Novel neural circuit biomarkers of major depression response to computer-augmented CBT

NCT: NCT03096886

Document Date: November 8, 2022

UNIVERSITY OF PENNSYLVANIA
RESEARCH SUBJECT
INFORMED CONSENT FORM AND HIPAA AUTHORIZATION FORM
HEALTHY CONTROL

Protocol Title:	Novel Neural Circuit Biomarkers of Major Depression Response to Computer-Augmented CBT
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Center for Neuromodulation in Depression and Stress:	Frederick Nitchie Clinical Research Coordinator Email: fnitchie@pennmedicine.upenn.edu Office Phone: 215-573-9058 (Scheduling/general questions)
Emergency Contact:	If you have a study related medical emergency, please contact the study staff or call 911

Summary

You are being invited to participate in a research study. Your participation is voluntary and you should only participate if you completely understand what the study requires and what the risks of participation are. You should ask the study team any questions you have related to participating before agreeing to join the study. If you have any questions about your rights as a human research participant at any time before, during or after participation, please contact the Institutional Review Board (IRB) at (215) 898-2614 for assistance.

The research study is being conducted to learn more about computer-augmented cognitive behavioral therapy (CCBT) and to examine connections in the brains of patients with depression using functional Magnetic Resonance Imaging (fMRI). This study is also examining the effects of sleep-wake patterns, microbiome, and total physical activity on treatment outcomes in individuals experiencing depression.

If you agree to join the study, you will be asked to complete the following research procedures: clinical interviews, self-report questionnaires, and an fMRI scan.

Your participation will last for 8 weeks, depending on your availability.

As a healthy control participant, you will not receive computer-augmented cognitive behavioral therapy. You will not have direct benefits from being in this study. The most common risks of participation are discomfort during fMRI scans and clinical interview assessments.

Please note that there are other factors to consider before agreeing to participate such as additional procedures, use of your personal information, costs, and other possible risks not discussed here. If you are interested in participating, a member of the study team will review the full information with you. You are free to decline or stop participation at any time during or after the initial consenting process.

Why am I being asked to volunteer?
You are being asked to voluntarily participate in a research study because you are a person between the ages of 18-60 years old and are considered a "healthy control." As a healthy control, you do not have symptoms of depression or other psychiatric diagnoses. Participants with depression will be asked to sign a separate informed consent form. The details in this consent form are only applicable to you as a "healthy control."

Your participation is voluntary, which means you can choose whether or not you want to take part. If you choose not to participate, there will be no loss of benefits to which you are otherwise entitled.

Before you can make your decision, you will need to know what the study is about, the possible risks and benefits of being in this study, and what you will have to do in this study. The study doctor and/or a member of the research team will talk to you about the research study, and they will give you this consent form to read. You are encouraged to discuss this study and consent form with your family, friends, or family doctor. You may find some of the medical language difficult to understand. Please ask the study doctor and/or the research team about this form. If you decide to participate, you will be asked to sign this form and you will receive a signed copy.

Your doctor may be an investigator in this research study. As an investigator, your doctor is interested both in your clinical welfare and in the conduct of this study. Before entering this study or at any time during the research, you may want to ask for a second opinion about your care from another doctor who is not an investigator in this study. You do not have to participate in any research study offered by your doctor.

What is the purpose of this research study?
The National Institute for Health (NIH) is funding this research study. The purpose of the study is to learn more about the treatment success of computer-augmented cognitive behavioral therapy (CCBT) and to examine neural circuits in the brains of patients with depression.
Cognitive behavioral therapy (CBT) is the psychotherapy with the best evidence base for the treatment of depression. Moreover, it is a form of treatment for depression that has

been shown to have more durable or sustained effects that persist for months after therapy is stopped. CBT works by helping patients change the way they think about and approach different situations.

Computer-augmented cognitive behavioral therapy (or CCBT) has now been established as another treatment option for depression. It is approved by the FDA as a form of treatment for depression. CCBT is done partly on the computer, and partly with a therapist. It was developed to help patients save time and money. *Good Days Ahead* (*GDA*) is the CCBT program that will be used for this research study. The program relies on the same concepts as normal CBT and may help you change the way you think about and approach different situations. Previous research studies have demonstrated that the CCBT treatment offered through this study is comparable to standard CBT in treating depression.

There are two groups for participants with depression in the study: Early CCBT and Later CCBT. The computer will randomly generate a number, and assign them to one of the two groups. We will learn more about CCBT and the connections in the brains of patients with depression by comparing these two groups before and after treatment.

Healthy control participants are needed to help establish any differences that exist between the neural circuits in the brain of people with depression and those without depression.

How long will I be in the study?
If you agree to take part in this research, your participation will last approximately 8 weeks. The MRI scan is completed within 1 week from the screening visit.

What am I being asked to do?
As a healthy control, you will not be exposed to CCBT. Only participants with depression will receive this treatment. Your involvement will include 3 study visits.

Please tell study staff of any new medications you begin taking. Medications that are not related to mental health treatment may still impact your participation in this study.

Procedure	Visit #1 (3-4 hours)	Visit #2 (3-4 hours)	Visit #3 (30 minutes)
Informed Consent	30 min		
Clinical Interviews and Assessments	2 hour	30 min	
Self-report Questionnaires	30 min		30 min
Neurocognitive Testing		1.5 hour	
Computer Task		15 min	
fMRI		1 hour	
Remote Monitoring Phone Set-Up		15 min	
Saliva Collection		5 min	

NOTE: If you are also participating in "Dimensional Connectomics of Anxious Misery" (AKA Anxious Misery), the information we collect from you for that study will also be used in this study. The interviews and neurocognitive assessments are the same between both studies; you will not be required to complete these more than once. Additionally, the 2 hour fMRI scan you complete for the Anxious Misery study will be used for the first fMRI for this study (CCBT). If you are also participating in "Dimensional Connectomics of Anxious Misery" (AKA Anxious Misery): Visit 1 and Visit 2 will be combined with the 2 study visits for the Anxious Misery study and will take approximately 4-5 hours total for each visit.

Please refer to the table below for the list of study procedures you will be completing, their descriptions, and amount of time.

Procedure	Description	Time
Clinical interviews and assessments	Asking about your psychiatric and medical history, use of alcohol and other substances, your thoughts, feelings, and behaviors, and thoughts of death, dying, or suicide.	- 2 hours at Visit 1 -30 minutes at Visit 2
Self-report questionnaires	Asking about your thoughts, feelings, and behaviors.	- 30 minutes at Visits 1 and 3
Neurocognitive testing	Completed on an electronic tablet and on the computer. This involves doing a variety of activities that test areas of brain cognition, such as memory and attention.	-1.5 hours at Visit 2
Computer Task	This computer task is measuring reward seeking behaviors. Instructions will be given during the task.	-15 minutes at Visit 2
fMRI scans	This is a noninvasive test that requires you to lay in an MRI scanner, which will take pictures of your brain to measure brain activity as you do different tasks, such as responding to images you may see on a screen.	- 1 hour at Visit 2
Surveys on cell phone apps	**Beiwe:** You will answer survey questions regarding your current feelings every other day starting at Visit 2, each time for about 3 minutes. Beiwe will also collect passive information, including the number of phone calls and SMS, as well as activity levels via GPS location.	- 3 minutes every other day
Actigraphy	You will be asked to wear an actigraph, which is a watch-like device for the duration of the study. This device will measure your sleep-wake patterns and physical activity because these measures are indicative of symptoms of depression and treatment outcome.	- 8 weeks starting at Visit 2
Saliva Collection for DNA testing	The inside of your cheek will be swabbed by study staff or by yourself with direction from study staff. This testing is being done to determine any additional biomarkers that may play a role in depression.	- 5 minutes at Visit 2

What are the possible risks or discomforts?
You may experience one or more of the risks indicated below from being in this study. In addition to these, there may be other unknown risks, or risks that we did not anticipate, associated with being in this study. Please inform the study staff about any discomforts, illnesses, or injuries that occurs while you are participating in this study.

Risks of Clinical interviews and assessments: Some discomfort may be associated with the clinical assessments conducted in this study. You may experience emotional discomfort when answering some questions in the questionnaires or when talking about personal information. You may choose not to answer any of the questions and terminate your participation.

Risks of MRI scan: There is no known health risk associated with exposure to magnetic fields during an MRI.

- **Likely/Common:** There are minimal risks from the loud noise associated with the MRI scanner and from the discomfort of lying on a hard surface. We shall provide you with protective earplugs as necessary and make every attempt to ensure your comfort with blankets, etc. during your time in the scanner. You may experience claustrophobia (fear of enclosed spaces and/or anxious feelings accompanied by fast heart rate or shortness of breath) within the MRI scanner. If you have a problem with feeling uncomfortable while inside the scanner you may stop this study. Some of the pulse sequences and/or RF coils are not FDA approved but are considered to pose no more than minimal risk.
- **Rare:**
  - Implanted medical devices and metallic foreign fragments inside your body may pose a risk if you were to enter the MRI magnet room. Devices such as Pacemakers, Internal Cardiac Defibrillators, Insulin Pumps, and other medical devices may also prevent you from safely having the MRI. Therefore, questions regarding medical and work history will be asked prior to your exam. Patients who have metallic devices in their bodies will not be permitted to be scanned using MRI. There are no known risk factors associated with MRI scans for healthy subjects.
  - This MRI is not a clinical scan. It is possible that during the course of the research study, the research staff may notice an unexpected finding(s). Should this occur, the finding(s) will be considered by the appropriate personnel and the PI will inform you. These possible finding(s) may or may not be significant and may lead to anxiety about your condition and to further work-up by your physician.
  - Although there are no known risks related to MRI on pregnant women or a fetus, there is a possibility of yet undiscovered pregnancy related risks. Since there is no possible benefit from participating in this protocol for a pregnant woman, we will exclude pregnant women. A woman of child-bearing potential can participate in this study after attesting that she is not pregnant.
  - A MRI scanner has a strong magnet which attracts certain metals. If anyone has these types of metal in their body, the MRI's strong magnetic field can cause them to move which may cause injury. The MRI will not be performed on anyone having these types of metal in their body. To prevent an injury, you

will be asked questions or given a form requesting information about any metal in your body and if you work with metals. Some dyes in tattoos and permanent eyeliner contain metals which may move during the MRI scan causing the area with the tattoo to become irritated and swollen.

- The greatest risk is a magnetic object flying through the air toward the magnet and hitting you. To reduce this risk we require that all people involved with the study remove all magnetic metal from their clothing and all magnetic metal objects from their pockets. No magnetic metal objects are allowed to be brought into the magnet room at any time except by approved personnel. In addition, once you are in the magnet, the door to the room will be closed so that no one inadvertently walks into the room.
- Before you are scanned, you must tell the MRI technologist if there is any chance that you may be pregnant. Your pregnancy status needs to be determined. If you are pregnant, then consultation with your physician is required before having an MRI scan. You should provide your physician with a copy of this research protocol.

Risks of using Beiwe phone application: The primary risk to participants is loss of confidentiality and privacy. The following measures have been put in place to offset such risk:

- Research staff will instruct you on how to lock your phone or take other safety measures as is needed.
- Behavior data is only stored on the device until the data is uploaded to the secure server. If the phone is lost or replaced, only data that was never uploaded is on the phone.
- Content of phone calls and SMS messages are never captured. Audio data is never captured.
- Only trained researchers have access to the data that is protected with security measures.
- Participants have the right to withdraw from the study at any time and have Beiwe uninstalled.
- Personal data can be permanently deleted from our databases if requested.

Risks of Actigraphy: You may potentially experience skin irritation from prolonged wear of the actigraph device.

Risks of DNA Testing through Saliva Sample

- Saliva sample is collected for DNA testing because research has shown that microbiome colonies may moderate treatment outcome.
- Even without your name or other identifiers, your genetic information is unique to you. The researchers believe the chance that someone will identify you is very small, but the risk may change in the future as people come up with new ways of tracing information.
- There can be a risk in knowing genetic information. New health information about inherited traits that might affect you or your blood relatives could be found during a research study. Even though your genes are unique, you share some of the same genes with your blood relatives. Although we are not able to know all of

the risks from taking part in research on inherited traits, we believe that the risks to you and your family are very low, because your samples will be coded.
- Research results will not be returned to you or your doctor.
- Very rarely health or genetic information could be misused by employers, insurance companies, and others. For example, it could make it harder for you to get or keep a job or insurance, or life insurance companies may charge a higher rate based on this information. We believe the chance these things will happen is very small, but we cannot make guarantees.
- A federal law (Genetic Information Non-Discrimination Act, GINA) helps reduce the risk from health insurance or employment discrimination. The law does not include other types of misuse by life insurance or long term care insurance. If you want to learn more about GINA, you can find information about it on the internet or ask the study staff.
- **Saliva Collection:** Saliva collection is one way in which we can collect DNA. We do not anticipate risks due to the saliva collection process.

Risk of Breach of Confidentiality: There is a rare risk of breach of confidentiality. Breaches in confidentiality could impact future insurability and/or employability.

If you become ill or have an injury while participating in this study, you should inform your primary care doctor that you are in a research study.

What if new information becomes available about the study?
During the course of this study, we may find more information that could be important to you. This includes information that, once learned, might cause you to change your mind about being in the study. We will notify you as soon as possible if such information becomes available.

What are the possible benefits of the study?
You are not expected to get any benefit from being in this research study. The information gathered in this study will help us to better understand how the human brain works.

What other choices do I have if I do not participate?
You have the choice not to participate in this research study. Participation is voluntary and you do not have to participate if you do not want to.

Will I be paid for being in this study?
You will receive compensation for your time and participation. You will be compensated only for the tasks you complete, as follows:

- Visit 1: $20.00
- Visit 2: $95.00*
- Completion bonus: $15.00
    - Provided if 85% of the mood monitoring questions on Beiwe phone app are completed.

Therefore, individuals can receive up to **$130.00***.

> ***NOTE:** If you are also participating in "Dimensional Connectomics of Anxious Misery" (AKA Connectomics): you will not receive $95.00 for the MRI scan for this CCBT study; instead you will receive $200.00 in compensation for the 2 hour MRI scan that you complete for the Anxious Misery and you will not be asked to repeat the MRI scan for this CCBT study. Therefore, the total amount of compensation you would receive from this CCBT study is $35.00.

Your study payment will be given to you in the form of a Greenphire ClinCard at the end of your study participation. This is a reloadable prepaid card (similar to a debit/credit card) which allows funds to be available immediately. You can use it for in-store or online purchases by selecting the "Credit" option at check-out, or it can be cashed out by presenting to a teller at any MasterCard member bank (look for a MC logo on the bank window). Study staff will provide you with a "ClinCard Cardholder FAQ: US" document to help answer any questions you may have.

Please note: In order to be compensated for your participation in this study, you must complete the financial paperwork with your Social Security Number (SSN) or Taxpayer Identification Number (TIN). Additionally, please note that the University of Pennsylvania is required to report to the IRS any cumulative payments for participation in research studies that exceed a total of $600 in a calendar year.

Will I have to pay for anything?
You will not have any costs for participating in this research study. The administration of all procedures will be covered by the study.

Will I receive the results of research testing?
Most tests done in research studies are only for research and have no clear meaning for health care. We will inform participants whether they meet the diagnoses of major depressive disorder based on the clinical interview. Participants with unexpected MRI findings will be informed after the information has been reviewed by an appropriate physician. We do not conduct labs for this study.

What happens if I am injured from being in the study?
We will offer you the care needed to treat injuries directly resulting from taking part in this research. We may bill your insurance company or other third parties, if appropriate, for the costs of the care you get for the injury, but you may also be responsible for some of them.

There are no plans for the University of Pennsylvania to pay you or give you other compensation for the injury. You do not give up your legal rights by signing this form.

If you think you have been injured as a result of taking part in this research study, tell the person in charge of the research study as soon as possible. The researcher's name and phone number are listed in the consent form.

When is the Study over? Can I leave the Study before it ends?
This study is expected to end after all participants have completed all visits and all information has been collected; this is expected to take approximately 4 years.

This study is expected to end after all participants have completed all visits, and all information has been collected. This study may also be stopped at any time by your physician, the study Sponsor, or the Food and Drug Administration (FDA) without your consent because:

- The Primary Investigator feels it is necessary for your health or safety. Such an action would not require your consent, but you will be informed if such a decision is made and the reason for this decision.
- You have not followed study instructions.
- The Sponsor (NIH), the study Principal Investigator, or the Food and Drug Administration (FDA) has decided to stop the study.

If you decide to participate, you are free to leave the study at anytime. Withdrawal will not interfere with your future care.

How will my personal information be protected during the study?
We will do our best to make sure that the personal information obtained during the course of this research study will be kept private. However, we cannot guarantee total privacy.

An exception to confidentiality is if you report child abuse or neglect or if you report suicidal or homicidal ideation or intent to the research team. Any information about child abuse or intent to harm yourself or others will be reported to authorities, as required by law.

Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used. The Institutional Review Board (IRB) at the University of Pennsylvania will have access to your records. If this study is being overseen by the Food and Drug Administration (FDA), they may review your research records.

To help protect your confidentiality, your data will only be transported by qualified study team members, and only during actual subject participation. Once all hard copy records are collected, they will be kept in a double-locked environment. Data collected during the study will be entered and stored in a password-protected database, called REDCap, Your data will be accessible only to engaged study members. Electronic records will not be transported via external drives or any other means. All biological samples will be transported by trained members of the research team directly to the appropriate facility where processing and analysis of the samples will take place. All samples will only be identified by the participants' randomly generated study ID number, and the date and time of the sample collection. If we write a report or article about this study or share the study data set with others, we will do so in such a way that you cannot be directly identified.

All research data will be de-identified and assigned a randomly generated research identification number. All information obtained will be kept completely confidential and will be in locked files behind locked doors. Electronic data will be encrypted and password protected.

Protected Health Information (PHI) is health information that identifies you. PHI is protected by federal law under HIPAA (the Health Insurance Portability and Accountability Act). To take part in this research, you must give the research team permission to use and disclose (share) your PHI for the study as explained in this consent form.

Once your health information is shared with someone outside of the research team, it may no longer be protected by HIPAA.

The research team will only use and share your information as talked about in this form. When possible, the research team will make sure information cannot be linked to you (de-identified). Once information is de-identified, it may be used and shared for other purposes not discussed in this consent form.

Will information about this study be available to the public?
A description of this clinical trial will be available on www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify you.

What may happen to my information collected on this study?
Your samples may be used to create products, including some that may be sold and/or make money for others. If this happens, there are no plans to tell you, or to pay you, or to give any compensation to you or your family. Most uses of biospecimens or information do not lead to commercial products or to profit for anyone.

Whole genome sequencing will not be conducted on your samples. Whole genome sequencing involves analyzing your entire personal genetic code.

Your information and samples will be de-identified. De-identified means that all identifiers have been removed. The information and samples could be stored and shared for future research in this de-identified fashion. It would not be possible for future researchers to identify you as we would not share any identifiable information about you with future researchers. This can be done without again seeking your consent in the future, as permitted by law. The future use of your information and samples only applies to the information and samples collected on this study.

What information about me may be collected, used or shared with others?
During your participation, you will be asked to provide your name, date of birth, address, telephone number, email address, and your social security number (so that we may issue you a check to compensate you for participation). We may also obtain or create a medical record number (in the event that we need to order procedures and to access your medical records to collect information about your medical history). This identifiable information will be held in strict confidence and will be kept in password protected files behind locked doors. Your personally identifying information will not be linked to any of the data that is analyzed and reported. All data will be de-identified when reported. You will also be asked to answer questions about your medical history including questions about your physical and mental health. Information from your medical charts will be reviewed and documented for research purposes. Results from physical exams and cognitive assessments will be part of the research record.

Scientific collaborators may request access to de-identified data such as brain imaging data to aid them in their own research. Depositing deidentified data in a central repository is a federal requirement.

Why is my information being used?
Your information is used by the research team to contact you during the study. Your information and results of tests and procedures are used to:

- Do the research
- Oversee the research
- To see if the research was done right.
- To evaluate and manage research functions.

Who may use and share information about me?
The following individuals may use or share your information for this research study:

- The investigator for the study and the study team
- Other authorized personnel at Penn, including offices that support research operations
- Other research personnel with access to the databases for research and/or study coordination and as otherwise approved by the IRB

Who, outside of the School of Medicine, might receive my information?

- Those working under the direction of the investigator for the study, (e.g. under subcontracts).
- All research centers participating in the study, even if they are not part of the School of Medicine
- The funding sponsor and organizations supporting the sponsor
- Harvard University and Amazon Web Services (AWS) as Beiwe is owned by Harvard University and AWS.

Oversight organizations

- The Food and Drug Administration
- The Office of Human Research Protections
- The study data and safety monitoring board
- The National Institutes of Health, which require central deposition of data.

Once your personal health information is disclosed to others outside the School of Medicine, it may no longer be covered by federal privacy protection regulations.

The Principal Investigator or study staff will inform you if there are any additions to the list above during your active participation in the trial. Any additions will be subject to University of Pennsylvania procedures developed to protect your privacy.

How long may the School of Medicine use or disclose my personal health information?
Your authorization for use of your personal health information for this specific study does not expire.

Your information may be held in a research database. However, the School of Medicine may not re-use or re-disclose information collected in this study for a purpose other than this study unless:

- You have given written authorization
- The University of Pennsylvania's Institutional Review Board grants permission
- As permitted by law

Can I change my mind about giving permission for use of my information?
Yes. You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the investigator for the study. If you withdraw your permission, you will not be able to stay in this study.

What if I decide not to give permission to use and give out my health information?
Then you will not be able to be in this research study.

You will be given a copy of this Research Subject HIPAA Authorization describing your confidentiality and privacy rights for this study.

By signing this document you are permitting the School of Medicine to use and disclose personal health information collected about you for research purposes as described above.

How can we contact you?
We would like to contact you by phone, email, or mail in order to arrange your appointments. Some of these messages may contain information that identifies you. We will also be contacting you in the future, after the conclusion of the study, in order to follow-up on your status. Please provide us with contact information for an additional individual who knows where to find you in the event that we cannot reach you.

Electronic Medical Records and Research Results

What is an Electronic Medical Record and/or a Clinical Trial Management System?
An Electronic Medical Record (EMR) is an electronic version of the record of your care within a health system. An EMR is simply a computerized version of a paper medical record.

A clinical trial management system (CTMS) is used to register your information as a participant in a study and to allow for your research data to be entered/stored for the purposes of data analysis and any other required activity for the purpose of the conduct of the research.

If you are receiving care or have received care within the University of Pennsylvania Health System (UPHS) (outpatient or inpatient) and are participating in a University of Pennsylvania research study, information related to your participation in the research (i.e. laboratory tests, imaging studies and clinical procedures) may be placed in your existing EMR maintained by UPHS. Information related to your participation in clinical research will also be contained in the CTMS.

If you have never received care within UPHS and are participating in a University of Pennsylvania research study that uses UPHS services, an EMR will be created for you for the purpose of maintaining any information produced from your participation in this research study. The creation of this EMR is required for your participation in this study. In order to create your EMR, the study team will need to obtain basic information about you that would be similar to the information you would provide the first time you visit a hospital or medical facility (i.e. your name, the name of your primary doctor, the type of insurance you have). Information related to your participation in the study (i.e. laboratory tests, imaging studies and clinical procedures) may be placed in this EMR.
Once placed in your EMR or in the CTMS, your information may be accessible to appropriate UPHS workforce members that are not part of the research team. Information within your EMR may also be shared with others who are determined by UPHS to be appropriate to have access to your EMR (e.g. Health Insurance Company, disability provider, etc.).

Who can I call with questions, complaints or if I'm concerned about my rights as a research subject?
For general questions or for scheduling, please call the Center for Neuromodulation of Depression and Stress at 215-573-2637. If you have concerns or complaints regarding your participation in this research study or if you have any questions about your rights as a research subject, please call Frederick Nitchie at (215) 573-9058. If a member of the research team cannot be reached or you want to talk to someone other than those working on the study, you may contact the Office of Regulatory Affairs with any question, concerns or complaints at the University of Pennsylvania by calling (215) 898-2614.

Do you agree to have the information you provide for "Dimensional Connectomics of Anxious Misery" (AKA Connectomics) used for this study as well?

Please note that if you wish to participate in both studies, you must give us permission to share your information between studies. You may choose not to participate in the Anxious Misery study and still participate in this CCBT study.

☐ *Yes* ☐ *No*

_____ _____

Initials Date

Do you agree to be contacted for future studies by the Center for Neuromodulation of Depression and Stress?

☐ *Yes* ☐ *No*

_____ _____

When you sign this form, you are agreeing to take part in this research study. This means that you have read the consent form, your questions have been answered, and you have decided to volunteer. Your signature also means that you are permitting the University of Pennsylvania to use your personal health information collected about you for research purposes within our institution. You are also allowing the University of Pennsylvania to disclose that personal health information to outside organizations or people involved with the operations of this study.

A copy of this consent form will be given to you.

_____
Name of Subject (Please Print)

_____
Signature Date

_____
Name of Person Obtaining Consent (Please Print)

_____
Signature Date

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RESEARCH SUBJECT
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CCBT GROUPS

Protocol Title:	Novel Neural Circuit Biomarkers of Major Depression Response to Computer-Augmented CBT
Principal Investigator:	Yvette I. Sheline, M.D. Department of Psychiatry University of Pennsylvania 3700 Hamilton Walk, Suite 303 Philadelphia, PA 19104-4283 Email: sheline@pennmedicine.upenn.edu Office Phone: 215-573-4229
Sub-Investigator:	Michael E. Thase, M.D.
Center for Neuromodulation in Depression and Stress:	Frederick Nitchie Clinical Research Coordinator Email: fnitchie@pennmedicine.upenn.edu Office Phone: 215-573-9058 (Scheduling/general questions)
Emergency Contact:	If you have a study related medical emergency, please contact the study staff or call 911

Summary
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The research study is being conducted to learn more about computer-augmented cognitive behavioral therapy (CCBT) and to examine connections in the brains of patients with depression using functional Magnetic Resonance Imaging (fMRI). This study is also examining the effects of sleep-wake patterns, microbiome, and total physical activity on treatment outcomes in individuals experiencing depression.

If you agree to join the study, you will be asked to complete the following research procedures: clinical interviews, self-report questionnaires, fMRI scans, computer-

augmented cognitive behavioral therapy for 8 weeks, and therapy with a cognitive behavioral therapist.

You will start treatment within 4 weeks after your first MRI scan. The treatment itself lasts 8 weeks. Therefore, your overall participation will last for 8-12 weeks. You will be randomly assigned to one of two groups depending the random number generated by the computer: 1) Early CCBT or 2) Late CCBT. Early CCBT participants will begin CCBT after completing baseline assessments and Late CCBT participants will begin CCBT 2-4 weeks from completing baseline assessments. This is further detailed in the "What am I asked to do?" section of this consent form. There may be possible treatment delays due to scheduling availability, fMRI scanner availability, or other unforeseen circumstances.

You may not receive additional benefits from computer-augmented cognitive behavioral therapy (CCBT) compared to standard cognitive behavioral therapy (CBT) because the benefits of the computer-augmented portion of the cognitive behavioral therapy is untested. You may benefit from the cognitive behavioral therapy component within CCBT from this study. CBT is also available to you outside of this study. The most common risks of participation are discomfort during fMRI scans and clinical interview assessments.

Instead of taking part in this study, you may choose to receive other treatments for depression. These include transcranial magnetic stimulation (TMS), electroconvulsive shock therapy (ECT), medication treatment, and other types of therapy, among others. Further detail is provided on page 10.

Please note that there are other factors to consider before agreeing to participate such as additional procedures, use of your personal information, costs, and other possible risks not discussed here. If you are interested in participating, a member of the study team will review the full information with you. You are free to decline or stop participation at any time during or after the initial consenting process.

Why am I being asked to volunteer?
You are being asked to voluntarily participate in a research study because you are a person between the ages of 18-60 years old and have symptoms of depression.

Your participation is voluntary, which means you can choose whether or not you want to take part. If you choose not to participate, there will be no loss of benefits to which you are otherwise entitled.

Before you can make your decision, you will need to know what the study is about, the possible risks and benefits of being in this study, and what you will have to do in this study. The study doctor and/or a member of the research team will talk to you about the research study, and they will give you this consent form to read. You are encouraged to discuss this study and consent form with your family, friends, or family doctor. You may find some of the medical language difficult to understand. Please ask the study doctor and/or the research team about this form. If you decide to participate, you will be asked to sign this form and you will receive a signed copy.

Your doctor may be an investigator in this research study. As an investigator, your doctor is interested both in your clinical welfare and in the conduct of this study. Before entering this study or at any time during the research, you may want to ask for a second opinion about your care from another doctor who is not an investigator in this study. You do not have to participate in any research study offered by your doctor.

What is the purpose of this research study?
The National Institute for Health (NIH) is funding this research study. The purpose of the study is to learn more about the treatment success of computer-augmented cognitive behavioral therapy (CCBT) and to examine connections in the brains of patients with depression.

Cognitive behavioral therapy (CBT) is the psychotherapy with the best evidence base for the treatment of depression. Moreover, it is a form of treatment for depression that has been shown to have more durable or sustained effects that persist for months after therapy is stopped. CBT works by helping patients change the way they think about and approach different situations.

Computer-augmented cognitive behavioral therapy (or CCBT) has now been established as another treatment option for depression. It is approved by the FDA as a form of treatment for depression. CCBT is done partly on the computer, and partly with a therapist. It was developed to help patients save time and money. *Good Days Ahead* (*GDA*) is the CCBT program that will be used for this research study. The program relies on the same concepts as normal CBT and may help you change the way you think about and approach different situations. Previous research studies have demonstrated that the CCBT treatment offered through this study is comparable to standard CBT in treating depression.

You will be in one of the two groups in the study: Early CCBT and Later CCBT. The computer will randomly generate a number, and assign you to one of the two groups. We will learn more about CCBT and the connections in the brains of patients with depression by comparing these two groups before and after treatment.

How long will I be in the study?
If you agree to take part in this research, the duration of your participation after completing the first MRI scan varies between 8-12 weeks. All participants will receive 8 weeks of CCBT within 4 weeks from completing the first MRI scan and baseline assessments. The first MRI scan is completed within 1 week from the screening visit.

Participation duration may vary depending on the scheduling availability of the therapists, participants, and also our facilities. If you wish to schedule for treatment services outside of this research study during the time you are waiting to start CCBT and terminate your participation in the study, please contact clinical research coordinator Frederick Nitchie at (215)-573-9058.

What am I being asked to do?
Please tell study staff of any new medications you begin taking. You may not participate in this study if you take medications related to mental health. Medications that are not related to mental health may also impact your participation in this study. Medications must not be stopped solely for the purpose of allowing participation in this study.

If you participate in this study we will ask you not to initiate other types of treatment until the study has ended. However, upon completing, or voluntary withdrawal, you may pursue these other treatments. We are happy to provide you with more information about these other treatments if you are interested.

Your involvement will include 10-12 study visits detailed in the tables below.

Before CCBT Treatment			
Procedure	**Visit #1 Day 0 (3-4 hours)**	**Visit #2 Day 0-14 (3-4 hours)**	**Late CCBT group only: Visit #3 Day 12-28 (3-4 hours)**
Informed Consent	30 min		
Clinical Interviews and Assessments	2 hour		
Self-report Questionnaires	30 min	5 min	30 min
Neurocognitive Testing		1.5 hour	1.5 hour
Computer Task		15 min	
fMRI		1 hour	1 hour
Remote Monitoring Phone Set-Up		15 min	
Saliva Collection		5 min	

CCBT Treatment
Participants are randomized by a computer (like the flip of a coin) to one of two groups:

1) Early CCBT – Participants will have two pre-treatment study visits (detailed above) and will be scheduled to begin CCBT within 0-14 days from Visit #1 and after the completion of the first fMRI scan.
2) Late CCBT – Participants will have three pre-treatment study visits (detailed above) and will be scheduled to start CCBT within 15-28 days from Visit #1 and after completing two fMRI scans. The two fMRI scans must be at least 14 days apart from each other.

Details of the CCBT treatment schedule are outlined in the table below.

	During CCBT Treatment								
	Week 1	**Week 2**	**Week 3**	**Week 4**	**Week 5**	**Week 6**	**Week 7**	**Week 8**	**Week 9**
GDA Modules (Completed at home)	Lesson 1*	Lesson 2	Lesson 3	Lesson 4	Lesson 5	Lesson 6	Lesson 7	Lessons 8 & 9	
Therapy	60 min	30 min		30 min		30 min		30 min	Debriefing 30 min
Clinical Assessments	30 min	30 min		30 min		30 min		30 min	30 min
Self-Report Surveys	5 min	5 min		5 min		5 min		5 min	30 min
MRI									60 min
Neurocognitive Testing									1.5 hour

Computer Task									15 min

*Lesson 1 Good Days Ahead Module will be completed on site to orient participants to CCBT.

- Therapy visits during Weeks 1, 2, 4, 6, and 8 visits will take approximately 1-1.5 hours: therapy session, clinical assessments, and self-report measures
- Week 9 visit will take approximately 3-4 hours (this may be divided into 2 visits based on scheduling availability): Debriefing, clinical assessments, MRI scan, neurocognitive testing, and self-report measures

After CCBT Treatment

At the CCBT study visit during Week 9, participants will complete the post-treatment fMRI scan, neurocognitive assessments, self-report surveys, and a debriefing with the therapist. The actigraph device must be returned and cell phone applications for the study will be removed.

NOTE: If you are also participating in "Dimensional Connectomics of Anxious Misery" (AKA Anxious Misery), the information we collect from you for that study will also be used in this study. The interviews and neurocognitive assessments are the same between both studies; you will not be required to complete these more than once. Additionally, the 2 hour fMRI scan you complete for the Anxious Misery study will be used for the first fMRI for this study (CCBT). If you are also participating in "Dimensional Connectomics of Anxious Misery" (AKA Anxious Misery): Visit 1 and Visit 2 will be combined with the 2 study visits for the Anxious Misery study and will take approximately 4-5 hours total for each visit.

Please refer to the tables below for the list of study procedures that you will be completing, their descriptions, and amount of time.

Procedure	Description	Time
Clinical interviews and assessments	Asking about your psychiatric and medical history, use of alcohol and other substances, your thoughts, feelings, and behaviors, and thoughts of death, dying, or suicide.	- 2 hours at Visit 1 - 30 minutes at Visits 2, 3*, and all therapy visits
Self-report questionnaires	Asking about your thoughts, feelings, and behaviors.	- 30 minutes at Visits 1, 2, 3*, & Week 9 - 5 minutes at CCBT Weeks 1, 2, 4, 6, & 8
Neurocognitive testing	Completed on an electronic tablet and on the computer. This involves doing a variety of activities that test areas of brain cognition, such as memory and attention.	-1.5 hours at Visits 2, 3*, and Week 9
Computer Task	This computer task is measuring reward seeking behaviors. Instructions will be given during the task.	-15 minutes at Visit 2 and Week 9
fMRI scans	This is a noninvasive test that requires you to lay in an MRI scanner, which will take pictures of your brain to measure	- 1 hour at Visits 2, 3*, and Week 9

	brain activity as you do different tasks, such as responding to images you may see on a screen.	

Procedure	Description	Time
CCBT using Good Days Ahead	You will complete nine lessons online. The CCBT program relies on the same concepts as normal CBT and may help you change the way you think about and approach different situations.	- 30 minutes each
Therapy sessions	Six therapy sessions with a licensed psychiatrist or psychologist.	- 1 hour at CCBT Week 1, 30 minutes at all other visits
Surveys on cell phone apps	**Beiwe:** You will answer survey questions regarding your current feelings every other day starting at Visit 2, each time for about 3 minutes. Beiwe will also collect passive information, including the number of phone calls and SMS, as well as activity levels via GPS location. Tracking location based on longitude and latitude coordinates will be collected to allow us to calculate amount of activity. The duration of calls and contacts' phone numbers will not be collected.	- 2-3 minutes per day
	Ethica: You will complete daily surveys about *Good Days Ahead* lessons through Ethica when you begin CCBT Week 1, once a day each time for about 2 minutes.	
Actigraphy	You will be asked to wear an actigraph, which is a watch-like device for the duration of the study. This device will measure your sleep-wake patterns and physical activity because these measures are indicative of symptoms of depression and treatment outcome.	- 8-12 weeks starting at Visit 2
Saliva Collection for DNA testing	The inside of your cheek will be swabbed by study staff or by yourself with direction from study staff. This testing is being done to determine any additional biomarkers that may play a role in depression.	- 5 minutes at Visit 2

What are the possible risks or discomforts?
You may experience one or more of the risks indicated below from being in this study. In addition to these, there may be other unknown risks, or risks that we did not anticipate, associated with being in this study. Please inform the study staff about any discomforts, illnesses, or injuries that occurs while you are participating in this study.

Delayed Scheduling: There is a risk that your symptoms of depression may worsen while you are waiting to begin CCBT. The following measures have been put in place to offset such risk:

- Your responses to the mood monitoring questions on Beiwe will be reviewed throughout the time you are waiting to be scheduled.

- If your symptoms appear to have worsened, research staffs will contact you to provide additional resources.
- You may also contact research staff Frederick Nitchie at (215) 573-9058 if you feel that your symptoms are worsening or if you are concerned about your condition.
- Participants have the right to withdraw at any time if they experience discomfort.

Risks of Clinical interviews and assessments: Some discomfort may be associated with the clinical assessments conducted in this study. You may experience emotional discomfort when answering some questions in the questionnaires or when talking about personal information. You may choose not to answer any of the questions and terminate your participation.

Risks of MRI scan: There is no known health risk associated with exposure to magnetic fields during an MRI.

- **Likely/Common:** There are minimal risks from the loud noise associated with the MRI scanner and from the discomfort of lying on a hard surface. We shall provide you with protective earplugs as necessary and make every attempt to ensure your comfort with blankets, etc. during your time in the scanner. You may experience claustrophobia (fear of enclosed spaces and/or anxious feelings accompanied by fast heart rate or shortness of breath) within the MRI scanner. If you have a problem with feeling uncomfortable while inside the scanner you may stop this study. Some of the pulse sequences and/or RF coils are not FDA approved but are considered to pose no more than minimal risk.
- **Rare:**
  - Implanted medical devices and metallic foreign fragments inside your body may pose a risk if you were to enter the MRI magnet room. Devices such as Pacemakers, Internal Cardiac Defibrillators, Insulin Pumps, and other medical devices may also prevent you from safely having the MRI. Therefore, questions regarding medical and work history will be asked prior to your exam. Patients who have metallic devices in their bodies will not be permitted to be scanned using MRI. There are no known risk factors associated with MRI scans for healthy subjects.
  - This MRI is not a clinical scan. It is possible that during the course of the research study, the research staff may notice an unexpected finding(s). Should this occur, the finding(s) will be considered by the appropriate personnel and the PI will inform you. These possible finding(s) may or may not be significant and may lead to anxiety about your condition and to further work-up by your physician.
  - Although there are no known risks related to MRI on pregnant women or a fetus, there is a possibility of yet undiscovered pregnancy related risks. Since there is no possible benefit from participating in this protocol for a pregnant woman, we will exclude pregnant women. A woman of child-bearing potential can participate in this study after attesting that she is not pregnant.
  - A MRI scanner has a strong magnet which attracts certain metals. If anyone has these types of metal in their body, the MRI's strong magnetic field can

cause them to move which may cause injury. The MRI will not be performed on anyone having these types of metal in their body. To prevent an injury, you will be asked questions or given a form requesting information about any metal in your body and if you work with metals. Some dyes in tattoos and permanent eyeliner contain metals which may move during the MRI scan causing the area with the tattoo to become irritated and swollen.

- No metal objects are allowed to be brought into the MRI scan room at any time, because the MRI magnet will quickly and strongly pull those items into the scanner. To prevent any injury to patients and staff and any damage to the MRI scanner, you will be asked to remove all jewelry and clothing containing metal before you enter the MRI scan room. Also, since the MRI magnet will erase credit cards, they must not be taken into the scan room. Once you are positioned in the scanner, the door to the room will be closed to prevent anyone with any metal object entering the scan room.
- Before you are scanned, you must tell the MRI technologist if there is any chance that you may be pregnant. Your pregnancy status needs to be determined. If you are pregnant, then consultation with your physician is required before having an MRI scan. You should provide your physician with a copy of this research protocol.

Risks of using Beiwe and Ethica phone applications: The primary risk to participants is loss of confidentiality and privacy. The following measures have been put in place to offset such risk:

- Research staff will instruct you on how to lock your phone or take other safety measures as needed.
- Behavior data collected by Beiwe and survey responses collected by Ethica are only stored on the device until the data is uploaded to the secure server. If the phone is lost or replaced, only data that was never uploaded is on the phone.
- Content of phone calls and SMS messages are never captured by Beiwe. Audio data is never captured.
- Only trained researchers have access to the data that is protected with security measures.
- Participants have the right to withdraw from the study at any time and have Beiwe and Ethica uninstalled.
- Personal data can be permanently deleted from our databases if requested.

Risks of Actigraphy: You may potentially experience skin irritation from prolonged wear of the actigraph device.

Risks of DNA Testing through Saliva Sample

- Saliva sample is collected for DNA testing because research has shown that microbiome colonies may moderate treatment outcome.
- Even without your name or other identifiers, your genetic information is unique to you. The researchers believe the chance that someone will identify you is very small, but the risk may change in the future as people come up with new ways of tracing information.

- There can be a risk in knowing genetic information. New health information about inherited traits that might affect you or your blood relatives could be found during a research study. Even though your genes are unique, you share some of the same genes with your blood relatives. Although we are not able to know all of the risks from taking part in research on inherited traits, we believe that the risks to you and your family are very low, because your samples will be coded.
- Research results will not be returned to you or your doctor.
- Very rarely health or genetic information could be misused by employers, insurance companies, and others. For example, it could make it harder for you to get or keep a job or insurance, or life insurance companies may charge a higher rate based on this information. We believe the chance these things will happen is very small, but we cannot make guarantees.
- A federal law (Genetic Information Non-Discrimination Act, GINA) helps reduce the risk from health insurance or employment discrimination. The law does not include other types of misuse by life insurance or long term care insurance. If you want to learn more about GINA, you can find information about it on the internet or ask the study staff.
- **Saliva Collection:** Saliva collection is one way in which we can collect DNA. We do not anticipate risks due to the saliva collection process.

Risk of Breach of Confidentiality: There is a rare risk of breach of confidentiality. Breaches in confidentiality could impact future insurability and/or employability.

If you become ill or have an injury while participating in this study, you should inform your primary care doctor that you are in a research study.

What if new information becomes available about the study?
During the course of this study, we may find more information that could be important to you. This includes information that, once learned, might cause you to change your mind about being in the study. We will notify you as soon as possible if such information becomes available.

What are the possible benefits of the study?
You may not benefit more than you would with cognitive behavioral therapy (CBT) received through standard care outside of this study. It is untested whether computer-augmented cognitive behavioral therapy (CCBT) adds additional benefit.

There is no benefit to you from the fMRI scan. However, your participation could help us understand how the human brain works in people with depression, which can benefit you indirectly. In the future, this may help other people with depression.

You may not get any benefit from being in this research study.

What other choices do I have if I do not participate?
You have the choice not to participate in this research study. Participation is voluntary and you do not have to participate if you do not want to.

Computer-augmented cognitive behavioral therapy (CCBT) is offered through research studies, such as this one. Cognitive behavioral therapy (CBT) may be offered through standard of care outside of this study. Instead of taking part in this study, you may choose to receive other treatment for depression, some a FDA approved and some are not. These include transcranial magnetic stimulation (TMS), electroconvulsive shock therapy (ECT), medication treatment, and other types of therapy, among others. The study doctor will discuss your options with you and explain the good and bad things that could happen with these other treatments. She will answer any question you may have. You may also discuss with your personal physician.

Will I be paid for being in this study?
You will receive compensation for your time and participation. You will be compensated only for the tasks you complete, as follows:

- 1st MRI scan: $75.00*
- 2nd MRI scan: $100.00
- 3rd MRI scan (if applicable): $125.00
- Completion bonus: $50.00
    - Provided if 100% of the *Good Days Ahead* homework for CCBT is completed and 85% of the mood monitoring questions on Beiwe and Ethica phone apps are completed.

Therefore, individuals can receive up to **$225.00*** or **$350.00***.

> ***NOTE:** If you are also participating in "Dimensional Connectomics of Anxious Misery" (AKA Anxious Misery): you will not receive $75.00 for the first MRI scan for this CCBT study; instead you will receive $200.00 in compensation for the 2 hour MRI scan that you complete for the Anxious Misery and you will not be asked to complete the first MRI scan for this CCBT study. Therefore, the total amount of compensation you would receive from this CCBT study is up to $150.00 (2 MRI scans) or $275.00 (3 MRI scans).

Your study payment will be given to you in the form of a Greenphire ClinCard at the end of your study participation. This is a reloadable prepaid card (similar to a debit/credit card) which allows funds to be available immediately. You can use it for in-store or online purchases by selecting the "Credit" option at check-out, or it can be cashed out by presenting to a teller at any MasterCard member bank (look for a MC logo on the bank window). Study staff will provide you with a "ClinCard Cardholder FAQ: US" document to help answer any questions you may have.

Please note: In order to be compensated for your participation in this study, you must complete the financial paperwork with your Social Security Number (SSN) or Taxpayer Identification Number (TIN). Additionally, please note that the University of Pennsylvania is required to report to the IRS any cumulative payments for participation in research studies that exceed a total of $600 in a calendar year.

Will I have to pay for anything?
You will not have any costs for participating in this research study. The administration of all procedures will be covered by the study.

Will I receive the results of research testing?
Most tests done in research studies are only for research and have no clear meaning for health care. We will inform participants whether they meet the diagnoses of major depressive disorder based on the clinical interview. Participants with unexpected MRI findings will be informed after the information has been reviewed by an appropriate physician. We do not conduct labs for this study.

What happens if I am injured from being in the study?
We will offer you the care needed to treat injuries directly resulting from taking part in this research. We may bill your insurance company or other third parties, if appropriate, for the costs of the care you get for the injury, but you may also be responsible for some of them.

There are no plans for the University of Pennsylvania to pay you or give you other compensation for the injury. You do not give up your legal rights by signing this form.

If you think you have been injured as a result of taking part in this research study, tell the person in charge of the research study as soon as possible. The researcher's name and phone number are listed in the consent form.

When is the Study over? Can I leave the Study before it ends?
This study is expected to end after all participants have completed all visits, and all information has been collected; this is expected to take approximately 4 years. This study may also be stopped at any time by your physician, the study Sponsor, or the Food and Drug Administration (FDA) without your consent because:

- The Primary Investigator feels it is necessary for your health or safety. Such an action would not require your consent, but you will be informed if such a decision is made and the reason for this decision.
- You have not followed study instructions.
- The Sponsor (NIH), the study Principal Investigator, or the Food and Drug Administration (FDA) has decided to stop the study.

If you decide to participate, you are free to leave the study at anytime. Withdrawal will not interfere with your future care.

How will my personal information be protected during the study?
We will do our best to make sure that the personal information obtained during the course of this research study will be kept private. However, we cannot guarantee total privacy.

An exception to confidentiality is if you report child abuse or neglect or if you report suicidal or homicidal ideation or intent to the research team. Any information about child abuse or intent to harm yourself or others will be reported to authorities, as required by law.

Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used. The Institutional Review Board (IRB) at the University of Pennsylvania will have access to your records. If this study is being overseen by the Food and Drug Administration (FDA), they may review your research records.

To help protect your confidentiality, your data will only be transported by qualified study team members, and only during actual subject participation. Once all hard copy records are collected, they will be kept in a double-locked environment. Data collected during the study will be entered and stored in a password-protected database, called REDCap, Your data will be accessible only to engaged study members. Electronic records will not be transported via external drives or any other means. All biological samples will be transported by trained members of the research team directly to the appropriate facility where processing and analysis of the samples will take place. All samples will only be identified by the participants' randomly generated study ID number, and the date and time of the sample collection. If we write a report or article about this study or share the study data set with others, we will do so in such a way that you cannot be directly identified.

All research data will be de-identified and assigned a randomly generated research identification number. All information obtained will be kept completely confidential and will be in locked files behind locked doors. Electronic data will be encrypted and password protected.

Protected Health Information (PHI) is health information that identifies you. PHI is protected by federal law under HIPAA (the Health Insurance Portability and Accountability Act). To take part in this research, you must give the research team permission to use and disclose (share) your PHI for the study as explained in this consent form.

Once your health information is shared with someone outside of the research team, it may no longer be protected by HIPAA.

The research team will only use and share your information as talked about in this form. When possible, the research team will make sure information cannot be linked to you (de-identified). Once information is de-identified, it may be used and shared for other purposes not discussed in this consent form.

Will information about this study be available to the public?
A description of this clinical trial will be available on www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify you.

What may happen to my information collected on this study?
Your samples may be used to create products, including some that may be sold and/or make money for others. If this happens, there are no plans to tell you, or to pay you, or to give any compensation to you or your family. Most uses of biospecimens or information do not lead to commercial products or to profit for anyone.

Whole genome sequencing will not be conducted on your samples. Whole genome sequencing involves analyzing your entire personal genetic code.

Your information and samples will be de-identified. De-identified means that all identifiers have been removed. The information and samples could be stored and shared for future research in this de-identified fashion. It would not be possible for future researchers to identify you as we would not share any identifiable information about you with future researchers. This can be done without again seeking your consent in the future, as permitted by law. The future use of your information and samples only applies to the information and samples collected on this study.

What information about me may be collected, used or shared with others?
During your participation, you will be asked to provide your name, date of birth, address, telephone number, email address, and your social security number (so that we may issue you a check to compensate you for participation). We may also obtain or create a medical record number (in the event that we need to order procedures and to access your medical records to collect information about your medical history). This identifiable information will be held in strict confidence and will be kept in password protected files behind locked doors. Your personally identifying information will not be linked to any of the data that is analyzed and reported. All data will be de-identified when reported. You will also be asked to answer questions about your medical history including questions about your physical and mental health. Information from your medical charts will be reviewed and documented for research purposes. Results from physical exams and cognitive assessments will be part of the research record.

Scientific collaborators may request access to de-identified data such as brain imaging data to aid them in their own research. Depositing deidentified data in a central repository is a federal requirement.

Why is my information being used?
Your information is used by the research team to contact you during the study. Your information and results of tests and procedures are used to:

- Do the research
- Oversee the research
- To see if the research was done right.
- To evaluate and manage research functions.

Who may use and share information about me?
The following individuals may use or share your information for this research study:

- The investigator for the study and the study team
- Other authorized personnel at Penn, including offices that support research operations
- Other research personnel with access to the databases for research and/or study coordination and as otherwise approved by the IRB

Who, outside of the School of Medicine, might receive my information?

- Those working under the direction of the investigator for the study, (e.g. under subcontracts).
- All research centers participating in the study, even if they are not part of the School of Medicine
- The funding sponsor and organizations supporting the sponsor
- Harvard University and Amazon Web Services (AWS) as Beiwe is owned by Harvard University and AWS.

Oversight organizations

- The Food and Drug Administration
- The Office of Human Research Protections
- The study data and safety monitoring board
- The National Institutes of Health, which require central deposition of data

Once your personal health information is disclosed to others outside the School of Medicine, it may no longer be covered by federal privacy protection regulations.

The Principal Investigator or study staff will inform you if there are any additions to the list above during your active participation in the trial. Any additions will be subject to University of Pennsylvania procedures developed to protect your privacy.

How long may the School of Medicine use or disclose my personal health information?
Your authorization for use of your personal health information for this specific study does not expire.

Your information may be held in a research database. However, the School of Medicine may not re-use or re-disclose information collected in this study for a purpose other than this study unless:

- You have given written authorization
- The University of Pennsylvania's Institutional Review Board grants permission
- As permitted by law

Can I change my mind about giving permission for use of my information?
Yes. You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the investigator for the study. If you withdraw your permission, you will not be able to stay in this study.

What if I decide not to give permission to use and give out my health information?
Then you will not be able to be in this research study.

You will be given a copy of this Research Subject HIPAA Authorization describing your confidentiality and privacy rights for this study.

By signing this document you are permitting the School of Medicine to use and disclose personal health information collected about you for research purposes as described above.

How can we contact you?

We would like to contact you by phone, email, or mail in order to arrange your appointments. Some of these messages may contain information that identifies you. We will also be contacting you in the future, after the conclusion of the study, in order to follow-up on your status. Please provide us with contact information for an additional individual who knows where to find you in the event that we cannot reach you.

Electronic Medical Records and Research Results

What is an Electronic Medical Record and/or a Clinical Trial Management System?
An Electronic Medical Record (EMR) is an electronic version of the record of your care within a health system. An EMR is simply a computerized version of a paper medical record.

A clinical trial management system (CTMS) is used to register your information as a participant in a study and to allow for your research data to be entered/stored for the purposes of data analysis and any other required activity for the purpose of the conduct of the research.

If you are receiving care or have received care within the University of Pennsylvania Health System (UPHS) (outpatient or inpatient) and are participating in a University of Pennsylvania research study, information related to your participation in the research (i.e. laboratory tests, imaging studies and clinical procedures) may be placed in your existing EMR maintained by UPHS. Information related to your participation in clinical research will also be contained in the CTMS.

If you have never received care within UPHS and are participating in a University of Pennsylvania research study that uses UPHS services, an EMR will be created for you for the purpose of maintaining any information produced from your participation in this research study. The creation of this EMR is required for your participation in this study. In order to create your EMR, the study team will need to obtain basic information about you that would be similar to the information you would provide the first time you visit a hospital or medical facility (i.e. your name, the name of your primary doctor, the type of insurance you have). Information related to your participation in the study (i.e. laboratory tests, imaging studies and clinical procedures) may be placed in this EMR.
Once placed in your EMR or in the CTMS, your information may be accessible to appropriate UPHS workforce members that are not part of the research team.
Information within your EMR may also be shared with others who are determined by UPHS to be appropriate to have access to your EMR (e.g. Health Insurance Company, disability provider, etc.).

Who can I call with questions, complaints or if I'm concerned about my rights as a research subject?
For general questions, scheduling, concerns, or complaints regarding your participation in this research study and/or questions about your rights as a research subject, please call

Frederick Nitchie at (215) 573-9058. If a member of the research team cannot be reached or you want to talk to someone other than those working on the study, you may contact the Office of Regulatory Affairs with any question, concerns or complaints at the University of Pennsylvania by calling (215) 898-2614.

Do you agree to have the information you provide for "Dimensional Connectomics of Anxious Misery" (AKA Anxious Misery) used for this study as well?

Please note that if you wish to participate in both studies, you must give us permission to share your information between studies. You may choose not to participate in the Anxious Misery study and still participate in this CCBT study.

☐ *Yes* ☐ *No*

_____ _____

Initials Date

Do you agree to be contacted for future studies by the Center for Neuromodulation of Depression and Stress?

☐ *Yes* ☐ *No*

_____ _____

Initials Date

When you sign this form, you are agreeing to take part in this research study. This means that you have read the consent form, your questions have been answered, and you have decided to volunteer. Your signature also means that you are permitting the University of Pennsylvania to use your personal health information collected about you for research purposes within our institution. You are also allowing the University of Pennsylvania to disclose that personal health information to outside organizations or people involved with the operations of this study.

A copy of this consent form will be given to you.

_____

Name of Subject (Please Print)

_____

Signature of Subject Date

_____

Name of Person Obtaining Consent (Please Print)

_____

Signature Date