RESEARCH PARTICIPANT INFORMATION AND CONSENT FORM
Cocaine Dependent Subjects

TITLE: 5-HT2AR:5HT2CR Balance in Brain Connectivity in Cocaine Dependence

VCU IRB PROTOCOL NUMBER: HM15289

INVESTIGATOR: Dr. F. Gerard Moeller

Study Sponsor: National Institute on Drug Abuse (NIDA)

If any information contained in this consent form is not clear, please ask the study doctor or the study staff to explain any information that you do not fully understand. You may take home an unsigned copy of this consent form to think about or discuss with family or friends before making your decision.

INVITATION TO TAKE PART

You are invited to take part in a project called "5-HT2AR:5HT2CR Balance in Brain Connectivity in Cocaine Dependence" conducted by Dr. F. Gerard Moeller, of Virginia Commonwealth University (VCU) School of Medicine. For this research project, he will be called the Principal Investigator or PI.

We are inviting you to take part in this research study as a person who has been using cocaine to compare your reactions on computer tasks and brain scans with other people who do not use cocaine. We ask you to read this form. If you find that the research and what we ask you to do is acceptable, you may sign the form and begin the screening process to find out if you are able to take part in this study.

This research project has been reviewed by the Office of Research Subjects Protection of Virginia Commonwealth University as protocol no. HM 15289.

PURPOSE OF THE STUDY

The main purpose of this study is to find out how the brain reacts to the medication called mirtazapine and how this is related to cocaine addiction. Mirtazapine is a medicine that is approved by the FDA for the treatment of depression. More information about how the brain reacts to mirtazapine may be helpful to develop new treatments for cocaine addiction. Measures of your memory and reaction time while you are in a magnetic resonance imaging (MRI) scanner will be tested to find out whether there are differences in brain scans between people who have been using drugs and people who do not use drugs.

This is a local study. The study will enroll a total of 400 people all at VCU.

PROCEDURES

You have already completed the screening procedure as per the protocol (HM 20000294, PRE-SCREEN, Keyser-Marcus (PI)) and have qualified to participate in this study. In this study, you will be asked about your possible drug or alcohol use and will also undergo some computer tests that measure attention and reaction time. In addition you will be required to undergo two MRI scans.

If you have ever had any pieces of metal enter your eye, then MRI may be potentially dangerous, and you should tell the study staff about this right away. Also, if you have a pacemaker or other metal such as bullet pieces in your body you need to tell the study staff as these may be dangerous as well. You will also be asked to fill out a standard metal screening check list to make sure that you do not have any metal in your body or conditions that might be dangerous for MRI. If you drink caffeinated beverages we ask that you abstain from these beverages prior to the scan.

You will begin with a baseline period that will last 1 week. During one of your baseline visits, you will have a practice MRI session that will take place in a mock MRI (which is not a real MRI machine) to allow you to practice the same tasks that you will do during the real MRI scan. The total time of the practice MRI session will be around 2 hours. After the practice MRI session is completed, you will have a real MRI session. Each real MRI scanning session consists of two 40-minute periods in which you will be inside the scanner. These periods are separated by a 10-minute bathroom break. While you are in the MRI scanner you will be asked to look at a screen and press some buttons in response to images on the screen, and you will be asked to perform tasks that measure decision-making, impulsivity, and attention. You will be paid $5 per task. As an incentive to do the tasks as accurately as possible, you may earn an additional sum of money that will be a reward based on your accuracy on each task (up to an additional sum of about $5 more per task). During the practice and the real scanning sessions, we will monitor your blood pressure with an automatic blood pressure cuff that is placed on your arm and your pulse with a small clip that is placed on your finger. The total time for the real MRI session, including preparation time outside the scanner, time in the scanner, and testing outside the scanner will take about 8 hours to complete.

For the real MRI session, you will arrive at our building at 7:30 a.m. to have a repeat ECG (heart test) to make sure that there are no medically dangerous changes in your ECG results. You will fill out several forms that ask questions about any problems you may be having. You will also receive one of the following study drugs to take by mouth before you go inside the scanner: Mirtazapine (15 mg) (also called Remeron); or Placebo (inactive pill). The drug you receive first will be assigned randomly, that means the decision is made "by chance", like the flip of a coin. Using the active study drug and placebo will test whether the medication reacts differently with the brain. You will also be asked to provide a urine sample for complete drug screen analysis, and a breath sample to screen for alcohol. If you are a woman, you will be asked to provide a urine sample for a pregnancy test. After you take the study medication, you will be monitored for up to 8 hours before being released. If there are any technical problems with the MRI scan during the baseline period, then you may be asked to provide an additional MRI session just like the first one.

One week after your first MRI session, you will have another MRI scanning session just like the first time. If there are any technical problems with this MRI scan, then you may be asked to provide an additional MRI session just like the previous one.

There will be times during the study when the research staff will need to contact you by telephone (for example, to reschedule an appointment).

If you need assistance with transportation to and from any of your clinic visits, please notify study staff in advance so they can make transportation arrangements for you (at no cost to you).

TIME COMMITMENT

The study elements and time are:

1. Baseline period (mock MRI scan, real MRI scan, computer tasks,) includes 3 visits per week for 1 week (about 12 hours total time for the baseline period)
2. Follow up MRI scan (real MRI scan, plus preparation time outside the scanner and testing outside the scanner, for total time of about 8 hours)

The total maximum number of hours is about 20 hours.

RISKS AND DISCOMFORTS

There are two kinds of risks; one is physical and the other is psychological (mental). You may have some pain and a bruise when the blood is drawn. There is also a slight chance of infection. Mirtazapine possible side effects include nausea, dry mouth, constipation, dizziness and feeling drowsy. The drowsiness associated with mirtazapine may impair a person's ability to drive, use machines, or perform hazardous tasks that require alertness. The drowsiness can be worse if you combine this medication with alcohol.

If you have metal in your body, such as a pacemaker, metal shavings, bullet pieces, or surgical clips, the MRI scan can cause injury to you. You will be carefully screened to eliminate this risk by a history, physical examination, and completing a standard MRI screening form.

Possible side effects will be monitored carefully. This will be done through a form that you fill out when you attend study visits.

The possible psychological effects are that mirtazapine, similar to other antidepressant medicines, can increase thoughts of death and suicide in people who are depressed. We will ask you about these thoughts during the study and you should tell us if you have these thoughts. You may experience the potential risk of feeling anxious or nervous due to being confined in a small, enclosed space such as the MRI scanner tube. You may become tired or bored during the memory testing.

Special note to women: Additional risks to an unborn child may exist with study drugs and with cocaine use. Therefore, pregnancy testing will be done every week during the study. In addition, pregnancy testing will be done before each MRI scan because of possible unknown risks to the fetus from MRI scanning. Women of childbearing potential must not be pregnant or breast feeding, and if sexually active, must be using acceptable methods of birth control to be enrolled in the study. Acceptable methods include:

a) Oral contraceptives
b) Barrier plus spermicide
c) Hormonal or surgical implants

Risks associated with having an ECG include: discomfort in learning of a potential health condition and the potential for hair removal where the ECG lead is applied to the chest. Some individuals who have allergies to tape adhesive may have a mild allergic reaction to the ECG electrode adhesive.

You will be asked to leave the study if you do not complete the requirements and fulfill your responsibilities to attend, give urine or breath samples, or complete forms. It may also be necessary for you to leave this study if you have other problems or illness during the study. If this happens, appropriate referrals will be given.

USE AND DISCLOSURE OF PROTECTED HEALTH INFORMATION

Authority to Request Protected Health Information

The following people and/or groups may request my Protected Health Information:

- Principal Investigator and Research Staff
- Research Collaborators
- Data Safety Monitoring Boards
- Others as Required by Law
- Study Sponsor
- Institutional Review Boards
- Government/Health Agencies

Authority to Release Protected Health Information

The VCU Health System (VCUHS) may release the information identified in this authorization from my medical records and provide this information to:

- Health Care Providers at the VCUHS
- Study Sponsor
- Data Coordinators
- Data Safety Monitoring Boards
- Others as Required by Law
- Principal Investigator and Research Staff
- Research Collaborators
- Institutional Review Boards
- Government/Health Agencies

Once your health information has been disclosed to anyone outside of this study, the information may no longer be protected under this authorization.

Type of Information that may be Released

The following types of information may be used for the conduct of this research:

■ Complete health record

Right to Revoke Authorization and Re-disclosure

You may change your mind and revoke (take back) the right to use your protected health information at any time. Even if you revoke this Authorization, the researchers may still use or disclose health information they have already collected about you for this study. If you revoke this Authorization you may no longer be allowed to participate in the research study. To revoke this Authorization, you must write to the Principal Investigator.

BENEFITS TO YOU AND OTHERS

The benefit you can expect as a result of taking part in this study is information regarding your physical and mental health status learned during the screening procedures.

It is also possible that information will be learned about how mirtazapine affects the brain, which may help develop new treatments for drug abuse in the future.

COSTS

All medical tests, brain scans, and study drug will be offered at no cost to you. If you receive a bill that you believe is related to your taking part in this research study, please contact Dr. F. Gerard Moeller at (804) 828-3793. with questions.

PAYMENT FOR PARTICIPATION

You will be compensated $20 for the practice scan, additional $5 for each task completed (up to $15) and earn bonus money based on task performance (up to $15). You will receive

$75 for each scanning session, an additional $5 for each task completed (up to $15) and earn bonus money based on task performance while inside the scanner (up to $15). You will receive $30 for each behavioral task session and earn bonus money based on task performance (up to $10). In addition a study completion bonus of $75 will be provided. Participants traveling more than 20 miles to the study site will be reimbursed for their travel expenses (mileage only at the current VCU rate). Compensation will be provided in the form of vouchers, which can be exchanged for cash or check (to be mailed to you), based on your preference. A counselor from the research center will meet with you to jointly decide upon how to spend the earnings in a manner that is consistent with individual treatment goals of increasing drug-free pro-social activities.

In addition, we can provide transportation to and from your clinic visits, if needed, at no cost to you.

If you complete the entire two-week study as per specified procedures, you will receive a maximum amount of $415 dollars. Total payments within one calendar year that exceed $600 will require the University to annually report these payments to the IRS and you. This may require you to claim the money you receive for participation in this study as taxable income. VCU is required by federal law to collect your social security number. Your social security number will be kept confidential and will only be used to process payment.

If you receive payment for taking part in this study please be informed that you will be asked to complete a W-9 form that will be forwarded to the accounting department as a requirement by the Internal Revenue Service. You will also be issued a 1099-Misc form from this study for tax reporting purposes.

ALTERNATIVE TREATMENT

This study is not intended to treat any medical condition. The alternative to taking part in this study is to not take part.

CONFIDENTIALITY

To help us protect your privacy, we have obtained a Certificate of Confidentiality from the National Institutes of Health. With this Certificate, the researchers cannot be forced to give out information that would identify you, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings. However, if we learn about abuse of a child or elderly person or that you intend to harm yourself or someone else, or about certain communicable diseases, we will report that to the proper authorities. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained. The Certificate cannot be used to resist a demand for information from employees of the United States Government that is used for auditing or evaluation of federally funded projects or for information that must be given in order to meet the requirements of the federal Food and Drug Administration (FDA). You should understand that a Certificate of Confidentiality does not prevent you or a member of your family from voluntarily giving information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the certificate to withhold the information.

No one outside the research staff may call and get information about you. If you decide you would like copies of your medical test results, you may sign a

form to release information to you or your physician. Only specific medical information, not research information, will be released.

You will not be personally identified in any reports or publications that may result from this study. Any personal information about you that is gathered during this study will remain confidential to every extent of the law. A special number will be used to identify you in the study and only the investigator and research staff will know your name.

You should know that research data or (medical information if applicable) about you may be reviewed or copied by Virginia Commonwealth University.

Although results of this research may be presented at meetings or in publications, identifiable personal information pertaining to participants will not be disclosed.

GENETIC TESTING

Background information: During this study, if you have not already provided an additional blood sample for genetic testing (as part of the intake screening conducted for HM 20000294, PRE-SCREEN, Keyser-Marcus (PI)), we will draw additional blood (about 2 tablespoons) to test your DNA. This sample will be used to do extra studies to learn more about the biology of drug or alcohol use. DNA is genetic material that we inherit from our parents. This material is made up of elements called genes that may affect our behavior and biology. DNA can be obtained from blood to study the relationship between specific genes and certain medical conditions, including mood disorders and drug dependence.

The research involves genetic testing. Genetic testing may reveal information about the likelihood that a person or his or her relatives may develop certain diseases. Genetic testing may reveal information about who is related to whom. If known to employers or insurance companies, the results of genetic testing might affect a person's ability to obtain a job or health or life insurance.

Future studies:

1. My blood/tissue samples may be stored and used for future research about drug or alcohol use.

   YES_____ NO_____
   initial initial

2. My blood/tissue samples may be stored and used for future research about other health problems (for example, heart disease, osteoporosis, depression, diabetes, etc.)

   YES_____ NO_____
   initial initial

Future contact concerning genetic testing results: Genetic testing in this study may help us understand the way the brain works that can lead to drug or alcohol use. There is no plan to test for genes that are known to cause cancer or other illnesses, so you will not be given the results of the genetic testing.

Withdrawal of genetic testing consent: In the future if you decide that you do not want us to use your DNA for genetic research you can tell us this and we will remove your DNA from our research samples for future studies.

Confidentiality: All genetic testing in this study is being done for research purposes only and is confidential. We have a certificate of confidentiality from the National Institute on Drug Abuse to help keep all research information in this study confidential.

COMPENSATION FOR INJURY or ILLNESS

If you suffer any injury as a result of taking part in this research study, please understand that nothing has been arranged to provide free treatment of the injury or any other type of payment. However, all needed facilities, emergency treatment and professional services will be available to you, just as they are to the community in general. You should report any injury to Dr. Moeller at (804) 828-3793. You will not give up any of your legal rights by signing this consent form.

If you are injured by, or become ill, from participating in this study, please contact your study doctor immediately. Medical treatment is available at the Virginia Commonwealth University Health System (VCU Health System). Your study doctor will arrange for short-term emergency care at the VCU Health System or for a referral if it is needed.

Fees for such treatment may be billed to you or to appropriate third party insurance. Your health insurance company may or may not pay for treatment of injuries or illness as a result of your participation in this study.

To help avoid research-related injury or illness it is very important to follow all study directions.

VOLUNTARY PARTICIPATION AND WITHDRAWAL

Your decision to take part is voluntary and you may refuse to take part, or choose to stop taking part, at any time. A decision not to take part, or to stop being a part of the research project will not change the services that are available to you from the research clinic or Virginia Commonwealth University School of Medicine. You do not have to take part in this study to take part in other research studies in the clinic.

You may refuse to answer any questions asked or written on any forms, however answering some questions about your health and safety are necessary to take part in this study.

Your participation in this study is voluntary. You may decide to not participate in this study. Your decision not to take part will involve no penalty or loss of benefits to which you are otherwise entitled. If you do participate, you may freely withdraw from the study at any time. Your decision to withdraw will involve no penalty or loss of benefits to which you are otherwise entitled.

Your participation in this study may be stopped at any time by the study doctor or the sponsor without your consent. The reasons might include:

- the study doctor thinks it necessary for your health or safety;
- you have not followed study instructions;
- the sponsor has stopped the study; or
- administrative reasons require your withdrawal.

QUESTIONS

The investigators of this study will be glad to answer any further questions at any time. In the event of problems due to this study you should report them to Dr. Moeller at (804) 828-3793. If you would like to withdraw your permission to use blood or tissue samples, mail address for sending a letter notifying us to 203 East Cary Street, Suite 202, Richmond, VA 23219.

If you have general questions about your rights as a participant in this or any other research, you may contact: Office of Research
Virginia Commonwealth University
800 East Leigh Street, Suite 3000
P.O. Box 980568
Richmond, VA 23298
Telephone: (804) 827-2157

Contact this number for general questions, concerns, or complaints about research. You may also call this number if you cannot reach the research team or if you wish to talk to someone else. General information about participation in research studies can also be found at http://www.research.vcu.edu/irb/volunteers.htm.

Do not sign this consent form unless you have had a chance to ask questions and have received satisfactory answers to all of your questions.

CONSENT

I have been provided with an opportunity to read this consent form carefully. All of the questions that I wish to raise concerning this study have been answered.

By signing this consent form, I have not waived any of the legal rights or benefits, to which I otherwise would be entitled. My signature indicates that I freely consent to participate in this research study. I will receive a copy of the consent form once I have agreed to participate.

_____
Participant Name, (Printed)

_____ _____
Participant Signature Date

_____
Name of Person Conducting Informed Consent Discussion/Witness (Printed)

_____ _____
Signature of Person Conducting Informed Consent Discussion / Witness Date

_____ _____
Principal Investigator Signature (if different from above) Date