RESEARCH CONSENT FORM

Basic Information

Title of Project: Facilitation of Reconsolidation Blockade by Intravenous (IV) Allopregnanolone in Posttraumatic Stress Disorder (PTSD)

IRB Number: H-40643

NCT04468360

Sponsor: National Institute of Mental Health (NIMH)

Principal Investigator: Ann M. Rasmusson, MD
amrasmus@bu.edu
72 East Concord St, Room R-623D, Boston, MA, 02118

Study Risk: greater than minimal risk.

Study-Related Phone Numbers: Regular business hours: 617-414-4782; 24-hour number: 617-414-4777

Overview

We are asking you to be in a research study funded by the National Institute of Mental Health (NIMH). A research study is an organized way of collecting information about scientific questions. This form will tell you what you should expect if you agree to be in the study. There are programs in place to make sure that investigators fulfill their obligations listed in this form.

It is your decision whether or not to join the study. We are doing the research to learn whether a natural stress steroid called allopregnanolone ("Allo") compared to an inactive drug called a "placebo" (given intravenously or by "IV") affects memory and startle reactions to a range of sensory stimuli (bursts of white noise through headphones, colored shapes on a computer screen, or sudden but not painful air blasts to the neck) in individuals with chronic post-traumatic stress disorder (PTSD). Results from the study may help with development of Allo for the treatment of PTSD. The study is being conducted in about 128 eligible females and males with chronic PTSD in: 1) Boston, Massachusetts, at Boston University Medical Campus (BUMC) and Boston Medical Center (BMC), and 2) Detroit, Michigan, at Wayne State University School of Medicine.

If you agree, you will first participate in a two-part screening evaluation to see if you qualify for the study. If you qualify, you will be scheduled to come to Boston Medical Center (BMC) 3 days in a row to take part in brief tests of memory, startle testing, alertness and psychiatric symptom ratings, and urine, saliva and blood collection. You will receive the IV study drug (Allo or placebo) only on the second day. About a week later, we will call to check-in and rate your PTSD symptoms. You will find *more information* about what will happen in this study later in this form.

The main risks of the study are:

1) Emotional discomfort from discussing your traumatic experiences or other mental health symptoms.
2) Pain or other side effects from blood drawing or placement of the IV.
3) Potential side effects of the study drugs (IV Allo or placebo).
4) Potential loss of confidentiality.

You will find more information about risks of the study later in this form.

Your doctor may be an investigator in this study. Being an investigator means your doctor is interested in both you and the study. You may want to get another opinion about being in the study. You can do so now or any time during the study. A doctor who is not part of this study could give you their opinion about being in the study. You do not have to agree to be in this study even if it is offered by your doctor.

Purpose

Exposure to extremely threatening events can result in PTSD. PTSD recovery can occur naturally over time or in response to treatment. PTSD improvement in response to treatment varies a lot among PTSD patients.

Research shows that some men and women with chronic PTSD have lower levels of Allo (and similar hormones). Low Allo is associated with more severe PTSD and depression, and interferes with recovery from traumatic stress. We will test whether IV Allo compared to IV placebo affects brain processes related to PTSD recovery. If this study is successful, we could potentially develop Allo to help treat PTSD and learn ways to increase natural Allo production.

You have been asked to participate in this study because you are 18 to 55 years old, were exposed to a traumatic event, and may have chronic PTSD. In addition, you have not yet reported medical or psychiatric disorders or use of medications or substances that would disqualify you from the study.

Your participation in this study is voluntary. This means that you have the right to choose if you want to participate. If you decide to participate and later change your mind, you are free to drop out at any time. Deciding not to take part in this research study will not change your legal rights or the quality of healthcare that you receive at this center. You can choose to stop participating for any reason at any time. If you decide to withdraw from the study, any information that has already been collected from you will be used and already collected samples will not be destroyed. However, you may choose to stop attending study visits and stop all future data collection.

What Will Happen in This Research Study

Location:

1. A mental health screening evaluation will take place remotely by phone or Zoom or in-person at the General Clinical Research Unit (GCRU) at the Boston University Medical Campus (BUMC) located at 72 East Concord St, Evans Building, 8th Floor, Boston, MA, 02118.
2. An in-person medical screening evaluation will take place at the GCRU.
3. The 3 days of experimental startle testing will take place at Boston Medical Center (BMC), which is near the GCRU; we will give you detailed instructions about how to find our laboratory.
4. The check-in a week later will take place remotely by phone or Zoom.

Eligibility:

- To participate in this study, you must be 18-55 years old and have chronic PTSD.
- You must be medically healthy in general and without sleep apnea, as well as free of medications *that may interact with the study drug or influence the study outcomes* for a time-period set by the study physician based on the specific medication under consideration. If it is in your best interest to remain on a medication that is not allowed, you will not be entered into the study.
- During screening for study eligibility, if you report use of illicit substances or prescribed opiates or benzodiazepines, or if these substances are detected on urine testing, you will be disqualified from the study.
- A positive saliva alcohol test at screening will disqualify you from participating in the study.

- A high blood gamma-glutamyl transferase "GGT" test at screening (which indicates recent heavy alcohol use) will exclude you from the study unless you: a) do not meet criteria for a moderate or severe alcohol use disorder within three months of screening, b) agree to abstain from drinking for 2 weeks before the experimental procedures, and c) have a normal follow-up GGT test.
- If you report non-dependent use of cannabinoids or nicotine or have a positive urine test for these substances at screening, you will be excluded unless you: a) agree to abstain from cannabinoids and nicotine for one month before the experimental procedures, b) have a negative follow-up test for these substances, and c) test negative for these substances on each morning of the experimental procedures. Please note that second-hand exposure to drugs or nicotine (due to inhaling smoke from someone else) may cause you to test positive on drug or nicotine screens and disqualify you from the study.
- On the days of experimental procedures, if you report use of medications or substances or test positive for medications or substances that may increase side effects of IV Allo or affect the experimental results, you will be excluded from further participation in the study.
- If you do not pass the hearing test, you will not be entered into the study.
- If you have a diagnosis of bipolar I disorder, a schizophreniform disorder, clinically significant psychotic symptoms apart from the presence of trauma-related sensory hallucinations or negative beliefs, moderate or severe substance misuse within 3 months of enrolling, or a severe traumatic brain injury (TBI), you will be excluded from this study.
- If you are a risk to yourself or others, you will not qualify for the study. Instead, you will be referred for further evaluation and treatment, against your will if that is clinically appropriate.
- If you were assigned female at birth, you must have a menstrual cycle and not be on hormonal birth control (with a few exceptions; see below). If you are gender non-conforming, you must not be on hormone therapy.
- Since this research could result in harm to a fetus, it should not be done during pregnancy. Therefore, 1) eligible females must have a negative pregnancy test at the in-person screening and on each of the 3 days of startle testing, and 2) females of childbearing potential must use two highly effective forms of contraception (other than contraceptives with hormones that circulate in the blood) for one week before IV Allo or placebo infusion and for 28 days after. **See the Study Procedures below for more details**.
- Nursing individuals may not participate in this study because IV Allo can enter the breast milk and could harm the baby. Levels of the biological chemicals measured in the study also may be affected by nursing.
- You may be excluded from further participation in the study at any point if you are unable to provide reliable study data, for example, by altering your urine sample or providing other misinformation.
- If you test positive for COVID-19 and cannot be rescheduled (see below), you will be discontinued from further participation in the study.

Study Procedures:

In addition to completing the screening evaluations below, you will be asked to consent to us contacting your healthcare providers and release of your medical records, as needed, to ensure your eligibility.

You will receive a rapid COVID-19 test at the beginning of each in-person study visit. If you test positive for COVID-19 at a screening evaluation or Day 1 visit, you will be rescheduled for that study visit in accordance with Center for Disease Control (CDC) Guidelines. However, if you test positive for COVID-19 at the Day 2 or Day 3 visit, you will be discontinued from further participation in the study.

Telephone/Zoom or In-Person Psychological Screening Evaluation (about 3 ½ hours)
This evaluation includes questions about your trauma exposure and history of psychiatric, substance misuse and medical disorders and treatments. The evaluation will be audio recorded to help the researchers accurately determine your eligibility. If necessary, the evaluation can be broken into multiple appointments, which will be conducted in-person at the GCRU or by telephone or Zoom if more convenient.

In-person Medical Screening Evaluation (about 2 ½ hours)
This evaluation at the GCRU will include more questions about your medical and psychiatric history (if needed), as well as a physical exam, tests for color blindness and hearing, EKG, pulse oximetry, cognitive testing, a blood draw, saliva collection, and urine collection. An EKG measures the heart's electrical activity; you will be asked to lie flat on a table and several small sticky electrode pads will be placed on your chest and limbs. A small pulse oximeter will be placed on your finger to measure the level of oxygen in your blood. Your saliva will be tested for alcohol. The urine will be used for standard medical testing and pregnancy testing (eligible females only). The urine also will be tested for a nicotine byproduct, cannabinoids, and illicit or prescribed drugs such as: amphetamines, barbiturates, benzodiazepines, buprenorphine, cocaine, marijuana, methadone, methamphetamine, MDMA, opiates, oxycodone, phencyclidine, tricyclic antidepressants, synthetic cannabinoids, methcathinones ("M-KAT or cat") and MDPV ("bath salts") that would exclude you from further participation. If you test positive for nicotine or cannabinoid products, you will not be excluded if you agree to abstain from them for one month prior to the experimental procedures, have a follow-up negative screening test, and test negative for these substances on the morning of experimental procedures. Medical blood tests will include a complete blood count (and other red blood cell, iron, B12 or folate tests if indicated), electrolytes, glucose (blood sugar) measures, cholesterol, lipids, and thyroid, kidney, and liver function tests. Some tests might need to be repeated to ensure accuracy or if they're abnormal due to a condition that goes away (e.g., if you had a urinary tract infection that got treated). If so, we will ask you to return to the GCRU for the repeat test (and you will be paid for that visit; see the Payment section below). Note that the urine fentanyl and medical blood test results <u>will</u> be put in your medical chart because these tests are conducted at the BMC clinical laboratory. The other test results will <u>not</u> be put in your medical chart.

Randomization to IV Allo or Placebo
If you are eligible for the 3 days of startle testing, you will be randomized (assigned by luck of the draw) to receive either IV Allo or placebo on the second day of testing. Neither you nor the researchers will know which study drug (IV Allo or placebo) you receive while this study is being conducted. If there is a need to know at any point for safety reasons, the research pharmacy will provide the information.

Scheduling of Eligible Participants for the 3-Day Startle Study
If you are eligible for startle testing based on the screening evaluation described above, you will be scheduled for startle testing 3 days in a row on: a) Monday, Tuesday and Wednesday, b) Tuesday, Wednesday and Thursday, or c) Wednesday, Thursday and Friday. You must be scheduled for Day 1 of startle testing $\leq$ 90 days of the remote psychological screening evaluation and in-person medical/cognitive screening evaluation. Out-of-window screening evaluations must be repeated before Day 1 startle testing to ensure your continued eligibility.

Special Procedures for Eligible Females
Females will be scheduled *either* during the early follicular phase of the menstrual cycle (2-6 days after the menstrual period begins) or during the mid-luteal phase (5-10 days after the luteinizing hormone or 'LH' surge). The LH surge occurs just before ovulation, about 2 weeks after the start of menstruation. If you are scheduled during the mid-luteal phase, you will be asked to test your urine for the LH surge every morning and every afternoon or evening with a dipstick beginning 6 days after your period starts and continuing until the dipstick is positive (usually 7-10 days later). If you have a menstrual cycle that is longer than the average 28 days, the timeframe for scheduling during the follicular phase or luteal phase may be extended.

As noted above, eligible females with childbearing potential must use two highly effective birth control methods for one week before IV Allo infusion and 28 days after. Systemic hormonal contraceptives are not allowed because they will interfere with the results of the study. Some hormonal intrauterine devices (IUDs) (e.g., Mirena, Kyleena, Liletta, and Skyla) or other contraceptive devices (e.g., Nuvaring) will be allowed if you still menstruate and ovulate when using them—because that means very little of the hormones are getting into your blood. [To see if you are ovulating, we will ask you to do urine dipstick testing at home for both the LH surge (as above) and a rise in pregnanediol glucuronide–or PdG–a metabolite of progesterone that increases after you ovulate.] Other effective contraceptive methods you or your partner can use include a diaphragm or cervical cap with spermicide, condoms with spermicide, vasectomy, and the copper IUD. If you suspect you have become pregnant while participating in the study, please contact the study physician immediately.

Procedures During the 3 Days of Experimental Testing

Day 1 (about 3 ½ hours): We will ask you to arrive at our laboratory at BMC by about **9:30 a.m**. Your vital signs (such as temperature, respiratory rate, heart rate and blood pressure) will be taken and may be repeated later during this visit. You will eat breakfast and provide a urine sample for nicotine, drug and, if eligible female, pregnancy testing. You will also provide a saliva sample for an alcohol test. If any of these tests are positive, you will not be able to continue in the study (please see potential effects on payment in the **"Payment"** section below). If these tests are negative, we will prepare you for *startle testing* by cleaning your skin for sensor placement below your eye, behind your ear, and on your palm, chest, stomach and/or wrist. We will then use sticky tape to attach 8 small senso end of the hour, you will have your blood drawn and do startle testing for about 15 to 30 minutes. During *startle testing*, you will hear sudden bursts of white noise through headphones, see colored shapes on a computer screen, and feel sudden (not painful) blasts of air to your neck. The electrodes will allow us to record your eye blinks, sweating, and heart rate reactions to these stimuli, which may startle you a little at times. The startling sounds will be about as loud as a train and last a fraction of a second. While you listen, we ask you to sit quietly with your eyes open. You will be discharged after the startle testing.

Day 2 (about 9 hours): We will ask you to arrive at our laboratory at BMC by about **9:30 a.m**. Your vital signs will be taken and repeated several times later during this visit. You will be weighed, eat breakfast and provide a urine sample for nicotine, drug and, if eligible female, pregnancy testing. You will also provide a saliva sample for an alcohol test and a small pulse oximeter will be placed on your finger to monitor the oxygen in your blood. If any of these tests are positive or your blood oxygen level is low, you will not be able to continue in the study (please see potential effects on payment in the **"Payment"** section below). If these tests are negative, 1) an IV will be placed and kept open by a slow stream of IV fluid, 2) you will be prepared for startle testing (as described above), and 3) you will sit for about 1 hour while doing a brief memory test and ratings of alertness and your psychiatric symptoms. Then a blood sample will be drawn through the IV and you will participate in brief startle testing. Afterwards, blood will be drawn again through the IV, study drug (IV Allo or placebo) will be given over 30 minutes, and IV fluids only will be continued for the next 4-5 hours. During this time, blood will be drawn up to 14 more times through the IV while you are monitored for any potential side-effects (see below). A neurological exam then will be performed to ensure that you are safe to leave. As sedation is a possible side effect of IV Allo infusion, you must have someone drive you home or use a transportation service paid for by the study. For your safety, you should avoid using alcohol or drugs or medications not approved by the study team the evening after the infusion, and we recommend that you have a trusted person available.

Day 3 (about 3 ½ hours): We will ask you to arrive at our laboratory at BMC by about **9:30 a.m**. Your vital signs will be taken and may be repeated later during this visit. You will eat breakfast and provide a urine sample for nicotine, drug and, if eligible female, pregnancy testing. You will also provide a saliva sample for an alcohol test.

If any of these tests are positive, you will not be able to continue in the study (please see potential effects on payment in the **"Payment"** section below). If the tests are negative, you will be prepared for startle testing and sit for 1 hour while doing a brief memory test and ratings of alertness and your psychiatric symptoms. At the end of the hour, you will participate in startle testing again. Your blood will be drawn by needle stick once before and once after the startle testing.

Follow-up Phone/Zoom Call (about 45 minutes; about 1 week after the experimental testing is complete)
This follow-up telephone/Zoom call will include interviews and questionnaires about your psychiatric and medical symptoms. If you prefer, some of the questionnaires can be filled out online instead. The call will be audio recorded. If no other safety measures are necessary, you will be discharged from the study after this call.

Genetic Testing
We plan to test for genomic factors linked to PTSD and PTSD-related psychiatric or medical conditions. Testing may focus on the genetic code itself (i.e. DNA sequences), "epigenetic" factors that influence gene expression. We also may test for effects of IV Allo vs. placebo on gene regulation. No genomic findings will be returned to you or your genetic relatives. You have the right to not participate in genomic testing while still participating in the rest of the study. Please inform the research staff at any point in the study or afterwards if you do not want genomic testing of your blood samples. If genomic analyses already have been completed, the results will remain in our databases without personal identifiers. However, any blood samples for genomic testing still in storage will be destroyed. If genomic analyses already have been completed, the results will remain in our databases without personal identifiers. However, any blood samples for genomic testing still in storage will be destroyed.

Please initial your current choice regarding genomic testing below:

You may use my blood samples for genomic testing _____

You may not use my blood samples for genomic testing _____

Pertinent and Incidental Findings
The research measurements we make are not necessarily the same as tests done by your primary care provider. We are collecting information on many people to answer our research questions. Not everyone doing the research tests is a doctor or a nurse. You or your primary care provider should not rely on the research measurements to make any diagnosis, treatment, or health planning decisions. We may find that you have an undiagnosed psychiatric or medical condition during our screening evaluation. If this is the case, we will inform you and your primary care or other relevant healthcare provider. If you or your provider decides that follow-up tests and treatments are necessary, then you or your insurance will be billed for those costs.

Storage of Samples in the GCRU Biorepository & Shipping of Samples or Data to Other Laboratories for Analysis
Blood samples (including those collected for genomic testing) will be stored in the GCRU biorepository. They will be used to look at Allo-related steroids, other biological chemicals, and genomic factors associated with PTSD and other PTSD-related conditions, or your responses to the IV Allo infusion. The GCRU biorepository will be responsible for storing, monitoring, pulling, and shipping the biological samples. The biological samples will be labeled with your Study ID (never your real name). Researchers from Wayne State University, with whom we are currently collaborating on this study, or other researchers may request the release of data and biological samples for future studies. Data that will accompany the biological samples may include demographic or diagnostic information, or study results. Your samples or data will only be identified by a Study ID to others who receive them, so no one will be able to identify you by looking at the samples or data.

Data Sharing with the NIMH Data Archive (NDA)
Data from this study also will be submitted to the NIMH Data Archive (NDA) at the National Institute of Health (NIH). The NDA is a large database where de-identified study data from NIMH-funded studies (like this one) are stored, managed, and shared with other approved researchers. De-identified study data means that all personal information about you (such as name, address, birthdate and phone number) has been removed and replaced with a code number. Sharing your de-identified study data with the NDA helps researchers learn new and important things about mental health and substance use more quickly than before.

Risks and Discomforts

Emotional Discomfort: You may feel embarrassment or stress when talking about your trauma, emotional health or medical experiences. To minimize discomfort, all telephone/Zoom or in-person visits will take place in a private, comfortable setting. If you experience a lot of distress during the interview, the person conducting the interview will work with you to provide support or connect you to a mental health provider if needed. Additionally, if you feel upset or uncomfortable with any question, you can refuse to answer or stop as needed until the distress lessens. If your symptoms bother you after you go home, you should contact the study team. We will provide you with additional clinical support or a safety evaluation and management if needed. If you are at risk of injuring yourself or another, you may be referred (against your will if necessary) for an emergency evaluation at a local emergency room.

Interview Burden*:* You may get tired or anxious from a long interview. However, if you do feel tired or stressed, you can take a break or stop the visit early and continue by phone or in person, as appropriate, at a later date.

Scheduling Inconvenience: We aim to schedule your appointments for the study as soon as possible and at your convenience. However, unexpected delays could occur, for example, due to the COVID-19 pandemic. If you test positive for COVID-19 at a screening evaluation or Day 1 visit, you will be rescheduled for that study visit in accordance with the Center for Disease Control (CDC) guidelines. *For eligible females:* Scheduling the 3-day startle testing during the desired menstrual cycle phase can sometimes be a challenge and may have to be delayed until the next month.

Potential Delay in Starting Clinical Treatment: We expect there to be minimal delays to you starting any desired clinical treatments for PTSD due to being in this study—though for the reasons described above, eligible females may experience greater delays. You will be allowed to participate in certain treatments that do not directly target PTSD symptoms. If you think that a delay in getting clinical care is too long or puts you at risk, you are free to stop participating in the study at any time.

Financial Costs: You will be compensated for travel and paid for study sessions to help offset time away from work or other costs, such as childcare. If you decide to stop participating in the study, you will be paid for sessions in which you already participated. If a visit is ended by the investigators because you tested positive for COVID-19, you will be paid for that study visit*. If a visit is ended by the investigators because you are disqualified from the study based on reporting or testing positive for prohibited nicotine, drug or alcohol use, you will not be paid for that study visit.*

Electrocardiogram (EKG): The test may cause some redness, swelling or itching are placed, which involves mild rubbing, shaving of hair and the use of alcohol to cleanse the surface of your skin.

Blood Draw or Intravenous (IV) Placement: IV placement and blood draws by needle stick may cause discomfort or pain, bruising at the site, lightheadedness, fainting, or infection (rare). To reduce these risks, a trained phlebotomist or research nurse will use standard techniques and infection precautions when performing these procedures. To increase the ease of blood drawing, we will ensure that you are well hydrated.

Sometimes a needle stick or IV placement may need to be attempted more than once. You will be asked if this is okay with you. If not, it may not make scientific sense for you to continue in the study or you might decide you don't want to continue in the study. If so, you will be paid for the sessions in which you already participated.

The amount of blood collected over the entire study is up to 404 cc (about 27 tablespoons or 4/5ths of a standard blood donation). If you have anemia (a low red blood cell count) due to iron, B12 or folate deficiency at your screening evaluation, you must be treated for the anemia before proceeding to the startle study.

Startle Testing: Startle testing may cause some brief anxiety but is not harmful. Mild skin irritation or an allergic reaction could result from electrodes placement, which involves use of alcohol and mild rubbing to cleanse the surface of your skin. Study team members have received careful training in these procedures to minimize discomfort.

IV Allo or Placebo Infusion:

a) IV Allo infusion may cause dizziness, dry mouth, mild nausea, feelings of alcohol-like intoxication, drowsiness, excessive sedation (extreme sleepiness), or sudden loss of consciousness (i.e., passing out). It also has been associated in some individuals with thoughts of hurting oneself, hot flushes, or increased anxiety. We are using a lower dose of IV Allo than studies reporting some of these side effects (such as excessive sedation or passing out), but similar side effects still may occur. For scientific reasons, if you feel sleepy during the 4-5 hours in the afternoon during the IV Allo infusion, you should let the researchers know and they will encourage you to try to stay awake.

b) To reduce the risks of excessive sedation or sudden passing out, we will test your urine for drugs and your saliva for alcohol, which could increase such side effects. You also will be monitored continuously for excessive sedation or sudden passing out in accordance with FDA regulations by: a) direct staff observation, and b) placement of a pulse oximeter, which sets off an alarm if your blood oxygen gets low due to slowed breathing. The IV infusion will be stopped immediately if you have signs or symptoms of excessive sedation or pass out. If the symptoms resolve, we will resume the IV Allo infusion at the same or a lower dose, as appropriate. Before discharge, an MD or other qualified healthcare provider will evaluate you to ensure that it is safe for you to leave. You will be cautioned against engaging in potentially dangerous activities that require mental alertness. We also require that someone else drive you home (friend, family member, commercial ride service paid by the study). If you experience an alcohol intoxication-like reaction to the IV Allo, we will help support you to avoid relapse to alcohol use if that has been a problem for you in the past. For your safety, you should avoid using alcohol or drugs or medications not approved by the study team the evening after the infusion, and we recommend that you have a trusted person available.

c) Although not likely, you may have an allergic reaction to the substance in which the Allo is dissolved (sulfobutyl ether beta-cyclodextrin). If you do have an allergic reaction, the IV Allo infusion will be stopped and appropriate medication or other treatment will be provided (please see the "**Compensation for Injury"** section on page 12 of this form for possible costs associated with such treatment).

d) The infusion used in this study has the potential to cause kidney damage at high doses, at doses given over long periods of time, and among people with end stage kidney disease. In the current study, IV Allo is given at a lower dose over a much shorter period of time. We also test your kidney function at the in-person screening evaluation to ensure that your kidney function is normal. To be especially cautious we test it again just before and a day after the IV Allo or placebo infusion. If we see any abnormalities, we will call and refer you for further evaluation.

e) There is limited information on the reproductive safety of IV Allo. The general class of medications to which IV Allo belongs may cause degeneration of the developing brain. Therefore, this research should not be done during pregnancy, and in accordance with FDA regulations, we test eligible females for pregnancy during the

screening evaluation and on each of the 3 days of startle testing. In addition, eligible females of childbearing potential must use two highly effective forms of contraception (see the Study Procedures section above for details). If you suspect that you have become pregnant while in the study, please contact the study MD immediately.

f) There may be additional unknown or unanticipated reactions to the IV Allo or placebo infusion.

Potential Benefits

You will receive no direct benefit from being in this study. It is possible that you might benefit from the diagnosis of mental or medical health disorders of which you were unaware or uncertain of and will be offered a referral for appropriate treatment outside of the study if desired. Your being in this study may help the investigators advance development of more effective treatments for PTSD or increase our understanding of factors that influence recovery from trauma.

Alternatives

This study is not intended to provide treatment for PTSD or other psychiatric symptoms. You may receive psychiatric services at BMC and other hospitals that include diagnosis of mental or medical health disorders and referral for appropriate treatment without participating in this study. You are also free to withdraw from this study at any time.

Costs

The study drugs (IV Allo and placebo) are manufactured by the University of California, Davis, and paid for by the NIMH. There are no costs to you for being in the study. Items and services done only for study purposes will be provided at no cost to you. They will not be billed to your health insurance either. You can ask any questions now about insurance coverage for this study or about the research activities paid for by the sponsor. You can also ask the investigator later, using the number on the first page of this form.

Payment

You will be paid for participation in study sessions unless you are disqualified at that session based on a positive saliva alcohol test or positive urine drug or nicotine test. Payments for the study sessions are: $50 for the psychological screening evaluation, $50 for the medical screening evaluation, $60 for the first day of startle testing, $175 for the second day of startle testing, $100 for the third day of startle testing, and $15 for the follow-up telephone/Zoom call. Therefore, you can receive up to $450 for taking part in all regular study visits. If you return to the GCRU to repeat a lab test, you will be paid $20. We also will reimburse you for transportation or parking if needed. You will receive these payments on a Clin Card (which can be used as a debit card) at the end of participation. You will be required to give us your Social Security Number or Individual Taxpayer Identification Number to receive these payments. Also, please note: While the research may lead to new drugs, tests, or procedures with commercial value, you will not receive additional payment for your contribution to their development.

Confidentiality

General Considerations: To do this research, we must use information that shows your identity. Information already collected about you will remain in the study record even if you later withdraw. We will store your information in ways we think are secure. However, we cannot guarantee confidentiality.

We will protect your information by using a Study ID (number code). A Study ID is a way to identify you without using your personal information, such as your name, on data collected from you. This will be the only way to identify you in our data. Study documents with personal information about you will be stored in a locked cabinet

within a locked office at Boston University School of Medicine. Your personal information will not appear anywhere in the data that we collect from you. Electronic data will be password protected and stored on a secure network. All information will be kept confidential. We will store audio recordings and paper copies of the data for at least seven years after the study is over. Biological samples taken from your body (such as blood and urine) also will be labeled with your Study ID. We will store biological samples in the GCRU biorepository with only your Study ID and date of collection on the sample. The repository has standard operating procedures to protect your confidentiality.

As previously noted, there will be no way to tell that you participated in this study by looking at the samples or data. A master list linking participant names and their study IDs will be stored electronically and kept separate from the rest of the data. Only the research team will have access to this list, which will be destroyed when the study is over. Any collaborators performing data analysis at other institutions will not have access to the master list; they will only have access to data that will not identify you. The reported data will represent groups of participants without their identifiable information. Access to all study data will only be for the investigator and the research team.

Zoom, a video conferencing platform, may be used to conduct study interviews, and interviews will be audio recorded. Although we use a secure Zoom account through Boston University School of Medicine/Boston Medical Center, we cannot guarantee that it is completely confidential.

Confidentiality Issues Related to Genetic Testing: The use of your blood for genetic testing raises special issues of confidentiality, because it is possible that information about your genes could be used against you or your genetic relatives if the wrong people knew it. For example, if it became known that you carried certain genes, an insurance company could try to deny benefits, or an employer could try to deny employment. The following measures will be taken in order to protect the confidentiality of genetic testing of your blood:

- The genetic testing of your DNA is for research purposes only. No results of genetic testing from this study will appear in your medical record.
- Genetic test results will not be made available to you, your family members, your insurance company, your employer, your doctors, your other clinicians, or any other clinical staff. We do not expect genetic testing done in this study to become part of treatment for PTSD at any time during this study or in the next few years to come.
- Your DNA sample and test results will carry a study ID without personal identifying information.

There are state and federal laws that protect against genetic discrimination. There is a federal law called the Genetic Information Nondiscrimination Act (GINA). In general, this law makes it illegal for health insurance companies, group health plans, and most employers (those with 15 or more employees) to discriminate against you based on your genetic information. However, it does not protect you against discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

This study is also covered by a Certificate of Confidentiality (CoC) from the NIH. All studies funded by the NIH that involve identifiable information or biological samples are covered by a CoC**.** The CoC provides for how we can share research information or biological samples. Because we have a CoC, we cannot give out research information or biological samples that may identify you to anyone that is not involved in the research, except as we describe below. Even if someone tries to get your information or biological samples in connection with a legal proceeding, we cannot give it to them. The CoC does not prevent *you* from giving your own research information. We will record some information from this study in your medical record, such as information related to your medical care. Please ask us if you have any questions about what information will be included in your medical records. You should know that once information has been put into your medical records, it is not covered by the CoC. However, information in your medical records is protected in other ways.

If you agree to be in the study and sign this form, we will share information or biological samples that may show your identity with the following groups of people:

- People who do the research or help oversee it, for example, by doing safety monitoring.
- People from federal and state agencies who audit or review the research, as required by law. Such agencies may include the U.S. Department of Health and Human Services, the Food and Drug Administration, the NIH, NIMH and the Massachusetts Department of Public Health.
- People from Wayne State University may get your information as described under **"What Will Happen in This Research Study"**. They are expected to protect it like we protect it.
- People who are authorized to see your medical records.
- Any people for whom you give us separate permission to share your information.

You should know that we are required to report information about child abuse or neglect, elder abuse, specific reportable diseases, and harm to others.

If you are in immediate danger of hurting yourself at any time in the study, the study team will try to work with you on a plan to keep you safe. Because study staff will be trying to protect you, it is possible that your information will be shared with others as part of a plan for safety.

We will share research data only after removing anything we think would show your identity. There still is a small chance that someone could figure out that the information is about you. Such sharing includes:

- Publishing results in a medical book, journal, or other scientific forum.
- Adding data and results to the NIMH Data Archive (NDA) or other Federal government database.
- Using research data in future studies, done by us or by other scientists.
- Using biological samples in future studies, done by us or by other scientists.

Potential Breaches of Confidentiality: Breach of confidentiality (your private information being disclosed to other people without your consent) is always a concern when participating in a research study. Information will not leave Boston University Medical Campus/Boston Medical Center in any form that would identify you. We might use our research data and your biological samples in future studies. These future studies might be done by us or by other investigators. Before we use your data or samples, we will remove any information that shows your identity. Any data transportation will take place together with many other sets of data, and you will only ever be identified by a Study ID (never your real name) to others who receive the data. Transfer of samples and data between sites will only occur using secure methods including use of a Certificate of Confidentiality, institutional training, and enforcement of privacy and confidentiality rules. If a breach in confidentiality occurs, you will be informed.

Your primary care provider will be informed of your participation in the research. The study monitors, auditor, IRB, and regulatory authorities will be granted direct access to your original medical and research records for verification of research procedures and/or data.

There are certain cases for safety in which the study staff may need to breach confidentiality. This includes reporting cases of suspected abuse or neglect of children, the elderly, or disabled persons, reporting of communicable diseases, and acting on information received about potential harm to yourself or others. If you report that you plan to harm yourself or someone else, we may have you meet with a social worker or another qualified provider at BMC to make sure you are safe. There may be other unknown risks or discomforts involved.

NIMH Data Archive (NDA) Confidentiality Risks: During and after the study, the study researchers will send de-identified study data about your health and behavior to the NDA. Other researchers across the world can then request your de-identified study data for other research. Every researcher (and institutions to which they belong) who requests your de-identified study data must promise to keep your data safe and promise not to try to learn your identity. Experts at the NIH who know how to keep your data safe will review each request carefully to reduce risks to your privacy. Sharing your study data does have some risks, although these risks are

rare. Your study data could be accidentally shared with an unauthorized person who may attempt to learn your identity. The study researchers will make every attempt to protect your identity.

You may not benefit directly from allowing your study data to be shared with the NDA. The study data provided to the NDA may help researchers around the world learn more about mental health and substance use and how to help others with mental health and substance use problems. The NIMH will also report to Congress and on its website about the different studies using NDA data. You will not be contacted directly about study data that you contributed to the NDA.

You may decide now or later that you do not want your study data to be added to the NDA. You can still participate in this research study even if you decide that you do not want your data to be added to the NDA.

Please initial your current choice below:

I want my data to be added to the NDA _____

I do not want my data to be added to the NDA _____

If you decide any time after today that you do not want your data to be added to the NDA, call or email the study staff, and they will tell the NDA to stop sharing your study data. Once your data is part of the NDA, the study researchers cannot take back study data shared before you notified them that you changed your mind. If you would like more information about the NDA, it is available on-line at http://nda.nih.gov.

NIH Genomics Database and Confidentiality Risks: Samples collected from you in this study may be analyzed to find out information about your genetics. Genetics and health information that we publish without your name or other data that could easily identify you will be put in a database run by the NIH. This may include your whole genome information. Other researchers can ask the NIH to get your genetic information from the database. You should know that it is possible that your genetics information might be used to identify you or your family, although we believe it is not too likely that this will happen. Once your information is added to the NIH database, you can ask to have NIH stop sharing it, but NIH can't take back information that was already shared.

ClinicalTrials.gov Confidentiality Risks: As required by U.S. Law, a description of this clinical trial will be available on http://www.ClinicalTrials.gov This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

Use and Sharing of Your Health Information

The research team has to use and share your health information to do this study, including information that may identify you. By agreeing to be in this study and signing this form, you are giving us your permission where needed to use and share your health information as described in this form.

Health information that might be used or shared during this research includes:

- Information that is in your hospital or office health records at Boston Medical Center or elsewhere. The records we will use or share are those related to the aims, conduct, and monitoring of the research study. If health information is needed from your doctors or hospitals outside of Boston Medical Center, you will be asked to give permission for these records to be sent to the researcher.
- Health information from tests, procedures, visits, interviews, or forms filled out in this study.
- The health information specifically includes:
    - Mental health communications (with a psychiatrist, psychologist, clinical nurse specialist, marriage-, family-, rehabilitation-, or mental-health-counselor, or educational psychologist).
    - Domestic violence counseling.
    - Social work communications.

- Rape victim counseling.
- HIV/AIDS information.
- Sexually transmitted disease information.
- Communicable disease information.
- Alcohol, nicotine or drug use disorder diagnoses or treatment records or results of urine drug or saliva alcohol tests that may disqualify you from participation in the study
- Genetic and genomic testing.
- Medical laboratory test or EKG results.
- Results from physical examinations.

The reasons that your health information might be used or shared with others are:

- To do the research described here.
- To make sure we do the research according to certain standards set by ethics, law, and quality monitoring groups.
- To comply with laws and regulations. This includes safety-related information. As we explained above, we also have to share any information from you about child abuse or neglect; elder abuse; specific reportable diseases; harm to others.
- To protect you. As we explained above, if you are in immediate danger of hurting yourself, it is possible that your information will be shared with others as part of a plan for safety.

The people and groups that may use or share your health information are:

- Researchers involved in this research study from Boston Medical Center, Boston University, Wayne State University, and/or other organizations.
- Other people within Boston Medical Center and Boston University who may need to access your health information to do their jobs such as for treatment, research administration, payment, billing, or health care operations.
- People or groups that the researchers use to help conduct the study or to provide oversight for the study.
- The Institutional Review Boards that oversee the research and other people or groups that are part of the Human Research Protection Program that oversees the research.
- Research monitors, reviewers, or accreditation agencies and other people or groups that oversee research information and the safety of the study.
- The sponsor of the research study listed on the first page, and people or groups they hire to help them do the research.
- Public health and safety authorities who receive our reports about child abuse or neglect; elder abuse; specific reportable diseases; harm to others.
- Other care providers and public safety authorities that may be involved in helping to protect you if you express thoughts about hurting yourself.

We ask anyone who gets your health information from us to protect the privacy of your information. However, we cannot control how they may use or share your health information. After your information has been shared with others, we cannot promise that they will keep it completely private.

The time period for using or sharing your health information:

- Because research is an ongoing process, we cannot give you an exact date when we will either destroy or stop using or sharing your health information.

Your privacy rights include:

- You have the right not to sign this form that allows us to use and share your health information for research. If you do not sign this form, you cannot be in the research. This is because we need to use the health information to do the research. Your decision not to sign the form will not affect any treatment,

health care, enrollment in health plans, or eligibility for benefits.

- You have the right to withdraw your permission to use or share your health information in this research study. If you want to withdraw your permission, you must write a letter to the Principal Investigator at the address listed on the first page of this form. If you withdraw your permission, you will not be able to take back information that has already been used or shared with others. This includes information used or shared to do the research study or to be sure the research is safe and of high quality. If you withdraw your permission, you cannot continue to be in the study.
- When the study has been completed for everyone, you have the right to request access to the health information that we used or shared to make your treatment or payment decisions. If you ask for research information that is not in your medical record, we might not give it to you, but we will explain why not. You may use the contact information on the first page of this form to find out how to get your health information. You may also contact the HIPAA Privacy Officer at Boston University at HIPAA@BU.EDU.

Compensation for Injury

If you think that you have been injured by being in this study, please let the investigator know right away. Use the phone number on the first page of this form. You can get treatment for the injury at Boston Medical Center or at any healthcare facility you choose. There is no program to provide compensation for the cost of care for research related injury or for other expenses. Other expenses might be lost wages, disability, pain, or discomfort. You or your insurance will be billed for the medical care you receive for a research injury. You are not giving up any of your legal rights by signing this form.

Subject's Rights

By consenting to be in this study you do not waive any of your legal rights. Consenting means that you have been given information about this study and that you agree to participate in the study. You will be given a copy of this form to keep.

If you do not agree to be in this study or if at any time you withdraw from this study, you will not suffer any penalty or lose any benefits to which you are entitled. Your participation is completely up to you. Your decision will not affect your ability to get health care or payment for your health care. It will not affect your enrollment in any health plan or benefits you can get.

During this study, we may find out something that might make you not want to stay in the study. If this happens, we will tell you as soon as possible. We may decide to have you stop being in the study even if you want to stay. This could happen if staying in the study may be bad for you, or if the study is stopped.

Questions

The investigator or a member of the research team will try to answer all of your questions. If you have questions or concerns at any time, or if you need to report an injury while in this study, contact Kayla Brown at 617-414-4782. If there is no answer at that phone number or if you are calling after normal business hours, call Dr. Ann Rasmusson at 617-414-4777.

You may also call 617-358-5372 or email medirb@bu.edu. You will be talking to someone at the Boston Medical Center and Boston University Medical Campus IRB. The IRB is a group that helps monitor research. You should call or email the IRB if you want to find out about your rights as a research subject. You should also call or email if you want to talk to someone who is not part of the study about your questions, concerns, or problems.

Re-Contact

We would like to ask your permission to contact you again in the future. This contact would be after your participation in the study has ended. **Please <u>initial</u> your choice(s) below**:

1. You may contact me again to ask for additional information related to this study _____Yes _____No
2. You may contact me again to ask for additional biological samples related to this study _____Yes _____No
3. You may contact me again to let me know about a different research study _____Yes _____No
4. You may contact me again to let me know when the study findings are published _____Yes _____No

Subject: _____
Printed name of subject

Preferred gender pronoun (optional): _____
(He/She/They)

By signing this consent form, you are indicating that:

- you have read this form (or it has been read to you).
- your questions have been answered to your satisfaction.
- you voluntarily agree to participate in this research study.
- you permit the use and sharing of information that may identify you as described, including your health information.

_____ _____
Signature of subject Date

Researcher: _____
Printed name of person conducting consent discussion

I have personally explained the research to the above-named subject and answered all questions. I believe that the subject understands what is involved in the study and freely agrees to participate.

_____ _____
Signature of person conducting consent discussion Date