IRB Protocol# 2000034829
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COMPOUND AUTHORIZATION AND CONSENT FOR PARTICIPATION IN A RESEARCH STUDY

YALE UNIVERSITY

Study Title: **Role Of non-Specific Effects in The Treatment of depression with Esketamine**

Principal Investigator (the person who is responsible for this research):
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Research Study Summary:

- We are asking you to join a research study.
- The purpose of this research study is to see if showing you a presentation about esketamine will help you understand more about the treatment.
- Study activities will include a screening visit, presentation prior to your first treatment with esketamine, 3 follow up sessions, and an end of study follow up session.
- Your involvement will require approximately two and one half hours in total for presentations and follow up assessments, much of which can be done virtually from home.
- There may be some risks from participating in this study such as worsening of anxiety associated with discussing your illness and the treatment.
- The study may have no benefits to you. You may or may not benefit from the study through improvement in your clinical outcomes. The results of this study would benefit the field by providing a better understanding of how to present information to patients prior to treatment.
- Taking part in this study is your choice. You can choose to take part, or you can choose not to take part in this study. You also can change your mind at any time. Whatever choice you make will not have any effect on your relationship with Yale psychiatry hospital team.
- If you are interested in learning more about the study, please continue reading, or have someone read to you, the rest of this document. Ask the study staff questions about anything you do not understand. Once you understand the study, we will ask you if you wish to participate; if so, you will have to sign this form.

Why is this study being offered to me?
We are asking you to take part in a research study because you are diagnosed with a depressive episode, it has been determined by your primary mental health provider that esketamine is an appropriate treatment, and you have already been deemed eligible and scheduled for clinical esketamine treatment at Yale Interventional Psychiatry Service. We are looking for 34 participants to be part of this research study.

Who is paying for the study?
The Yale Center for Clinical Investigation (YCCI) is paying for this study.

What is the study about?
The purpose of this study is to see if showing you a presentation about esketamine will help you understand more about the treatment.

APPROVED BY THE YALE UNIVERSITY IRB 3/17/2024

Participants will be randomized (like the flip of a coin) into one of two groups, either the “72 hours” (intervention) or the treatment as usual (TAU) group.

If you are assigned to the intervention group, you will be given a presentation virtually (via Zoom or another HIPAA compliant telehealth tool) about esketamine by a physician. You will also receive a follow-up session after your first esketamine treatment where you will be given another much shorter presentation virtually. Additionally, you will be asked to complete questionnaires about your depressive symptoms, expectations, mood, health, and side effects.

If you are assigned to the TAU group, you will not be shown the presentation; however, you will be asked to complete questionnaires about your depressive symptoms, expectations, mood, health, and side effects. More details are included in the next section below.

Participants in both the intervention and TAU groups will be asked to schedule an appointment at the end of the 8th clinical treatment for a follow up research visit.

What are you asking me to do and how long will it take?

If you decide to participate in this study and sign the consent form, you will have a Screening/ Baseline Visit to see if you are eligible to participate. The following procedures will be performed:

- Study staff will collect demographic information from you (such as age, gender, race) and will ask questions about your medical and psychiatric history including reviewing any medication you take and psychiatric treatment you receive
- Study staff will conduct a depression severity rating scale (same as what would be done clinically)
- You will fill out a questionnaire about your mood and health
- Study staff will ask some questions about your expectations from treatment
- In total, this screening visit will take about half an hour to complete (Which can be done virtually)

After the screening/ baseline visit you will be “randomized” into a study group by chance, like a coin toss. You have a 1 out of 2 or 50% chance of being placed in one of the two groups. You will either receive information about treatment virtually, within 72 hours, or you will be randomized into treatment as usual group and will receive the usual care without receiving a presentation 72 hours before the first treatment.

You cannot choose your study group. You will know what group you are in, but some members of the study team will not. Once you are assigned to your study group, you will have some visits or study appointments in which we evaluate your mood, expectation from treatment and side effects in both groups. Some of these study appointments can be done over phone or over a video call. The study team will let you know if the study visit is remote or in person.

Within 72h before treatment 1

- If you were randomized to the intervention group, you will receive an informative presentation 72 hours prior to first treatment. You will be asked about the quality of the presentation.
- For all participants, before treatment 1, you will be asked about your expectations from treatment.

24 hours post dose 1

- If you were randomized to the intervention group, you will have a follow up session after the first treatment to see if there is any improvement in your depression symptoms.

For all participants:

- Your depressive symptoms will be assessed, and you will be asked about your expectations of treatment. Depressive symptoms will be assessed through an interview with a trained research staff member.
- You will fill out a questionnaire about your mood and health.
- You will be asked about any side effects since the start of treatment.

Immediately before treatment 2 (all participants)

- Your depressive symptoms will be assessed, and you will be asked about your expectations of treatment

Within 72 hours after 8th treatment (all participants)

- Your depressive symptoms will be assessed again after the eighth treatment.
- You will fill out a questionnaire about your mood and health.
- You will be asked about any side effects after the start of treatment.
- End of study session to provide additional information about the goals of the study and to give you another opportunity to ask questions about the research.

We think that the study will take two and one half hours of your time in total.

Table 1: Visit schedule table

Timeline based on ketamine/esketamine treatments	Screening/Baseline session	Within 72h before treatment 1	Immediately before Treatment 1	24hr post dose 1	Immediately before Treatment 2	Within 72 hours after 8th treatment

Day (subject to clinical treatment schedule)	-16±14	-3	0	1	5±3	30±3
Interventions						
Pre-treatment Presentation		**X (for intervention group only)**				
Follow up session				**X (for intervention group only)**		
End of Study Session						**X**
Assessments						
Demographics	**X**					
Montgomery-Asberg Depression Rating Scale (MADRS)	**X**			**X**		**X**
Quick Inventory of Depressive Symptomatology (QIDS)	**X**			**X**		**X**
Presentation quality feedback			**X (for intervention group only)**			
Assessment of side effects				**X**		**X**
Review expectations	**X**		**X**	**X**	**X**	

Are there any risks from participating in this research?

Discussing symptoms or past experiences can sometimes be stressful. If you decide to take part in this study, you may experience worsening of anxiety. All included evaluations are non-invasive and have been used without difficulty or adverse events in previous studies and clinical practice. There is also the possible risk of loss of confidentiality; however, we are taking precautions to minimize this risk as we discuss in the "How will you keep my data safe and private?" section below.

How can the study possibly benefit me or others?

You may or may not benefit from taking part in this study in terms of improvement in your clinical outcomes. However, possible benefits to you include learning more about the use of esketamine/ketamine as an antidepressant. The results of this study are expected to benefit the field by providing a better understanding of how to present information to patients prior to treatment.

Are there any costs to participation?

You will not have to pay for taking part in this study. The only costs may include transportation and your time coming to the study visits.

Will I be paid for participation?

You will be paid for taking part in this study. A breakdown of payments is given below. You will receive compensation in the form of a prepaid debit card after consenting to participate in the study. According to the rules of the Internal Revenue Service (IRS), payments that are made to you as a result of your participation in a study may be considered taxable income.

Study Day	Payment
Screening/Baseline session	$50
24hr post dose 1	$50
Within 72 hours after 8th treatment	$50

The total amount you are expected to be compensated for completing the study is $150.

How will you keep my data safe and private?

All of your responses to the study questionnaires will be held in confidence. Only the researchers involved in this study and those responsible for research oversight (such as representatives of the Yale University Human Research Protection Program, the Yale University Institutional Review Boards, and others) will have access to any information that could identify you that you provide. We will share it with others if you agree to it or when we have to do it because U.S. or State law requires it. For example, we will tell somebody if we learn that you are hurting a child or an older person.

All possible steps to keep your data private and safe will be taken. These measures will include the following:

- All participants will be assigned a unique number to ensure anonymity on study documents. The document linking you to your assigned study number will kept securely and privately. After up to 5 years, this document will be destroyed.
- Hard copies of study documents will be stored in a locked office in a locked building.
- Digital study forms and data will be kept on secure, password-protected data management program called REDCap.

Information about your study participation will be entered into your Electronic Medical Record (EMR). Once placed in your EMR, these results are accessible to all of your providers who participate in the EMR system. Information within your EMR may also be shared with others who are appropriate to have access to your EMR (e.g., health insurance company, disability provider).

When we publish the results of the research or talk about it in conferences, we will not use your name. If we want to use your name, we would ask you for your permission.

We will also share information about you with other researchers for future research, but we will not use your name or other identifiers. We will not ask you for any additional permission.

Data collected in this research might be deidentified and used for future research or distributed to another investigator for future research without your consent.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to

the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

What Information Will You Collect About Me in this Study?

The information we are asking to use and share is called "Protected Health Information." It is protected by a federal law called the Privacy Rule of the Health Insurance Portability and Accountability Act (HIPAA). In general, we cannot use or share your health information for research without your permission. If you want, we can give you more information about the Privacy Rule. Also, if you have any questions about the Privacy Rule and your rights, you can speak to Yale Privacy Officer at 203-432-5919.

The specific information about you and your health that we will collect, use, and share includes:

- Research study records
- Medical and laboratory records of only those services provided in connection with this Study or your esketamine treatment.
- The entire research record and any medical records held by Yale and Yale New Haven Hospital
- Records about phone calls made as part of this research
- Records about your study visits
- Information obtained during this research regarding
    - Questionnaires
    - The diagnosis and treatment of a mental health condition

How will you use and share my information?

We will use your information to conduct the study described in this consent form.
We may share your information with:

- The U.S. Department of Health and Human Services (DHHS) agencies
- Representatives from Yale University, the Yale Human Research Protection Program and the Institutional Review Board (the committee that reviews, approves, and monitors research on human participants), who are responsible for ensuring research compliance. These individuals are required to keep all information confidential.
- Governmental agencies to whom certain diseases (reportable diseases) must be reported
- Health care providers who provide services to you in connection with this study.
- Principal Investigator of the study
- Co-Investigators and other investigators
- Study Coordinator and Members of the Research Team
- Other individuals authorized to monitor the conduct of the Study

We will do our best to make sure your information stays private. But, if we share information with people who do not have to follow the Privacy Rule, your information will no longer be protected by the Privacy Rule. Let us know if you have questions about this. However, to better protect your health information, agreements are in place with these individuals and/or companies that require that they keep your information confidential.

Why must I sign this document?

By signing this form, you will allow researchers to use and disclose your information described above for this research study. This is to ensure that the information related to this research is available to all parties who may need it for research purposes. You always have the right to review and copy your health information in your medical record.

What if I change my mind?

The authorization to use and disclose your health information collected during your participation in this study will never expire. However, you may withdraw or take away your permission at any time. You may withdraw your permission by telling the study staff or by writing to **Sina Nikayin, MD** at Yale Psychiatry Hospital, 184 Liberty Street, New Haven, CT 06520.

If you withdraw your permission, you will not be able to stay in this study but the care you get from your doctor outside this study will not change. No new health information identifying you will be gathered after the date you withdraw. Information that has already been collected may still be used and given to others until the end of the research study to ensure the integrity of the study and/or study oversight.

What if I want to refuse or end participation before the study is over?

Taking part in this study is your choice. You can choose to take part, or you can choose not to take part in this study. You also can change your mind at any time. Whatever choice you make will not have any effect on your relationship with Yale Psychiatry Hospital or Yale University**.**

Who should I contact if I have questions?

Please feel free to ask about anything you don't understand.

If you have questions later or if you have a research-related problem, you can call the Principal Investigator at **203 430 7212**.

If you have questions about your rights as a research participant, or you have complaints about this research, you call the Yale Institutional Review Boards at (203) 785-4688 or email hrpp@yale.edu.

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.

Authorization and Documentation of Consent

Your signature below indicates that you read and understand this consent form and the information presented and that you agree to be in this study.

We will give you a copy of this form.

Participant Printed Name	Participant Signature	Date

Person Obtaining Consent Printed Name	Person Obtaining Consent Signature	Date