Stimulant Oxytocin Study

NCT03016598

08/08/2019

Department of Veterans Affairs	INFORMED CONSENT FORM
Subject Name:	**Date:**
Title of Study: 6-week trial of oxytocin for co-occurring cocaine and opioid use disorders.	
Principal Investigator: Christopher Stauffer, MD	**San Francisco VAMC**

CONSENT TO PARTICIPATE IN A RESEARCH STUDY

This is a research study designed to examine how the hormone, oxytocin, affects the behavior of patients with cocaine use disorder and amphetamine use disorder. The study Principal Investigator, Chris Stauffer, M.D., from the San Francisco VA Medical Center (SFVAMC) Research Department and the University of California, San Francisco (UCSF) Department of Psychiatry, or one of his research assistants, will explain this study to you.

Research studies include only people who choose to take part. Please take your time to make your decision about participating and discuss your decision with your family or friends if you wish. If you have any questions, you may ask the researchers.

You are being asked to take part in this study because you have been identified as an individual over age 18 who uses cocaine or amphetamines and receives methadone maintenance therapy.

Why is this study being done?

The purpose of this study is to test the effects of oxytocin on thoughts and behavior in individuals who use cocaine or amphetamines.

Who is funding this study?

This study is funded by the Department of Veterans Affairs.

What is oxytocin and what is the dosage in this study?

Oxytocin is a hormone found naturally in both men and women and has an effect on social behavior, response to stress, and addiction behavior.

Synthetic versions of oxytocin are approved by the U.S. Food and Drug Administration in intravenous form (Pitocin) to induce uterine contraction during childbirth and in intranasal form (Syntocinon) to help with breastfeeding. It is not currently approved for use in people with substance use disorders; therefore, its use in this study is considered experimental.

Intranasal oxytocin has been widely studied and administered at the dose you may receive - 40 International Units (IU). It is considered very safe.

How many people will take part in this study?

Approximately 50 people will take part in this study. Half of these participants will receive oxytocin and half will receive a placebo. A placebo is an inactive substance.

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

If you agree, the following procedures will occur:

Before you begin the main part of the study:

Your eligibility for the study will be assessed in a 3-4-hour visit. This will include receiving your written consent and determination of eligibility. We will conduct some basic baseline measures including a urine toxicology screen, a urine pregnancy test (female participants), surveys/questionnaires, and an interview about your mental health and past/current substance use.

During the main part of the study:

The testing portion of the study will include intranasal study drug administration (oxytocin or placebo) twice daily for six weeks. On the days that you receive your opioid replacement at OTP, a dispensing nurse, or member of the study staff will administer morning oxytocin doses. If you come to OTP to receive your methadone dose, but do not receive your study drug, you will lose $1. For individuals who receive more than 3 take home doses, you will be trained to video chat via Zoom, a HIPAA compliant video conferencing app, during your screening visit. You will contact the study staff on weekdays you do not receive your opioid replacement therapy; during these video calls, you will self-administer the study drug in view of the study staff. If you do not self-administer oxytocin over Zoom with the study staff during the days you are scheduled to, you will lose $1 per day.

You will be given a take-home bottle containing your take-home study drug doses to be self-administered; Evening doses should happen 8-12 hours after each morning dose. We ask that you return your self-administration bottle, empty or not, each week when you meet with us. There will not be any penalty for forgetting to take an evening dose, so return it even if doses have not been administered However, your compensation for the week will be reduced if you do not return your bottle. It is important that you take the evening dose as often as possible and that you not share the medication with anyone else, which would hinder our ability to determine if this medication might be a helpful treatment option.

In addition to twice daily study drug administration, your participation will include seven weekly in-person visits with study staff. At each in-person visit, you will provide a urine sample and complete some questionnaires. Each visit will be about a half hour, except for the first and final (seventh) visits, which will be two hours. For visits 2-7, you will be asked to return your self-administration bottles. Below is a detailed list of additional procedures that you will be asked to complete throughout the study:

- Urine Drug Screen: We will ask you for a urine sample to test for drug use (and pregnancy for female participants) at each of the seven visits. Your results will not affect your participation with the exception of a positive pregnancy test, which will lead to study termination.
- Urine pregnancy test (female participants): We will also perform a urine pregnancy test at each visit. If a pregnancy test is positive at any point, study participation will end in order to avoid medical risks.
- Birth Control (female participants): Women of childbearing potential wishing to participate in this study must agree to use an adequate form of non-hormonal birth control throughout the six weeks of study participation. A study physician will ask you questions about your current birth control methods. Not of childbearing potential is defined as permanent sterilization, postmenopausal, or assigned male at birth.
- Alcohol Breath Test: You may be asked to perform an alcohol breath test to ensure that you are not intoxicated during study sessions. If you test >0.00 on the breath test, you will not be eligible to complete testing and you will not be paid for your time that day.
- Randomization: You will be randomized to receive either oxytocin or placebo. You will receive the same

study drug throughout the study duration. Randomization means that you are put into a group by chance. A computer program will place you into one of the groups. Neither you nor the study staff can choose the group you will be in and neither of you will know which study drug you are receiving during the study. You will have an equal chance of being placed in either the oxytocin or placebo group.

- Oxytocin/Placebo: We will train you how to self-administer the intranasal study drug. The study drug will be dosed twice daily for six weeks
- Surveys/Questionnaires: Throughout the study, you will be given surveys and questionnaires. These questionnaires will ask you about how you feel physically and mentally and ask about past and recent drug use and mental health symptoms.
- Speech Task: You will be asked to give a 5-minute speech on a topic we have selected for you. The speech will be video recorded and it will be adjudicated for quality and delivery.
- Arithmetic Task: You will be asked to complete an arithmetic task while being video recorded. The recording will be adjudicated for correctness, speed, and cognitive abilities. During the task, a live adjudicator will correct any mistakes.
- Video recording: You will be video recorded during the speech and arithmetic tasks. We will inform you before starting the video recording. The recording will be kept secure, private, and confidential. The researchers will use this content to look at your experience of and judge your performance on the speech and arithmetic tasks.
- Physiologic measurements: You will be asked to wear a harness with sensitive physiology instruments in order to measure your psychophysiological responses during various tasks.
- Daily Video Calls: If you receive 3 or more take-home opioid replacement therapy (ORT) doses, in order to monitor adherence, the study staff will ask you to video chat with them while you take your morning dose of the study drug on days you use your take home does of ORT.

Additional Information:

- If at any point in this study you report that you have thoughts of hurting yourself or harming others, you will consult with one of the study psychiatrists. If necessary, a staff member will contact emergency services for further evaluation.
- With your permission, we may contact your primary physician in case of emergency or if we need additional information about your current symptoms and medications that you cannot provide.

Study location: All testing will be conducted at the San Francisco Veterans Affairs Medical Center, 4150 Clement St, San Francisco, CA 94121

How long will I be in the study?

Participation in the study will include: administering study drug twice daily, an initial 3-4 hour visit to determine eligibility, and seven weekly visits. The first and last of the weekly visits will be 2-hours long and the five visits between will be a half-hour each. Total participation in the study will be around 10 hours over about six weeks.

Can I stop being in the study?

Yes. You can decide to stop at any time. Just tell the study researcher or staff person right away if you wish to stop being in the study.

Also, the study researcher may stop you from taking part in this study at any time if he or she believes it is in your best interest, if you do not follow the study rules, or if the study is stopped for unforeseen reasons.

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

- Urine Drug Screen/Alcohol Breath Test: There is a possibility that your test may come back falsely positive.

A positive alcohol breath test will make you ineligible to participate in that day's study session; however, you are welcome to participate in the study on another occasion when you do not test positive for alcohol. Results from the urine drug screen and alcohol breath test will only be used for the purposes of the study and will not be available to any third party.

- Randomization risks: You will be assigned to a treatment group by chance, and the treatment you receive may prove to be less effective or to have more side effects than the other study treatment(s) or other available treatments.
- Oxytocin Nasal Spray: The most common side effects of oxytocin nasal spray include a runny, stuffy, or irritated nose. Potential, rare, adverse effects of the preservatives in the nasal spray include skin rashes and anaphylactoid reactions associated with shortness of breath, low blood pressure, or shock. Side effects that are uncommon include irregular heartbeats, nausea and vomiting. Water intoxication is also an uncommon side effect which may result from high dose or prolonged use of oxytocin and large water consumption. These uncommon side effects are associated with intravenous infusion of oxytocin rather than intranasal administration. No studies using intranasal administration of oxytocin have provided evidence for any of these side effects and it is widely considered safe. A medically licensed doctor will be available on-site throughout study participation.
- Psychological distress: The sensitive nature of topics in assessments or self-report questionnaires may lead to psychological distress. You may take a break from assessments or questionnaires at any time. Additionally, the speech and arithmetic tasks may cause some psychological distress. However, research participation will not be any more distressing than situations you may encounter in everyday life. If there are any concerns over your immediate safety or the safety of others, we may escort you to emergency services or contact appropriate emergency personnel.
- Risks of Cue-Induced Craving: Some of the questionnaires and discussion topics may lead to mild emotional discomfort or a temporary increase in substance craving. The stimuli are generally no more triggering than what is found in your environment.
- Video recording: Video recording during study tasks increases the risk that your confidentiality and privacy may be compromised given the identifiable nature of video contents. Such recordings will be saved on password-protected computers that are within the SFVAMC network or on a secure, encrypted, and password- protected hard drive. Recordings will only be viewed by researchers involved in the study to examine facial and body expressions and evaluate performance in the speech and arithmetic tasks and will be kept indefinitely.
- Video Chat (if applicable): Video conferencing during the study increases the risk that your confidentiality and privacy may be compromised given the identifiable nature of video contents. Study staff will talk with you via the HIPAA compliant video conferencing app, Zoom. Password protected tablets will be used in a private room in the SFVAMC to ensure confidentiality. Videos will not be recorded or kept. Only study-approved research staff will talk with you over Zoom.
- Physiologic measurements: The physiology instrument that we use is like a harness that goes around your chest and shoulder. It is non-invasive and causes no physical pain. Some people experience some mild discomfort while wearing the harness, but that quickly goes away after removing it. Should you begin to experience discomfort such as redness or itching at any point while wearing the harness, we can remove it.
- 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, feel free to ask your study doctor.

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

It is important that you tell your study doctor 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/her at (415) 221-4810 x2-3673.

Treatment and Compensation for Injury: If you are injured as a result of being in this study, VA will ensure that treatment is made available at a VA medical facility. If you are eligible for veteran's benefits, the costs of such treatment will be covered by the Department of Veterans Affairs. If you are not eligible for veteran's benefits, the

costs of treatment may be billed to you or your insurer just like any other medical costs, or covered by the Department of Veterans' Affairs or the University of California, depending on a number of factors. The Department of Veterans Affairs and the University do not normally provide any other form of compensation for injury. For further information about this, call the VA Regional Counsel at (415) 750-2288 or the office of the UCSF Institutional Review Board at (415) 476-1814.

Are there benefits to taking part in the study?

Detailed psychological assessments before and during the participation in the study may assist you in better understanding your substance use history and current psychosocial functioning. The treatment interventions may also help you with your substance use, although this is certainly not guaranteed. While doctors hope oxytocin will be beneficial to you, there is no proof of this yet. We do know that the information from this study will help doctors learn more about oxytocin as a treatment for substance use disorders and contribute to our scientific understanding of substance use and social engagement. This information could help future patients struggling with substance use issues.

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

You are free to choose not to participate in the study. If you decide not to take part in this study, there will be no penalty to you. You will not lose any of your regular benefits, and you may continue receiving other medical and psychological treatment as usual without participating in the study. You may enter a treatment program without taking part in this study.

Will information about me be kept private?

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. If you do not have a VAMC medical record, one will be created for you.

For studies that involve a medical intervention, a progress note entry should indicate that an individual has been enrolled in a research study, any details about study interventions that might affect the subject's clinical care, and the name and contact information for the investigator conducting the study. Subjects' informed consent forms and HIPAA authorization documents are not to be included in the health record. Study tests that are performed by research labs, and 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.

In this study, you will be asked about and tested for illegal drug use. The researchers will keep information about you as confidential as possible, but complete confidentiality cannot be guaranteed. On rare occasions, research records have been subpoenaed by a court. 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 disclose information that may identify you, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings.

Exceptions: A Certificate of Confidentiality does not prevent researchers from voluntarily disclosing information about you, without your consent. For example, we are obligated under State and Federal law to report information about incidents such as child abuse, intent to harm yourself or others. In the case of being a danger to yourself or others, if necessary, study staff may contact emergency services for further evaluation. In addition, a Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing 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 that information.

Finally, the Certificate may not be used to withhold information from the Federal government needed for auditing or evaluating federally funded projects or information needed by the FDA.

Organizations that may look at and/or copy your research records for research, quality assurance, and data analysis include:

- UCSF's Institutional Review Board
- VA Regulatory Personnel
- The U.S. Food and Drug Administration

Participation in research may involve a loss of privacy, but information about you will be handled as confidentially as possible.

What are the costs of taking part in this study?

You will not be charged for any of the study treatments or procedures.

Will I be paid for taking part in this study?

You will be compensated for participating in this study to cover your time and travel expenses. You can make up to $350 for your full participation in the study. After today's screening visit you will receive $50. For the remaining visits, you will receive some of the money you earned for your participation, at the time of your visit, while the remainder will be put into a completion bonus pot. The money you earn towards your completion bonus pot will be provided to you after your final visit with us.

Visit 1: You will earn $50 after completing the first visit; you will receive $30 immediately after your visit and $20 will go towards your completion bonus.

Visits 2-6: You can earn up to $40 at each follow-up visit. At the time of the visit, if you remember to return your nasal spray bottles, you will receive $30. If you do not return your nasal spray bottle during the visit, $10 will be subtracted from your earnings that day and you will only receive $20. After each of these visits, $10 will be added to your completion bonus pot whether or not you remember to bring your bottle. If you have take home ORT doses do not complete a study drug self-administration in the view of study staff, you will forfeit $1 from the next week's pay. If you arrive at OTP and do not receive your study drug, you will lose $1 from next week's pay.

Visit 7: You will earn $50 after completing the final visit; you will receive $30 ($10 will be subtracted from this if you do not bring your bottle back) plus $20 that will go towards the completion pot. Upon completing this visit, you will also receive your completion bonus pot earnings, which can be up to $90.

Remember: it does not matter if the bottle you bring is full or empty, just that you return it for adherence monitoring.

Examples:

- If you attend all visits, your completion bonus will be $90 ($20 for the first and last visits, $10 for visits 2- 6).
- If you attend all but one study visit, you will forfeit your $40 for that visit ($30 the day of and $10 in the bonus pot, making your total bonus pot $80).
- If you miss two follow-up visits total, you will forfeit the $30 for those visit days and your completion

bonus will be $70, and so on.
- If you miss the final session, you will not receive your bonus pot or you final $30 payment.
- If you forget to video call the study staff three days, you will forfeit $3 from your next visit pay. You will receive $27 if you bring back your spray bottle instead of the possible $30.

This means that in order to receive the full $350, **you must attend every single visit ,return all of your nasal spray bottles, video chat with the study staff every weekday (if applicable,) and receive the study drug dose during every visit to OTP.**

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 the researcher(s) about any questions or concerns you have about this study. Contact the

	Screening Visit	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6	Visit 7	TOTAL
Take home on visit day	$50	$30	$30	$30	$30	$30	$30	$30	$260
Loss if do not bring bottle in	n/a	n/a	-$10	-$10	-$10	-$10	-$10	-$10	(up to -$60)
Loss no observed AM dose	n/a	n/a	(up to -$5 each missed dose)	(up to -$5 each missed dose)	(up to -$5 each missed dose)	(up to -$5 each missed dose)	(up to -$5 each missed dose)	(up to -$5 each missed dose)	(up to -$30)
Completion Bonus	n/a	+$20	+$10	+$10	+$10	+$10	+$10	+$20	+$90
									$254-**$350**

researchers at (415) 221-4810 x2-3673.

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

If you have any questions, comments, or concerns about taking part in this study, first talk to the researchers (above). If for any reason you do not wish to do this, or you still have concerns after doing so, you may contact the office of the Committee on Human Research, UCSF's Institutional Review Board (a group of people who review the research

to protect your rights).

You can reach the IRB office at (415) 476-1814, 8 am to 5 pm, Monday through Friday. Or you may write to: Committee on Human Research, Box 0962, University of California, San Francisco (UCSF), San Francisco, CA 94143.

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Please read each sentence below and think about your choice. After reading each sentence, put your **initials** in the "Yes" or "No" box.

No matter what you decide to do, it will not affect your care.

1) Someone may contact me in the future to ask me to take part in more research.

YES	NO

2) I agree to being videotaped and/or audio taped during the study as specified in the consent.

YES	NO

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

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

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

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

_____
Participant's Name *(print)*

_____ _____
Date Participant's Signature for Consent

_____ _____
Date Person Obtaining Consent

Date of Document

VA 10-1086