Project Title: Neurobehavioral Substrates of Propranolol's Effects on Drug Cue Reactivity

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DUKE UNIVERSITY HEALTH SYSTEM

Consent to Participate in a Research Study
Neurobehavioral substrates of propranolol's effects on drug reactivity

CONCISE SUMMARY

This is a research study to determine the potential effects of propranolol, a common blood pressure medication, on smoking behavior. Participants will complete five visits that vary in length from 1 to 3 hours over a period of about one month. The first visit is a screening visit and involves questionnaires, interviews and laboratory. At the second visit, you will practice some study tasks and be trained to take pictures of places you visit with a study camera. You will return the camera and complete some additional forms and tasks at the third visit. A medical exam will be conducted at one of these first three visits. If you complete them successfully, you will be scheduled for an MRI visit. You will be asked to abstain from smoking for 24 hours, given a single dose of propranolol and receive an MRI scan during which you will view and rate different pictures while we measure brain activity. At your last visit, you will take another dose of propranolol and complete a computer task during which you will have the opportunity to smoke cigarettes.

Risks for the study include the experience of nicotine withdrawal, bruising, fainting or excess bleeding from the blood draw, injury from the MRI if safety precautions are not followed, discomfort from answering certain questions, potential for loss of confidentiality and side effects of propranolol. A more detailed description is provided in this document.

If you are interested in learning more about this study, please continue reading below.

You are being asked to take part in a research study in the Department of Psychiatry, Duke University Medical Center (DUMC), on the neural and behavioral effects of propranolol in adult smokers. Research studies are voluntary and include only people who choose to take part. Please read this consent form carefully and take your time making your decision. As your study doctor or study staff discusses this consent form with you, please ask him/her to explain any words or information that you do not clearly understand. We encourage you to talk with your family and friends before you decide to take part in this research study. The nature of the study, risks, inconveniences, discomforts, and other important information about the study are listed below.

Please tell the study doctor or study staff if you are taking part in another research study.

A grant from the National Institute on Drug Abuse (NIDA) is sponsoring this study. Portions of Dr. Jason Oliver's research team salaries will be paid by this grant.

WHO WILL BE MY DOCTOR ON THIS STUDY?

If you decide to participate, Dr. Jason Oliver will be your doctor for the study and will be in contact with your regular health care provider throughout the time that you are in the study and afterwards, if needed. Dr. Rachel Dew, MD, a member of the study team, will serve as medical monitor for the study.

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WHY IS THIS STUDY BEING DONE?

The purpose of this study is to investigate the effects of propranolol on adult smokers. Propranolol is approved by the Food and Drug Administration and is a commonly prescribed beta-blocker medicine used to treat heart or circulatory conditions, such as high blood pressure and arrhythmia. Propranolol is not approved for use to help people quit smoking. In this study, this medication is being investigated to examine potential effects on smoking behavior. You are being asked to be in this study because you are an adult right-handed smoker who has no plans to quit smoking during the course of this study. The drugs that you will be given include propranolol and/or a placebo (a capsule that contains no active drug). We will measure your brain activity while you are in a MRI machine after you have taken these drugs. You will return back to the office on a separate day and complete some additional tasks after taking another dose of the medication.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

Approximately 75 people between the ages of 18 and 55 will be recruited for this study at Duke University Medical Center.

WHAT IS INVOLVED IN THE STUDY?

If you agree to be in this study, you will be asked to sign and date this consent form prior to any tests or procedures. Then, you will have the following tests and procedures to make sure that you are eligible. The first visit will last around 2.5-3 hours.

- *General Information*: We will need to know your name, age, date of birth, sex, race, address, medical history, phone number, and social security number. We will need your social security number to process your participant payment. If you choose not to provide your social security number, we will not be able to reimburse you for your participation.
- *Urine Sample Collection*: The urine sample will be used to test for drugs of abuse. Some prescription drugs can also be detected by this urine drug screen. If you test positive for any of the drugs measured by the drug screen, you will not be allowed to participate in this study.
- *Expired Breath Collection*: Breath samples will be used to measure the CO (carbon monoxide) and alcohol in your exhaled breath.
- *Medical History:* You will provide information about your medical history.
- *Physical Exam:* Participants will undergo a full physical exam by the study physician to ensure safety of propranolol administration. This will include blood pressure readings and EKG. A blood sample will be drawn and submitted for analysis.
- *Nicotine Use History:* You will provide detailed information about your current and past use nicotine. You will also identify places where you do smoke, as well as places where you do not smoke.
- *Psychiatric Screen:* You will undergo a psychiatric evaluation for symptoms for psychiatric disorders
- *MRI Safety Questionnaire:* This questionnaire will help determine it if is safe for you to enter the MRI scanner.
- *Mock scanner:* You will enter a mock MRI scanner to assess if you do feel comfortable in order to complete a real MRI session

The results of the screening tests and procedures will be reviewed by the study staff to determine if you continue to qualify for this study. Portions of these exams may occur at the 2nd or 3rd visit depending on staff and scheduling. Your responses during some of these tests may be audio recorded. If the results of your tests indicate that you cannot continue in the study, your participation in the study will end. If you continue to qualify and you feel comfortable in continuing to participate in the study, you will then begin the study.

In the next part of the study, you will fill out a series of questionnaires regarding your personality, and behavior, and then be trained on how to take pictures using the study camera. You will complete practice versions of tasks you will do later. be asked to take at least 5 photographs of smoking and non-smoking environments as identified earlier. This visit will last around 1.5 hours. At the end of this session, you will be scheduled to return for a camera return session.

In the camera return session, we will view the images that you had taken and decid if they are appropriate for the study. You will also complete a short computer task. This visit will also last about 1.5 hours.

The next visit will be the MRI session. You will be asked to abstain from smoking for 24 hours before your scheduled fMRI. You will submit a breath sample to be tested for carbon monoxide to ensure that you have abstained. If you do exceed the allowed amount of carbon monoxide measure, you will not be allowed to complete the scan. Afterwards, you will be administered either propranolol or a placebo medication. A placebo is an inactive substance given in the same forma sat the active drug, propranolol. You will be randomly assigned (like the flip of a coin) to receive either propranolol or placebo. You have a 1 in 2 chance of receiving study drug. For the next 1.5 hours, you fill out questionnaires and your blood pressure and heart rate will be monitored. During the scan, you will be viewing images that you had photographed, as well as other images. This visit will last about 3 hours.

The final visit will back in our office that will require you to be abstinent from smoking for six hours before your appointment time. As with the last visit, you will be asked to submit a breath sample and if you exceed the allowed amount of carbon monoxide, you will not be allowed to complete the visit and may be withdrawn from the study. In this visit you will again be administered either propranolol or placebo, fill out questionnaires and complete another computer task. You will view pictures of smoking locations and will have the opportunity to smoke cigarettes. We will video tape your smoking behavior during this part of the session. At the end of this session, we will discuss how much money you have earned for the entire study. This last visit will last about 2.5 hours.

HOW LONG WILL I BE IN THIS STUDY?
All subjects will have a total of 5 visits (1 screening visit, 1 training visit, 1 camera return session, a fMRI session, and laboratory session). This study can be completed within 2 – 4 weeks based on availability and schedule preferences.

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You can choose to stop participating at any time without penalty or loss of any benefits to which you are entitled. However, if you decide to stop participating in the study, we encourage you to talk to your doctor first.

WHAT ARE THE RISKS OF THE STUDY?
For Women of Childbearing Potential:
Being a part of this study while pregnant may expose the unborn child to significant risks, some of which may be currently unforeseeable. Therefore, pregnant women will be excluded from the study. If you are a woman of childbearing potential, a blood pregnancy test will be done (using 2 teaspoons of blood drawn from a vein by needle-stick), and it must be negative before you can continue in this study. Urine pregnancy tests will also be conducted prior to receiving the study medications. These tests must be negative before you can continue in the study. If sexually active, you must agree to use appropriate contraceptive measures for the duration of the study. Medically acceptable contraceptives include: (1) surgical sterilization (such as a tubal ligation or hysterectomy), (2) approved hormonal contraceptives (such as birth control pills, patches, implants or injections), (3) barrier methods (such as a condom or diaphragm) used with a spermicide, or (4) an intrauterine device (IUD). Contraceptive measures such as Plan B (TM), sold for emergency use after unprotected sex, are not acceptable methods for routine use. If you do become pregnant during this study or if you have unprotected sex, you must inform your study physician immediately.

Risks of Blood Drawing:
Risks associated with drawing blood from your arm include momentary discomfort and/or bruising. Infection, excess bleeding, clotting or fainting are also possible, although unlikely. The total amount of blood drawn for the entire study will not exceed 4 teaspoons (20 ml).

Propranolol Side Effects:
The primary risk associated with this study are the side effects associated with the study medication.

Common side effects include hypotension, bradycardia (slow heart rate), cold extremities, transient fatigue, sleep disturbance, drowsiness, agitation and irritability, dizziness, and Raynaud's phenomenon (e.g. coldness/numbness in the fingers and toes).

Most of the side effects are minor and resolve quickly on their own. In order to minimize risks, we do ask that you give your medical history and completely and accurately as possible. We will monitor these risks by closely monitoring you and your blood pressure and heart rate during experimental sessions.

Effects of Nicotine Withdrawal:
You may experience the following symptoms when you abstain from smoking for the two periods (one for 24-hours and another for 6-hours) in the study: cravings for nicotine, anxiety, irritability, restlessness, mood changes, nervousness, disruptions of you sleep, drowsiness, trouble concentrating, increased appetite, headaches, muscular pain, constipation and fatigue. These may begin almost immediately after you stop smoking.

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Functional Magnetic Resonance Imagining (fMRI) Risks:
Magnetic resonance imaging (MRI) uses a magnet and radio waves to make diagnostic medical images of the body. There have been no ill effects reported from exposure to the magnetism or radio waves used in this test. However, it is possible that harmful effects could be recognized in the future.

A known risk is that the magnet could attract certain kinds of metal. Therefore, we will carefully ask you about metal within your body (this includes certain dyes found in tattoos). If you have metal within your body, tell us immediately, since it will be dangerous for you to be in an MRI machine. If there is any question about potentially hazardous metal within your body, you will be excluded from participating in this research study. We will also keep the MRI locked so that no one carrying metal objects can enter while you are in the scanner.

The study involves entering a large room in which a magnet is present. You will be placed on a narrow bed and then slid into a small tunnel approximately 6 feet in length and 25 inches in diameter. You will be asked to lie still for about one hour on this bed and will hear loud noises during this time. Some people who are claustrophobic (afraid of being in cramped places like closets or crowded elevators) may experience extreme anxiety when placed in a MRI machine. You may be asked to have a harmless monitoring device applied during the study. During the study, you will have voice contact with the technician in between scans.

There may be risks, discomforts, drug interactions or side effects that are not yet known.

Psychiatric Assessment Risks:
This is a research study that involves questions that ask about your mental state which may cause discomfort. As researchers, we do not provide mental health services. It is possible that we will not view your responses for several days, weeks, or months after you complete the surveys. Therefore, we will not know of any immediate risks that you may have for harming yourself or others, including suicidality. Should you decide you need assistance at any time while enrolled in this study, please contact the study doctor (919-681-0031) or principal investigator (919-668-0093) for clinic referrals, or the National Suicide Prevention Lifeline (1-800-273-8255).

Confidentiality:
The information obtained as a result of your participation in this research will not be included in your medical record by research staff. Information from which you may be personally identified will be maintained in a confidential, locked file at DUMC or on a secured department server accessible only to the study. Information will not be disclosed to third parties except with your permission or as may be required by law. There is a potential risk of loss of confidentiality. Every effort will be made to keep your information confidential; however, this cannot be guaranteed. Some of the questions we will ask you as part of this study may make you feel uncomfortable. You may refuse to answer any of the questions and you may take a break at any time during the study. You may stop your participation in this study at any time.

There may be risks, discomforts, drug interactions or side effects that are not yet known. Your risk of being harmed by participating in this study may increase if you do not give your health history as accurately and as completely as you can.

The Department of Health and Human Services (HHS) has issued a Certificate of Confidentiality to further protect your privacy. With this Certificate, the investigators may not disclose research information that may identify you in any Federal, State, or local civil, criminal, administrative, legislative, or other proceedings, unless you have consented for this use. Research information protected by this Certificate cannot be disclosed to anyone else who is not connected with the research unless:

1) there is a law that requires disclosure (such as to report child abuse or communicable diseases but not for legal proceedings);
2) you have consented to the disclosure, including for your medical treatment; or
3) the research information is used for other scientific research, as allowed by federal regulations protecting research subjects.

Disclosure is required, however, for audit or program evaluation requested by the agency that is funding this project or for information that is required by the Food and Drug Administration (FDA).

You should understand that a Confidentiality Certificate does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it. This means that you and your family must also actively protect your own privacy.

Finally, you should understand that the investigator is not prevented from taking steps, including reporting to authorities, to prevent serious harm to yourself or others.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?
You will not benefit from being in this study, although the knowledge gained may benefit others.

WILL MY INFORMATION BE KEPT CONFIDENTIAL?
Participation in research involves some loss of privacy. We will do our best to make sure that information about you is kept confidential, but we cannot guarantee total confidentiality. Your personal information may be viewed by individuals involved in this research and may be seen by people including those collaborating, funding, and regulating the study. We will share only the minimum necessary information in order to conduct the research. Your personal information may also be given out if required by law.

As part of the study, results of your study-related laboratory tests, x-rays, and procedures may be reported to NIDA and its affiliates. In addition, your records may be reviewed in order to meet federal or

state regulations. Reviewers may include from the National Institutes of Health, the Duke University Health System Institutional Review Board, and others as appropriate. If any of these groups review your research record, they may also need to review your entire medical record.

The study results will be retained in your research record for at least six years after the study is completed. At that time either the research information not already in your medical record may be destroyed or information identifying you will be removed from such study results at DUHS. Any research information in your medical record will be kept indefinitely.

This information may be further disclosed by the sponsor of this study. If disclosed by the sponsor, the information is no longer covered by federal privacy regulations. If this information is disclosed to outside reviewers for audit purposes, it may be further disclosed by them and may not be covered by federal privacy regulations.

While the information and data resulting from this study may be presented at scientific meetings or published in a scientific journal, your name or other personal information will not be revealed.

Some people or groups who receive your health information might not have to follow the same privacy rules. Once your information is shared outside of DUHS, we cannot guarantee that it will remain private. If you decide to share private information with anyone not involved in the study, the federal law designed to protect your health information privacy may no longer apply to the information you have shared. Other laws may or may not protect sharing of private health information.

All of the laboratory tests and questionnaires are being given only because you are in this study. The study results will not be given to you to send or be sent to your physician to include in your medical record. Any significant new findings found out during this research, which may change your willingness to continue to be in the research, will be given to you.

There are certain situations in which confidentiality may be broken. Possible legal exceptions to confidentiality may occur if necessary to protect yourself or others from abuse or neglect, or in cases of potential harm to oneself or others. In such cases, confidentiality would only be broken in order to protect you or others from significant harm or death.

WHAT ARE THE COSTS?
There will be no additional costs to you as a result of being in this study. We do provide hospital parking passes if you choose to drive to your MRI session. Visitor parking is free at our office.

WHAT ABOUT COMPENSATION?
You will be compensated $20 for the screening visit, provided you test negative for drugs and alcohol and testing confirms you are a smoker. If you are eligible and complete this study, you will earn $25 for the training visit and $25 for the camera return session, $150 for the fMRI session, and $150 for the laboratory session. You can earn an additional $50 for completing the entire study. Therefore, the total

maximum compensation for this study is $420. In order to be compensated, you do need to provide your social security number. You can participate in this study without giving a social security but you will not be compensated for your time. In addition to financial compensation, you will be able to receive an electronic or paper copy of an image of your brain derived from the MRI scan (for entertainment purposes only), assuming a sufficient quality image is obtained. In addition, at your final session you will receive a report based on some of the information we learned about you during your participation.

WHAT ABOUT RESEARCH RELATED INJURIES?
Immediate necessary medical care is available at Duke University Medical Center in the event that you are injured as a result of your participation in this research study. However, there is no commitment by Duke University, Duke University Health System, Inc., or your Duke physicians to provide monetary compensation or free medical care to you in the event of a study-related injury. For questions about the study, contact Dr. Jason Oliver at 919-668-0093 during regular business hours. For a research-related injury, contact Dr. Rachel Dew at 919-681-0031 during regular business hours and at 919-970-8541 after hours and on weekends and holidays.

WHAT ABOUT MY RIGHTS TO DECLINE PARTICIPATION OR WITHDRAW FROM THE STUDY?
You may choose not to be in the study, or, if you agree to be in the study, you may withdraw from the study at any time. If you withdraw from the study, no new data about you will be collected for study purposes unless the data concern an adverse event (a bad effect) related to the study. If such an adverse event occurs, we may need to review your entire medical record.

Your decision not to participate or to withdraw from the study will not involve any penalty or loss of benefits to which you are entitled, and will not affect your access to health care at Duke. If you do decide to withdraw, we ask that you contact Dr. Oliver in writing and let him know that you are withdrawing from the study. His mailing address is 2608 Erwin Rd, Suite 300, Durham, NC 27705.

Nonparticipation or withdrawal from this study will not affect your job status if you are a Duke employee and will not affect your grades if you are a Duke student.

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

INCIDENTAL FINDINGS:
Although we will not be testing for any disorders or genetic diseases, it is possible that this study will identify information about you that was previously unknown, such as disease status or risk. There are no plans to provide this information to you or your physician unless the information indicates that you may be at risk for a disease known at the time of testing to potentially cause premature death if untreated, including suicidality. In that case, we will attempt to notify you using the contact information you have provided, so that you can speak with Dr. Oliver at Duke University Health System (DUHS). DUHS staff will not provide this information in a voice mail, email, or otherwise prior to contacting you. Please

notify us of any change in your contact information. If you do not want to be notified of any incidental findings, please place your initials below.

_____ (initials) Please do not notify me of any incidental findings obtained from this research.

If you prefer, we can ask you at the time of notification whether or not you want to receive incidental findings information. In this case, please place your initials below.

_____ (initials) Please ask me at the time of notification whether or not I want to receive incidental findings information.

It is possible that MRI scan will identify information about you that was previously unknown. Such incidental findings, if any, will not be shared with you unless the incidental finding is determined to be likely to cause premature death if untreated. Should such life-threatening results be uncovered, the principal investigator of the study will be informed. The information will be shared with you as follows: you will be notified via certified mail to contact Jason Oliver, PhD at Duke University Medical Center (DUMC). Notification will be sent to the address you provided to us. The DUMC staff will not release these specific research findings over the telephone or in the mail. Dr. Oliver will arrange for you to meet with him and/or other appropriate health care providers either at DUMC or another medical institution near your residence to review the research information.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?
For questions about the study, contact Dr. Oliver at 919-668-0093 during regular business. For a research-related injury, or if you have problems, concerns, questions or suggestions about the research, contact Dr. Rachel Dew at 919-681-0031 during regular business hours and at 919-970-8541 after hours and on weekends and holidays.

For questions about your rights as a research participant, or to discuss problems, concerns or suggestions related to the research, or to obtain information or offer input about the research, contact the Duke University Health System Institutional Review Board (IRB) Office at (919) 668-5111.

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STATEMENT OF CONSENT
"The purpose of this study, procedures to be followed, risks and benefits have been explained to me. I have been allowed to ask questions, and my questions have been answered to my satisfaction. I have been told whom to contact if I have questions, to discuss problems, concerns, or suggestions related to the research, or to obtain information or offer input about the research. I have read this consent form and agree to be in this study, with the understanding that I may withdraw at any time. I have been told that I will be given a signed and dated copy of this consent form."

_____	_____	_____
Signature of Subject	Date	Time
_____	_____	_____
Signature of Person Obtaining Consent	Date	Time

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FUTURE RESEARCH
Dr. Oliver and his colleagues are often interested in follow-up or related studies. These may involve a return visit to the laboratory to complete similar questionnaires and tasks, or there may be a new study for which you might qualify to participate. If you are interested in possible future participation in such studies, we would keep your name on file and contact you about them in the future. The sole purpose of this initial contact would be to determine if you are interested in participating in a future study. There is no obligation to participate and your refusal for future contact will in no way affect your participation in the present study.

Please indicate whether or not you agree to be contacted in the future about participation in any follow-up or related research studies by initialing one of the blanks below:

____ **I WOULD LIKE TO BE CONTACTED** in the future to be provided more information about participation in follow-up or related research studies.

____ **DO NOT CONTACT ME** in the future to provide more information about participation in follow-up or related research studies.

Preferred method of contact (check 1 or more):

☐ Telephone # ( ) _____

☐ Mail (address) _____

☐ E-mail (address) _____@_____

_____		_____	_____
Signature of Subject	Printed Name	Date	Time

_____	_____	_____
Signature of Person Obtaining Consent	Date	Time