Temple IRB Approved

12/1/2021

Temple University
Research Participant Informed Consent

Title of Research: Phase 1B, Double Blind, Placebo-Controlled Pharmaco-MRS study of Clavulanic acid after repeated administration

Investigator and Department:

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Sponsor: National Institute of Drug Abuse

Study-Related Phone Numbers:

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Sub Investigator: M. Ingre Walters, M.D.

Study Supervisor: Helene Philogene-Khalid, Ph.D.
Office: 215-707-8980

Study Coordinator: Eric Cunningham, B.A.
Office: 215-707-7915
Cell: 267-332-1751

Research Project Associate: Yaminah Carter, B.S.
Office: 215-707-8980

EMERGENCY CONTACT INFORMATION:

Please call 911 for any emergencies that require immediate medical attention. For an urgent medical problem after working hours, please contact the study doctor using the 24-Hour phone number at 610-247-2126.

Document Revision Date: November 15th, 2021

RESEARCH CONSENT SUMMARY

You are being asked for your consent to take part in a research study. This document provides a concise summary of this research. It describes the key information that we believe most people need to decide whether to take part in this research. Later sections of this document will provide all relevant details.

What should I know about this research?

- Someone will explain this research to you.
- Taking part in this research is voluntary. Whether you take part is up to you.
- If you don't take part, it won't be held against you.
- You can take part now and later drop out, and it won't be held against you
- If you don't understand, ask questions.

Ask all the questions you want before you decide. During this consent process, a physician will be present to answer any questions you have about the study.

Why is this research being done?

The main purpose of this study is to determine how an experimental study drug, clavulanic acid, is associated with decreases in glutamate, a chemical in the brain. Using a brain scan method called Magnetic Resonance Spectroscopy (MRS), a way of studying brain chemicals using magnetic waves, we will look at the brain area known as the anterior cingulate (ACC). You will also undergo a different type of magnetic scan called structural Magnetic Resonance Imaging (MRI) and have a functional MRI (fMRI) that examines brain activity when you are shown different images.

How long will I be in this research?

This is an eleven (11) day inpatient study with at least three (3) outpatient visits.

What happens if I agree to be in this research?

In this study you will undergo five (5) MRS, structural MRI and fMRI scans. MRS, MRI, and fMRI scans do not use radiation, and each scanning session takes approximately one (1) hour.

Could being in this research hurt me?

The most serious potential side effect from being in this study is an allergic reaction to our study drug, Clavulanic acid. Clavulanic acid is commonly given as part of the antibiotic Augmentin and may pose a risk to individuals with a preexisting allergy to penicillins, or individual with no known allergies. If you have had an allergic reaction or are aware of any penicillin allergies, you should notify the study team immediately.

A full list of side effects and other minor risks will be included in the detailed section of the consent.

Will being in this research benefit me?

Your participation in this research study does not offer direct benefits to your health.
However, possible benefits of this study include the potential to develop an effective treatment for cocaine abuse which may benefit others with cocaine use disorder in the future.

What other choices do I have besides taking part in this research?

This research study is voluntary, which means you are under no obligation to participate. If you choose not to participate in this study, then you have the following options available to you:

- If you are interested in substance abuse treatment options, or behavioral therapy, and have medical insurance, we will provide you with options and refer you to substance abuse treatment. Treatment for drug abuse will focus on cocaine use disorders because of health risks.
- You may seek these treatment options on your own outside of the Temple University Health System.
- If you do not have medical insurance and desire any form of treatment, we will give you information about applying for medical insurance and how to pursue any available treatment options.
- You have the right to not seek any treatment options, if you choose to do so.

What else do I need to know about this research?

Please ask questions about the study and study procedures. If you want to proceed with assessment for the study, please sign and date below. You have a right not to sign this form. If you sign this form, that allows us to use and share your health information for research purposes. However, if you do not sign it, you cannot take part in this research study. You will receive a copy of this form for your records.

DETAILED RESEARCH CONSENT

You are being invited to take part in a research study. A person who takes part in a research study is called a research subject, or research participant.

You are being asked for your consent to take part in a research study. This document provides a concise summary of this research. It describes the key information that we believe most people need to decide whether to take part in this research. Later sections of this document will provide all relevant details.

Why am I being invited to take part in this research?

We invite you to take part in this research study because you are an adult with history of cocaine use who does not currently use cocaine and potentially meets the requirements for enrollment into the study. The research team will discuss this study with you. You may find some of the medical language or parts of this form difficult to understand. If you have any questions during or after reviewing this form, please ask the study doctor or the research team about anything you do not understand. If you decide to volunteer for this study, then you will be asked to sign this form.

What should I know about this research?

- Someone will explain this research to you.
- Taking part in this research is voluntary. Whether you take part is up to you.
- If you don't take part, it won't be held against you.
- You can take part now and later drop out, and it won't be held against you
- If you don't understand, ask questions.

Ask all the questions you want before you decide. During this consent process, a physician will be present to answer any questions you have about the study.

Who can I talk to about this research?

If you have questions, concerns, or complaints, or think the research has hurt you, contact the Study Supervisor, Dr. Helene Philogene-Khalid, or the Study Coordinator, Eric Cunningham:

You can also speak with Dr. Morrison whose contact information is on Page 1. This research has been reviewed and approved by an Institutional Review Board (IRB) at Temple University. You may talk to them at 215-707-3390 or e-mail them at: irb@temple.edu for any of the following:

- Your questions, concerns, or complaints are not being answered by the research team.
  - You cannot reach the research team.
  - You want to talk to someone besides the research team.
  - You have questions about your rights as a research participant.
  - You want to get information or provide input about this research.

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How long will I be in this research?

This is an eleven (11) day inpatient study with at least three (3) outpatient visits. The timeline of the study is as follows:

- An outpatient day of screening to complete written assessments and receive a Covid-19 test
- An outpatient day of screening to complete medical assessments
- A coronavirus screening test within 96 hours before your baseline visit
- Ten (10) days of inpatient sessions with study medication, with five (5) MR scans
- One (1) discharge day with an MR scan
- One (1) follow-up visit 5-8 days after the day of discharge

How many people will be studied?

We expect twelve (12) people will complete the trial. This entire study is expected to take one (1) year to complete.

Why is this research being done?

The main purpose of this study is to determine how an experimental study drug, clavulanic acid, is associated with decreases in glutamate, a chemical in the brain. Using a brain scan method called Magnetic Resonance Spectroscopy (MRS), a way of studying brain chemicals using magnetic waves, we will look at the brain area known as the anterior cingulate (ACC). You will also undergo a different type of magnetic scan called structural Magnetic Resonance Imaging (MRI) and have a functional MRI (fMRI) that examines brain activity when you are shown different images.

What happens if I agree to be in this research?

The study will take place at both the Temple Episcopal Hospital and at Temple University Brain Research and Imaging Center (TUBRIC) on the Temple University main campus. In the event that space is unavailable at the Episcopal Hospital, you will be admitted to the Temple University Hospital Main (TUH-Main) or Jeanes Hospital instead. TUBRIC is in the basement of the Temple University Weiss Hall building, located at 1701 N 13th street in Philadelphia. You will be provided transportation for any visit that requires you to go to TUBRIC. A staff member will travel with you to the building to sign you in and escort you to the imaging center.

In this study you will undergo five (5) MRS, structural MRI and fMRI scans. MRS, MRI, and fMRI scans do not use radiation, and each scanning session takes approximately one (1) hour.

Study Medication:

You will receive the study drug (clavulanic acid) or placebo to take daily. A placebo is commonly called a “sugar pill”, though there is no sugar in it. A placebo has no active ingredients. Neither you nor the study team will know whether you have been given clavulanic acid or placebo. You will be given the same number of pills whether you receive placebo or clavulanic acid.

The study drug comes in 250 milligram (250 mg) capsules. The first day you will take one (1) pill after your first MR scan, and you will be given a second pill later in the day if you don’t have bad side effects from the first pill. If you experience bad side effects from the first pill or have any questions

about the study medication after taking the first dose, you can contact the study team or your inpatient nurse, who can contact the study team.

On days two (2) and three (3) of the study, you will take both pills at the same time after eating food in the morning. If you tolerate the medication on days 1-3, you will be given a total of 3 pills (750mg) on days 4-6, and 4 pills (1000mg) on days 7-10 if you tolerate the 750mg dose.

This study is so that we can understand whether clavulanic acid, given once a day, is helpful in treating cocaine addiction. Currently, there is no available medication treatment for cocaine addiction and prevention of return to cocaine use. The clavulanic acid being used in this study is investigational. The study has been approved by the Food and Drug Administration (FDA).

Additional details about each study day are listed in the next section.

Outpatient Screening Visits (About 2.5-3 hours in two visits)

The screening period consists of two (2) outpatient screening days to collect information from you about your health and substance use to determine if you are eligible and healthy enough to participate in the study. The first visit takes about 1.5-2 hours and the second visit takes about 1 hour. At the screening visits, the following will occur:

Visit 1 (90-120 minutes)

1. You will be asked about your demographic information (race, age, ethnicity, etc.) and asked to provide contact information, including emergency contacts.
2. You will be interviewed by the study physician about your medical history, including any prescription and over-the-counter medications.
3. You will be asked questions and complete forms about past and present psychiatric symptoms and drug and alcohol use disorders.
4. You will answer questions about whether it is safe for you to have an MRI/MRS scan.
5. You will have a medical record review to confirm you do not have any medical history which would make you ineligible for the study
6. You will undergo a Covid-19 test via nasopharyngeal swap (long Q-tip) at an offsite testing location. Researchers will provide you with a medical Lyft to the testing location. You are not

responsible for cost related to testing or transportation. You will need to provide photo identification to the test center staff.

Visit 2 (About 60 minutes)

1. If you attend screening part 2 more than 30 days after screening part 1 we will update your medication history, medical history and recent substance use information.
2. The physician will conduct a physical examination. A study team member will take your vital signs, including heart rate, blood pressure, temperature, respiratory rate, and height and weight.
3. You will have an Electrocardiogram (EKG) to collect information about your heart.
4. Routine laboratory tests will assess your safety for this study. Blood will also be collected for infectious diseases, including human immunodeficiency virus (HIV) type 1 and 2. About 15 milliliter (ml) or about 1 tablespoon (tbsp) of blood will be collected in total along with a urine sample for analysis.
5. You will have a urine drug test to screen for drugs of abuse. Females less than 56 years of age will also undergo a urine pregnancy test.
6. You will have a breathalyzer test to assess recent alcohol use.
7. You will need to provide any of the following government issued photo identification:
   - Driver's License
   - Non-driver ID
   - Passport
   - Military ID

   Or, you can provide non-governmental photo ID supported by additional documentation (social security card or birth certificate) that includes the same name on the photo ID.

If we discover any health concerns (mental health or physical) through the course of the screening process that the study physician believes requires follow up, we will refer you to the appropriate medical or mental health services. You will be reminded that you will be responsible for any costs related to treatment.

Following the outpatient screening day, the screening period may last up to thirty (30) days prior to your second MR outpatient screen visit.

If you complete the screening phase and are found to be eligible and healthy enough to participate in the study, you will be enrolled in the inpatient phase of the study.

Prior to enrollment, you must have a negative Coronavirus PCR nasopharyngeal viral test within 96 hours prior to admission. A nasal swab will be used to collect a sample for testing. You are not responsible for any costs related to testing.

If you test positive for Coronavirus, we will ask you to seek appropriate medical care. If you do not have a primary physician, we will provide a referral. Temple University will not be responsible for any costs related to your Coronavirus treatment.

The study team will continue to follow up with you until symptoms resolve. You can be rescheduled for your baseline visit a minimum of 14 days after your Coronavirus symptoms resolve. You may be asked to take another Coronavirus test within 96 hours before the rescheduled visit to confirm you can no longer transmit Coronavirus.

Inpatient Study Period

The inpatient study period consists of eleven (11) days during which you will stay in the hospital unit. You can watch television, read books, and listen to music with headphones on the unit. You will need to bring your own music and headphones.

Each day, you will have your vital signs taken (blood pressure, pulse) and be assessed for any side effects of the study drug.

Each day, you will be asked to fill out several surveys related to your mental health, substance abuse history, and drug use. Other questions will include feelings related to the study drug, including mood, cocaine craving, and mental functioning. These surveys and questions are expected to take about 25-30 minutes total each time you complete them.

There will be five (5) MR scan days during the inpatient period. During these days, staff will provide travel to the scanning center.

Baseline (Approximately 180 minutes)

If you are eligible for the study, you will be scheduled for a baseline visit (Day 1) at TUBRIC. Upon arrival, you will be asked to complete a breathalyzer test and provide a urine sample to confirm you have not used illicit substances. You will also complete a record of your substance use covering the time back to the screening visit and complete assessments.

After the assessments, the study team will perform the first MR scan session. After the scans' completion, you will self-administer the first dose of study drug CLAV 250 mg dose or placebo (1 capsule). You will self-administer the second 250 mg capsule under study personnel supervision later in the day if the initial dose is tolerated.

After the completion of the MR scan and initial study drug dose, the study team will accompany you to the inpatient unit. Upon arrival, you will need to provide a photo ID so you can be registered as an inpatient on the unit. Aside from the times you need to travel to TUBRIC, you will remain on the inpatient unit until discharge. A study team member will remain with you at all times during travel between sites.

The baseline visit will take approximately 3 hours to complete.

Study Day 2 (About 30 minutes)

This session will include questions about side effects and study surveys. Vital signs (blood pressure, pulse) will be obtained. You will self-administer study drug (2 pills) under study personnel supervision. This session will take approximately 30 minutes.

Study Day 3 (About 180 minutes)

This session will include MR scan session 2, laboratory tests, questions about side effects, and study surveys. The MR scans will take 1 hour. Approximately 15 ml (1 tablespoon) of blood will be collected at this visit for lab tests. Vital signs (blood pressure, pulse) will be obtained. You self-

administer study drug (2 pills) under study personnel supervision. This session will take approximately 3 hours.

If you have been given the study drug and safely tolerated it, your dose will increase to 750 mg (3 pills) on study day 4. If you have been given placebo, you will be given 3 placebo pills to take. You will not be told which you have received.

Study Days 4-5 (About 30 minutes)

These sessions will include questions about side effects and study surveys. Vital signs (blood pressure, pulse) will be obtained. You will self-administer study drug (3 pills) under study personnel supervision. These sessions will take approximately 30 minutes.

Study Day 6 (About 180 minutes)

This session will include MR scan session 3, laboratory tests, questions about side effects, and study surveys. The MR scans will take one (1) hour. Approximately 15 ml (1 tablespoon) of blood will be collected at this visit for lab tests. Vital signs (blood pressure, pulse) will be obtained. You will self-administer study drug (3 pills) under study personnel supervision. This session will take approximately 3 hours.

If you have been given the study drug and safely tolerated it, your dose will be increased to 1000 mg (4 pills) on study day 7. If you have been given placebo, you will be given 4 placebo pills to take. You will not be told which you have received.

Study Days 7-9 (About 30 minutes)

These sessions will include questions about side effects and study surveys. Vital signs (blood pressure, pulse) will be obtained. You will self-administer study drug (4 pills) under study personnel supervision. These sessions will take approximately 30 minutes.

Study Day 10 (About 120 minutes)

This session will include MR scan session 4, questions about side effects, and study surveys. Vital signs (blood pressure, pulse) will be obtained. You will self-administer the final dose of study drug (4 pills) under study personnel supervision. An EKG will be performed and reviewed. Approximately

15ml (1 tablespoon) of blood will be collected at this visit for laboratory tests. This session will take approximately 3 hours and will occur both before and after you are discharged from the hospital. This session will take approximately 2 hours.

Study Day 11 (About 180 minutes)

This session will include MR scan session 5, questions about side effects, study surveys, and laboratory tests. Vital signs (blood pressure, pulse) will be obtained.

Follow up Visit (About 60 minutes)

Five to eight (5-8) days after discharge, you will return for a follow up visit. The visit will involve an assessment of side effects to determine any withdrawal symptoms and study surveys. This visit will take approximately 1 hour.

If you have side effects that remain at the follow up visit, we will continue to contact you until they have gone away. We may ask you to come in for additional visits if we believe your side effects require an in-person exam.

Early Termination (End of Study) Visit (About 60 minutes)

If your study participation ends earlier than planned, we will ask you to complete the day 11 tasks. You will be compensated at the day 11 discharge rate ($230). After you are discharged from the hospital we will ask you to return for a follow-up visit after you leave the study so that we may collect information about any possible side-effects, physical problems, or discomfort you have had since you left the study. This is also to make sure that you are safe and that we refer you to the proper care if you continue to feel any side effects. At this visit, you will receive the final payment for your time and travel for the study in the form of gift cards or cash. After completing the follow up session, we will contact you in a follow-up phone call. The early termination (end of study) visit will take approximately 1 hour. Only people who do not finish the study will have this visit.

MR Scanning Details

Before beginning the MR scans, you will have the option to go inside a mock (pretend) scanner to create the feeling of the MR setting. If you decide that you are uncomfortable being inside the mock scanner, you do not have to proceed with the study.

During the scans, you will be asked to lie down on a table, which will be slid into the MRI. An MRI coil will be placed around your head. This coil is simply wires covered in plastic. You will not come into contact with the metal wires during the procedure. Foam pads will be placed around your head to keep you from moving during the study. You will then be slid into the machine. You will be asked to lie down and stay still for approximately one (1) hour, when we will take several pictures of your brain. A study staff researcher will be present during the MRI scan and will keep you updated on how much time is left in the scan.

You will have two fMRI scans: a resting state fMRI and an imaging cue fMRI. During the resting state fMRI, you will be instructed to keep your eyes open and keep your eyes on a cross that is projected on a screen. During the imaging task, you will be exposed to different types of imagery that are flashed on the screen. At certain points the images will include cocaine related imagery.

While the purpose of this study is for research purposes only, there is a risk that an MRI scan will reveal a possible brain abnormality. If we think we may have observed such an abnormality, we will seek the opinion of a professionally licensed radiologist at no cost to you. In the event that the radiologist recommends clinical follow-up, we will inform you of the recommendation, make images from the scan session available to you, and provide a referral to a professional. We are not responsible for any medical costs incurred after this point as a result of this potential anomaly.

Table 1: Study Assessments

	Screening visit (-30 to 0 days)	Screening Visit 2 (-30 to 0 days)	Day 1 Baseline	Day 2	Day 3	Day 4 (Dose Increase 750)	Day 5	Day 6	Days 7-9 (Dose Increase 1000)	Day 10	Day 11	Follow Up (Day 16 - 19)
MRS scan			X		X			X		X	X	
Consent with HIPAA	X											
Cocaine Use Questionnaire	X											
Drug Use TLFB (preceding 30 days or less on follow up)	X		X									X
Medical record review	X											
Demographics	X											
Vital signs	X[1]	X	X	X	X	X	X	X	X	X	X	X
Medical History	X											
Nasopharyngeal swab (Covid-19 test)	X	X										
Physical Exam		X										
Labs (Blood Count, Metabolic Panel)		X			X			X		X		
Labs (Hepatitis B, C, HIV)		X										
EKG		X								X		
Breathalyzer		X	X									X
Urine Drug Screen		X	X									X
Urine Pregnancy		X	X		X			X		X		
Urinalysis		X								X		
MINI (Psychiatric Exam)	X											
ASI	X											
Craving Assessments (CCQ-Brief, Craving VAS			X	X	X	X	X	X	X	X	X	X
Subjective Assessments (POMS, VAS)			X	X	X	X	X	X	X	X	X	X
CANTAB (Cognitive Tests)			X		X			X		X	X	
C-SSRS scale	X		X								X	
MED-Q					X					X		
Assessment of AEs (Side Effects)			X	X	X	X	X	X	X	X	X	X
Assessment for Dose Escalation					X			X				

[1] Vital signs will only be taken at the first part of Screening if it is done in person

This research will be conducted at the Episcopal, Health Sciences, Jeanes Hospital, and Main campus of the Temple University Health System and Temple University.

What are my responsibilities if I take part in this research?

If you take part in this research, you will be responsible for:

- Not taking non-prescription medications and vitamins during the study that have not been approved by the study physician.
- Taking precautionary measures to not become pregnant during the study period as the risks of the study drug are unknown. This means that you must either agree to abstain from sexual activity starting at least 14 days prior to the study or use double barrier contraception during sexual activity. The double barrier method means that you must use two methods of contraception, for example oral contraceptives and condom, contraceptive patches and condom, vaginal rings and condom, contraceptive implant and condom, medroxyprogesterone (Depo Provera) injection and condom, a diaphragm and condom, intrauterine device and condom, or sponge and condom. This must continue for 30 days after the last dose of study drug.
- Providing a urine specimen during the outpatient and baseline visits for drug testing.

What other choices do I have besides taking part in this research?

This research study is voluntary, which means you are under no obligation to participate. If you choose not to participate in this study, then you have the following options available to you:

- If you are interested in substance abuse treatment options, or behavioral therapy, and have medical insurance, we will provide you with options and refer you to substance abuse treatment. Treatment for drug abuse will focus on cocaine use disorders because of health risks.
- You may seek these treatment options on your own outside of the Temple University Health System.
- If you do not have medical insurance and desire any form of treatment, we will give you information about applying for medical insurance and how to pursue any available treatment options.
- You have the right to not seek any treatment options, if you choose to do so.

What happens if I agree to be in this research, but I change my mind later?

This study is completely voluntary, and you should contact the study team if you wish to completely discontinue the study medication. Phone numbers for the study team are on page 1. If you experience a side effect or physical problem, let us know. You will be asked if you are comfortable continuing with the study, and the study physician will evaluate whether it is safe for you to continue.

If you decide to leave this research, contact the research team so that the physician can evaluate you and stop the study. Once you decide to leave the study and put that wish in writing, you will be considered withdrawn from the research study. If you wish, you will be referred for ongoing medical care.

If you stop being in this research, data that was already collected may not be removed from the research database. You may be asked whether the study team and physician can collect data from your routine medical chart. If you agree, this data will be handled the same as research data.

Is there any way being in this research could be bad for me?

Medication Side Effects:

The primary risks of this study are those of possible side effects to the study drug, clavulanic acid. Clavulanic acid has a risk of allergic reactions both for those with known penicillin allergy and for those with no known allergy. If you have any allergies to Augmentin®, penicillins, cephalosporins, or beta-lactam related drugs, then you will not be enrolled in the study.

There is no safety data in the scientific literature on clavulanic acid alone. Clavulanic acid has been used in combination with amoxicillin as a part of the antibiotic Augmentin®. Augmentin has been associated with a risk of hepatitis estimated to be between 1 out of every 10,000 and 1 out of every 100,000 people, with a higher risk for older men. A small percentage of patients taking Augmentin® have diarrhea (14.5%), vaginal mycosis (fungal infection of the vagina-often itchy) (3.3%), nausea (2.1%), and loose stools (1.6%). Clavulanic acid is unavailable by itself, without amoxicillin. Side effects associated with clavulanic acid from the FDA approval data from 250 mg up to 750 mg doses include: nausea (sometimes with a change in heart rate), vomiting, drowsiness, fatigue, diarrhea, indigestion, headache, increased stomach noises, flatulence (passing gas), “very slight increase in liver

size" with increased liver tests, cholestatic jaundice, dizziness, lightheadedness, and priapism (prolonged penile erection). If you are a man, and you experience a penile erection for 4 hours or more while you are in the hospital, we recommend that you contact your nurse or doctor immediately. The study team will transfer you to the emergency room for the doctors to determine whether your prolonged erection (priapism) is high flow or low flow priapism. Temple Psychiatry (our study team) completed a drug safety trial with 10 participants that were administered 3 doses (250 mg, 500 mg, 750 mg) of clavulanic acid in combination with cocaine to determine the safety of the combination. The most common side effects were headache and gastrointestinal symptoms (nausea, vomiting, gas, etc.). All 10 participants tolerated doses of 250 mg and 500 mg without serious side effects. The 750 mg dose was added later to the study, and 5 participants received the 750 mg dose of CLAV and tolerated it without serious side effects. In a follow up outpatient study, participants tolerated CLAV 500 mg/day for 10 days without serious side effects, only mild side effects. Based on those studies, and longstanding experience with clavulanic acid as part of the antibiotic Augmentin, we believe that clavulanic acid 500-1000 mg/day for 10 days can be safely studied in an inpatient study for people with a problem with recent cocaine use disorders.

MR Scans: There is little risk associated with the MR studies. The levels of energy used to make the pictures of your brain are far less than those used in a single x-ray, and many patients have been safely studied with multiple MR (magnetic resonance) sessions. The study will use non-significant risk investigational studies to measure glutamate (brain chemical) in the brain. The measurement is painless, but it will be noisy inside the magnet due to a hammering sound made when the magnetic fields are turned on and off. You will be given earplugs. Because of the strong magnetic field, people with pacemakers or certain metallic implants (inserted devices or metal splinters/bullets) cannot be a part of this study. You should inform the study doctor if you are aware of any known metallic implants or foreign metallic objects in your body. In addition, there may be a possibility of a metallic object flying toward the magnet and hitting you. To reduce this risk, we require that all people involved in the study remove all metal from their clothing and all metal objects from their pockets. No metal objects are to be brought into the magnet room at any time. Once you are in the magnet, the door to the room will be closed so that no one inadvertently walks in during the study by mistake. You should inform the doctor if you are claustrophobic or become nervous in small or tight spaces. If you become uncomfortable inside the magnet, you should tell the research staff so that you may leave the study. Some powerful magnets rarely provoke a metallic taste or dizziness or a twitchy feeling in your muscles, but this sensation does not last long and goes away as soon as the study is over.

Although there are no known risks of MR scans on pregnant women or a fetus (developing baby inside the woman), there is a possibility of yet undiscovered pregnancy-related risks. Since there is no direct benefit from participating in this study, no pregnant women are allowed into the study. A urine pregnancy test will be administered by study staff during each MR scan visit. A negative urine pregnancy test is required before a woman of child-bearing potential can participate in this study.

Other Risks:

Drawing blood may result in discomfort when the needle is inserted into the skin. Minor temporary bruising may occur at the site of needle insertion.

There is a risk of your confidential information being disclosed.

For both your safety and staff safety, you can only participate in the study if you do not have an active Covid-19 (Coronavirus) infection. The test for Covid involves a nasopharyngeal swab (long Q-tip) put into your nose for about 20-30 seconds with a twisting motion while in your nose. Before testing you should avoid eating, drinking, using nose drops, aerosol inhalers and antibiotic treatment for 2 hours. Both nostrils are tested with a swab. The swab can be uncomfortable and there may be mild bleeding from your nose afterwards (5-8% patients). Headache and ear discomfort after the swab test are rarely experienced (1-5% patients).

In addition to these risks, this research may hurt you in ways that are unknown. These may be minor inconveniences or may be severe enough to cause death.

Will being in this research benefit me?

Your participation in this research study does not offer direct benefits to your health.
However, possible benefits of this study include the potential to develop an effective treatment for cocaine abuse which may benefit others with cocaine use disorder in the future.

What happens to the information collected for this research?

To the extent allowed by law, we limit the viewing of your personal information to people who have to review it. We cannot promise complete secrecy. The Institutional Review Board at Temple (IRB), Temple University, Temple University Health System Inc. and its affiliates, and if applicable,

regulatory agencies, such as the Food and Drug Administration (FDA), the National Institutes of Health (NIH), the Office of Human Research Protections (OHRP), and the Department of Health and Human Services (HHS) may inspect and copy your information. By signing this document, you are authorizing this access. You will also need to sign a separate "Authorization to use and disclose your protected health information" to be a part of this research. We may publish the results of this research. However, we will keep your name and other identifying information confidential, meaning it will not be a part of published research.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. 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.

Federal law provides additional protections of your personal information. These are described in an attached document titled "Authorization to use and disclose your protected health information".

Certificate of Confidentiality for Health Information and Other Identifying Information from the Research

For this study, we have a Certificate of Confidentiality from the Department of Health and Human Services (HHS) of the U.S. government. In granting the Certificate, HHS is not approving the research itself but is helping us strengthen the privacy protections for your information and other identifying information from the research. With the Certificate, we cannot be forced (for example, by court order) to disclose your health information or other identifying information from the research in any federal, state, local civil criminal, administrative, legislative or other proceedings. The Certificate does not protect you or a member of your family from voluntarily (freely) releasing any information about you or your involvement in this study. Note that if an employer or insurer learns about your participation and obtains your consent to receive this information, the study team cannot use the Certificate of Confidentiality to withhold this information. This means that your family and you must also actively protect your own privacy.

Finally, you should understand that the study doctor is not prevented from taking steps, including reporting to the authorities, to prevent serious harm to yourself or others. The Certificate of Confidentiality will not be used to prevent disclosure to local authorities of child abuse and neglect, or harm to self or others.

Information from the research, such as allergies to medications or results from standard blood tests done at the hospital lab, that relates to your general medical care may be included in your electronic medical record. This information may be accessible by court order and may not be protected by the Certificate of Confidentiality. Please ask your study doctor if you have any questions about what information will be included in the electronic medical record.

Can I be removed from this research without my OK?

The person in charge of this research or the sponsor can remove you from this research without your approval. For instance, you can be removed if the study doctor feels it necessary for your health or safety. You will be informed if such a decision is made and the reason for this decision. Possible reasons for removal include:

- You experience very bad side effects from the study drug.
- You show new or worsening mental or medical symptoms that require treatment.
- You experience a substance abuse problem that requires treatment.
- You are unable to tolerate the MR scans.
- You are unable to follow study procedures.
- The sponsor (NIDA), principal investigator, or the Food and Drug Administration (FDA) has decided to stop the study.
- Any other reason we do not foresee at this time.

We will tell you about any new information that may affect your health, welfare, or choice to stay in this research.

What if I am injured because of taking part in this research?

If you are injured as a result of taking part in this research, immediately notify the research team or the inpatient team and they will arrange for you to get appropriate medical care. There is no commitment by Temple University, Temple University Health System or its subsidiaries to provide monetary compensation or free medical care to you in the event of a research-related injury. If you have a research-related injury, please contact Dr. Mary F. Morrison or study physician covering the study at 215-707-8688 during regular hours and at 610-247-2126 after-hours and on weekends and holidays.

What will I be paid for taking part in this research?

Payment schedule					
Visit	**Visit Compensation**	**Medical Compensation**	**MRI Compensation**	**Survey Compensation**	**Participant Compensation**
Outpatient screen-Visit - 1	$20	$0	$0	$0	**$20**
Outpatient Visit 2	$0	$20	$0	$0	**$20**
Covid Test 1+2	$20[1]	$0	$0	$0	**$25**
Day 1	$30	$0	$150	$30	**$210**
Day 2	$30	$0	$0	$30	**$60**
Day 3	$30	$20	$150	$30	**$230**
Day 4	$30	$0	$0	$30	**$60**
Day 5	$30	$0	$0	$30	**$60**
Day 6	$30	$20	$150	$30	**$230**
Day 7	$30	$0	$0	$30	**$60**
Day 8	$30	$0	$0	$30	**$60**
Day 9	$30	$0	$0	$30	**$60**
Day 10	$30	$0	$150	$30	**$210**
Day 11	$30	$20	$150	$30	**$230**
Outpatient Follow up visit	$70	$0	$0	$30	**$100**
Study Completion Bonus					**$730**
Total Payment for Full Participation					**$2340**

*You will be compensated for reasonable travel costs [up to a maximum of $100 over the course of study with qualifying receipts. Travel compensation will also be distributed for the required visits for urine samples for participants.

[1] Covid-19 test compensation will be given in the form of gift cards

You will be compensated (paid) for travel costs and time spent. Your payments are determined by how much of the study you complete. You can choose to receive payment is in the form of cash gift cards, or by ClinCard, . a secure, reloadable MasterCard debit card supported by Greenphire. If you choose Greenphire as your payment method we will give you the card. You will be given one card for the entire time of your participation. You will also get a pamphlet about how to use this card and whom to call if you have any questions. Be sure to read this information, including the cardholder agreement from Greenphire if you choose ClinCard as your payment option.

If you choose ClinCard money will be added to your card based on the study's payment schedule. You may use this card online or at any store that accepts MasterCard.

Greenphire is a company working with Temple University to manage and process payments. Greenphire will be given your name, address, date of birth, and social security number. They will use this information only as part of the payment system, and it will not be given or sold to any other company. They will not receive any information about your health status or the study in which you are participating.

Payment will be made after each of the initial screening visits, the discharge day of the inpatient session, and at the follow up visit. If you are discharged from the study early, you will receive compensation for completed days at the time of the outpatient follow-up visit. If you attend all study days and complete all study activities, you will receive a $730 completion bonus at the time of the follow up visit.

You will receive a $25 gift card for completing two Covid-19 tests. You will receive it after the second test.

If you agree to take part in this research, we will pay you ***a maximum of $2340*** for your time and effort and up to $100 for travel. You will be required to provide a receipt for all travel reimbursement. If you do not provide a receipt, you will be given $5.00 to compensate you for the cost of public transportation. Federal tax law requires you to report this payment as income to the Internal Revenue Service (IRS). You will be asked to tell us your social security number. If all study payments and travel reimbursements total more than $599.00 in a year, Temple will report them to the Internal Revenue Service. We will ask you to fill out a W-9 form so that you can be sent a 1099-MISC form.

Participating in Future Research Studies

We would like to contact you in the future to see if you would be interested in participating in another research study. Please indicate below if you are willing to be contacted about any future research studies

____**Yes**, I agree to be contacted about future research studies.

Name of Participant (Please Print)	Signature of Participant	Date

____**No**, I do not want to be contacted about future research studies

Name of Participant (Please Print)	Signature of Participant	Date

What else do I need to know about this research?

Please ask questions about the study and study procedures. If you want to proceed with assessment for the study, please sign and date below. You have a right not to sign this form. If you sign this form, that allows us to use and share your health information for research purposes. However, if you do not sign it, you cannot take part in this research study. You will receive a copy of this form for your records.

WOMEN OF CHILDBEARING POTENTIAL MUST READ PAGE 24, AND COMPLETE PAGE 25. ALL OTHER POTENTIAL PARTICIPANTS SKIP TO PAGE 26

Reproductive Risks for Women of Childbearing Potential:

If you are pregnant or currently breast-feeding, you may not participate in this research study. If you are pregnant, become pregnant, or are breast-feeding during this study, you or your fetus (developing child) may be exposed to unknown risks. You should not become pregnant while in this research study. You must agree to take precautionary measures to not become pregnant during the study period as the risks of the study drug are unknown. This means that you must either agree to abstain (give up) from sexual activity starting at least 14 days prior to the study or use double barrier contraception during sexual activity. The double barrier method means that you must utilize two methods of contraception, for example oral contraceptives and condom, intrauterine device (IUD) and condom, or sponge and condom. You need to continue these methods for 30 days after the last day of study drug.

To confirm to the extent medically possible that you are not pregnant, you are required to agree to have a urine pregnancy test three times: at screening, baseline, and the follow up visit. You must also agree to remain abstinent (have no sex) or use a birth control method as outlined below for at least 30 days after this study ends. Because birth control is not guaranteed to be 100% effective at preventing pregnancy, you may still become pregnant even with responsible contraceptive use. You agree to notify the study staff or doctor if you become pregnant at any time during the study or within 30 days after completing the study.

If you have any questions about this form, what you are agreeing to, or about any of the methods of birth control described, please ask the study doctor.

Select One Option and Initial Below:		**Agreement for Women of Childbearing Potential:**
☐ I agree _____ Initial	☐ I disagree _____ Initial	I understand that if I choose to participate in this research study, I will agree to have **three** urine pregnancy tests: • At screening • On the first scanning day • At the follow up visit
☐ I agree _____ Initial	☐ I disagree _____ Initial	If I participate in this research study, I agree to use an effective form of birth control during and for a minimum of 30 days after study participation. Effective forms of birth control include: • complete abstinence from sexual intercourse • oral contraceptives, contraceptive patches, contraceptive implants, vaginal rings, Depo-Provera, Norplant, or intrauterine progesterone contraceptive system **AND** condom by partner • diaphragm **AND** condom • intrauterine device (IUD) **AND** condom • sponge **AND** condom
☐ I agree _____ Initial	☐ I disagree _____ Initial	I agree to notify the study doctor if I become pregnant at any time during the study or within 30 days after completing the study.

_____ _____
Name of Participant (Please Print) Signature of Participant Date

_____ _____
Name of Study Personnel Obtaining Consent Signature of Study Personnel Date

Signature Block for Adult Participant Capable of Consent

Your signature documents your permission to take part in this research study.

Signature of Participant	Date
Printed name of Participant	
Signature of person obtaining consent	Date
Printed name of person obtaining consent	
Signature of Physician present	Date
Printed name of Physician present	