COMPOUND AUTHORIZATION/CONSENT FOR PARTICIPATION IN A RESEARCH PROJECT YALE UNIVERSITY SCHOOL OF MEDICINE – YALE MAGNETIC RESONANCE RESEARCH CENTER

Study Title: Influence of medication on functional connectivity
Principal Investigator: Sarah W. Yip, PhD
Funding Source: National Institute on Drug Abuse & departmental account

Invitation to Participate and Description of Project

You are invited to participate in a research study designed to assess potential sources of variance for neuroimaging studies. This research study will use functional magnetic resonance imaging (fMRI) to measure changes in the flow of blood through the brain during periods of rest. The proposed research will explore the effects of a single dose of oxycodone (15mg) on brain activity during neuroimaging measures (fMRI). You are invited to participate in this study because you are a medically healthy adult. If you are eligible, you will be one of approximately 40 individuals participating in this study.

In order to decide whether or not you wish to be a part of this research study you should know enough about its risks and benefits to make an informed judgment. This consent form gives you detailed information about the research 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, possible benefits and possible alternative treatments. Once you understand the study, you will be asked if you wish to participate; if so, you will be asked to sign this form.

Description of Procedures

Screening:

The total time of this process is estimated to be from 3-4 hours and may take more than 1 visit to complete either in person or virtually via Zoom. To determine if you are eligible for this study, we will ask you questions about different aspects of your life including your health, smoking, sexual behaviors, substance use behaviors and attitudes, and the ways in which you view yourself. If you are determined to be eligible we may ask you to complete additional interviews and questionnaires. You may also be asked for a urine drug test. If the drug test is positive then this would exclude you from participation in this study and these results would be destroyed to maintain your privacy. If you have recently (within the past 6 months) participated in another study under Dr. Yip involving an intake/medical screening, you will not need to complete a second screening.

Baseline assessments:

If you are determined to be eligible for study participation we will ask you to complete a few more assessment measures involving interviews and questionnaires. This also may be conducted either

in person or virtually via Zoom. This will take about 1½ hours. During this visit we will also schedule your first MRI appointment.

The researcher will also interview you to determine if it is safe for you to participate in MRI scanning. To be sure that you are free of major medical illnesses and that it is safe for you to receive the medication, you will also receive a medical evaluation by a study physician. This examination will be in person and include a medical history and physical examination and may also involve routine cheek swab tests, urine analysis, and urine toxicology to test your urine for drugs of abuse such as heroin, cocaine, marijuana, and benzodiazepines, as deemed necessary by the study physician. This will take about 1 hour. Results of the medical evaluation will be made available to you or your personal physician upon your written request. Before admission into the study, a study physician reviews all results. Once admitted into the study, the study physician will access your Yale medical chart once for the purpose of attaining your medical record number for the prescription of oxycodone. We will also ask you for a small cheek swab sample, to be taken by the study physician during your medical screening session. The cheek swab in this sample will be used to test for a common genetic variation that can influence how fast your body metabolizes medications such as oxycodone. Your sample will only be used to test for this variation and will not be saved for other purposes.

This research study will use functional magnetic resonance imaging (fMRI) to measure changes in the flow of blood through the brain during resting states or performance of a behavioral task. If you have significant metal implants in your body (for example, a metal skull plate), you will be excluded from the study. We are also excluding from this study women who are pregnant or nursing because oxycodone could be harmful to an unborn baby and because oxycodone does enter breast milk. If you become pregnant while you are in the study, please let us know as soon as possible. Women of child-bearing age will be given a pregnancy test prior to scanning to rule out pregnancy. You will be required to abstain from the use of any alcohol or drugs (other than prescription) 24 hours prior to your scan. If at any time during the study you are found to be at risk for hurting yourself you may be hospitalized as a safety measure.

MRI scanning:

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.

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, as well as devices to measure things such as your heart rate.

You will be asked to participate in up to two 90 minute fMRI sessions. For one of the sessions we will require you take a single dose of oxycodone (15mg) just prior to the scan. For one of the

session we will require you to take a placebo pill just prior to the scan. The order in which you receive oxycodone or placebo pills will be randomized and will not be known to you or the primary researcher. A licensed physician will be on-call for both scans.

During the MRI session, you will be able to communicate with the research staff with headphones and a microphone. We may 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. We will take a series of pictures while you are simply resting with your eyes open and laying still. In between each series of resting pictures (approximately 6 minutes each), we will ask you to answer some questions about how you are feeling and you will indicate your responses using a simple button or lever press. We will also take another series of pictures will be taken for a more detailed image of your brain. During this time you will be asked to simply lie still. You may close your eyes during this time. We may also take pictures of your brain while you are performing a simple emotion regulation task (described below). The entire imaging procedure may last between 60 and 90 minutes. In addition to the MRI operator, a member of the research team will accompany you and will stay for the MRI. For all scans a trained medical professional will also be on hand in addition to a licensed medical doctor being available by pager.

During fMRI scanning, you may be participating in a task called the Monetary Incentive Delay Task (MID). The basic goal of the task is to press a button as quickly as possible when you see a target, in order to win or avoid losing money. At the start of each trial, you will see a screen indicating the amount of money that can be won or lost ($0, $1, or $5). Then there will be a short delay and a box will flash on the screen. Your job is to press the button as soon as you see the target – in other words 'hit the box'. After each trial, you will receive feedback indicating whether or not you hit the target and also telling you how much money you have won so far. Some of the trials will be trials for which you may win money, as indicated via a cue (for example, 'WIN $1'). Other trials will be trials for which you may lose money, as indicated via a cue (for example 'LOSE $1'). For both trial types, your goal is to press the button as quickly as possible in response to the target. The task takes about 12 minutes. In order to help you to perform your best during task performance we will give you the opportunity to practice the task before the MRI scan.

Risks and Inconveniences

During the study you will be asked questions related to your mental health and drug use history that may make you feel uncomfortable or sad. If this happens, you will be allowed to take a break for as long as is necessary before proceeding. We would like you to tell us about any times you use cannabis or any other drugs while you are in the study. It is not illegal to report past substance use and we will make every effort to insure your confidentiality. However, you should understand that there is a risk that you may be recognized by other participants or staff involved in the study, but this is no greater than the usual risk of identification that occurs in our usual treatment in this clinic.

Magnetic Resonance Imaging:

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

You will be watched closely throughout the MR study. Some people may feel uncomfortable or anxious. If this happens to you, you may ask to stop the study at any time and we will take you out of the MR scanner. On rare occasions, some people might feel dizzy, get an upset stomach, have a metallic taste or feel tingling sensations or muscle twitches. These sensations usually go away quickly but please tell the research staff if you have them.

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

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

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

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.

<u>Oxycodone</u>

Risks associated with oxycodone use include gastrointestinal upset, constipation, nausea, vomiting, tiredness, dizziness, light-headedness, itching, headache, blurred vision and dry mouth. Among these, the most common risks include constipation (in 25-30% of individuals), nausea (25%), drowsiness (25%), dizziness (15%) and vomiting (10-15%). It is possible that serious, life-threatening or fatal respiratory depression may occur. As you will only be taking a single 15 mg oxycodone pill, risks are minimal and trained staff will be on hand to monitor you.

Should these side effects occur, you will be offered symptomatic relief by the study physician (Dr. Camenga or her designee) as appropriate based on her clinical judgement. You will be monitored closely until side effects have subsided. The study physician, Dr. Camenga has significant expertise in adolescent and young adult substance use and addiction and adolescent medicine. She is therefore extremely well qualified to deal with possible oxycodone-associated side effects, in the unlikely event that they arise.

A dose of naloxone will be on hand to counteract any effects from the opioid should the need arise (as determined based on the discretion of the study physician), although this is highly unlikely to be necessary given the low dose of oxycodone. Other risks associated with oxycodone include the risk of possible interactions with other opioids, alcohol, benzodiazepines and other medications. For this reason, participants taking medications that could interact with oxycodone are not eligible for this study, and we will ask you to abstain from drugs or alcohol for 24 hours prior to each study visit.

You will not be allowed to drive after the scan on the day when you take the medication. As such, you will need to arrange for transportation home following the scan.

As with most opioid medications, oxycodone has abuse liability and its prolonged use may lead to addiction and drug seeking behavior. These adverse events are unlikely to develop when oxycodone is used at approved doses and for a short time (single administration) as in this study. In addition to being closely monitored during study visits, you will be contacted via phone following each study visit and at one-month follow-up by a trained member of the research staff to check for any possible any adverse effects and will be referred to the study physician if necessary. You will also be given a card to keep in your wallet with the contact information for the study physician. The study physician, Dr. Camenga, has significant expertise in adolescent and young adult substance use and addiction and adolescent medicine. She is therefore extremely well qualified to deal with possible oxycodone-associated risks, in the unlikely event that they arise.

Baseline assessments

Completing the baseline assessments has minimal potential for harm. We will do everything in our power to minimize any risks or inconveniences. We would like you to feel comfortable in our testing environment. Also, please note that at any time during the course of this study, you may ask us to stop.

Benefits

The study will be of no direct benefit to you. It will provide us with information on the possible influence of acute opioid use on parts of the brain. We hope and believe this information will prove useful in the future ultimately with respect to determining if these conditions affect neuroimaging results.

Economic Considerations

There are no additional costs to you for participation in this study except for transportation to the study visits and your time. You will be paid $25 to participate in an initial screening session and $10 in a medical screening session. Eligible participants will be paid $145 for participation in each of the fMRI sessions, with a bonus of $75 for completing both sessions. The total possible compensation is therefore up to $400. If you leave the study prior to completing it, you will be paid only for those parts you have completed.

In addition, you may be eligible for a referral payment up to $25 for each eligible participant you refer to this study.

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

This is not a treatment study. The only alternative in this study is simply to not participate. You are free to choose not to participate and if you do become a subject, you are free to withdraw from the study at any time. If you withdraw it will not adversely affect your relationship with this clinic or the clinicians or doctors here.

Confidentiality and Privacy

If you decide to be in this study, the researchers will get information that identifies you and your personal health information. This may include information that might directly identify you, such as your name and address. All personal information will be coded and stored in a locked cabinet to protect your confidentiality.

We will replace your identifying information with a code that does not directly identify you. The principal investigator will keep a link that identifies you to your coded information until all analyses and publications arising from this research are complete, but 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. The research team will only give this coded information to others to carry out this research study. After termination of this study and completion of all analysis and publications, all data and screening information will be de-identified, thereby making the data anonymous, and kept in a secure fashion for the purpose of further analyses indefinitely unless prevailing University or Federal guidelines at the time require a change.

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

- Past and present medical records
- Research records
- Records about phone calls made as part of this research
- Records about your study visits
- Information obtained during this research about:
    - Laboratory test results
    - The diagnosis and treatment of a mental health condition

Information about you and your health, which might identify you, may be given to

- Yale University School of Medicine personnel involved in the study on a need to know basis
- Members of the Human Investigations Committee or ethics Committee(s)
- Key Investigators: Sarah Yip, PhD; Dustin Scheinost, PhD; Deepa Camenga, MD
- Key Study Personnel
- The Secretary of the Department of Health and Human Services, if needed for an audit of the study
- The National Institutes of Health, study funding source
- The Food and Drug Administration (FDA)
- Those individuals at Yale who are responsible for the financial oversight of research including billings and payments

The research team can only give information about you to others for research with your permission. We will make every effort to insure your confidentiality. In all records of the study you will be identified only by a number. Your name will not appear in any publication or be released to anyone without your written consent. However, you should understand that there is a risk that you will be recognized by other participants or staff involved in the study, but this is no greater than the usual risk of identification that occurs in our usual treatment in this clinic. If you find this risk unacceptable you should not sign this consent form.

The data we collect from you may be shared across other protocols the Principal Investigator is running. 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 and APT Foundation 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.

If you decide to take part in this research study, you will be required to give us information about your substance use (e.g., past or current opioid use). To protect this information, this research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation by the Department of Health and Human Services through NIDA which is funding this project or for information that must be disclosed 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 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.

The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law such as child abuse and neglect, or harm to self or others].

You have the right to review and copy your health information in your medical record in accordance with institutional medical records policies. However, by deciding to take part in a single or double blinded treatment study and sign this permission form, you will not be allowed to look at or copy your study related information until after the research is completed. 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 while on study, seek treatment and contact the study doctor as soon as you are able, (203) 737-4358. Yale School of Medicine and [Specify health care facility, e.g., Yale-New Haven Hospital, 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 (the person who has been scheduling your appointments) 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.

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

Withdrawing Your Authorization to Use and Disclose Your Health Information

You may withdraw or take away your permission to use and disclose your health information at any time. You may withdraw your permission by telling the study staff or by writing to the principal investigator, Sarah Yip, PhD; 1 Church Street, 7th Floor, New Haven, CT, 06510-0333.

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

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 Person Obtaining Consent or PI Date

APPROVED BY THE YALE UNIVERSITY IRB 3/8/2022

Authorization and Permission:

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

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

Name of Subject:_____

Signature:_____

Date:_____

_____ _____
Signature of Principal Investigator Date

or

_____ _____
Signature of Person Obtaining Consent Date

If 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. Sarah W. Yip at (203) 737-4358. 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.