Non-invasive Vagal Nerve Stimulation in Opioid Used Disorders

NCT04556552

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You Are Being Asked to Be in a Research Study

Concise presentation of key concepts

You are being asked to be in a research study. A research study is designed to answer a scientific question. If you agree to be in the study you will be one of 20 people who are being studied, at Emory and elsewhere.

Why is this study being done?

This study is being done to answer the question: what are the effects of Vagal Nerve Stimulation (VNS) on behavior as well as blood and brain responses to craving in patients with OUDs? You are being asked to be in this research study because you have been diagnosed with an OUD.

Do you have to be in the study?

It is your decision to be part of this research study. You do not have to be in it. Your choice will not affect your access to medical care for your condition. Before you make your decision, you should take time to learn about the study.

What do I have to do if I choose to participate in this study?

If you are eligible and want to be part of the study, you will participate for 2 or 3 study visits and a follow up call around 6 weeks after your visits. The researchers will ask you to do the following: complete several psychiatric questionnaires/interviews, blood draws, physiological monitoring with several devices (explained below), VNS testing, and brain imaging. ALL of these procedures will be paid for by the study.

How is this study going to help you?

If you are in the study, you will be helping the researchers answer the study question.

What are the risks or discomforts I should know about before making a decision?

The study will take time. The drug/device/procedure that is being tested may not work any better than regular care, and may even cause harm. All studies have some risks. Some risks are relatively small, like being bored or losing time. Some are more serious – for this study, these include an increase in opioid craving, anxiety during scans, skin irritation, tingling/pricking/twitching feeling where the VNS device is applied, radiation exposure, loss of privacy, and breach of confidentiality. A full list of expected risks, their frequency and severity are in the “What are the possible risks and discomforts?” section of this document.

Alternatives to Joining This Study
Since this is not a treatment study, the alternative is not to participate.

Costs
You WILL NOT have to pay for any of the study procedures.

What Should I Do Next?
Read this form, or have it read to you. Make sure the study doctor or study staff explains the study to you. Ask questions (e.g., about exact time commitment, about unfamiliar words, more details on specific procedures, etc.) Make sure you understand. Take time to consider this, and talk about it with your family and friends.

Emory University
Consent to be a Research Subject / HIPAA Authorization

Title: Non-invasive Vagal Nerve Stimulation in Opioid Used Disorders – Study 2

Principal Investigator: J Douglas Bremner, MD

Sponsor-Investigator: J Douglas Bremner, MD

Study Supporter: National Institute on Drug Abuse (NIDA)

Introduction
You are being asked to be in a medical research study. This form is designed to tell you everything you need to think about before you decide if you want to be a 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. If you decide not to take part in this study, your doctor will continue to treat you.

Before making your decision:
- Please carefully read this form or have it read to you
- Please listen to the study doctor or study staff explain the study to you
- Please ask questions about anything that is not clear

You can take a copy of this consent form, to keep. Feel free to take your time thinking about whether you would like to participate. You may wish to discuss your decision with family or friends. Do not sign this consent form unless you have had a chance to ask questions and get answers that make sense to you. 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 can search this Web site at any time.

What is the purpose of this study?
The purpose of this study is to look at Opioid Use Disorders (OUDs) and Vagal Nerve Stimulation (VNS). OUDs are conditions involving misuse or addiction to opiate-containing prescription pain medications or opioid-containing substances including heroin. OUDs are associated with symptoms of withdrawal upon discontinuation of the substance, which can include problems with concentration and sleep, irritability, rapid heart rate, and craving for opioids. Vagal Nerve Stimulation (VNS) is a procedure where the vagus nerve, which is in the neck, is electrically stimulated, much like a pacemaker is used to stimulate the heart. Branches of the vagus nerve travel throughout the brain and the body. Vagal nerve stimulation is felt to have positive effects on the brain and body by blocking the sympathetic (adrenaline) response that occurs with withdrawal from opioids, as well as changes in the brain that drive craving for opioids. A surgically implantable VNS has been approved by the Food and Drug Administration (FDA) for the treatment of both epilepsy and severe depression. Studies have shown that VNS stimulation is helpful for both conditions. We are using a non-invasive hand-held VNS device made by a company called ElectroCore. It is applied directly to the neck and does not require surgery. It is approved in Europe for the treatments of epilepsy, anxiety, depression, headaches, and other conditions, and in the US by the FDA for the treatment of headaches. We have studied its use at Emory for PTSD and have found it to be well tolerated and there have been no adverse events or untoward effects with the device. It has not yet been approved in the US by the FDA for the treatment of OUDs and is considered investigational in this study.

You have been selected to participate in this study because you have been diagnosed with and Opioid Use Disorder (OUD). The main purpose of this study is to look at the effects of VNS on behavior as well as blood and brain responses to craving in patients with OUDs. Study procedures include a screening, mental health assessment, medical assessment, lab work, and brain imaging with and without VNS and opioid use related videos. Brain imaging will be done with positron emission tomography (PET) and Magnetic Resonance Imaging (MRI). It is possible that you may not have the brain imaging (PET and/or MRI) during the study. The study will be completed in up to 3 visits.

What will I be asked to do?

After signing the consent form, you will begin research procedures.

Screening Description (Visit 1): If a screening was not done over the phone then you will be carefully screened during this study visit. You will be screened to make sure you qualify for the study and to make sure you do not have any contraindication to the brain imaging or other study procedures. If you qualify for the study, you may undergo an initial group of tests, which include questionnaires about your behaviors, experiences, and medical history. We may ask you to complete a urine drug test and we will also go over psychiatric questionnaires with you. These will be either be collected in paper form or using a computer or tablet. This visit, if needed, will take around 1-2 hours.

We may also ask if you are willing to be a backup participant. If you are, we may ask you to come in for an hour or two on the PET day. If the scheduled participant is not able to complete the study then we would proceed for the full day with you. If the other participant is able to complete the study then we would reschedule your visit for another day.

Visit 2 Description (PET Day): If not previously screened then you will begin with this. If you have been screened then you will undergo brain imaging using PET. We may ask you to hold all of your morning medications on the day of your testing. You may take these medications once you are done with the testing. Specific medications may exclude you from being qualified for the study. These medications may include antipsychotic or other psychotropic medication treatment during the last month. You will be asked not to eat or drink anything except water for two hours before your visit. Please eat a light breakfast around 6am. Eight brain scans sessions will be performed using PET during one study visit with neutral and opioid use related videos. We will ask you about your medical history, health behaviors such as smoking status, clinical events and procedures, and medications. We will also ask questions about your mood and stress level. And we will go over psychiatric questionnaires with you. Blood and urine tests, including a urine pregnancy test if you are a woman of child bearing potential, will be done. **Women who are positive for pregnancy will not be eligible for participation in this study.** Blood vessel testing, VNS, physiological monitoring, and heart monitoring will be performed. You may be fitted with a Biopac monitor that will measure things like heart rate and skin temperature and/or fitted with a temperature-controlled glove-like patch at each visit. You may be given an activity monitor to wear on your wrist of either arm. This visit will occur at the Emory Center for Systems Imaging (CSI) and will take around 3-4 hours. You may be given a VNS device to take home for 4-6 weeks. A prepaid return mailer will be given to you. Successful return of the device will be included as a requirement for your study compensation.

PET scan: You will undergo PET scanning of your brain at the Emory Center for Systems Imaging (CSI). A PET scan is an imaging system which provides a picture of the functioning or activated areas of the brain. You will also be wearing a set of noninvasive sensors on your body to measure physiological signals. These signals may include the following: brain activity, heart activity, blood vessel function, and skin activity and temperature. You will also be wearing the sensor on your finger for the PAT test during the scans and a pair of smart glasses that will allow you to view videos in the camera. Prior to the PET scan, a small needle (intravenous catheter or i.v.) will be placed in a vein in your arm to allow for the administration of radioactive water by a physician, nurse, or Nuclear Medicine Technologist and to allow for the blood collections. After the IV is in place, you will be asked to lie on a narrow table with your head inside of an open tunnel. The first scan will be to measure the position and size of your head. You might hear a very faint sound during scanning (most people don't hear anything). The procedure will consist of eight PET scans of the brain. The scans will be done along with neutral and opioid use related videos and/or receiving VNS. You will receive either VNS or a fake or sham

stimulation. You will be randomly assigned the order by a computer program. You have a 50/50 chance of ending up in either group. Blood samples will be drawn from the i.v. to measure molecules in the blood that may be involved in the stress response (for example: cortisol and norepinephrine and other biomarkers) at various time points during the study visit (a total of around 18 tablespoons). The PET procedure will take about 90 minutes, plus about a half hour of preparation time, and an hour and a half after the PET scans for blood draws.

Visit 3 Description (MRI Day): You will undergo scanning of your head with MRI at the Emory Center for Systems Imaging (CSI). Magnetic Resonance Imaging (MRI) uses a powerful magnet to take pictures of your body. Because the MRI machine exposes the body to a very strong magnetic force, you will have to follow certain safety precautions to make sure you do not have any metal objects in or on your body. Before you undergo your MRI scan, a researcher or technician will ask whether or not your body contains any metallic medical devices or equipment, including heart pacemakers, metal prostheses, implants or surgical clips. You also will be asked whether you have had any prior injury from shrapnel or grinding metal, and you will be asked whether your eyes may have been exposed to metal particles. You or the researcher or technician will also complete a checklist that addresses issues of MRI safety. You will be asked to remove all jewelry and other metal-containing objects, like a belt. You will lie flat on a table with your head positioned in the scanner part of the machine for a little less than an hour. No part of the machine will come into contact with your body. When you are inside the scanner, you will be able to see out through a mirror. You will occasionally hear loud noises as the scanner takes pictures of your head. If you have a claustrophobic reaction to being scanned, you will be removed from the scanner. The whole session will take about 1 hour of your time.

Follow up call: After 6 weeks, the study team may call you to see how you are doing. We may ask you to repeat a few of the questionnaires you completed during the study visits. If you took a VNS device home with you we will ask you a few questions about that and remind you to return this to us.

Optional Studies

Optional Study – future research: In the future, we would like to contact you to offer you the chance to participate in additional studies. This future contact would be made by one of the investigators, coordinators, or recruiters of this study. The contact would initially be made by phone, email, or by sending you a letter in the mail. This contact might include a questionnaire for you to fill out and return. If you do not want to participate or fill out the questionnaire, you will simply be asked to return a card in the mail to us, email, or call us. If we do not hear from you then we may have our study coordinator call you. There is no additional compensation for this future contact.

Optional Study - Storage of Samples for Future Research: With your permission, we would like to store part of your blood sample in a freezer for future studies. The sample will not be used for genetic testing. If a future study were to be done, we may share the blood with other researchers. Your sample will be stored for as long as it is useful, unless you ask us to destroy it sooner. The Principal Investigator and members of the research team will have access to the samples. The sample will be stored using your identification code, not your name or other identifying information. Donating blood is completely voluntary and will not affect your care in any way. You can refuse to have your sample stored and still be able to participate in this study. The information that is obtained from the study of your blood may be used by the sponsors of other research. The study of your blood sample may contribute to the creation of new diagnostic tests or new medicines in the future. However, you will receive no financial benefits from such developments nor will we be able to tell you the results of any tests run with your sample.

Optional Study - Blood Sample Link:
If you give us permission to store part of your blood sample, we will store it with an identification code. In order to protect your privacy, all samples from your blood will be given an identification code that does not include any of your personal information. This code will allow researchers to link clinical information about you with your blood sample. Unless you disagree, the Principal Investigator will keep a private list that links your sample code with your name, allowing him/her to know which samples were collected from you. You can request that we not keep any information

linking your name with your sample. Please understand that once we lose the ability to know which sample(s) came from you, we also lose the ability to destroy your samples upon request, or to respond to any future requests you may make regarding results or new information. If you allow the Principal Investigator to keep the list that links your sample code with your name then you may request that your sample be destroyed at any time by contacting the Principal Investigator, J. Douglas Bremner, MD at 404-712-9569.

Who owns my study information and samples?

If you join this study, you will be donating your samples and study information. You will not receive any compensation if your samples or information are used to make a new product. If you withdraw from the study, data and samples that were already collected may be still be used for this study.

What are the possible risks and discomforts?

There may be side effects from the study procedures that are not known at this time. The most common risks and discomforts expected in this study are: (1) the stress of the psychological questionnaires/interview; (2) physiological monitors; (3) the intravenous catheters and blood draw; (4) the PET scan with a radioactive substance; (5) the MRI scan; (6) opioid use related videos; (7) VNS testing; (8) reproductive risks; (9) fasting.

1. **Psychological questionnaires/interview**: Being asked questions about the stress in your life or your mood and opioid use may cause you to have unpleasant and/or upsetting feelings or have an increase in opioid craving. If this happens, then you can take a break from the interviews. You can also slow down and take longer to do the tests. If needed, an assessment by the study psychiatrist may be performed. A referral for treatment or assessment will be made available if needed.

2. **Physiological monitors: (Biopac, Glove, EDA, PPG, SCG, etc.)** These monitors require you to have sensors attached to your skin which may represent an inconvenience to you e.g. when adhesives are removed. They may also cause mild skin irritation or itching. The glove cold application may cause temporary numbness, which stops after application. The hot application may cause temporary redness/skin sensitivity. You may feel itchiness due to sensor hookups on hands (due to sticky electrodes and gels) and temporary numbness of the arm is possible, since you will remain in the same position for half an hour. The EDA requires you to wear a bracelet-type device during (and possibly after) the visit, which may represent an inconvenience to you.

3. **Intravenous (IV) catheter and blood draw.** The IV can result in infection, bruising of the skin, or a blood clot in the vein. These complications are not common when the catheter is inserted by a professional under clean conditions. Dizziness and fainting are rare risks of blood draws. There are no long-term side effects. You may have some discomfort from the blood drawing. The risk from blood drawing is minimal, but may include bruising and infection. The use of sterile precautions will decrease the risk of infection. However, you may develop a bruise at the site of the puncture, but this will go away in two to three days. If we are unable to get IV access then you may not be eligible for the study.

4. **PET scan:** This research study involves exposure to radiation from a Positron Emission tomography (PET) scan. This PET scan procedure is routinely used for medical purposes; however, radioactive water is investigational and not approved by the FDA. This radiation dose is not necessary for your medical care and will occur only as a result of your participation in this study. If you have had any significant exposure to radiation over the past year or plan to participate in other research studies involving radioactivity over the next year please consult with the study team and Dr. Bremner first. Some people experience anxiety from the PET scan procedure. Viewing videos on smart glasses may cause wooziness or motion sickness. A nurse or technologist will be with you during the PET scan procedure. If you should become claustrophobic, anxious or agitated, or otherwise feel unwell in the PET scanner, the scan will be stopped. If you are not able to complete the first PET scan, you may not be able to continue in the study. This study will expose you to a small amount of radiation. The radiation dose that you will receive is equal to or less than the annual radiation exposure limit allowed for persons who are occupationally exposed to radiation (x-ray technicians, radiologist). The principal risk associated with a radiation dose is the possibility of developing a

radiation-induced cancer later in life. The risk for radiation-induced cancer from this study is minimal. Although the risk from radiation is cumulative it is not expected to adversely affect your condition or treatment. The risk from radiation exposure of this magnitude is considered to be comparable to other everyday risks.

5. **MRI scan:** MRI is used routinely for diagnosis of medical conditions. Although MRI, like X-ray, is used to take pictures of structures in the brain and other parts of the body, there is no radiation with MRI. If you have any metal in your body (such as shrapnel or a pacemaker), you may not be eligible for the study because it would be unsafe for you to have an MRI. An MRI scan can make some people feel anxious, particularly if they do not like enclosed spaces or noise. If you feel very anxious or uncomfortable during the scanning, you should inform the study team and if needed the study will be stopped. You are free to stop the MRI at any time. 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.

   You will be getting scans (PET/MRI) for research purposes only. The research does not require the scans to be read for healthcare purposes. However, if the researchers are concerned about something they see on the scans they will tell you, and ask you if you want the scans to be reviewed for healthcare purposes (possibly by other clinicians), and you may then be referred for medical treatment. You or your insurance company may have to pay for the review for healthcare purposes, and for any such treatment.

6. **Opioid Use Related Videos.** The viewing of opioid use related videos may cause some anxiety or feelings of craving for opioids. You may stop this test at any time if you experience anxiety, excessive cravings, or other problems or are uncomfortable with the procedure.

7. **VNS Testing**. Sometimes, you may experience hoarseness, shortness of breath, throat pain, cough, abdominal pain, headache, and/or change in voice during treatment. A tingling/pricking/twitching feeling where the device is applied is normal, but should not cause major discomfort. These effects usually stop right away once the treatment is completed. Mild skin irritation or dizziness are other possible side effects. We will not use the VNS device if you have any of the following conditions: an active implantable medical device, such as a pacemaker, defibrillator, cochlear implant, and other implanted electronic device; a history of significant carotid atherosclerosis; or a cervical vagotomy.

8. **Reproductive Risks. Women please note**: Since this research may have bad effects on a fetus and should not be done during pregnancy, it is necessary that a pregnancy test be done first, even if, to the best of your knowledge, you are not pregnant now. Women of childbearing potential will take a urine pregnancy test when you arrive for your visit. If the test is positive you will not be able to participate in the study. This study may be hazardous to a breast-feeding child. Breast feeding mothers may not participate in this study.

   Women who may be pregnant should not be in this study because of possible effects of radiation exposure on their unborn child. Both men who may later father children and women of childbearing potential should be aware that exposure to radiation poses a very slight risk of genetic mutation in the next generation.

9. **Fasting**. In order to undergo study testing (PET day), you need to be fasting before your study visit until the scans are completed. Some people may show discomfort from this prolonged fasting, although true hypoglycemia is rare. A sweetened beverage will be administered if patients complain of lightheadedness or other fasting-related symptoms.

It is possible that the researchers will learn something new during the study about the risks of being in it. If this happens, they will tell you about it. Then 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 the effects of VNS on behavior as well as blood and brain responses to stress. The study results may be used to help others in the future. In general, we will not give you any individual results from the study of the samples you give us. If we find something of urgent medical importance to you, we will inform you, although we expect that this will be a very rare occurrence.

Will I be compensated for my time and effort?

You will be compensated for your time and effort for participating in this study. Compensation ranges from $75 to a total of up to $350 for the study. A breakdown of payments is listed below. We will also pay for parking, if needed, at each clinical visit. The return of the VNS/Sham device is necessary for you to receive full compensation.

If used as a backup participant: $50 to cover time and transportation costs
Visit 2: $150 (PET Day)
Visit 3: $75 (MRI Day)
If you are given a VNS device to take home, you will get $75 after successful return of the device.

You may 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. Another method of payment is using "ClinCard", which works like a debit card and is provided by Greenphire. When visits are completed, funds will be loaded onto your card. You will be able to use the funds in approximately 1 business day. You will have up to 3 visits over the period of the study (total that you can receive is $350). To issue your card, we need to give Greenphire some of your personal information. If you do not wish to provide this information, you can still take part in the study, but you will not be paid (or paid through a different mechanism if applicable). Banks and other financial institutions can access this information if they need to verify your identity when you use your card. Emory is required by law to report any payments we make to the IRS. To do this, the Finance department needs to keep your social security number on file. We are asking you to allow us to give your name, address, date of birth, research study name and social security number to Greenphire. If you want to receive email or text alerts when payments are made to you, we will ask you to provide your email 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 or use of your personal information. 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.

What are my other options?

If you decide not to enter this study, there is care available to you outside of this research study. This study is not designed to prevent or treat you. The alternative to participating in this study is to not participate. Emory, Grady and other healthcare facilities are available to provide care for your medical problems.

How will you protect my private information that you collect in this study?

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.

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.

Storing and Sharing your Information

De-identified data from this study (data that has been stripped of all information that can identify you), including your de-identified genetic information, may be placed into public databases where, in addition to having no direct identifiers, researchers will need to sign data use agreements before accessing the data. We will remove or code any personal information that could identify you before your information is shared. This will ensure that, by current scientific standards and known methods, it is extremely unlikely that anyone would be able to identify you from the information we share. Despite these measures, we cannot guarantee anonymity of your personal data.

Your data [and specimens] from this study may be useful for other research being done by investigators at Emory or elsewhere. To help further science, we may provide your deidentified data and/or specimens to other researchers. If we do, we will not include any information that could identify you. If your data or specimens are labeled with your study ID, we will not allow the other investigators to link that ID to your identifiable information.

In general, we will not give you any individual results from the study of the samples you give us. If we find something of urgent medical importance to you, we will inform you, although we expect that this will be a very rare occurrence.

Medical Record

If you have been an Emory Healthcare patient before, then you already have an Emory Healthcare medical record. If you 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 gives you any services or procedures for this study.

Copies of the consent form/HIPAA authorization that you sign will be put in any Emory Healthcare medical record you have now or any time during the study.

Emory Healthcare may create study information about you that can help with your care. For example, the results of study tests or procedures. These study results will be put in your Emory Healthcare medical record. Anyone who has access to your medical records will be able to have access to all 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 and procedures will be used only for research purposes and will *not* be placed in your medical record. For this study, those items include:

- Labs – blood and urine testing
- PET and MRI scans
- Psychological/psychiatric assessments/interviews/questionnaires
- Physiological monitoring
- VNS testing

Tests and procedures done at non-Emory places may not become part of your Emory medical record. Also, if you decide to be in this study, it is up to you to let your other health providers know.

In Case of Injury

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

If you get ill or injured from being in the study, Emory will help you get medical treatment. Neither Emory nor the study-supporter will pay for your medical treatment. Your insurer will be billed for your treatment costs. If you do not have insurance, or if your insurance does not pay, then you will have to pay these costs.

Emory and the study supporter have not, however, set aside any money to pay you or to pay for this medical treatment. The only exception is if it is proven that your injury or illness is directly caused by the negligence of an Emory or sponsor employee. "Negligence" is the failure to follow a standard duty of care. *You do not give up any legal rights you may have by being in this study, including any right to bring a claim for negligence.*

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. If the study procedures result in any medical complications that would not fall under "injury" as discussed above, the cost of treatment for those complications may be charged to you or your insurance.

Withdrawal from the Study

You have the right to leave a study at any time without penalty. The researchers also have the right to stop your participation in this study without your consent for any reason. Especially if they believe it is in your best interest or if you were to object to any future changes that may be made in the study plan.

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 main study and for any optional studies in which you may choose to participate.

Main Study

PHI that Will be Used/Disclosed:

The PHI that we will use or share for the research study includes:

- Demographic information such as your name, date of birth, and other identifiers
- Medical information about you including your medical history and present/past medications.
- Results of exams, procedures and tests you have before and during the study.

Purposes for Which Your PHI Will be Used/Disclosed:

We will use and share your PHI for the conduct and oversight 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, vital status or contact information.

Use and Disclosure of Your Information That is Required by Law:
We will use and disclose your PHI when we are required to do so by law. This includes laws that require us to report child abuse or abuse of elderly or disabled adults. We will also comply with legal requests or orders that require us to disclose your PHI. These include subpoenas or court orders.

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 form. You do not have to sign this form to allow the use and disclosure of your PHI. If you do not sign this form, then you may not participate in the research study.

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

- The Principal Investigator and the research staff will use and share your PHI to conduct the study
- Emory may use and disclose your PHI to get payment for study procedures and to run normal business operations.
- Greenphire, an independent company specializing in payments for research studies and clinical trials.
- The Principal Investigator and research staff will share your PHI with other people and groups to help conduct the study or to provide oversight for the study.
- Doug Bremner, MD is the Sponsor of the study. The Sponsor may use and disclose your PHI to make sure the research is done correctly and to collect and analyze the results of the research. The Sponsor may disclose your PHI to other people and groups like study monitors to help conduct the study or to provide oversight for the study.
- The National Institute on Drug Abuse (NIDA) is the study supporter. The study supporter may use and disclose your PHI to make sure the research is done correctly and to collect the results of the research. The study supporter may disclose your PHI to other people and groups like study monitors to help conduct the study or to provide oversight for the study.
- The research team and the Sponsor may use and disclose your PHI, including disclosure to insurance carriers to administer payment for subject injury.
- The following people and groups will use your PHI to make sure the research is done correctly and safely:
    - 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.
    - Government agencies that regulate the research including: Office for Human Research Protections or the Food and Drug Administration.
    - Public health agencies.
    - Research monitors and reviewer.
    - Accreditation agencies.
    - Georgia Institute for Technology IRB
- Sometimes a Principal Investigator or other researcher moves to a different institution. If this happens, your PHI may be shared with that new institution and their oversight offices. PHI will be shared securely and under a legal agreement to ensure it continues to be used under the terms of this consent and HIPAA authorization.

Optional Studies: future research, storage of samples for future research, and blood sample link:

PHI That Will be Used/Disclosed for Optional Studies:

The PHI that we will use and/or disclose (share) for the optional research studies includes: The same people and groups who will use and disclose your PHI for the main study will also do so in connection with the optional research study.

Purposes for which your PHI will be Used/Disclosed for Optional Studies:

We will use and disclose your PHI for the conduct and oversight of the optional research study.

Authorization for This Use of PHI is Required to Participate in Optional Studies, but Not in Main Study:

You do not have to authorize the use and disclosure of your PHI. If you do not authorize the use and disclosure of your PHI for the optional studies, then you may not participate in the optional research studies. You can still be in the main research study even if you don't participate in the optional studies.

People Who Will Use/Disclose Your PHI for Optional Studies:

The following people and groups will use and disclose your PHI in connection with the optional research studies:

- The same people and groups who will use and disclose your PHI for the main study will also do so in connection with the optional research study.
- Future researchers

Expiration of Your Authorization

We will add your PHI to a database that we are compiling for research purposes. There is no date or event after which your authorization will expire and your PHI will no longer be used for this purpose.

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 contact the principal investigator at:

J Douglas Bremner, MD
Professor of Psychiatry and Radiology
[redacted]
Atlanta, GA 30329

At that point, the researchers would not collect any more of your PHI. But they may use or disclose the information you already gave them so they 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 main study.

Other Items You Should Know about Your Privacy

Not all people and entities are covered by the Privacy Rules. HIPAA only applies to health care providers, health care payers, and health care clearinghouses. If we disclose your information to people who are not covered by the Privacy Rules, including HIPAA, then your information won't 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.

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. When the study ends, and at your request, you generally will have access to your PHI that we maintain in a designated record set. A designated record set is data that includes medical information or billing records that your health care providers use to make decisions about you. If it is necessary for your health care, your health information will be provided to your doctor.

We may remove identifying information from your PHI. Once we do this, the remaining information will not be subject to the Privacy Rules. Information without identifiers may be used or disclosed with other people or organizations for purposes besides this study.

Contact Information

Contact [redacted] Research Associate, at [redacted]

- if you have any questions about this study or your part in it,
- if you feel you have had a research-related injury or a bad reaction to the study procedures, or
- if you have questions, concerns or complaints about the research

Contact the Emory Institutional Review Board at [redacted] irb@emory.edu:

- if you have questions about your rights as a research participant.
- if you have questions, concerns or complaints about the research.
- 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

Consent and HIPAA Authorization for Optional Studies:

Please initial below if you opt to participate in and authorize use and disclosure of your PHI in the optional studies previously described:

Future Research _____Initials

Storage of Samples for Future Research _____Initials

Blood Sample Link _____Initials

TO BE FILLED OUT BY SUBJECT ONLY

Please **print** your name, **sign**, and **date** below if you agree to be in the main 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.

_____

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**