INFLAMMATION-RELATED ALTERATIONS IN NEUROCIRCUITRY: REVERSAL WITH LEVODOPA

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You Are Being Asked to Be in a Research Study

What Is a Research Study?

The main purpose of research studies is to gain knowledge. This knowledge may be used to help others. Research studies are not intended to benefit you directly, though some might.

Do I Have to Do This?

No. Being in this study is entirely your choice. If you decide to join this study, you can change your mind later on and withdraw from the research study.

Taking part in a study is separate from medical care. The decision to join or not join the research study will not affect your status as a patient.

What Is This Document?

This form is an informed consent document. It will describe the study risks, procedures, and any costs to you.

This form is also a HIPAA Authorization document. It will describe how your health information will be used and by whom.

Signing this form indicates you are willing to take part in the study and allow your health information to be used.

What Should I Do Next?

1. Read this form, or have it read to you.
2. Make sure the study doctor or study staff explains the study to you.
3. Ask questions (e.g., time commitment, unfamiliar words, specific procedures, etc.)
4. If there will be medical treatment, know which parts are research and which are standard care.
5. Take time to consider this, and talk about it with your family and friends.

Emory University School of Medicine
Department of Psychiatry and Behavioral Sciences
Consent to be a Research Subject/ HIPAA Authorization

Title: Inflammation-related Alterations in Neurocircuitry: Reversal with Levodopa

Principal Investigator: Jennifer C. Felger, Ph.D.

Study-Supporter: National Institute of Mental Health; Dana Foundation

Introduction

You are being asked to be in a medical research study. This form will tell you everything you need to think about before you decide if you want to be part of the study. **It is entirely your choice. If you decide to take part, you can change your mind later on and withdraw from the research study**. The decision to join or not join the research study will not cause you to lose any medical benefits.

Before making your decision:

- Please carefully read this form
- Please listen to the study doctor or study staff explain the study to you
- Please ask questions about anything that is not clear
- Feel free to take home an unsigned copy of this form and take your time to think about it and talk it over with family or friends

If you agree to join this research study, you will receive a copy of this consent form with your signature and the date, to keep. Do not sign this consent form unless you have had a chance to ask questions and get answers that make sense to you. Nothing in this form can make you give up any legal rights. By signing this form you will not give up any legal rights.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. law. This Web site will not include information that can identify you. At most the Web site will include a summary of the results. You may search this Web site at any time.

What is the purpose of this study?

The goal of this study is to learn more about what happens in the brain and the body when you are depressed. We may also learn about drugs that increase certain molecules in the brain, which may help people with depression. You are being asked to be in this study because you have expressed feelings of depressed mood. This study will include 225 people who are depressed.

The main goal of the study is to see if the level of inflammation in the body is related to depression. We will also look at how well you think, and how some of your brain regions work with each other. We may also record physiological measures including heart rate and activity. Inflammation is when your body's immune system becomes too activated. We will measure inflammation in your body using a blood test for a C-reactive protein (CRP). CRP is a protein made by the liver during inflammation. We will also measure other molecules related

to inflammation in your blood and in your spinal fluid by performing an optional spinal tap procedure, referred to as a lumbar puncture (LP).

During the study visits you will take an FDA-approved medication called Levodopa (L-DOPA, also called Sinemet). This medication increases dopamine, a nerve chemical in the brain that can make you feel energetic, and that is decreased in the brain by inflammation. Before and after you take the medication, we will use magnetic resonance imaging (MRI) scans to look at your brain activity. You will also perform tests looking at how you think.

What will I be asked to do?

During this study you will meet with study doctors, research faculty, a clinical social worker, research nurses, study coordinators and other study staff.

The study consists of a minimum of 4 visits to Emory University:

- 1-2 initial office visit(s) for study overview and consent signing
- 1-2 outpatient screening visit(s) including baseline computer tasks and training
- 1 outpatient visit for lumbar puncture (optional)
- 2 treatment visits (Study Visit 1 & 2) with MRI scans and behavioral assessments

Initial Office Visit(s): First, you will come and meet with us to see if you are able to be in the study. During this visit, a study staff member will ask you questions about your health and how you are feeling. You will also be asked about problems with drugs or alcohol and current medications you are taking. If you have significant problems with your health, you cannot be in the study. You also cannot be in the study if you have significant problems with drugs or alcohol. This visit will last 1–2 hours. After the consent has been reviewed and signed, screening lab work may be done at this visit or at a screening visit, as described below. You may also be asked during this visit or at a future visit to have one to two drops of blood collected from a finger prick conducted by trained research staff.

Medications to Avoid:

It is important that you do not take some medications while you are in the study. Please do not take the following: Aspirin or Aspirin-like compounds, Ibuprofen or Naproxen Sodium (for example: Advil, Aleve, Motrin IB), Cholesterol medications (for example: Simvastatin, Lipitor, Pravachol), Antibiotics, Topical Steroids (i.e. hydrocortisone), Vaccinations, Herbal Medications, and Omega-3 supplements. Please contact us if your doctor prescribes any new medication while participating in the study. Please also contact us if you plan on starting any new over-the-counter medications between study visits. Please do not stop taking any prescribed medications.

Screening Visit A:

You will come to Emory Clinic Building B for your screening visit. The study team will ask you about any psychiatric symptoms you may have now or in the past. You will be asked about your medical history and will fill out some self-report forms about yourself. You will have a physical examination. You will have an electrocardiogram (ECG) at the clinic. You may be asked to give a small sample of blood, collected from a vein in your arm by an Emory Healthcare professional to make sure you are in good physical health. Up to 4 tablespoons of blood will be drawn from your arm vein. We will also take a urine sample to know more about your health and to find out whether any drugs of abuse are in your body. You will not be charged for the

physical exams, psychiatric evaluation, or blood and urine tests. This visit will last up to approximately 6 hours. Some assessments may be repeated if necessary.

Screening Visit B:
You will come to Emory Clinic Building B in the morning for your second screening visit. If research blood work will be conducted at this visit, you will be asked not to eat or drink anything but water after midnight, planning for blood to be drawn first thing in the morning. You will be asked to give a small sample of blood, collected from a vein in your arm by an Emory Healthcare professional, to measure your inflammation level and to look at your genes related to inflammation and metabolism. A little over 1 tablespoon of blood will be drawn from your arm vein. After the blood draw, you will be able to eat and drink as normal. Any previous screening lab work including blood and urine and a physical examination may be repeated if 4 weeks has passed or at the discretion of the study physician. We may also place an ECG patch(s) on your chest and/or leg that will allow us to record your heart rate and activity over 24 hours. If you are given an ECG patch(s), you will be asked to remove the ECG patch(s) the following day and return it to the Emory Clinic, Building B at your next study visit, or in a pre-paid envelope that we will provide to you. At this visit, you will also complete tests of your thinking ability. These tests will last about 90 minutes, and you will be given a 15-minute break in the middle. For the first block of computer tasks, additional compensation will depend on the choices you make. After a break, you will complete the second block of tasks. For these tasks you will receive compensation simply for completing them. These tasks are similar to those that will be done when you return for Study Visits 1 & 2 and will allow you to get used to the procedures. This visit will last approximately 3-4 hours. You may be asked to come in for additional screening visits to repeat any lab work or assessments. If possible, screening visits A and B may be combined into a full day visit.

Optional Visit- Lumbar Puncture:
You may be asked to come in for an additional visit, which will consist of a lumbar puncture. This portion of the study is optional. If you choose to participate in this portion of the study, you will arrive at ACTSI-CRN (Research Unit inside Emory University Hospital) between 7-10am, an IV line will be inserted by research nurses at ACTSI. If you are asked to be given a small sample of blood for research at this visit, then you will also be asked not to eat or drink anything but water after midnight, in planning for a fasting research blood sample draw. You will be given a bag of saline (normal saline is water with some salt in it) through an IV in your arm. After receiving fluids for at least 30 minutes, you will have a spinal tap (Lumbar puncture or LP). The LP procedure allows us to collect a sample of your spinal fluid for the purpose of measuring inflammatory markers. A senior Attending Anesthesiologist from Emory University with experience in performing spinal taps will directly oversee the procedure. Before the procedure, you will be offered pre-LP sedation with Versed through IV. The procedure will involve inserting a special long bore needle into the spine to obtain about two teaspoons full of fluid. This is a safe procedure and is often used to identify and treat brain diseases. The procedure would be carried out at a research unit dedicated to aid in such procedures by personnel who are well trained in conducting these procedures. Following the LP you will be instructed to rest until the research nurse determines that it is safe for discharge. You will be carefully observed for any side effects prior to discharge. A family member or friend will need to drive you home from the hospital after discharge. In total, ~6 hours will be required from you for this visit.

Treatment Visits (Study Visits 1 & 2):
You are being asked to participate in magnetic resonance imaging (MRI) scan sessions where you will take a tablet of medication called levodopa (L-DOPA, also referred to as Sinemet) on one visit, and a placebo tablet (an inactive substance like sugar) on the other visit. The order of the L-DOPA and placebo will be randomly

assigned (similar to a flip of a coin). You will have a one in two chance of getting L-DOPA and a one in two chance of getting placebo on the first visit. On the second visit, you will be given the other tablet that you did not get on the first visit. Neither you nor the study doctor will know which day you will receive L-DOPA or placebo. The tablets will be prepared specially for the study to be identical. However, if a medical emergency occurs, the information about whether you received L-DOPA or placebo will be available to your study doctor. The L-DOPA medication is FDA approved to treat Parkinson's disease. It increases a molecule in the brain called dopamine, which may also be low in depression.

In preparation for these visits, you will be asked not to eat or drink anything but water and/or juice 3 hours before your scheduled MRI scan. On the day of the study visit, you will come to the Clinical Research Network in the Emory University Hospital outpatient unit, or to the Emory Behavioral Immunology Program in The Emory Clinic Building B in the morning. You will give a urine sample in order to test for any drugs of abuse. A trained Behavioral Immunology Program staff or a nurse will take your body temperature, heart rate, and blood pressure. During either study visit, a physical examination may be repeated if 4 weeks has passed. You will fill out some self-report forms about yourself and you will be asked questions about how you are feeling.

You will have 2 MRI scans with a 45-60 minute break in between. A study staff member will escort you to the Emory University Imaging Facility where the MRI scanner is housed. The scanner uses a very strong magnet to take pictures of your brain. MRI scans are painless and contain no radiation. You will have a functional MRI scan (fMRI) and perform a task looking at how you think. fMRI is used to look at brain activity using the MRI scanner. This will be done to see how brains of people with depression are activated while at rest, during passive viewing of faces, or when performing a task on a computer. We will give you instructions about the task. You will also have a practice session outside of the scanner. This will let you become familiar with task instructions. During the task, you can either win or lose money based on how fast you can press a button. The smallest amount of money you may win is zero. The highest amount of money you can win is $20 in cash, regardless of your total reported earnings. You will receive your total money won after the scan ends.

You will be asked to remove all jewelry and other metal-containing objects. You will then be placed on a narrow table, which will slide into the MRI scanner. The scanner is a large closed box with a tube in the middle. You will lie in the tube while the scan is being done. The tube is about 6 feet long and 25 inches wide. You will then be asked to lie still during the scan for about 30-45 minutes. For 9 minutes you will be asked to lie with your eyes open while looking at a cross that you will see in a mirror above your head. For 5 minutes, you will also be asked to passively look at faces presented above your head. During the last part of the scan you can rest with your eyes closed. You will hear some loud noises as the scanner takes pictures of your head. You will be offered earplugs to wear to decrease how loud the noise seems to you. Occasionally, people have an extreme fear reaction (claustrophobia) to being in the scanner. If this occurs you will be removed from the scanner and the experiment will be stopped.

After the first scan, you will be escorted to a waiting room near the MRI facility by the study staff. You may be offered a low protein snack a few minutes prior to receiving the medication. You will then be asked to take one tablet of medication (either L-DOPA or the placebo tablet). The study doctor or nurse will ask if you feel any unlikely side effects from the medication tablet. The study doctor or nurse will take your temperature, heart rate and blood pressure. If your temperature changes by more than 2 degrees, your heart rate or blood pressure increases or decreases above normal, the study will be paused and appropriate medical care will be given. These changes are rare and if they do happen, they are not expected to last a long time. The study doctor or nurse will

check on you while you relax quietly for about 45 minutes. During this time, you will also complete a practice session of the task.

You will then be escorted back to the room with the MRI scanner where you will have a similar MRI scan as before but will be asked to make choices on a response pad during the task. The total time for the second scan will be 45-55 minutes. Afterwards, you will be escorted back to the Clinical Research Network or the Emory Clinic. Less than 1 tablespoon of blood will be drawn from your arm vein, though more may be drawn if necessary for additional safety labs. You will be asked to complete self-report forms and assessments of your thinking ability. You will complete a task on the computer similar to the ones you completed at the screening visit. For this task, you can earn between $0 and $60. You will also be given lunch. You will be asked to stay at Emory until the nurses see that you have normal vital signs. Before you leave, the nurse will take your body temperature, heart rate, and blood pressure. You should be able to walk without wobbling, talk without slurring, and show no signs of dizziness. These visits will last about 5-6 hours. When you come in for the second treatment visit, a similar schedule will be followed.

Procedure	**Initial Visit(s)**	**Screening A**	**Screening B**	**Lumbar Visit (optional)**	**Additional screening (if needed)**	**Study Visit #1**	**Scan Visit #2**
Consent*	X						
Self-report Forms	X	X	X	[X]	[X]	X	X
Psychiatric assessments	[X]	X	[X]	[X]	[X]	X	X
Screening labs (blood draw, EKG, and urine)	[X]	X	[X]	[X]	[X]	[X]	[X]
History and Abbreviated Physical		X	[X]	[X]	[X]	[X]	[X]
Placement of ECG patch(s)		[X]	[X]		[X]		
Urine Drug screen	[X]	[X]	[X]	[X]	[X]	X	X
MRI scan						X	X
Computer tasks/Cognitive testing			X	[X]	[X]	X	X
Fasting research blood draw			X	[X]	[X]	X	X
Lumbar Puncture (optional)				X			

[X]- To be completed if needed
*- If our consent form is updated you will be notified of any applicable changes. You will be asked to sign the newest version of our consent form.

Storage of blood samples for future, unknown research:
Your blood will be used in several ways for this study. Some will be used for the tests mentioned above. Some will be used as a source of material for future studies. By doing this, we can do research for a long time without needing to ask for fresh blood samples from you. Any products made from your sample will become the property of Emory University. Some samples may be sent to other labs for additional analysis. In order to protect your privacy, all samples and products from your blood will be given an identification code. This code will not include any of your personal information. Your sample will be stored for as long as it is useful, unless you ask us to destroy it sooner. You may request that your sample be destroyed at any time, simply by contacting the Principal Investigator Jennifer C. Felger, Ph.D. [redacted]

What are the possible risks and discomforts?
The most common risks and discomforts expected in this study are:

Blood Draws: The risks of a syringe are minimal. They include swelling, tenderness, discomfort, bruising, infection, bleeding, and fainting. To minimize these risks, the procedures will be done in a sterile manner while you are comfortably seated. Blood draws will be done by nurses or trained phlebotomists. The blood volume collected from you during the study is within the American Red Cross safety guidelines.

Psychiatric Assessments: The psychiatric assessments may bring up disturbing memories or feelings. To minimize this, we will give you time during the assessment to talk about those feelings. We will be careful not to cause you unneeded distress during the psychiatric assessment.

Computer Testing: There are no known risks for the tests of your thinking ability.

Magnetic resonance imaging (MRI): Because the MRI is performed in an enclosed narrow space, some people may eventually experience fear, shortness of breath, rapid heartbeat, or claustrophobia. If this happens to you, you may ask to stop the scan immediately. Metallic implants may move due to the procedure and may cause damage to your body. Therefore, you will be carefully screened for any type of metal objects in your body prior to receiving the scan. If you have metal implants in your body you will not participate in the scan. No other known risks are associated with receiving MRI scans.

L-DOPA administration: The dose of L-DOPA given in this study is very small compared to doses given for treatment of diseases like Parkinson's disease. Nausea and vomiting are frequent side-effects of taking levodopa. Carbidopa is given with the L-DOPA to reduce these side effects. Other symptoms you may experience include dizziness, sleepiness or trouble sleeping, and headache. It may also cause increased eye blinking/twitching, fainting, mood changes, or worsening of involuntary movements and spasms. People who take L-DOPA every day for Parkinson’s disease have also reported more serious but rare symptoms. These include: easy bleeding or bruising, signs of infection such as fever or sore throat, tingling in the hands and feet, blurred or double vision, chest pain, seizures, vomit that looks like coffee grounds, black or tarry stools, muscle stiffness, confusion, sweating, fast heartbeat, rapid breathing or trouble breathing, erection lasting more than 4 hours in males, and rash, itching or swelling. If you agree to participate in this study, we require you to stop taking nonselective monoamine oxidase (MAO) inhibitors at least 4 weeks before the first study visit.

Delay in Treatment for Depressed Volunteers: Being in the study will delay treatment for your depression. This may mean that you have continued symptoms of depression, distress, and difficulty in your daily functioning. Your depressive symptoms could also get worse, including the risk of suicidality. The risk of suicide is always possible with depression. Please tell the study clinician, Bobbi Woolwine, LCSW or the study doctors, Andrew H. Miller or Ebrahim Haroon, immediately if you have thoughts of suicide.

Storage of blood samples for future, unknown research: It is possible that the storage of your blood for future research may pose risks that we haven't thought of. Future research could show that you have genes for special medical illnesses. This could affect your insurability or employability in the future if the information were released. It could also cause other social or financial problems. To guard against this, your name will not be stored with your blood samples. All samples will be identified by number only. The privacy of your blood samples will be protected to the full extent allowed by law. Laboratory staff performing assays on your samples will not have access to your name or any of your information.

ECG monitor: This requires you to wear patch devices attached to your chest, which may represent an inconvenience to you. It is possible that study personal will ask you to shave a small section of your chest. It is possible that the adhesive (sticky substance that will attach it to your skin like a band-aid) or shaving could cause irritation. This is an optional component of the study.

Lumbar puncture**:** A lumbar puncture procedure involves inserting a needle between the bones of your spine to collect a small amount of cerebrospinal fluid. This is the fluid that surrounds the brain and the spinal cord. About 2 teaspoons of fluid will be withdrawn. This fluid will allow us to measure the amounts of inflammation-related molecules surrounding your brain. Prior to the LP procedure, you will have the choice of receiving a sedative. A sedative is a medication administered by the Anesthesiology physician that will produce a calming effect on the body. This sedative can interact with other sedative drugs. You will be asked to refrain from taking sedative drugs during your participation in the study, and a family member or friend will need to drive you home after the procedure. For the LP, the physician will carefully sterilize the skin over a small area of your lower back. Then he or she will inject local anesthesia to numb the area. The physician will then insert a thin needle between the bones of your spine to collect the fluid.

Some of the side effects of this procedure include bruising at the site of needle insertion, infection, bleeding and headache (post-LP headache). To reduce risks associated with receiving an LP, an experienced physician will conduct the procedure under standard sterile conditions. Subjects will receive two liters of normal saline prior to the procedure. This has been found to reduce the incidence of post-LP headache. Subjects will lie flat for up to two hours after the procedure and will be observed for the emergence of any significant adverse effects. If subjects develop a headache they will be treated with pain medication or application of blood patch. The blood patch involves injecting a small amount of your own blood at the site of the LP. Your blood acts as a patch to close the small opening made by the needle. Very rarely, some individuals develop neurological symptoms following the procedure, in which they would be evaluated by the Emory Emergency Room Physicians and treated accordingly. The Department of Anesthesiology at Emory University has 24 hour coverage of the ACTSI-CIN if more emergent side effects develop following LP. In addition, the entire procedure will be conducted in the Emory research unit at ACTSI-CIN and/or pre-operational unit, which have immediate access to EKG monitoring, cardiac resuscitation equipment and are located in close proximity to the Emory University Hospital Emergency room. You will be encouraged to call your study doctor right away if you have any of these side effects:

- you feel faint, or unsteady on your feet, when you stand up after you have been sitting or lying down
- you have lost power or sensation of one or both your lower limbs
- you have a headache that is not relieved by several doses of painkillers

- you feel confused
- your neck feels sore and stiff
- you develop nausea or vomiting

If you are a woman: To protect against possible risks of the study, women who are pregnant or nursing a child may not take part in this study. If you are a female and could possibly become pregnant, a serum pregnancy test will be conducted at a screening visit. Additional pregnancy tests (either serum or urine) may be performed if 4 weeks have passed since the last test.

New Information

It is possible that we will learn something new during the study about the risks of being in it. If this happens, we will tell you about it so you can decide if you want to continue to be in this study or not. You may be asked to sign a new consent form that includes the new information if you decide to stay in the study.

Will I benefit directly from the study?

This study is not designed to benefit you directly. This study is designed to learn more about depression and inflammation. The study results may be used to help other patients in the future.

Will I be compensated for my time and effort?

Our preferred method of compensation will be the use of Clincards. All payments are made using a personal payment card. We issue this to you for free. The payment card is a prepaid debit card. It can be used exactly like a MasterCard. We load money onto your card electronically every time you need to be paid. The card scheme is run by Greenphire, an independent company specializing in payments for research studies and clinical trials. To issue your card, we need to give Greenphire some of your personal information. Banks and other financial institutions can access this information if they need to verify your identity when you use your card.

Emory University is required by law to report any payments we make to the IRS. Research payments in cash or cash equivalents that exceed $600.00 per calendar year must be reported to the Internal Revenue Service (IRS) by the University. The level of reimbursement for this study is at a level that the potential exists for the federal tax reporting to the IRS for your participation in this study. To do this, Emory University Department of Finance needs to keep your Social Security Number on file. We are asking you to allow us to communicate your name, address, date of birth, research study name and Social Security Number to Greenphire and Emory University Department of Finance. If you want to receive e-mail or text alerts when payments are made to you, we will ask you to provide your e-mail or phone number as well. All of this information will be stored on computers owned by Greenphire. Greenphire will not have access to any other information collected during this study. Full instructions about using your card are included when we issue it. Please ask if you have any questions or concerns about the card scheme.

We would also like the option of compensating you in the form of cash, check or gift card if ClinCard accessibility is not available. You will be asked to fill out a tax form, including your Social Security or Taxpayer Identification Number, in order to be reimbursed, depending on the amount and method of payment. Some payment methods involve mail coming to your house, which may be seen by others in your household. You can decline payment if you are concerned about confidentiality, or you can talk to the study team to see if there are other payment options. You will need to fill out a W-9 form.

Initial Office Visit: You will be compensated $25 for this visit.

Screen A: You will be given $50 that day. Further compensation (an additional $25 per visit) will be provided to cover travel expenses for you if you live equal to or greater than 50 miles outside of the Atlanta city limits.

Screen B: You will be given $25 for the visit, to be paid to you at the end of that day. If you decide to wear the ECG patch(s), you will also receive an additional $25 paid to you at the end of the visit. If research blood work is collected at this visit, $25 will also be paid to you to you at the end of the study visit. For the computer testing, you will receive $50 total simply for completing these tasks, which will be uploaded to your ClinCard after you complete the study. Additional compensation for computer testing will depend on the choices you make. Please read each task's instructions very carefully. On one of the tasks you will receive payment for your winnings from two completed trials. All earnings paid to you at the end of the study visit will be rounded to the nearest $5.
Additional Screening (if needed): You will be paid up to $50 for each additional screening visit.

Lumbar Puncture visit (optional): If you decide to complete the lumbar puncture, you have $500 uploaded to your ClinCard after you complete the study. You will also receive $25, to be paid to you at the end of that day, if you are asked to have a research blood draw or lab work at this visit.

Treatment Visits (Study Visits 1 & 2): For the L-DOPA and placebo study visits, you will be given $200 for the completion of each visit. $50 for each visit will be paid to you at the end of that day and $150 of each visit will be uploaded to your ClinCard after you complete the study. If you are unable to complete a scan session or if you are excluded from the study on the day of the scan, you will be paid $25 that day. For the computer tasks inside the scanner, you will receive 1/3 of your winnings at the end of the session, up to $20. For the computer task outside of the scanner, you may earn up to $60 that will be paid to you at the end of the study visit. All earnings paid to you at the end of the study visit will be rounded to the nearest $5. You can receive a maximum earning of $280 at each of these study visits.

The maximum compensation you can earn after completing two screening visits and two treatment visits is $800. If you decide to do the LP procedure you can receive an additional $500

Disclosure
Dr. Treadway (one of the co-investigators for this study) is a co-inventor of the EEfRT task software, which is one of the computerized tests used in this study. Emory University and Vanderbilt University licensed this software to BlackThorn Therapeutics. Under the IP Policies of both universities, Dr. Treadway receives licensing fees and royalties from BlackThorn Therapeutics. Additionally, Dr. Treadway has a paid consulting relationship with BlackThorn. The terms of this arrangement have been reviewed and approved by Emory University in accordance with its conflict of interest policies.

What are my other options?
This study is not designed to treat depression. You are free to choose not to be in it.

How will you protect my private information that you collect in this study?
Emory will keep any research records that it creates private to the extent that it is required by law. Whenever possible, a study number, rather than your name, will be used on study records. Your name and other identifying information will not appear when we present or publish the study results.

Medical Record

If you are or have been an Emory Healthcare patient, you have an Emory Healthcare medical record. If you are not and have never been an Emory Healthcare patient, you do not have one. An Emory Healthcare medical record will be made for you if an Emory provider or facility does any service for you in this study.

We will take reasonable steps to keep copies of this form out of Emory Healthcare's medical records system. If we aren't successful in keeping these forms out, we will take steps to remove them. If they cannot be removed, we will take steps to limit others from seeing them. Your healthcare record will identify you as a study participant with our contact information. Neither the study title nor the type of research will be published in your medical record for this study.

Emory Healthcare may create study information about you that can help with your care. For example, all safety and medical laboratory tests from the study will be put in your Emory Healthcare medical record. Anyone who has access to your medical records will be able to see the study information placed there. The confidentiality of the study information in your medical record will be protected by laws like the HIPAA privacy rule. State and federal laws may not protect the research information from disclosure.

The results of some study tests will be used only for research and will *not* be placed in your medical record. These results will not be reviewed to make decisions about your health or treatment. These items include: computer tests, medical and psychiatric history, health status updates, questionnaires, urine drug screen results, research lab work for looking at inflammation, and MRI scans. These study results will be kept only in a research record. We will take steps to make sure that these results are not placed in your Emory Healthcare medical record. These results will not be made available to any other healthcare providers who may be giving you treatment. These results are not intended for clinical use and will not be available to you or your doctor.

Tests done at non-Emory places may not become part of your Emory medical record. Emory also does not have control over any other medical records that you may have with other healthcare providers. Emory will not send any test or procedure results from the study to these providers. Also, if you decide to be in this study, it is up to you to let your other health providers know.

Incidental Findings

This type of brain scan is not designed to detect problems of the brain. A radiologist will not be reading the scan. However, it is still possible that we will see something on your scan that is potentially abnormal but may be nothing. If this happens, we will discuss it with you. This may cause you to seek further medical treatment and incur costs associated with that.

In Case of Injury

If you get ill or injured from being in the study, Emory will help you to get medical treatment. However, Emory and the Sponsor, the National Institute of Mental Health and Dana Foundation, have not set aside any money to pay you or to pay for this medical treatment. The only exception is if it is proved that your injury or illness is directly caused by the negligence of an Emory employee. "Negligence" is the failure to follow a standard duty of care. If you become ill or injured from being in this trial, your insurer will be billed for your treatment costs. If you do not have insurance, or if your insurer does not pay, then you will have to pay these costs.

If you believe you have become ill or injured from this research, you should contact Dr. Jennifer C. Felger at telephone number [redacted]. You should also let the health care provider who treats you know that you are in a clinical research study.

Costs
There will be no costs to you for participating in this study, other than basic expenses like transportation. You will not be charged for any of the research activities.

Withdrawal from the Study
You have the right to leave a study at any time without penalty. If you leave the study before the final planned study visits, the study doctor may ask you to have some of the final steps done.

The study doctor and sponsor also have the right to stop your participation in this study without your consent if:
1. They believe it is in your best interest;
2. You were to object to any future changes that may be made in the study plan;
3. You become too severely depressed and/or suicidal to participate
4. You are found to have used drugs of abuse
5. or for any other reason as determined by the PI or study doctor.

30 Day Off-Study Policy
There may be situations based on your schedule or ours that require more than 30 days to occur between study visits. If this is the case, for the purposes of your care and safety, a research assistant will inform you of the delay and temporarily remove you from the study. In the meantime, you should feel free to start or resume any form of treatment. When you return for your next study visit, you will be reevaluated for study eligibility and re-consented by a study clinician or coordinator. Based on your status, we will continue the study where you left off and will use as much previously collected data as possible. However you may be asked to repeat some bloodwork or assessments to evaluate any changes in your status.

Authorization to Use and Disclose Protected Health Information

The privacy of your health information is important to us. We call your health information that identifies you, your "protected health information" or "PHI." To protect your PHI, we will follow federal and state privacy laws, including the Health Insurance Portability and Accountability Act and regulations (HIPAA). We refer to all of these laws as the "Privacy Rules." Here we let you know how we will use and disclose your PHI for the study.

PHI that Will be Used/Disclosed:
The PHI that we will use or share for the main research study includes:
1. Medical information about you including your medical history and present/past medications.
2. Results of exams, procedures and tests you have before and during the study.
3. Laboratory test results

Purposes for Which Your PHI Will be Used/Disclosed:
We will use and share your PHI for the conduct of the research study. We will use and share your PHI to provide you with study-related treatment and for payment for such treatment. We will also use and

share your PHI to conduct normal business operations. We may share your PHI with other people and places that help us conduct or carry out the study, such as laboratories, data management centers, data monitors, contract research organizations, Institutional Review Boards (IRBs) and other study sites. If you leave the study, we may use your PHI to determine your health status or contact information.

Authorization to Use PHI is Required to Participate:
By signing this form, you give us permission to use and share your PHI as described in this document. You do not have to sign this form to authorize the use and disclosure of your PHI. If you do not sign this form, then you may not participate in the research study or receive research-related treatment. You may still receive non-research related treatment.

People Who will Use/Disclose Your PHI:
The following people and groups will use and disclose your PHI in connection with the research study:

1. The Principal Investigator and the research staff will use and disclose your PHI to conduct the study and give you study-related treatment.
2. Emory may use and disclose your PHI to get payment for study-related treatment and to run normal business operations.
3. The Principal Investigator and research staff will share your PHI with other people and groups to help conduct the study.
4. The following people and groups will use your PHI to make sure the research is done correctly and safely:
    1. Emory offices that are part of the Human Research Participant Protection Program and those that are involved in study administration and billing. These include the Emory IRB, the Emory Research and Healthcare Compliance Offices, and the Emory Office for Clinical Research.
    2. Government agencies that regulate the research including: Office for Human Research Protections; Food and Drug Administration.
    3. Public health agencies including the sponsor of the study, the National Institute of Mental Health (NIMH).
    4. Research monitors and reviewer.
    5. Accreditation agencies.

Expiration of Your Authorization
Your PHI will be used until this research study ends.

Revoking Your Authorization
If you sign this form, at any time later you may revoke (take back) your permission to use your information. If you want to do this, you must write to:

[redacted]

At that point, we will not collect any more of your PHI. But we may use or disclose the information you already gave us so we can follow the law, protect your safety, or make sure that the study was done properly and the data is correct. If you revoke your authorization you will not be able to stay in the study.

Other Items You Should Know about Your Privacy
Not all people and entities have to follow the Privacy Rules. HIPAA only applies to health care providers, health care payers, and health care clearinghouses. If we disclose your information to people do not have to follow the Privacy Rules, including HIPAA, then your information will not be protected by the Privacy Rules. People who do not have to follow the Privacy rules can use or disclose your information with others without your permission if they are allowed to do so by the laws that cover them. Let us know if you have questions about this.

To maintain the integrity of this research study, you generally will not have access to your PHI related to this research until the study is complete.

We may "deidentify" your data by removing identifying information from your PHI. Once we do this, the rest of the information will not be subject to the Privacy Rules. Information with no identifiers may be used or disclosed with other people or organizations for purposes besides this study. For example, your deidentified data from this study may be shared with national repositories such as the National Institute of Mental Health Data Archive (NDA) or the Gene Expression Omnibus (GEO). A data repository is a large database where information from many studies is stored and managed. These national databases allow researchers to collect and share deidentified information with each other. With an easier way to share, researchers hope to learn new and important things about diseases more quickly than before.

Use of the ECG patch (MC10 BioStamp®) for collection of biometric data: If you choose to wear the ECG patch, the data that is collected from you for this study may be further used in analyses by Emory University, MC10, Inc. (the manufacturer of the Biostamp sensors used in this study), or outside academic researchers to answer additional scientific questions and for product development and other business purposes. We will take appropriate measures to protect your information and will only share de-identified data for this purpose. You may review MC10's Privacy Policy (www.mc10inc.com/privacy-policy) and Terms and Conditions of Use (www.mc10inc.com/terms-conditions).

If you decide to sign consent for enrollment into this study, there are a couple of items that you may opt to check on the signature pages. You do not have to check these items in order to be in the study. They are optional. The first item is whether or not you are willing to participate in the lumbar puncture procedure. If you are not willing to participate in the lumbar puncture procedure you may still participate in the study. The second item is whether or not you agree to wear the ECG patch(s) for collection of heart rate data over 24 hours. If you do not decide to wear the ECG patch(s), you may still participate in the study. The third item is whether or not you agree to participate in the texting service for appointment reminders. The fourth item is agreeing to allow the results of your screening assessments and any data collected from you during the study to be shared with other research studies of your choosing. If you decide not to sign this line you may still participate in the study.

Certificate of Confidentiality
There is a Certificate of Confidentiality from the National Institutes of Health for this Study. The Certificate of Confidentiality helps us to keep others from learning that you participated in this study. Emory will rely on the Certificate of Confidentiality to refuse to give out study information that identifies you. For example, if Emory received a subpoena for study records, it would not give out information that identifies you.

The Certificate of Confidentiality does not stop you or someone else, like a member of your family, from giving out information about your participation in this study. For example, if you let your insurance company know

that you are in this study, and you agree to give the insurance company research information, then the investigator cannot use the Certificate to withhold this information. This means you and your family also need to protect your own privacy.

The Certificate does not stop Emory from making the following disclosures about you:

- Giving state public health officials information about certain infectious diseases.
- Giving law officials information about abuse of a child, elderly person or disabled person.
- Giving out information to prevent harm to you or others.
- Giving the study sponsor or funders information about the study, including information for an audit or evaluation.

Contact Information

[redacted]

1. if you have any questions about this study or your part in it,
2. if you feel you have had a research-related injury, or
3. if you have questions, concerns or complaints about the research
4. [redacted]

Contact the Emory Institutional Review Board [redacted]

1. if you have questions about your rights as a research participant.
2. if you have questions, concerns or complaints about the research.
3. You may also let the IRB know about your experience as a research participant through our Research Participant Survey at http://www.surveymonkey.com/s/6ZDMW75.

Consent and Authorization

TO BE FILLED OUT BY SUBJECT ONLY

Please **print** your name, **sign**, and **date** below if you agree to be in the study. By signing this consent and authorization form, you will not give up any of your legal rights. We will give you a copy of the signed form to keep.

In the box below, please put your initials under "Yes" if you agree to the statement, or "No" if you do not agree and then sign on the appropriate line below:

Yes	No	
☐	☐	I AM willing to participate in the LP procedure, as described on page 4 of this consent form.
☐	☐	I AM willing to wear the ECG patch, as described on pages 4, 8 and 13 of this consent form.
☐	☐	I AM interested in receiving appointments reminders and scheduling information via text message.
☐	☐	I DO agree that the results of my screening tests (laboratory, medical, and psychiatric) and any data collected during my study visits may be shared with the study team of my choice. I also authorize the use of my PHI for this purpose.
☐	☐	May we contact you in the future regarding participation in future research studies? You may then decide if you are willing to participate.

Name of Subject

Signature of Subject (18 or older and able to consent) **Date** **Time**

TO BE FILLED OUT BY STUDY TEAM ONLY

Name of Person Conducting Informed Consent Discussion

Signature of Person Conducting Informed Consent Discussion **Date** **Time**