HIC#: **2000024444**

COMPOUND AUTHORIZATION AND CONSENT FOR PARTICIPATION IN A RESEARCH PROJECT
200 FR. 4 (2018-1)

YALE UNIVERSITY SCHOOL OF MEDICINE – YALE-NEW HAVEN HOSPITAL
YALE UNIVERSITY SCHOOL OF MEDICINE—CONNECTICUT MENTAL HEALTH CENTER

Study Title: Imaging the Neuroimmune Response to Alcohol
Principal Investigator: Ansel Hillmer, Ph.D., 2 Church Street South, Suite 314, New Haven, CT 06519
Funding Source:

All Subjects (Version .05) Aim 1/2 (50 Moderate Drinkers, 50 AUD)

Invitation to Participate and Description of Project

You are invited to take part in a research study designed to examine the effects of alcohol drinking on the chemistry of the brain. In particular we are interested in examining the neuroimmune system in the brain. The proposed non-treatment study will fill a major gap in our understanding of addiction. This information may help in the development of better treatments for various populations. You have been asked to take part because you are either a moderate drinker or may have an alcohol use disorder (AUD) and agree to abstain from drinking for 48 hours.

In order to decide whether or not you wish to be a part of this research study you should know enough about its risks and benefits to make an informed decision. This consent form gives you detailed information about the study, which a member of the research team will discuss with you. This discussion should go over all aspects of this research: its purpose, the procedures that will be performed, any risks of the procedures, and possible benefits. Once you understand the study, you will be asked if you wish to participate; if so, you will be asked to sign this form.

Summary of Procedures

If you agree to this study, you will have a screening evaluation to determine eligibility, an MRI (magnetic resonance imaging) brain scan, and up to two [C11]PBR28 PET Scans. After your first baseline PET scan you will be asked to drink a supplied alcoholic beverage targeting a blood alcohol level of .08 prior to having the second PET scan. After the second scan you will be admitted to an inpatient unit overnight, during which time you will be medically evaluated. If you are participating as an AUD subject and have higher dependence levels you will be asked to go inpatient the night prior to the first scan to assure overnight drinking abstinence. The details are below.

Sequence of procedures:

Order	Study procedure	When/where
1.	Screening visit (medical evaluation)	2 Church St South Suite 511, CNRU, or PET Center
2.	Alcohol abstinence and inpatient admission overnight at CMHC or HRU	Before PET scan for High Level dependence AUD subjects, after PET

APPROVED BY THE YALE UNIVERSITY IRB 10/13/2021

		scan for AUD subjects, optional for Moderate Drinkers and AUD subjects with lower dependence levels.
3.	PET scans: 1 Baseline Pre-Alcohol Admin 1 Shortly After Alcohol Admin	After overnight abstinence from alcohol, another shortly after alcohol administration (Same day),
4.	MRI scan	Within a week of PET scan

Description of Procedures:

Screening evaluation:
Before you are accepted into the study, you will be interviewed by a research assistant to find out if you qualify for the study. The screening evaluation will occur at the Connecticut Mental Health Center (CMHC) Clinical Neuroscience Unit (CNRU), 2 Church street South Suite 511, or the Yale PET center. If you are already staying inpatient at the CNRU and participating in another study, by signing this consent you agree to allow us to contact that study team to ensure there are no conflicts or safety concerns. During the screening, you will have a medical evaluation including a breathalyzer, medical history, physical examination, blood tests and urine tests, and an electrocardiogram (ECG) to ensure that you are medically healthy. Women will also have a serum pregnancy test during screening. The blood sample will be tested for hepatitis and HIV in addition to the other required blood tests listed above for this study. Results of these tests are confidential. A qualified physician will report any clinically important results of these tests to you in person. Positive hepatitis and HIV tests must be, by law, reported to the State Department of Public Health and you will be given access to appropriate counseling and advice about the next steps to take. If any of these tests are positive, you will not be able to participate in the study. If you do not want to risk this possibility, you can refuse to have these tests done, but then you cannot participate in the study. The results of these tests will be handled according to the HIPAA section outlined below under the section on Confidentiality and Privacy, which among other things, explains the importance and commitment to protecting the privacy of your medical information. This information is protected by a Certificate of Confidentiality (mentioned on page 10).

If you are medically healthy and meet study requirements, you will be scheduled for the scans as well as a possible admission to the inpatient unit located at CMHC or Yale New Haven Hospital (HRU) for the same night as the alcohol administration. If you are participating as an AUD subject and have higher levels of dependence, you will also be scheduled to go inpatient the night before your first scan to confirm alcohol abstinence. Carbon monoxide (CO) levels may be taken before every session. We also ask that you not take medications such as aspirin, acetaminophen (Tylenol), ibuprofen (Advil, Motrin), naproxen (Aleve), or celecoxib (Celebrex) for 3 days before the PET scans.

<u>MRI Scans</u>
You will be asked to go to the MRRC at The Anlyan Center for Medical Research & Education (TAC, 300 Cedar Street) to have an MRI (Magnetic Resonance Imaging) scan of your brain. A member of the research team will accompany you and remain for the duration of the scan. The purpose of the MRI is to help us identify the different regions of your brain on the PET scans. MRI scans are a routine way to get pictures of the inside of the body. In the MRI Center, we will review whether you are carrying any metallic objects before you move toward the MRI system. These objects will be held for you in the MRI Center to avoid having these objects fly toward the magnet when you approach it. You will also be asked to walk through a metal detector. You will be asked to lie still in the MRI scanner. The scanner looks like a deep tunnel. You will be inside the tunnel from head to knees. You will not be able to see out of it, but you will be able to hear us and be heard if you wish to say anything. You will hear a drumming noise when the camera is taking pictures of your brain. If you feel

uncomfortable during the scan, we can end the scan at any time you wish to do so. However, if you cannot complete the MRI scans, you may not be able to participate in any more of these studies. If you have a recent MRI that is already on file at the PET center you may not need to repeat this scan.

PET Scans

Before your [C11]PBR28 PET scan you will need to be abstinent from alcohol for 48 hours. For AUD subjects who have higher level of dependence you will be asked to stay the night prior to the first scan at CMHC's CNRU to ensure overnight abstinence. AUD subjects with higher dependence levels will be required to stay overnight at the CNRU after having the alcohol administration, moderate drinkers and AUD subjects with lower dependence levels will have the option to stay overnight, either at the CNRU or YCCI's HRU. PET scans will be conducted at the Yale University PET Center on 801 Howard Avenue, New Haven. You will have up to 2 scans, 1 before alcohol administration, one shortly after alcohol administration(same day as the first). The purpose of these scans is to measure brain neuroimmune response to alcohol. If a scan fails after radiotracer injection, you may have an additional scan.

When you arrive at the PET Center you will be asked to provide a urine sample to check for drug use and/or nicotine use. You will also be checked with a breathalyzer device for recent alcohol use . Your vital signs (blood pressure, heart rate, respiration) will be taken several times throughout the test day. If female, you will be given a urine pregnancy test on the day of the PET procedures prior to imaging. You cannot participate in this study if you are pregnant or nursing.

A trained nurse or CNMT (Certified Nuclear Medicine Technologist) will place plastic catheters (tubes) in your arm (for the radiotracer injection and to take venous blood samples) during the PET scan. Blood draws will occur throughout each scan and during the alcohol administration. Total blood drawn for the entire study not exceed 32 tablespoons.

An experienced physician will insert an arterial catheter in your wrist area. The arterial catheter is about 2 inches long and looks like a regular IV tube, but it is inserted into an artery, not a vein. The blood flow in the arteries can tell us about your blood pressure. If an arterial catheter is in place, we can measure your blood pressure continuously. The other main reason to put in an arterial catheter is to be able to draw blood samples rapidly, repeatedly, and without causing you pain. Here is what happens when an arterial line in placed. First, the skin is cleaned with betadine solution (contains iodine). This skin cleansing with an antiseptic aims to reduce the microorganisms present on the skin and therefore reduce the risk of an infection. Second, the insertion area is numbed with a local anesthetic, so that you feel less pain when the catheter is inserted. You will probably just feel pressure but may also feel pain. This pain is usually like the pain you feel when an IV is placed and only rarely is it worse. Third, the catheter will be flushed regularly during your scan with saline (a salt solution), which prevents clogging of the catheter with a blood clot. Fourth, after the catheter is removed, local pressure is applied for a minimum of 15 minutes to prevent bleeding under the skin. A pressure dressing (Coban) and clear dressing (Tegaderm) will then be applied and you will be asked to keep it clean and dry, avoid strenuous exercise, refrain from lifting heavy objects weighing more than 5 pounds, and to avoid repetitive movements for 48 hours. You may remove the pressure dressing at bedtime and the clear dressing after 48 hours, but do not submerge your hand and wrist in water for a full 72 hours. Since the catheter is in for a minimal period, there is a low risk of infection.

After the arterial catheter is inserted, a PET scanner will be used to take pictures of your brain. As part of the PET scanning session, you will be asked to lie very still on a table. The radiotracer, [C11]PBR28, which is a minimal amount of a drug that is labeled with a very small amount of a radioactive substance, will then be injected into the tube in your vein. Following this injection, the PET scanner camera will detect the radiotracer

present in brain areas. This information will be used to create pictures of your brain showing the patterns of microglia in your brain. Blood samples during the PET scanning sessions will be used to measure the amount of radiotracer in your blood. We will also collect blood samples for measurement of certain substances in the blood such as levels of glutamate. The PET scanning session will require a few hours. If you ask, we can stop the scan at any time. However, if you can't complete the PET scan, you may not be able to do any more of our scanning studies in the future. A transmission scan or low dose CT scan will be completed immediately before or after each PET scan. This information is used to increase the accuracy of the PET data. You will be asked to drink several glasses of water at the close of the PET scanning session to wash out the radiotracer. A light meal will be provided at the conclusion of the PET scanning day. After the PET scan you will be discharged from the PET center. You will be provided with a telephone number you can call any time after the scan if you need assistance for problems related to the study procedures.

*Alcohol administration :*Between the first and second scans you will be given an alcoholic beverage to drink. This will be 80 proof vodka mixed with a zero-calorie, caffeine free, decarbonated beverage of your choice. You will be monitored throughout this time and be asked to continue drinking over a period of 90 minutes, drink strength is calculated based on your weight and drinks are dispersed evenly over the 90 minutes. Moderate drinkers may be discharged after the PET scan once a breath alcohol of 0.02 has been reached, transportation will be provided if this is the case.

We will also perform sessions of testing of your memory, attention, behavior, cognition, and concentration. This will take approximately 1.5 hrs total. This testing will take place on each of the PET scan days.

During a scan visit, you may earn additional compensation (up to $60) if you play two computer games, one called the Face Game and the other being the Card Game. The goal of the Face Game is to win as much money as possible. You may earn money by quickly and correctly pressing one of two keys on the keyboard, each time you see a face on the screen. You will press one key if you think that the mouth on the face is long, and the other if you think it is short. The goal of the Card Game is to earn as much money as possible by picking the best deck. You will be presented with a series of card decks, and you must choose the one you think will win you the most money.

Please initial below if you agree to participate in the 20 hr post alcohol administration scan (3rd scan)

_____Yes _____No

Stay at CMHC

If you agree to participate in this study you agree to be admitted to CMHC. The Connecticut Mental Health Center is located at 34 Park St, New Haven. The Clinical Neuroscience Research Unit is a closed inpatient facility within CMHC primarily used for research purposes. While there you will be monitored by the CNRU or HRU staff.

While at CMHC, you can ask to meet with a clinical psychologist to review treatment options for alcohol use disorders if you so choose.

During your stay in the CNRU, you may be placed in a room with another inpatient if the unit is at capacity, however it is likely you will be in a private room. Before entering the facility, you will need to sign a CNRU rules agreement which will outline basic unit rules regarding your stay. The CMHC is a smoke-free facility. If you smoke nicotine products, you will be provided replacement nicotine in the form of gum and/or transdermal patches to use if desired. Subjects who smoke will be allowed to have smoke breaks while on the CNRU when

accompanied by study personnel. Subjects wishing to quit smoking will be offered a referral to a smoking cessation program upon completion of the study. The unit is also Caffeine free which means no products that contain caffeine while in the CNRU, i.e. Coffee, Energy Drinks, Chocolate. 3 Meals a day plus snacks will be provided for you, you are also allowed to order delivery. There is a small exercise room that is available for use. Guests are welcome during visiting hours, however whenever you are off unit you will need to be accompanied by either CMHC staff or a member of the study team. The CNRU rules agreement will go over these items in more detail.

Optional Specimens for Future Storage/Genetic Testing

You are invited to allow some of your samples (called specimens) and related information to be stored (banked) for future research for genetic testing. This may help researchers in the future learn more about how to prevent, find and treat certain illnesses risks due to variations in some genes.

Your specimens will be stored for an unlimited time and may be used to make a cell line that will live indefinitely. Future research may look at your genes, which are the units of inheritance that are passed down from generation to generation. Genes are responsible for many things about you such as eye color, hair color, blood type and hundreds of other traits. Future genetic analysis may possibly include finding out the details of how your DNA is put together, such as whole exome or genome sequencing, or genome wide association studies (that is, looking at genes other than those associated with a specific disease).

When your specimens and information are stored, we are careful to try to protect your identity from discovery by others. Your samples and information will receive a unique code. Other researchers will only receive coded samples and information, and will not be able to link the code to you. Strict security safeguards are in place to reduce the chance of misuse or unplanned release of information.

Using your specimens for research will probably not help you. We do hope the research results will help people in the future.

There is a risk that your information could be misused. The chance of this happening is very small. We have protections in place to lower this risk. There can also be a risk in uncovering genetic information. New health information about inherited traits that might affect you or your blood relatives could be found during a research study. Very rarely, health or genetic information could be misused by employers, health insurance companies, and others. There is a federal law called the Genetic Information Nondiscrimination Act (GINA) that, in general, makes it illegal for health insurance companies, group health plans, and most employers (except those with fewer than 15 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.

Your specimens and information will only be used for research and will not be sold. There is a possibility that this research may lead to development of products that will be commercialized. If this happens, there is no plan to share any financial gain with you.

Research results will not be returned to you or your doctor. If research results are published, your name and other personal information will not be given.

The choice to take part is up to you. You may choose not to let us store and use your samples, and your care will not be affected by this decision. If you decide that your samples can be kept, you may change your mind at any time. Contact the study staff at 203-737-4833 to let them know you do not want your samples used any longer. Your samples will be destroyed.

I agree to allow my samples and information to be stored and used for future research as described above: (initial your choice)

_____YES _____No

Risks and Inconveniences

Possible risks from participation in this study include 1) Alcohol Administration 2) Risk of alcohol withdrawal 3) radiation exposure, 4) having intravenous lines placed/blood drawing, 5) having arterial lines placed in your arteries, 6) MRI scanning, 7) risks to pregnancy and breastfeeding, 8) genetic testing, 9) Allergic Reactions, and 10) Unanticipated Events.

1. Alcohol Administration

The risks of alcohol administration for this study include: Nausea, Reduced Coordination, Reduced Judgement. You will be monitored throughout the administration process and after the scan at the CNRU to ensure your safety.

2. Alcohol Withdrawal

The risks of untreated alcohol withdrawal include seizure, psychosis, agitation, hypertension, hyperthermia, tremor, and confusion. To reduce these risks, if you have an Alcohol Use Disorder your symptoms will be monitored upon admission to the CNRU and HRU and throughout the PET scan. If your symptoms are severe enough you will be transferred to the Yale-New Haven Hospital for continued evaluation and treatment.

3. Radiation Exposure

This research study involves exposure to radiation from positron emission tomography (PET). Please note that this radiation exposure is **not** necessary for your medical care and is for research purposes only.

The targeted amount of radiation you will receive from participating in up to 2 PET scan sessions in this study is from up to 2 injections of [C11]PBR28 and from transmission scans, or low dose CT scans, used to help obtain the PET images. Although each organ will receive a different dose, the amount of radiation exposure you will receive from *a single injection* of [C11]PBR28 is equal to a uniform whole-body exposure of **0.814** rem, for a total of **1.63 rem** for two injections. In addition, you may have a low dose CT scan before or after each PET scan. One additional low dose CT scan may be obtained, in the event that PET scans are interrupted for any reason, for a total of 3 CT scans. The total radiation exposure, including CT scans would be **3.51 rem** (1.63 rem from [C11]PBR28 and **1.88 rem** from CT) . This is the equivalent of approximately **11.5 years** of natural environmental exposure from sources such as naturally occurring radioactive forms of water and minerals.

This value is known as the "effective dose equivalent" and is used to relate the dose received by each organ to a single value. This amount of radiation exposure is below the annual limit of 5 rem set by the federal government for research subjects.

The effects of radiation exposure on humans have been studied for over 60 years. In fact, these studies are the most extensive ever done of any potentially harmful agent that could affect humans. In all these studies, no harmful effect to humans has been observed from the levels of radiation you will receive by taking part in this research study. However, scientists disagree on whether radiation doses at these levels are harmful. Even though no effects have been observed, some scientists believe that radiation can be harmful and may cause cancer at any dose- even low doses such as those received during this research.

Please tell your study doctor if you have taken part in other research studies at Yale or other places/hospitals that used radiation. This way we can make sure that you will not receive too much radiation. You should consider x-rays taken in radiology departments, cardiac catheterization, and fluoroscopy as well as nuclear medicine scans in which radioactive materials were injected into your body. Before you take part in any future studies that use radiation, you should also tell those study doctors about your participation in this study.

4. Risks associated with IV line and blood draws

Drawing blood and inserting an intravenous line (IV) into an arm vein are safe and standard medical procedures. Sometimes a bruise will occur at the puncture site and rarely a blood clot or infection will occur in the vein. You should not donate blood for at least 8 weeks after the study. The total volume of blood collected during this study will be up to 32 tablespoons, including screening laboratories and blood drawn from your vein and/or artery during your PET scan day(s). This amount of blood is safe for study participants.

5. Risks Associated with Use of an Arterial Catheter

Important: If you have a history of a bleeding disorder or are taking medication to thin your blood, you will not be allowed to participate in this study.

Putting in the plastic tube into the artery in the wrist area may cause bruising, and potentially infection. The arterial puncture may also cause spasm or clotting of the artery with a temporary decrease in blood flow, hematoma (swelling of blood within the tissues), bleeding, or inflammation. If this occurs, signs and symptoms will dissipate over time, usually 24 to 72 hours after the event. In rare instances, blocking of the artery, poor healing, or infection at the catheter insertion site may occur. Insertion of arterial catheters for sampling blood may be associated with mild-to-moderate pain or bruising at the puncture site. To minimize these risks, an experienced physician will insert the arterial line and a trained nurse will oversee subject care.

For two days following the placement of the arterial line, you should check your wrist/arm daily. If you experience any excessive pain, tenderness, swelling, redness, drainage, skin color changes, numbness, pins and needles, or decreased strength in the arm that had the catheter, you should immediately call your study team or the PET Center Physicians Dr. David Matuskey at 203-370-1403 (pg) or Dr. Ming-Kai Chen 203-766-4241 (pg) (You will need to punch in your tel. number with area code followed by the, "#," sign).

You may experience a rare allergic reaction to the medicine used to numb your skin prior to placement of the arterial catheter. If you have had a bad reaction to lidocaine, Novocain, or other anesthetic agents used to numb the skin in the past, please tell us about this experience before you go through the arterial line placement. Severe allergic reactions can be life threatening. You will also be asked to abstain from using aspirin and other anti-inflammatory drugs (such as Motrin or Aleve) for 7-10 days before arterial line placement and 7-10 days after arterial line removal.

6. MRI Scan

Risks and Inconveniences

Magnetic resonance (MR) is a technique that uses magnetism and radio waves, not x- rays, to take pictures and measure chemicals of different parts of the body. The United States Food and Drug Administration (FDA) has set guidelines for magnet strength and exposure to radio waves, and we carefully observe those guidelines.

You will be watched closely throughout the MR study. Some people may feel uncomfortable or anxious. If this happens to you, you may ask to stop the study at any time and we will take you out of the MR scanner. On rare

occasions, some people might feel dizzy, get an upset stomach, have a metallic taste or feel tingling sensations or muscle twitches. These sensations usually go away quickly but please tell the research staff if you have them.

There are some risks with an MR study for certain people. If you have a pacemaker or some metal objects inside your body, you may not be in this study because the strong magnets in the MR scanner might harm you. Another risk is the possibility of metal objects being pulled into the magnet and hitting you. To lower this risk, all people involved with the study must remove all metal from their clothing and all metal objects from their pockets. We also ask all people involved with the study to walk through a detector designed to detect metal objects. It is important to know that no metal can be brought into the magnet room at any time. Also, once you are in the magnet, the door to the room will be closed so that no one from outside accidentally goes near the magnet.

We want you to read and answer very carefully the questions on the MR Safety Questionnaire related to your personal safety. Take a moment now to be sure that you have read the MR Safety Questionnaire and be sure to tell us any information you think might be important.

This MR study is for research purposes only and is not in any way a complete health care imaging examination. The scans performed in this study are not designed to find abnormalities. The principal investigator, the lab, the MR technologist, and the Magnetic Resonance Research Center are not qualified to interpret the MR scans and are not responsible for providing a health care evaluation of the images. If a worrisome finding is seen on your scan, a radiologist or another physician will be asked to review the relevant images. Based on his or her recommendation (if any), the principal investigator or consulting physician will contact you, inform you and your parents of the finding, and recommend that you seek medical advice as a precautionary measure. The decision for additional examination or treatment would lie only with you and your physician. The investigators, the consulting physician, the Magnetic Resonance Research Center, and Yale University are not responsible for any examination or treatment that you receive based on these findings. The images collected in this study are not a health care MR exam and for that reason, they will not be made available for health care purposes.

7. Risks associated with pregnancy and breastfeeding.

WOMEN PLEASE NOTE: Since the acceptable levels of radioactivity are lower for pregnant individuals, you may not participate in this study if you are currently pregnant or if you might become pregnant during the study, or you are breastfeeding an infant. You will be tested for pregnancy as part of the routine lab tests. If the test is positive, you will not be included in the study. Before starting the study, we will ask you to avoid becoming pregnant and ask you what precautions you plan to take. If you change your mind about becoming pregnant or how you will avoid becoming pregnant, we ask that you to tell us immediately. You will be given a pregnancy test during screening and on the day of each PET scan.

8. Genetic (DNA and RNA) Testing

Since the results of these genetic tests may allow prediction of risk of illness in some cases, we will keep the results confidential. Only scientists working on this research project will know the results; under certain circumstances the Yale Human Investigation Committee (HIC), may access this information. We will not make any of our lab results available to you, nor will we add them to your medical record. If you want to know your risk for genetic diseases, we will refer you to a genetics counselor. Sometimes, knowledge of genetic information may be a risk of discrimination in insurance coverage, jobs, or education opportunities. 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 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.

9. Allergic Reactions

All drugs have a potential risk of an allergic reaction, which if not treated promptly, could become life threatening. You will be asked to monitor and report the following symptoms: trouble breathing, or swelling of the face, mouth, lips, gums, tongue or neck. Other allergic reactions may include rash, hives, or blisters.

10. Unanticipated Events

Your health and safety will always be the primary concern of the doctors and staff performing the study. In the event of an unanticipated event, all necessary medical action will be taken. Medication might be administered as needed, per the Yale PET Center standard operating procedure for medical emergencies, in order to treat any unanticipated events/complications.

Possible Participation in Future Studies

We would like to be able to contact you in the future to offer you participation in other studies. Giving your permission for the research team to contact you does not obligate you to answer any future questions or to participate in any future research – you always have the right to decline further participation in research. If you agree to participate in another study, we would ask you to read and sign a new consent form. Please initial if you would like to be contacted to participate in other studies.

I agree to be contacted for future research studies: _____.

Participant's Initials

Benefits

There are no direct benefits to you for participating in this study. We hope that your participation will benefit society in the future by helping us to learn more about alcohol addiction.

Economic Considerations

You will be compensated for your participation as follow: $50 for screening, $400 for each PET scan and $50 for each arterial line placement, $50 the MRI scan, $100 per night inpatient stay, and $150 bonus for completing the study. If you participate in the face game and the Card Game, you may earn up to an additional $60. If you arrive for a scheduled PET test day and the procedure is cancelled due to technical difficulties then you will be compensated $50 or more (not to exceed PET scan compensation) and we may reschedule your test day. You may receive the payments in the form of a check several weeks after your participation has ended. You may also receive your payment in a form of cash or pre-paid credit card. Also, all medical evaluations and laboratory tests will be conducted without charge to you. Reasonable transportation and some meal costs may be reimbursed. Please contact the study coordinator prior to your study date to discuss your transportation and meal plans and confirm that they will be appropriate for reimbursement. You are responsible for paying state, federal, or other taxes for the payments you receive for being in this study. Taxes are not withheld from your payments.

Treatment Alternatives/Alternatives

This is not a treatment study. The alternative to participating in this study is to not participate. Alcohol treatment programs will be discussed with you if you are interested. You will be given information about other places where you may receive treatment for alcohol abuse.

Confidentiality and Privacy

Any identifiable information that is obtained in connection with this study will remain confidential and will be disclosed only with your permission or as permitted by U.S. or State law. Examples of information that we are legally required to disclose include abuse of a child or elderly person, or certain reportable diseases. You will be tested for hepatitis and HIV in study, and positive results are reportable to the State of Connecticut. When the results of the research are published or discussed in conferences, no information will be included that would reveal your identity unless your specific consent for this activity is obtained.

By signing this form, you authorize the use and/or disclosure of the information described above for this research study. The purpose for the uses and disclosures you are authorizing is to ensure that the information relating to this research is available to all parties who may need it for research purposes.

We understand that information about you obtained in connection with your health is personal, and we are committed to protecting the privacy of that information. If you decide to be in this study, the researcher will get information that identifies you and your personal health information. This may include information that might directly identify you, such as your name and date of birth and address. This information will be de-identified at the earliest reasonable time after we receive it, meaning we will replace your identifying information with a code that does not directly identify you. The principal investigator will keep a link that identifies you to your coded information, and this link will be kept secure and available only to the PI or selected members of the research team. Any information that can identify you will remain confidential. Additionally, all data is securely stored in locked filing cabinets or on a password-protected computer server**.** De-identified PET subject data will be kept for a minimum of 7 years.

The information about your health that will be collected in this study includes:

- Records about phone calls made as part of this research
- Records about your study visits
- Information obtained during and regarding this research
- Questionnaires

Information about you and your health which might identify you may be used by or given to:

- The U.S. Department of Health and Human Services (DHHS) agencies
- Representatives from Yale University and the Human Investigation Committee (the committee that reviews, approves, and monitors research on human subjects), who are responsible for insuring research compliance. These individuals are required to keep all information confidential.
- Those individuals at Yale who are responsible for the financial oversight of research including billings and payments
- The Principal Investigator (Ansel Hillmer, Ph.D.) and appropriate research staff
- Yale University PET Center where your PET scans will occur.
- Yale University Magnetic Resonance Center where your MRI/MRS scans will occur.
- FDA
- Laboratories and other individuals and organizations that analyze your health information in connection with this study, according to the study plan
- Yale University Radiation Safety Committee (YU RSC)
- Yale New Haven Hospital Radiation Safety Committee (YNHH RSC)

<u>Certificate of Confidentiality</u>

If you decide to take part in this research study, you will be required to give us information about your substance use, mental health, criminal history, and physical health. We will obtain a Certificate of Confidentiality (CoC)

issued by the NIH. Once granted, the researchers can use this Certificate to legally refuse to disclose information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if there is a court subpoena. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below. The protection offered by the CoC does not stop us from voluntarily reporting information about suspected or known sexual, physical, or other abuse of a child or older person, or a participant's threats of violence to self or others. If any member of the research team is given such information, he or she will make a report to the appropriate authorities. Because this research is sponsored by the Department of Health and Human Services through NIDA, staff from that and other DHHS agencies, including the FDA, may review records that identify you only for audit or program evaluation. They cannot report anything that would harm you or other research subjects. Even when a CoC is in place, you and your family members must still continue to actively protect your own privacy. If you voluntarily give your written consent for anyone to receive information about your participation in the research, then we may not use the CoC to withhold this information.

By signing this form, you authorize the use and/or disclosure of the information described above for this research study. The purpose for the uses and disclosures you are authorizing is to ensure that the information relating to this research is available to all parties who may need it for research purposes.

All health care providers subject to HIPAA (Health Insurance Portability and Accountability Act) are required to protect the privacy of your information. The research staff at the Yale School of Medicine, Connecticut Mental Health Center and Yale PET Center is required to comply with HIPAA and to ensure the confidentiality of your information. Some of the individuals or agencies listed above may not be subject to HIPAA and therefore may not be required to provide the same type of confidentiality protection. They could use or disclose your information in ways not mentioned in this form. However to better protect your health information; agreements are in place with these individuals and/or companies that require that they keep your information confidential.

If you decide to be in this study, and you may be visiting the Connecticut Mental Health Center (CMHC) as part of your study procedures, some information about your participation in this research study will become part of your CMHC medical record that identifies you. If you do not already have a medical record at CMHC, one will be made for your visit. The information that will be entered into your medical record may include the following: medical and laboratory records of only those services provided in connection with this study, research study records, and personal information.

You have the right to review and copy your health information in your medical record in accordance with institutional medical records policies

In Case of Injury

If you are injured as a result of your participation in this study, treatment will be provided. You or your insurance carrier will be expected to pay the costs of this treatment. No additional financial compensation for injury or lost wages is available. You do not waive any legal rights by signing this form.

Voluntary Participation and Withdrawal

Participating in this study is voluntary. You are free to choose not to take part in this study. Refusing to participate will involve no penalty or loss of benefits to which you are otherwise entitled (such as your health care outside the study, the payment for your health care, and your health care benefits). However, you will not be able to enroll in this research study and will not receive study procedures as a study participant if you do not allow use of your information as part of this study.

Withdrawing From the Study

If you do become a subject, you are free to stop and withdraw from this study at any time during its course. If you sign this authorization, you may change your mind at any time, but the researchers may continue to use information collected before you changed your mind to complete the research

To withdraw from the study, you can call a member of the research team at any time and tell them that you no longer want to take part. This will cancel any future appointments *(if applicable)*.

The researchers may withdraw you from participating in the research if necessary. The conditions in which you may be withdrawn from participating include a positive pregnancy test for women, positive drug screen, or your non-compliance with the research study.

Withdrawing from the study will involve no penalty or loss of benefits to which you are otherwise entitled. It will not harm your relationship with your own doctors or with *Yale*-New Haven Hospital

Withdrawing Your Authorization to Use and Disclose Your Health Information

You may withdraw or take away your permission to use and disclose your health information at any time. You may withdraw your permission by telling the study staff or by writing to
Ansel Hillmer, Ph.D.
Yale University School of Medicine
2 Church Street South, Suite 314
New Haven CT 06519

If you withdraw your permission, you will not be able to stay in this study.

When you withdraw your permission, no new health information identifying you will be gathered after that date. Information that has already been gathered may still be used and given to others until the end of the research study, as necessary to insure the integrity of the study and/or study oversight.

Questions

We have used some technical terms in this form. Please feel free to ask about anything you don't understand and to consider this research and the consent form carefully – as long as you feel is necessary – before you make a decision.

HIC#: **2000024444**

Authorization and Permission

I have read (or someone has read to me) this form and have decided to participate in the project described above. Its general purposes, the particulars of my involvement and possible hazards and inconveniences have been explained to my satisfaction. My signature also indicates that I have received a copy of this consent form.

By signing this form, I give permission to the researchers to use [and give out] information about me for the purposes described in this form. By refusing to give permission, I understand that I will not be able to be in this research.

Name of Subject:_____

Signature:_____

Date:_____

_____ _____
Signature of Principal Investigator Date

or

_____ _____
Signature of Person Obtaining Consent Date

If you have further questions about this project or if you have a research-related problem, you may contact the Principal Investigator *Ansel Hillmer, Ph.D. 203-737-6969 or David Matuskey, MD at 203-737-6316*. If you would like to talk with someone other than the researchers to discuss problems, concerns, and questions you may have concerning this research, or to discuss your rights as a research subject, you may contact the Yale Human Investigation Committee at (203) 785-4688. If after you have signed this form you have any questions about your privacy rights, please contact the Yale Privacy Officer at 203/436-3650

APPROVED BY THE YALE UNIVERSITY IRB 10/13/2021