UNIVERSITY OF CALIFORNIA, SAN FRANCISCO
CONSENT TO PARTICIPATE IN A RESEARCH STUDY

Study Title: The Effect of Chronic Pain on Delay Discounting in Methadone Patients
NCT04473950

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This is a clinical research study. Your study doctor, D. D. Andrew Tompkins, MD MHS, Ellie Ahmadi, Charlotte Evans, or Gabrielle Agin-Liebes from the UCSF Department of Psychiatry will explain the study to you.

STUDY SUMMARY

Introduction: We are asking you to consider taking part in a research study being done by Dr. D. Andrew Tompkins at UCSF.

The first part of this consent form gives you a summary of this study. We will give you more details about the study later in this form. The study team will also explain the study to you and answer any questions you have.

Research studies include only people who choose to take part. It is your choice whether or not you want to take part in this study. Please take your time to make a decision about participating. You can discuss your decision with your family, friends and health care team.

Purpose of the study: The researchers want to learn about the usefulness of measuring delay discounting, a model of impulsive decision-making, in patients with opioid use disorder (OUD). Researchers want to know if delay discounting may be affected by stressors, like chronic pain or opioid withdrawal. If successful, delay discounting may be developed as a clinical tool to help guide treatment of patients with OUD.

Study Procedures: If you choose to be in this study, you will be asked to receive an injection of the study drug, naloxone, or a placebo (an injection that looks like the study drug but has no drug in it) once at the beginning of each of two sessions. You will then be assessed for pain and opioid withdrawal every 15 minutes until two hours after the injection. Lastly, you will answer delay discounting questions approximately 30 minutes after each injection.

You will be in this study about 2-4 weeks. You will come to the clinic 3 times, including today's screening visit. The screening visit should last 3 hours and the study sessions should last about 4

hours. Study sessions will occur in Building 90, Ward 95 and Building 5, Unit 5B on the campus of ZSFG.

For your safety and the safety of others, you will be screened for recent positive tests, exposures, symptoms of COVID-19 and will be asked to wear a mask for the duration of all study visits.

Possible Risks: There are risks to taking part in a research study. Some of the most likely risks of participation in this study include:

- Opioid withdrawal symptoms, including nausea, vomiting, diarrhea or loose stools, body aches, dysphoric mood, worsening anxiety symptoms, including tunnel vision or panic attacks, and gooseflesh
- Boredom or fatigue from answering questions

There are also rare but serious risks of participation, like:

- Relapse to opioid or other substance use
- Infection at the site of injection

We'll tell you about the other risks later in this consent form.

Possible Benefits: There will be no direct benefit to you from participating in this study.

Your Other Options: You do not have to participate in this study. Your other choices may include:

- Not joining the study

Please talk to your doctor about your choices before agreeing to participate in this study.

Following is a more complete description of this study. Please read this description carefully. You can ask any questions you want to help you decide whether to join the study. If you join this study, we will give you a signed copy of this form to keep for future reference.

DETAILED STUDY INFORMATION

This part of the consent form gives you more detailed information about what the study involves.

Research studies include only people who choose to take part. Please take your time to make your decision about participating. You may discuss your decision with your family and friends and with your health care team. If you have any questions, you may ask your study doctor.

You are being asked to take part in this study because you have opioid use disorder and are on a stable dose of methadone for the past 21 days.

Why is this study being done?

The purpose of this study is to learn about how stressors like chronic pain or opioid withdrawal may influence decision making ability in patients on methadone for OUD. We will be using a

series of questions that ask you to choose between a reward now and a larger reward at a time in the future. You will not earn these rewards, but we ask that you consider each question as if you could receive the reward. This series of questions is known as delay discounting. This study is a first step. If successful, delay discounting may be developed as a clinical tool to help guide treatment of patients with OUD.

The National Institute on Drug Abuse, part of the National Institutes of Health is funding this study.

Naloxone, an FDA approved medication for the reversal of opioid overdose, is being used in this study to precipitate mild symptoms of opioid withdrawal.

How many people will take part in this study?

About 130 people will take part in this study. We will recruit roughly equal numbers of people with and without chronic pain to take part.

What will happen if I take part in this research study?

Before you begin the main part of the study:

You will need to have the following exams, tests or procedures to find out if you can be in the main part of the study. All of those exams can be completed in one day or separated out to two days depending on a number of factors.

Additionally, you will be screened for COVID-19 symptoms by phone (or telehealth) prior to and at the time of arrival for a screening visit. You will be asked about recent positive tests, exposures, and symptoms not explained by a pre-existing condition. If the answer to any of these screening questions is yes, the visit will be postponed and you will be referred to the medical team for further evaluation.

Study-related activities will take place via Zoom/iPads as much as possible. All study staff and participants will wear personal protective equipment (PPE) as necessary for the duration the visit.

- Questions about
    - Demographics
    - Drug use history
    - Medical history
    - Psychiatric history
    - Pain
- Physical exam including vital signs
- Verify your methadone dose by contacting your opioid treatment program. (We must have your permission to do this.)
- Collect urine for urine drug screen and pregnancy test (if female)
- Collection of an ECG (electrocardiogram – an electronic tracing of your heart)

During the main part of the study:

If the exams, tests and procedures show that you can be in the main part of the study, and you choose to take part, then you will need the following tests and procedures. The same tasks will be done in the same order in each session and the sessions will need to be at least 48 hours apart.

You will again be screened for COVID-19 symptoms by phone (or telehealth) as described above prior to and at the time of arrival for session visits. The same precautionary measures for COVID-19 as described above will be taken during session visits.

- Collect urine for urine drug screen and pregnancy test (if female). The results of the urine drug screen must be positive for methadone and negative for illicit substances. Otherwise, the session will be rescheduled. A positive pregnancy test will result in withdrawal or the participant from the study and referral to appropriate resources.
- Must be without signs of intoxication as evidenced by ability to receive full dose of methadone prior to research activities.
- Contact your opioid treatment program to verify you have not yet taken your methadone dose on the day of your session. Your dose on session one must be the same dose on session two.
- Administer your current methadone dose at OTOP / Ward 93.
- If you are a smoker, you will be asked to smoke 1 cigarette 20 minutes prior to session and then refrain from smoking until the session is complete.
- Collect baseline responses on
    - Current pain level
    - Current symptoms of withdrawal
    - Vital signs
    - Take a picture of your eye
- Administer one injection in your upper arm muscles approximately 2 hours after your methadone dose. You and the study team will not know what you are given. One of the doses will be a placebo, an inactive substance, and one of the doses will contain 0.1 mg of naloxone. The order of the injections will be randomized, like flipping a coin.
- Every 15 minutes after the injection up to 2 hours the study team will collect responses on
    - Current pain level
    - Current symptoms of withdrawal (if any)
    - Vital signs
    - Take a picture of your eye
- Collect responses on the delay discounting task approximately 30 minutes after study medication is administered.

In addition, you will be asked to answer questions about the following:

- Impulsivity
- Sleep problems (insomnia)
- Anxiety, somatization and depressive symptoms
- Pain catastrophizing

How long will I be in the study?

You will be asked to complete two sessions that will last about 4 hours each in addition to a screening visit. The sessions must be at least 48 hours apart. On average, you will be spend 11 hours in study related activities spread out over 2-4 weeks.

Can I stop being in the study?

Yes. You can decide to stop at any time. Tell the study doctor if you are thinking about stopping or decide to stop. He will tell you how to stop your participation safely.

It is important to tell the study doctor if you are thinking about stopping so any risks from naloxone or placebo can be evaluated by your doctor. Another reason to tell your doctor that you are thinking about stopping is to discuss what follow-up care and testing could be most helpful for you.

The study doctor may stop you from taking part in this study at any time if he/she believes it is in your best interest, if you do not follow the study rules, or if the study is stopped.

What side effects or risks can I expect from being in the study?

You may have side effects while on the study. Everyone taking part in the study will be watched carefully for any side effects. However, doctors don't know all the side effects that may happen. Side effects may be mild or very serious. Your health care team may give you medicines to help lessen side effects.

You should talk to your study doctor about any side effects you experience while taking part in the study.

Risks and side effects related to the study medications include those which are:

Likely

- Opioid withdrawal, including body aches, headache, nausea, vomiting, sweating, diarrhea or loose stools, tearing, depressed mood, worsening anxiety, including tunnel vision or panic attacks, and gooseflesh
- Changes in vital signs, including elevations in heart rate and blood pressure
- Injection site reaction, including pain and redness
- Dizziness

Less Likely

- Bruising at the site of injection
- Boredom or fatigue at answering questions
- Sleepiness after receiving study medication

Rare but serious

- Relapse to substance use. If this does occur, we would communicate this to your opioid treatment program.
- Infection at site of injection

Reproductive risks: You should not become pregnant or father a baby while on this study because the drugs in this study can affect an unborn baby. Women should not breastfeed a baby while on this study. It is important to understand that you need to use birth control while on this study. Check with your study doctor about what kind of birth control methods to use and how long to use them.

Unknown Risks: The experimental treatments may have side effects that no one knows about yet. The researchers will let you know if they learn anything that might make you change your mind about participating in the study.

For more information about risks and side effects, ask your study doctor.

Are there benefits to taking part in the study?

There will be no direct benefit to you from participating in this study. However, this study will help doctors learn more about how stressors may affect delay discounting, and it is hoped that this information will help in the treatment of future patients with OUD.

What other choices do I have if I do not take part in this study?

You do not have to join this study. Your care at OTOP and ZSFG will not be affected if you choose not to enter this study. Please talk to your doctor about your choices before deciding if you will take part in this study.

How will my information be used?

Researchers will use your information to conduct this study. Once the study is done using your information, we may share them with other researchers so they can use them for other studies in the future. We will not share your name or any other personal information that would let the researchers know who you are. We will not ask you for additional permission to share this de-identified information.

How will information about me 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 privacy. Some information from your medical records will be collected and used for this study. Information gathered directly from you by the researchers will be part of your research records but will not be added to your medical record. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

Authorized representatives from the following organizations may review your research data for the purpose of monitoring or managing the conduct of this study:

- Representatives of the National Institutes of Health
- Representatives of the University of California

What is a Certificate of Confidentiality?

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. This means that the researchers cannot release or use information, documents, or samples that may identify you in any action or suit unless you say it is okay. They also cannot provide them as evidence unless you have agreed. This protection includes federal, state, or local civil, criminal, administrative, legislative, or other proceedings. An example would be a court subpoena.

There are some important things that you need to know. The Certificate DOES NOT stop reporting that federal, state or local laws require. Some examples are laws that require reporting of child or elder abuse, some communicable diseases, and threats to harm yourself or others.

Researchers may release information about you when you say it is okay. For example, you may give them permission to release information to insurers, medical providers or any other persons not connected with the research. The Certificate of Confidentiality does not stop you from willingly releasing information about your involvement in this research. It also does not prevent you from having access to your own information.

Are there any costs to me for taking part in this study?

No.

Will I be paid for taking part in this study?

In return for your time, effort and travel expenses, you will be paid up to $300 for participation in study related activities. You can earn $50 for study screening, $75 after completion of each study session, and an additional $100 bonus for completion of both sessions.

If you pass study screening and complete at least one study session, you will then also be eligible to refer participants to the study. If participants that you have referred also pass study screening and complete at least one study session, you will receive a referral bonus of $50. The referred participant must also mention your name during their study screening for you to receive this referral bonus.

What happens if I am injured because I took part in this study?

It is important that you tell your study doctor, Dr. D. Andrew Tompkins, if you feel that you have been injured because of taking part in this study. You can tell the doctor in person or call him at 628-206-3645.

Treatment and Compensation for Injury: If you are injured as a result of being in this study, the University of California will provide necessary medical treatment. The costs of the treatment may be billed to you or your insurer just like any other medical costs or covered by the University of California depending on a number of factors. The University and the study sponsor do not normally provide any other form of compensation for injury. For further information about this, you may call the office of the Institutional Review Board at 415-476-1814.

What are my rights if I take part in this study?

Taking part in this study is your choice. You may choose either to take part or not to take part in the study. If you decide to take part in this study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your regular benefits. Leaving the study will not affect your medical care. You can still get your medical care from our institution.

We will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

Who can answer my questions about the study?

You can talk to your study doctor about any questions, concerns, or complaints you have about this study. Contact your study doctor. Dr. D. Andrew Tompkins, at 628-206-3645.

If you wish to ask questions about the study or your rights as a research participant to someone other than the researchers or if you wish to voice any problems or concerns you may have about the study, please call the office of the Institutional Review Board at 415-476-1814.

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.

Future Contact:

We want to know if we may contact you in the future to see if you are interested in participating in other research studies. If you agree and we contact you to tell you about a study, you have no obligation to actually participate in any study. You can decide when you are told about the study if you want to receive more information about the study. There would be a new consent process for that study. If at any time you decide you no longer want to be contacted about future studies, please let us know by calling 628-206-3365.

Making Your Choices: Please read the sentence below and mark your choice by checking either the "Yes" or "No" box. If you have any questions, please talk to your doctor or nurse, or call our research review board at 415-476-1814. No matter what you decide to do, it will not affect your care or your participation in the main study.

I agree to allow someone to contact me in the future about taking part in more research:

YES ☐ **NO** ☐

CONSENT

You have been given copies of this consent form and the Experimental Subject's Bill of Rights to keep.

You will be asked to sign a separate form authorizing access, use, creation, or disclosure of health information about you.

PARTICIPATION IN RESEARCH IS VOLUNTARY. You have the right to decline to participate or to withdraw at any point in this study without penalty or loss of benefits to which you are otherwise entitled.

If you wish to participate in this study, you should sign below.

Date	Participant's Signature for Consent
Date	Person Obtaining Consent