COMPOUND AUTHORIZATION/CONSENT FOR PARTICIPATION IN A RESEARCH PROJECT

YALE UNIVERSITY SCHOOL OF MEDICINE
YALE NEW HAVEN HOSPITAL

YALE UNIVERSITY SCHOOL OF MEDICINE
CONNECTICUT MENTAL HEALTH CENTER

YALE UNIVERSITY SCHOOL OF MEDICINE
YALE POSITRON EMISSON TOMOGRAPHY CENTER

YALE UNIVERSITY SCHOOL OF MEDICINE
YALE MAGNETIC RESONANCE RESEARCH CENTER

Study Title: Investigation of cocaine addiction using mGluR5 PET and fMRI

Principal Investigator: Patrick D. Worhunsky, Ph.D.

Funding Source: National Institute on Drug Abuse (NIDA)

Consent for non-treatment seeking individuals with recent cocaine use

Invitation to Participate and Description of Project

You are invited to participate in a research study designed to look at the brain chemical glutamate and how it may be related to the way the brain processes information in people with cocaine use disorder. You have been asked to participate because you regularly use cocaine, are not currently seeking treatment for your cocaine use, you are in good physical and psychiatric health, and you are not having problems with other drugs. If you are eligible, you will be one of approximately 20 individuals with a cocaine use disorder participating in this study.

To decide if 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.

APPROVED BY THE YALE UNIVERSITY IRB 3/29/2022

Description of Procedures

If you agree to participate in this research, you will be asked to undergo a series of procedures that will allow us to 1) measure chemicals in your brain that are related to glutamate and 2) examine your brain activity. You will be asked to undergo medical and psychiatric exams that include blood and urine testing and tests of your cognitive performance. You will also be asked to spend approximately one week at our inpatient research unit while participating in this study. You may also be invited to remain on the unit for approximately one month to repeat brain scans and cognitive testing.

This study takes place at several locations at Yale University. The Clinical Neuroscience Research Unit (CNRU) is located on the 3rd floor of the Connecticut Mental Health Center (CMHC) and is a 13-bed, full-service inpatient psychiatric research unit where visitors are restricted and access to drugs is prevented. The Hospital Research Unit (HRU) is located on the 10th floor of the Yale New Haven Hospital (YNHH) and is equipped with medical, nursing, and laboratory services and suites for outpatient research studies. The Yale PET Center and Magnetic Resonance Research Center (MRRC) are located at the Yale School of Medicine and host state-of-the-art molecular and magnetic imaging facilities.

Screening and Evaluation:

If you received this consent form, it is because you already completed initial screening by telephone, or because you are participating in a similar study being conducted by the research team and are likely eligible to participate in this study. Before being admitted to participate in the study, you may be asked take part in an additional screening phase that will include an in person visit at the CNRU in order to determine your eligibility.

The screening phase will take approximately 2 hours and will include medical and psychiatric history, specialized diagnostic interviews to help us better understand your cocaine use patterns, how you use cocaine (e.g., snorting, smoking, IV), and other drug use history, physical and neurological exams, a study of the electrical activity in your heart (i.e., electrocardiogram or ECG), routine laboratory studies of blood (less than 4 tablespoons) and urine, including a toxicology screening. Portions of the screening (i.e., psychiatric interview and related questioning) may be conducted remotely over the phone or using tele-health platforms (e.g. video chat). The medical exam will be conducted at the CNRU. If you test positive for drug use other than cocaine, you may not be allowed to participate in the study. Women of childbearing age will also have a blood pregnancy test. If your pregnancy test result is positive, you may not participate in this study. The results of these tests will be discussed with you.

There will be no charge for these tests or interviews. If you qualify for the study and if you decide (i.e., consent) to participate, you will then be asked to participate further in the study. Lastly, we will ask you for a release of information so that study staff may contact your primary care doctor. If you do not have a primary care doctor, we will ask you for the name of a family member or close friend. The purpose of this release of information is to help confirm study eligibility and ensure it's safe for you to participate. Under no circumstances will the specifics of your study participation be revealed to your primary care doctor or your family member (e.g.,

they will not be informed that you're participating in a study for individuals who have a cocaine use disorder).

If you are participating in a similar study being conducted by the research team, you will already have completed this evaluation. By agreeing to participate in this study, you are authorizing the research team to share the data collected during that evaluation for use in this study as well. You may also be asked to repeat some of these procedures (e.g., urine drug screening).

Admission to the Clinical Neuroscience Research Unit (CNRU):

If you are eligible and would like to participate, you will be admitted to the CNRU. During Day 1 of your admission, you will meet with the medical and nursing staff who will complete additional interviews and a physical exam. If your screening visit was conducted more than 7 days prior to admission, staff will repeat your laboratory work (i.e. blood and urine tests). A few days (usually 2-4 days) after your admission, you will complete a PET scan and MRI scan (described below). You will return to the CNRU following each procedure.

You will be discharged from the CNRU upon completion of study procedures (unless your participation in another study has not been completed). If you agree to complete the initial set of study procedures, your stay at the CNRU may be up to 10 days (typically 5-8). If you are invited and agree to repeat the study procedures approximately 1-4 weeks later, you will stay at the CNRU until those procedures are completed (typically an additional 10-20 days).

Interviews, Questionnaires, and Cognitive Testing:

We will ask you questions about several topics including your cocaine use, how strong your desire for it is, your general functioning, history of medical problems, history of psychiatric problems, history of other drug use, and social aspects of your life such as years of education completed, whether you have legal problems or not, presence of supportive persons in your life, etc. Most of the questionnaires on cocaine use, medical problems, psychiatric/drug use, and social aspects of your life will be completed during the screening visit and could be repeated during the admission. Also at admission, we will also ask you to complete a brief series of questionnaires about your behavior, thoughts, and tendencies in general and as related to your drug use. You will also be asked to complete a brief series of cognitive tasks (e.g., to assess your memory and reasoning abilities) on a computer. We expect it may take about two hours to complete these questionnaires and computer tasks.

Positron Emission Tomography (PET) scan:

You will be asked to participate in a PET scanning session that will be conducted at the Yale PET Center in New Haven. PET scanning involves the use of a 'radiotracer', which is a small amount of a drug that is labeled with a very small amount of a radioactive substance. The radiotracer drug binds to the receptors in the brain and the radioactivity can be detected by a special camera in the PET scanner. In this study, you will receive the radiotracer [fluorine-18]F-PEB, a drug which is limited by Federal Law for research use only. This radiotracer binds to a receptor called the metabotropic glutamate receptor type-5 (mGluR5), and we will use the

information from the PET scan to measure the location and concentration of these receptors in your brain.

You may be asked to fast prior to the PET scan. On the day of your PET scan, a trained nurse or Certified Nuclear Medicine Technologist will place one or two plastic catheters (tubes) in your arms (one for the radiotracer injection and one to take venous blood samples, if necessary).
An experienced health care provider may 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. Thanks to an arterial catheter, we can draw blood quickly, more than once, and without causing you pain. Here is what happens when an arterial line is placed:

- We will clean the skin with betadine solution (contains iodine). It will reduce the risk of an infection.
- We will numb your skin 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. It would be similar to the pain you feel with an IV.
- We will flush the catheter often during your scan with saline (a salt solution) to make sure it does not clog.
- After we remove the catheter, we will apply pressure to your skin for a minimum of 15 minutes to prevent bleeding under the skin.
- We will apply a pressure dressing (coban) and clear dressing (tegaderm). You will need to keep it clean and dry. Do not exercise too much and do not lift heavy objects weighing more than 5 pounds. Avoid making the same movements for 48 hours.
- You may remove the pressure dressing at bedtime and the clear dressing after 48 hours, but do not put 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.

During the PET scanning session, the radiotracer will be injected into the tube in your vein. You may not feel anything as a result the drug; however, you may briefly experience nausea shortly after it is administered. You will then be asked to lie very still on a table for up to 2 hours while the scanner camera collects information.

After the PET scan, you will be asked to drink several glasses of water to help wash out the radiotracer, and a light meal may also be provided. You may be asked to return to the CNRU following the PET scan if you have not completed all other study procedures. You will also be provided with a telephone number you can call any time after the study if you need assistance for problems related to the study procedures.

Occasionally there may be problems making the radiotracer, such that there is not enough to perform the PET scan. If this happens, a member of the research team will discuss with you the options for participating in the study again within a few days or weeks.

<u>Magnetic Resonance Imaging (MRI) scan:</u>

You will be asked to participate in a MRI scanning session that will be conducted at the Yale Magnetic Resonance Research Center in New Haven. MRI scans are painless, do not involve the use of radiation, and are used routinely to diagnose neurological problems. You must inform the research staff if you have any metal (for example, shrapnel or surgical prostheses) in your body because having an MRI could be harmful. Some people feel mildly anxious in the scanner, and if it is too difficult for you to be in it, you may withdraw at any time. The scans will take place in New Haven, at the Yale MRI Research Center. The scan will be conducted by an MRI technologist, and a member of the research team will accompany you and stay for the MRI session.

During the MRI session, you will lie on your back on a comfortable mattress, which is then slid into a large tube until your head and the upper part of your body are inside the tube. Your head will be held still in a cushioned head rest, and you will wear earplugs to reduce the level of noise. You will also be wearing headphones to help communicate with the research staff and possibly additional devices to measure things such as your breathing and heart rate.

The MRI session may last up to 2 hours, during which you will be asked to lie very still. We will tell you when we begin taking pictures of your brain and you will notice a series of knocking noises made by the machine when the pictures start. Each series of pictures may last up to 10 minutes, and we may ask you some questions about how you are feeling in between series.

We will take some pictures while you are simply resting with your eyes open, and some pictures while you are performing a simple computer task. The computer task will be used to examine your brain activity while you push a button in response to letters or shapes displayed on a projection screen that you will be able to see in the MRI scanner using mirrors. For example, the letters ‘X’ and ‘K’ will be quickly presented one at a time, and you will be asked to push a button only when you see an X; and try not to push the button when you see a K. At times during the task, you may earn money depending on how well you perform the task (i.e., pushing and/or not pushing the button at the right times). We will give you the opportunity to practice this task outside the scanner before the MRI session. Following the MRI scan you may be asked to return to the CNRU if you have not completed all other study procedures.

Study timeline and duration

This study will take place over approximately one week. Following admission to the CNRU, you will complete the interviews, questionnaires, and cognitive testing at the CNRU and/or at the PET/MRI centers. A few days later you will complete the PET and MRI scans. When possible, we will schedule your PET and MRI scans on the same day, but they may also take place on separate days. In these instances, the scans will not be more than a few days apart. When you are not participating in the PET and MRI scans you will be asked to remain at the CNRU. Once you complete all the procedures for this study, you will be discharged from the CNRU.

Optional extended study:

You may be invited to participate in an optional extension of this study that would occur after you have successfully completed the procedures of the main study described above. The study involves remaining on the CNRU for an additional month (typically 10-20 days) before completing a second set of PET and MRI scans and cognitive tests. Your participation in the study extension is optional and you may participate in the main study without participating in the longer study.

Risks and Inconveniences

There are some risks associated with the procedures you will be asked to complete during this research study. It is important you fully understand these risks before you decide to take part in this study. A member of the research staff will discuss these risks with you, including the measures we will take to reduce these risks. You are encouraged to ask them any questions you may have regarding the procedures and their risks to help you decide whether to take part in this study. Please note that even if you do decide to participate, you may change your mind at any time during the study.

Risks Associated with Interviews, Questionnaires, and Cognitive Testing:

There are no significant risks known to be associated with the completion of the interviews, questionnaires, and cognitive testing. However, you may become tired and may feel uncomfortable/ashamed disclosing some of this information. The staff who will conduct the interviews have received training in empathetic/non-judgmental techniques, and you will be allowed to take a break for as long as is necessary before proceeding if you become tired or uncomfortable.

Since some of the data collected (e.g., history of drug use behavior) is private in nature and may have legal implications, risks related to loss of confidentiality also exist. The staff responsible for the data collection will explain to you how we handle confidential information. Any identifiable information that is obtained during this study will remain confidential and will be disclosed only with your permission or in specific cases. Examples of information that we would involuntarily disclose include abuse of a child or elderly person, or certain reportable diseases. All the information obtained in this study is stored in locked cabinets or on password protected computers. Only the medical personnel and the research staff involved in this study will have access to this information. When the results of the research are published or discussed in conferences, no information will be included that would reveal your identity.

Risks Associated with Blood Draws and Intravenous Lines:

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. Blood draws are done by expert personnel who will follow aseptic/antiseptic standards and who will stop the procedure after two failed attempts.

Blood draws have also been associated with feeling lightheaded or fainting in some people. You will be excluded from this study if you have a history of fainting during blood draws. Including screening, any possible admission laboratories and the PET scan, the total volume of blood collected during this study will be up to 16 tablespoons, which is half of the amount taken in a standard 1-pint blood donation. You should not donate blood for at least 8 weeks after the study.

Risks Associated with Arterial Lines:

Important: You cannot take part in the study if you have ever had a bleeding disorder or are taking medication to thin your blood.

The insertion of the arterial line may be painful and you can get bruises. The arterial puncture may cause a spasm, a temporary tightening (constriction) of the muscles in the wall of the artery. You may get a clot and your blood flow will slow down for a little while. You can get a hematoma (swelling of blood within the tissues). The site can bleed or get inflamed (become red, swollen, hot, and painful). These feelings will go away after some time, usually 24 to 72 hours after the procedure. Rarely, you may experience blocking of the artery or nerve damage to the insertion site. The insertion site may not heal as fast or you may get infection. This is why an experienced health care provider will insert the arterial line and a trained nurse will look after for you.

Check your wrist and arm every day for two days after the study visit with the arterial line. Call right away your study team or the PET Center Physicians, Dr. David Matuskey at 203-370-1403 (voice mail pager) or Dr. Ming-Kai Chen 203-675-0120 (cell), if you notice any of the following:

• You feel a lot of pain
• Your wrist or arm is tender, swollen, or red
• You see some blood or other fluids coming out of the injection site
• The color of your skin changes
• Your arms feel numb
• You feel pins and needles in your arm
• Your arm that had the catheter does not feel as strong

Tell us if you have had a bad reaction to lidocaine, novocain, or other drugs used to numb the skin in the past. You may experience a rare allergic reaction to the medicine used to numb your skin prior to placement of the arterial catheter. Severe allergic reactions can be life threatening. Some things that happen during an allergic reaction are:
• rash
• hives
• having a hard time breathing
• wheezing when you breathe
• sudden drop in blood pressure
• swelling around the face, mouth, lips, tongue, throat, or eyes
• fast pulse
• sweating

If you have any of the above allergy related side effects or symptoms, your study doctor will assess you and treat these symptoms.

Do not take aspirin and other anti-inflammatory drugs (such as Motrin or Aleve) for 7-10 days before arterial line placement and 7-10 days after the study visit.

Risks associated with cocaine withdrawal:

Upon admission to the CNRU, it is possible you may experience withdrawal. Unlike some substances of abuse (e.g. alcohol, benzodiazepines), cocaine withdrawal does not typically cause physiological changes that are life threatening. Cocaine-withdrawal symptoms may include depressed mood, lack of motivation, fatigue, sleep changes, increased appetite, and suicidal ideation. The medical and nursing staff on the inpatient unit is trained to assess for withdrawal symptoms and will be available 24 hours a day should you experience any symptoms of withdrawal. Depending on the severity of any potential symptoms, you will have the opportunity of receiving any appropriate treatment. If you are still experiencing withdrawal-related distress at the time of study completion, you will have the option of remaining on the inpatient unit to receive appropriate monitoring and treatment.

Although we are unaware of research situations where this has happened, if your emotional reaction to cocaine withdrawal puts your or other individuals' lives at risk, a physician would be obligated by law to keep you in the hospital until yours and others' safety could be assured.

Even if you are not currently interested in drug treatment, if you decide during the study to request treatment for your drug use, we are prepared and ready to refer you for treatment the moment you request it. The staff will give you information about drug treatment opportunities if you wish to take advantage of these in the future.

Risk Associated with Radiation

This research study involves exposure to radiation. The radiation you will receive in this study is from an injection of the radiotracer [fluorine-18]FPEB and transmission scans that will be used during PET imaging. This radiation exposure is **not** necessary for your medical care and is for research purposes only. Although each organ will receive a different dose, the amount of radiation exposure you will receive from one scan in this study is equal to a uniform whole-body exposure of 0.57 rem. If you agree to participate in the extended study or are asked to complete a second PET scan for technical problems, the total amount of exposure would be 1.14 rem for the two scans. In the unexpected case where you may be asked to undergo third PET scan, you would be exposed to an additional dose of radiation, totaling 1.71 rem for three injections. This calculated value is known as the “effective dose” and is used to relate the dose received by each organ to a single value. This amount of radiation is well below the dose guidelines established by the federal government (i.e., not more than 5 rem per year) and adhered to by the Yale-New Haven Hospital Radiation Safety Committee for research subjects. To give you an idea about how much radiation you will get, we will make a comparison with an every-day situation. Everyone receives a small amount of unavoidable

radiation each year. Some of this radiation comes from space and some from naturally-occurring radioactive forms of water and minerals. Each PET scan as part of this research gives your body the equivalent of about 2 extra years' worth of this natural radiation. That means two scans will be equivalent to 4 years, and three scans would be equivalent to 6 years' worth of this natural radiation.

Risks Associated with Magnetic Resonance Imaging (MRI):

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, we require that all people involved with the study 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 healthcare examination of the brain. 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 healthcare 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 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 healthcare MR exam and for that reason, they will not be made available for healthcare purposes.

If, during the screening for MRI, it is determined you may have metal in your body, we may require an X-ray to rule this out. If so, the risk of undergoing an X-ray are minimal as the radiation exposure is low and is no different than an X-ray you would receive from your dentist or doctor.

There are no additional risks associated with completing more than one MRI scan should you be asked to complete additional scans because of technical problems or if you agree to participate in the extended study.

There may be additional risks related to this study that are not yet known. You will be told of any new findings that may affect your decision to participate in the research.

Benefits

This research is not intended to benefit you directly. However, you will receive a thorough medical and psychiatric evaluation at no cost to you. The results obtained from this study will contribute to the knowledge of the medical and scientific community. This study may help inform future research toward better treatments to help people with addictive disorders.

Economic Considerations

You will not be responsible for payment of any study related procedures. You will be compensated for your participation for each procedure as follows:

Procedure	Amount
Screening interviews/exams (i.e., to determine eligibility)	$25
Baseline questionnaires, cognitive testing, and exams	$25
PET scanning	
Arrival and setup (including IV and/or arterial line placement)	$50
Administration of radiotracer and PET scan*	$350
MRI scanning	
Arrival and setup	$15
MRI scan*	$65
Task-performance earnings	up to $20
Inpatient stay (up to 10 days)	$100
Extended-study questionnaires, cognitive testing, and exams	$25
Extended-study inpatient stay (up to one additional month)	$200
* In rare cases of technical problems or early termination (either voluntarily or at the discretion of study staff) once procedures have been initiated, you will receive full compensation for that procedure.	

Thus, the total possible compensation for participating in the initial study is $650. If you are invited and complete the extended study, repeating questionnaires, cognitive testing, PET and MRI scans, and remain on the unit for up to an additional month, you would be compensated an additional $725 (for a total of $1375). You may also be reimbursed for travel expenses (please provide receipts for trains, buses, taxis, parking, etc.). You are free to stop the study at any time; however, if you choose to withdraw, you will be paid only for the parts of the study that you completed.

Payments will typically be made via a pre-paid debit card in loadable increments after completing individual study procedures. These pre-paid debit cards are provided by the Bank of America, and we will need to share with them with your name, address, and telephone number to order your debit card. The card may be mailed to you or provided in person. Reimbursements may also be made in the form of small cash payments (i.e., for the outpatient appointments) or checks.

According to the rules of the Internal Revenue Service (IRS), payments that are made to you as a result of your participation in a study may be considered taxable income. 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.

Alternatives

The purpose of this study is not diagnosing, preventing, or providing a treatment for cocaine use disorders. You have the alternative to decline participation in the study. Declining to participate has no effect on any relationship that you may have with your healthcare providers, the Connecticut Mental Health Center or the Yale New Haven Hospital. You should not feel pressured to participate in this. If you want formal treatment for cocaine dependence, please let us know and we may be able to help with the referral.

Confidentiality and Privacy

If you decide to take part in this research study, you will be required to give us information about your substance use. We have obtained a Certificate of Confidentiality (CoC) issued by the National Institutes of Health (NIH). 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. When the CoC is obtained, we will inform all active study participants.

Because this research is sponsored by the Department of Health and Human Services through the National Institute on Drug Abuse (NIDA), staff from that and other DHHS agencies 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.

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. Any identifying information will be stored in a locked cabinet. All research data will be coded with a participant number in place of any identifying information, and stored separately in locked cabinets or on password protected computers. 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.

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

If you decide to be in this study, you will 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: name, date of birth, date of admission to the CNRU, date of experiments at the YNHH HRU, date of discharge from the CNRU, phone number, address, medical history, individual and family history of psychiatric problems, and substance abuse history. One of the instruments used to assess substance abuse history will include questions related to legal problems.

As a participant in a clinical research study involving the Yale-New Haven Hospital (YNHH) Research Unit (HRU), it is important for you to know that if you do not already have a medical record at YNHH, one will be made for your admission. In addition, you need to know that if you have ever been a patient at YNHH at any time, your previous medical records of other visits or admissions will become available to the researchers and to the staff of the HRU when information regarding your participation in this study is added into the medical record.

These medical records, while not protected by the Certificate of Confidentiality issued by the NIH, are covered under federal HIPAA laws described further below.

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, birthday 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 (PI) 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. All your information will be kept on a study record in a locked filing cabinet, in a locked office. Any electronic data is stored on a secure server or in password protected computer files. The research team will only give this coded information to others to carry out this research study. The link to your personal information will be kept for up to five years, after which time the link will be destroyed and the data will become anonymous. The data will be kept in this anonymous form indefinitely.

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

- Research study records
- Medical and laboratory records of only those services provided in connection with this study
- The entire research record and any medical records held by Connecticut Mental Health Center and the Yale New Haven Hospital created from the date signed below to completion of all research procedures included in this form.
- The following information:
  - Records about phone calls made as part of this research
  - Records about your study visits
  - Information obtained during this research regarding:
    - Hepatitis infection
    - Other reportable infectious diseases
    - Physical exams
    - Laboratory, x-ray, and other test results
    - Diaries and questionnaires
    - The diagnosis and treatment of a mental health condition
    - Use of illegal drugs or the study of illegal behavior
  - Records about any study drug you received

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, the Human Investigation Committee (the committee that reviews, approves, and monitors research on human subjects), who are responsible for ensuring 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, Patrick D. Worhunsky Ph.D.
- The U.S. Food and Drug Administration (FDA). This is done so that the FDA can review information about the drug product involved in this research. The information may also be used to meet the reporting requirements of drug regulatory agencies.
- The study sponsor
- Governmental agencies to whom certain diseases (reportable diseases) must be reported
- Health care providers who provide services to you in connection with this study.
- Laboratories and other individuals and organizations that analyze your health information in connection with this study, according to the study plan.
- Co-Investigators and other investigators
- Study Coordinator and Members of the Research Team

- Data and Safety Monitoring Boards and others authorized to monitor the conduct of the study

The data we collect from you may be shared across other protocols the Principal Investigator is running. Similarly, if you are participating in another study being conducted by the research team, any data collected may be shared between studies. The data will be coded so your personal information cannot be determined.

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, Yale-New Haven Hospital, and the Connecticut Mental Health Center are 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.

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

This authorization to use and disclose your health information collected during your participation in this study will never expire.

In Case of Injury

If you are injured as a result of your participation in this study, seek treatment and contact the study doctor as soon as you are able.

Yale School of Medicine, Yale-New Haven Hospital, and the Connecticut Mental Health Center do not provide funds for the treatment of research-related 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 give up any of your 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.

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.

The researchers may withdraw you from participating in the research if necessary. Reasons why you could be withdrawn from the study include non-compliance with study procedures or if the medical/nursing or research staff determine it would be in your best interest to cease study procedures.

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, Yale-New Haven Hospital, the Connecticut Mental Health Center.

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 the principal investigator: Patrick D. Worhunsky Ph.D.; Yale University Department of Psychiatry; 1 Church Street, Room 730, New Haven, CT, 06510.

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 ensure 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 please consider this research and the consent form carefully – for as long as you feel is necessary – before you make a decision.

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.

Please initial below if applicable:

_____ I agree to participate in the extended study that involves remaining on the research unit for up an additional month to repeat study procedures.

_____ I am participating in other research being conducted by the study team and authorize the release of data collected during that research for use in this study.

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 after you have signed this form you have any questions about your privacy rights, please contact the Yale Privacy Officer at (203) 432-5919.

If you have further questions about this project or if you have a research-related problem, you may contact the Principal Investigator, Dr. Patrick D. Worhunsky at (203) 737-2668. 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.

Research Authorization/Permission to Contact for Future Research

I give permission for Yale research staff to approach me or to contact me in the future regarding other research studies I may be eligible for. (Please initial below your preference).

_____ Yes

_____ No

I understand that by agreeing to or declining this option in no way affects my eligibility for the present study.

_____
Name of Subject

_____ _____
Signature Date

_____ _____
Signature of PI or Person Obtaining Consent Date