved antidepressant medications such as Prozac, Zoloft, Effexor, etc., in addition to other types of medications are effective in the treatment of depression. You do not have to participate in the study to receive Lexapro/escitalopram and Cymbalta/duloxetine. These medications are available outside of this study's protocol. Additionally, psychotherapies such as Interpersonal Psychotherapy and Cognitive Behavior Therapy are available outside of this study to treat depression.

Procedures

- At the beginning of the study, you will start taking an antidepressant medication called escitalopram (Lexapro) or duloxetine (Cymbalta).
- You will speak with a doctor and study staff every two weeks to see how you are feeling.
- At the end of the study (8 weeks) you will undergo repeat administration of the rating scales and cognitive tests that you performed in the previous PTSD study.
- Some of these measures will be completed remotely using the telephone or using WebEx, a Health Information Portability and Accountability Act (HIPAA) compliant video teleconferencing service, while others will be conducted in-person.

Risks

This study includes some risks and discomforts (please refer to the consent form for further details and explanations of these risks). These include side effects associated with the antidepressant medication (such as nausea, insomnia, and inability to have an orgasm) and nervousness or discomfort associated with psychological tests. There are also risks associated with COVID-19 and travel for research purposes.

Please alert study staff if you feel your depression is getting worse.

Benefits

This research study is not meant to benefit you directly. You may contact the study doctor, Dr. Bret Rutherford at 646-774-8660 with any questions.

Informed Consent for Participation in Research

ANTIDEPRESSANT RESPONSE IN OLDER ADULTS WITH COMORBID PTSD

PURPOSE OF STUDY

The purpose of this research study is to understand whether antidepressant medication is effective treatment for depressive symptoms in older adults who have chronic Posttraumatic Stress Disorder (PTSD). Participants in this study will receive open (meaning you are assured of receiving 'real' medication) treatment with an FDA-approved antidepressant (either escitalopram [Lexapro] or duloxetine [Cymbalta] depending on your past experience). At the end of the 8 weeks of treatment, you will repeat the symptom scales, cognitive tests, and measures of physical functioning that you previously completed as part of your participation in the Columbia PTSD study (IRB# 7489).

This study is supported by an institutional grant from Columbia University.

VOLUNTARY

Participation in this study is voluntary. If you do not wish to participate in this study or decide to discontinue your participation in this study later, you will not lose any benefits to which you are otherwise entitled, including current or future treatment at New York State Psychiatric Institute or Columbia University Medical Center. We will notify you of any significant new findings that may relate to your willingness to continue to participate.

ALTERNATIVE TREATMENT

You do not have to participate in this study. The alternative to participating in this study is to seek treatment outside the research project. Approved medications for depression are available (e.g., fluoxetine (Prozac), sertraline (Zoloft), etc.), and evidence based psychotherapies (Interpersonal Psychotherapy, Cognitive Behavior Therapy) also may be helpful with depression, whether on their own or combined with medication. You do not have to participate in the study to receive Lexapro/escitalopram and Cymbalta/duloxetine. These medications are available outside of this study's protocol**.**

Information being collected is for research purposes only and is to learn more about changes in depressive symptoms and functioning in older adults with PTSD and depression, not about you.

STUDY PROCEDURES

This study will follow all applicable policies of the New York State Psychiatric Institute to ensure the safety of research participants and staff during the COVID-19 pandemic. We have reduced in-person visits to the minimum needed. Some of your visits may be conducted remotely using the telephone or WebEx, a HIPAA compliant video teleconferencing platform. When it is necessary for your participation for you to come to the New York State Psychiatric Institute, research staff will ask screening questions about your health beforehand, and it is required that you wear a face covering when in the building. We offer transportation via car services to reduce risks inherent in public transportation.

Evaluation: If you decide to participate in this study, we will utilize the blood tests, tests of thought processes such as memory, language, reasoning, and attention, and physical function tests that you already completed. No further evaluation procedures are needed.

Medication portion: In the medication part of the study, you will begin treatment with escitalopram (Lexapro). This is an antidepressant medication in the Selective Serotonin Reuptake Inhibitor (SSRI) family. If you have previously taken escitalopram (Lexapro) during the present time you have been depressed, then we will offer the medication duloxetine (Cymbalta) instead. This is an antidepressant medication in the Serotonin Norepinephrine Reuptake Inhibitor (SNRI) family.

You will be asked to speak with the study doctor and other research staff every 2 weeks to talk about how you are feeling. These visits will be conducted remotely using the telephone or WebEx, A HIPAA compliant teleconferencing platform. The results of these tests are for research purposes only and will not be shared with you. These meetings will last about 30 minutes. If you still have depressive symptoms after four weeks on the pills you are given, the dose will be increased to 20mg of escitalopram (or 60mg of duloxetine after 2 weeks). You will receive free medication for the duration of the study. Medication will be provided to you onsite or mailed to your home via FedEx.

You will take the study pills for 8 weeks. If you have trouble tolerating the study medication, we will lower your dose to one you previously tolerated. If you cannot tolerate any dose of the medication, your participation in the study will be discontinued. If the study doctor feels your condition worsens significantly, the current treatment will be stopped, and you will be offered different treatments for your depression.

The study doctor may stop your participation in the study at any time without your consent if you do not comply with the study procedures or for other reasons. The research study will end after 8 weeks, when you will again complete the tests you performed at the beginning of the PTSD study (tests of symptoms, thinking/memory, and physical functioning).

Following the study, you will still receive 3 months of free doctor visits in the clinic. The medications used in this study are available from pharmacies, so it is an option to

continue taking the medication following the study if you feel you have benefited from it. You will receive at least 1 month of free medication if you wish. Every effort will be made to provide free medication for 3 months total, but we cannot guarantee the availability of free medication beyond 1 month. If you do not wish to continue the medication after the study, the dose will be gradually decreased over 3 days before stopping it.

Study Visits will occur in person/virtually as outlined below:

- Week 0: In-person
- Week 2: Virtual
- Week 4: Virtual
- Week 6: Virtual
- Week 8: In-person

RISKS

The most common side effects reported for escitalopram and duloxetine are nausea, insomnia, and inability to have an orgasm. Less common side effects reported include constipation, dry mouth, dizziness, headache, insomnia, and sedation.

The FDA has concluded that antidepressants increased the risk of suicidal thinking and behavior (suicidality) in short-term studies in children and adolescents with Major Depressive Disorder (MDD) and other psychiatric disorders. No suicides occurred in any of these studies. It is unknown whether the suicidality risk in pediatric patients extends to longer-term use, i.e., beyond several months. It is also unknown whether the suicidality risk extends to adults. The FDA has directed the manufacturers of all antidepressant medications to add a "black box" warning that describes the increased risk of suicidality related to antidepressant use in children and adolescents (but not in adults). The warning urges that adults with MDD or co-morbid depression in the setting of other psychiatric illness being treated with antidepressants should be observed closely for clinical worsening and suicidality, especially during the initial few months of a course of drug therapy, or at times of dose changes, either increases or decreases. Please alert study staff if you feel your depression is getting worse.

You cannot participate in the study if you abuse alcohol or drugs. In any case, you should be careful about drinking alcohol, since it may have a greater effect on you in combination with medication. You must not take monoamine oxidase inhibitor (MAOI) drugs (tranylcypromine or Parnate, phenelzine or Nardil) during the study or within five weeks of ending the study. Serious reactions, including death, have been reported when MAOIs are co-administered with medications like citalopram.

Furthermore, specifically for in person visits to NYSPI, individuals are at increased risk for exposure to COVID-19 both in transit to NYSPI as well as during their time at

NYSPI. Procedures are in place to minimize this risk. We plan to offer car transportation subject to a maximum of $50 each way, which minimizes exposure to public transportation for those participants. At NYSPI, personal protective equipment such as masks will be utilized at all times both by staff and participants, and social distancing will be adhered to when possible (exceptions exist for procedures such as blood draws and EKGs). Screen shields between patient and staff will be used during neuropsychological testing to further minimize exposure risk. Please alert study staff if you feel your depression is getting worse.

BENEFITS

You may not benefit from this study, and no benefit is in any way guaranteed as a result of your participation. However, you may feel less depressed as a result of receiving medication for your depression.

CONFIDENTIALITY

Your records will be stored in a locked file. Records will be available to research staff, and to Federal, State and Institutional regulatory personnel (who may review records as part of routine audits). There are legal advocacy organizations that have the authority under State Law to access otherwise confidential records, though they cannot be redisclosed without your consent. All records will be kept confidential to the extent permitted by law. Your name and other personal identifying information will be stored in an electronically secure database at New York State Psychiatric Institute. Electronically stored data will be accessible only by password known to the study investigators and research assistants. For participants with email access, self-report measures will be sent via encrypted email.

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.

COMPENSATION AND ECONOMIC CONSIDERATIONS

You will not be charged for any procedures that are a part of this study, including the study medication.

To compensate you for the time required for the main assessment session after treatment is over, you will receive $25 for each biweekly visit (Week 0, 2, 4, 6) and $100 for the final treatment visit (Week 8). You will receive a total of $200 for the completion of all study visits. This money will be paid by gift card or check at the conclusion of each study visit.

IN CASE OF INJURY

Federal regulations require that we inform participants about our institution's policy with regard to compensation and payment for treatment of research-related injuries.

In case of injury, New York State Psychiatric Institute will provide 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 to provide. In addition, we will provide assistance in arranging follow up care in such instances.

New York State Psychiatric Institute and Research Foundation for Mental Hygiene do not provide compensation or payment for treatment of research related injuries. However, you should be aware that you do not give up your legal right to seek such compensation through the court by participating in this research.

Please be aware that:

1. The Research Foundation for Mental Hygiene, The New York State Psychiatric Institute, Columbia University and New York Presbyterian Hospital will furnish that emergency medical care determined to be necessary by the medical staff of this hospital
2. You will be responsible for the cost of such care, either personally or through your medical insurance or other form of medical coverage.
3. No monetary compensation for wages lost as a result of injury will be paid to you by the New York State Psychiatric Institute, Columbia University or by New York Presbyterian Hospital.
4. By signing this consent form, you are not waiving any of your legal rights to seek compensation through the courts.

QUESTIONS

If you have further questions about the research procedures, or about your response to the procedures research staff members are available to answer them to the best of their ability. You can reach Dr. Bret Rutherford at 646-774-8660 during general business hours. In an emergency, you may reach the on call doctor at 917-786-6940, 24 hours per day. If you have general questions, you may contact the research coordinator at 646-774-8664. We will notify you of any significant new findings that may relate to your willingness to continue to participate.

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 human subjects in research studies). You may call the IRB Main Office at (646) 774-7155 during regular office hours.

You will be given a copy of this consent form to keep.

DOCUMENTATION OF CONSENT

I have read the above and voluntarily agree to participate in the research study described above. To the best of my knowledge, I am not pregnant. I have been informed that my participation is voluntary, and that I can withdraw from the study at any time without penalty or loss of benefits to which I am otherwise entitled.

Print name: _____

Signed: _____

Date: _____

I have discussed the proposed research with this participant 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 is capable of freely consenting to participate in this research.

Print name: _____
Person Designated to Obtain Consent

Signed: _____

Date: _____