# UNIVERSITY OF PENNSYLVANIA
# RESEARCH SUBJECT
# INFORMED CONSENT AND HIPAA AUTHORIZATION FORM

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| **Protocol Title:** | Reducing neural perseveration through closed loop real time fMRI neurofeedback to alleviate depressive symptoms |
| **Principal Investigator:** | Yvette Sheline, M.D.<br>Department of Psychiatry<br>University of Pennsylvania<br>Richards Biomedical Building<br>3700 Hamilton Walk<br>Philadelphia, PA 19104<br>Email: sheline@pennmedicine.upenn.edu |
| **Emergency Contact:** | If you have a study related medical emergency, please present to your nearest emergency room or call 911 and contact CNDS at the number listed above |

## Research Study Summary for Potential Subjects

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 test the efficacy of a new psychotherapeutic strategy, closed loop real time fMRI neurofeedback, in reducing negative attention bias and depressive symptoms. You are being asked to voluntarily participate in a research study because you are between the ages 18-65 and currently experiencing symptoms of depression.

If you agree to join the study, you will be asked to complete the following research procedures: clinical assessments, self-report questionnaires, magnetic resonance imaging (MRI) scans at a 3T MRI scanner (with no use of contrast agents/injections), and behavioral tasks.

Your participation will last for approximately 6 weeks. This study requires 2 follow-up visits. This study may provide direct benefit to individual participants, but there is no guarantee that you will see a reduction in your depressive symptoms. Another potential benefit of participation would be the advancement of science. The most common risks of participation are discomfort during the clinical interviews, assessments, and magnetic

resonance imaging (MRI) scans. You may discontinue participation in this study at any time with no loss of benefits you're otherwise entitled to. The alternative to participation is simply not to participate.

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 invited to participate in a research study because you are between the ages of 18-65 and currently experiencing symptoms of depression.

This consent form describes what this study is about, the possible risks and benefits of being in this study, and what we will ask you to do. The research team will explain the study and answer any questions you may have. You may also discuss it with your family, friends, or doctor. You may find some of the medical language difficult to understand, so please ask the research team about anything you would like to know. If you decide to participate, you will be asked to sign this form.

## What is the purpose of this research study?

Behavioral training has been used in the past to reduce attentional biases in depression, specifically leading to reduced negative attention bias and depressive symptoms. A pilot study utilized fMRI data to create a "closed-loop" procedure to address attentional biases in participants. This is the first real time feedback therapy to use the participants' brain state (based on all of the individual participants' brain signal) for feedback training. This neural feedback provides data that is "close to the source" of the biases, which has the potential to be more sensitive and informative.

Thus, the purpose of this study is to test the efficacy of this new psychotherapeutic strategy, closed loop real time fMRI neurofeedback, in reducing negative attention bias and depressive symptoms.

## How long will I be in the study?

While the overall study duration will be for 5 years, your participation will be for an initial one-week period with one follow-up visit 1 months.

During the initial week, there will be one initial pre-training/screening visit (approx. 3-4 hours), 3 training visits (approx. 4-5 hours each), and one post-training visit (approx. 1 hour). Within 3 months, there are 2 follow-up sessions after the treatment is over (approx. 1 hour each).

**Please note that these times are approximates**, some participants may take more time and some may take less time to complete these visits.

## What am I being asked to do?

If you agree to take part in this research, you will be asked to complete the following:

- **Clinical assessments with study staff**: regarding your thoughts, feelings, and behaviors, and thoughts of death, dying, or suicide.
- **Self-report questionnaires**: regarding your thoughts, feelings, and behaviors.
- **Behavioral tasks**: gaze task that is part of neurofeedback training.
- **Randomization**: like a coin-flip, randomization allows researchers to assign participants to groups without bias. Participants in this study will be randomized after screening and eligibility check.
- **Magnetic Resonance Imaging (MRI) Scan**: an MRI uses electromagnetic radiation (radio waves) in a strong magnetic field to take clear pictures of your brain. You will be asked to lie still on a table in the MRI machine for 3 training sessions, each lasting approximately 2 hours per session.

| Procedure | Pre-training Session 1 | Training Session 1 | Training Sessions 2-3 | Post-training Session | Follow-up Sessions |
|---|---|---|---|---|---|
| Clinical Assessments | X (includes screening) | X | X | X | X |
| Self-Report Questionnaires | X | X | X | X | X |
| Medical History | X | | | | |
| Demographics Survey | X | | | | |
| MRI Scan at 3T scanner (no contrast agents/injections) | | X (includes baseline scan) | X | | |
| Behavioral Tasks | X | X | X | | |

## 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 unknown risks, or risks that we did not anticipate, associated with being in this study.

**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 to terminate your participation.

**MRI scan:**

- **Claustrophobia**: 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. An MRI scan requires you to be in a partially enclosed space inside the scanner. Some people may find this to be uncomfortable and claustrophobic. You need to inform the doctor ordering the scan, or the study staff, if you suffer from claustrophobia.
- **Magnetic Fields**: There is no known health risk associated with exposure to magnetic fields during an MRI. 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.
- **Medical Implants & Foreign Bodies**: There is also a potential risk of MRI for subjects with medical implants or other metallic objects in their body. All subjects undergoing MRI scanning must complete a screening evaluation risk in advance of the study for the presence of medical implants or other foreign bodies that could pose an injury. Every effort will be made to insure that disclosed implants or foreign bodies do not pose a risk to subjects. In cases where there is insufficient information to evaluate the risks associated with an implant or foreign body, the MRI study will not be allowed to proceed.
- **Flying Objects**: The greatest risk of MRI 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.
- **Incidental Findings**: 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 if necessary. 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.
- **Pregnancy**: 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. You will be asked to confirm pregnancy status during screening and prior to each MRI scan.

**Risk to confidentiality**: There is a rare risk that confidentiality could be breached in this study. Breaches in confidentiality could impact your future insurability and/or employability.

## 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?

Not all participants are expected to benefit from this study. It is possible that you may see a reduction in your depressive symptoms. However, we cannot guarantee that your depression will improve.

Your participation in this study could help us to better understand how the human brain works in people with depression. In the future, this information may be used to further help people with depression

## What other choices do I have if I do not participate?

The alternative to participation is to not participate. This is a voluntary study. If you choose not to participate, there will be no loss of benefit to you.

## Will I be paid for being in this study?

You will receive compensation for your time and participation: $25 for initial pre-training/screening, $50 for each training session, $25 for post-training session, and $25 for the 1-month follow-up session. You receive an additional $275 at the end for completing the study. This means it is possible to receive up to $500 total for participation.

Your payments will be given to you in the form of a Greenphire ClinCard. This is a reloadable prepaid card (similar to a debit/credit card) that allows funds to be available immediately. Please note that payments of $100.00 or more may take up to 1 full business day to appear available on your ClinCard. 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 provide your Social Security Number. 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.

## 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. If you feel this injury was caused by medical error on the part of the study doctors or others involved in the study, you have the legal right to seek payment, even though you are in a study. You do not give up your legal rights by signing this form.

This research may involve risks that are currently unforeseeable. University of Pennsylvania investigators and staff will try to reduce, control, and treat any complications from this research. If you feel you are injured because of the study, please contact the investigator, Dr. Yvette Sheline at: sheline@pennmedicine.upenn.edu

## 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 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, the study Principal Investigator, or the Food and Drug Administration (FDA) has decided to stop the study.
- Other administrative reasons
- Unanticipated circumstances

You may withdraw your consent to participate at any time and will immediately be removed from the study. If you wish to withdraw from the study, you can notify study staff in person, on the phone, or via email. Data already collected may still be used in analyses.

You may be withdrawn from the study by the principal investigator (study doctor) if you fail to attend study visits or notify the research team of cancellations in a timely manner. Additionally, you may be withdrawn from the study if there are concerns about your safety. If there are any concerns about your safety, the principal investigator and/or study staff will work with you to find immediate treatment options.

## 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. 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.

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.

## 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. At most, the web site will include a summary of the results. You can search this web site at any time.

## What may happen to my information collected on this study?

Any 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 research data will be de-identified when reported. De-identified means that all identifiers have been removed. This de-identified data will be 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.

**Future Use of Data and/or Specimens**

The information could be stored and shared for future research in this de-identified fashion. The information may be shared with other researchers within Penn, or other research institutions, as well as pharmaceutical, device, or biotechnology companies. 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 only applies to the information collected on this study.

## Will I receive the results of research testing that may be relevant to my health?

Many of tests done in research studies are only for research and have no clear impact on your healthcare. Research results for this study will not be returned to you because they would not be relevant to your healthcare. However, as discussed in the MRI scan risks section above, 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 if necessary. 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.

## What information about me may be collected, used or shared with others?

During your participation, you will be asked to provide your name, address, telephone number, email address, date of birth, and your social security number (so that we may compensate you for participation). 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. 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.

## 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.

## Where may my information be stored?

Information related to your participation in clinical research will be contained in a clinical trial management system (CTMS). A clinical trial management system (CTMS) is used to register your information as a participant in a study. This allows for your research data to be entered and stored for the purposes of study operational and financial applications and other activities required as part of the conduct of the research. Once placed in the CTMS your information may be accessible to other authorized personnel at Penn Medicine that support research operations. Your information may be held in other research databases.

## 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 the University of Pennsylvania and The University of Pennsylvania Health System and School of Medicine workforce who may need access to your information in the performance of their duties, 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 might receive my information?

We will keep your participation in this research study confidential to the extent permitted by law. However, it is possible that other people such as those indicated below may

become aware of your participation in this study and may inspect and copy records pertaining to this research. Some of these records could contain information that personally identifies you.

- Government representatives, (including the Office for Human Research Protections) to complete federal or state responsibilities
- The U.S. Food and Drug Administration
- Hospital or University representatives, to complete Hospital or University responsibilities
- University Pennsylvania's Institutional Review Board (a committee that oversees the conduct of research involving human participants).

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, accessible only to engaged study members. All electronic data will be coded and assigned a randomly generated research identification number. 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.

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; that is, the information will be de-identified. Once information is de-identified, it may be used and shared for other purposes not discussed in this consent form.

Once your personal health information is disclosed to others outside the University of Pennsylvania, 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 procedures developed to protect your privacy.

## How long may Penn 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, Penn 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 School of Medicine to use and disclose personal health information collected about you for research purposes as described above.

## Who can I call with questions, complaints or if I'm concerned about my rights as a research subject?

If you have questions, concerns or complaints regarding your participation in this research study or if you have any questions about your rights as a research subject, you should speak with the Principal Investigator listed on page one of this form. 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 IRB at the number on page one of this form.

## How will I be contacted?

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. We will ask you to provide contact information for an additional individual who knows where to find you in the event that we cannot reach you.

## 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 |