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Title: Effects of Intramuscular Oxytocin on Pupil Diameter and Heart Rate Variability
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Wake Forest®
School of Medicine

Department of Anesthesiology

Effects of intramuscular oxytocin on pupil diameter and heart rate variability in healthy volunteers

Informed Consent Form to Participate in Research
James C. Eisenach, M.D., Principal Investigator

SUMMARY

You are invited to participate in a research study. The purpose of this research is to evaluate the effects of oxytocin (naturally occurring hormone) given by an intramuscular (IM; into the muscle) injection, has on your parasympathetic nervous system. The parasympathetic nervous system is the part of the involuntary nervous system that is sometimes called the "rest and digest" system; the parasympathetic system conserves energy as it slightly slows the heart rate, increases intestinal and gland activity, and relaxes sphincter muscles in the gastrointestinal tract. You are invited to be in this study because you are a healthy subject. Your participation in this research will involve 2 study visits.

Participation in this study will involve receiving IM administration of oxytocin and we will record changes in your pupil size by using an infrared camera for video recording of your pupil. All research studies involve some risks. A risk to this study that you should be aware of is discomfort from the IM injection. There is not the possibility that you may benefit from participation in this study.

Your participation in this study is voluntary. You do not have to participate in this study if you do not want to. This is not a treatment study and there are no additional choices. You will not lose any services, benefits, or rights you would normally have if you choose not to participate.

The remainder of this form contains a more complete description of this study. Please read this description carefully. You can ask any questions if you need help deciding whether to join the study. The person in charge of this study is James C. Eisenach, M.D. If you have questions, suggestions, or concerns regarding this study or you want to withdraw from the study his/her contact information is: James C. Eisenach, M.D.
[redacted]

If you have any questions, suggestions or concerns about your rights as a volunteer in this research, contact the Institutional Review Board at 3[redacted] or the Research Subject Advocate at Wake Forest at [redacted].

INTRODUCTION

You are invited to be in a research study. Research studies are designed to gain scientific knowledge that may help other people in the future. You are being asked to take part in this study because you are a healthy adult. Your participation is voluntary. Please take your time in making your decision as to whether or not you wish to participate. Ask your study doctor or the study staff to explain any words or information contained in this informed consent document that you do not understand. You may also discuss the study with your friends and family.

WHY IS THIS STUDY BEING DONE?

The purpose of this research study is to evaluate the effects of oxytocin given by an intramuscular (IM) injection, has on your parasympathetic nervous systems; in particular your heart rate changes and pupil changes after receiving the study medication.

In this study oxytocin will be compared to placebo. A placebo is a substance, like a sugar pill, that is not thought to have any effect on your disease or condition. In this study you will receive the active study medication, oxytocin and the placebo which is not active, on different visits. On both visits you will receive one or the other by an IM injection. Placebos are used in research studies to see if the drug being studied really does have an effect.

This study is a double-blinded, randomized, crossover study. Neither you nor the investigator will know which study medication you are receiving. Cross-over means that you will get both the Oxytocin injection and a placebo injection; the order that you receive the injections will be randomized. Randomized means that you are put into a group by chance. It is like flipping a coin. This is done so that a fair evaluation of results can be made. This information is available to the researchers if needed in an emergency.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

We will enroll 22 people at this research site. In order to identify the 22 subjects needed, we may need to screen as many as 30 because some people will not qualify to be included in the study. To be considered for inclusion in this study, you must have been vaccinated against SARS-CoV-2 (COVID-19). We will request to see a copy of your verification record (vaccine card or North Carolina Health and Human Services printed form).

WHAT IS INVOLVED IN THE STUDY?

You will have 2 visits to the Pain Research Unit, located at Piedmont Plaza 2. Study visits1 and 2 will each last approximately 2.5 hours.

If you take part in this study, you will have the following tests and procedures:

PROCEDURES

Vital Signs: we will monitor your blood pressure, heart rate and oxygen saturation (amount of oxygen in your blood).

Laboratory Testing: female participants of child-bearing potential will have a urine pregnancy test to determine that they are not pregnant.

Non-Invasive Heart Rate Monitoring: we will attach a small portable heart monitor to you during your visits to record your heart rate during your testing. The monitor will be placed around your chest with an elastic strap.

Pupillometry Testing: we will have you sit in a comfortable chair and position your head so your chin is resting in a chinrest (very similar to the way an eye doctor would examine your eyes). We will ask you to stay in this position for the testing. A continuous video recording will be made of the size of your pupils while you are sitting with your chin in the chinrest. This video recording is being done so that we can record the changes in your pupil before we administer the oxytocin and afterward.

Intramuscular injection of Oxytocin or Placebo: we will give you an injection of oxytocin or placebo into the muscle in your arm.

Study Visit 1

You will report to the Pain Research Unit at Piedmont Plaza 2. You will review and sign the Informed Consent. After informed consent is adequately obtained, a detailed medical history will be obtained. During this visit we will measure your blood pressure, heart rate, respiratory rate, and we will place a clip on your finger which will measure the oxygen in your blood. Female participants of child-bearing potential will provide a urine sample for a pregnancy test. The heart rate monitor will be placed around your chest. We will then have you sit in a chair and place your chin in a chinrest, we will have you maintain your focus at a computer monitor that will have an image of a fixed color, and once we have calibrated the system to your pupil we will begin a recording of your pupil. We will have you sit with your chin in the chinrest for 20 second intervals every 5 minutes for 20 minutes. We will then administer an IM injection into your arm of Oxytocin or placebo. After administration of the study medication, we will have you return to the chinrest every 5 minutes for 20 second intervals over a period of 120 minutes. We will also measure your blood pressure, heart rate, respiratory rate and oxygen saturation at 30, 60, and 90 minutes after the injection.

Study Visit 2

On the second visit; at least 24 hours after visit 1, you will report to the Pain Research Unit at Piedmont Plaza 2, and the study staff will repeat the same procedures from visit 1 and you will receive an injection that is opposite from the first visit. We will complete study visit 2 within 4 weeks of study visit 1.

As part of this research study, you will be videotaped. We will only videotape the size of your pupils, your face or any other identifying characteristics will not be videotaped. This is being done so we can have a measurement of your pupils after the administration of oxytocin. You understand that you may request the filming or recording be stopped at any time during the course of the research study and withdraw from the study at this time. You can also withdraw your consent to use and disclose the photograph/videotape/audiotape before it is used. You should also understand that you will not be able to inspect, review, or approve the videotapes or other media (including articles containing such) before they are used in this study.

Please choose one of the following regarding the use and disclosure of the videotape used in this research study:

_____ I would like the videotapes of me to be destroyed once their use in this study is finished.

____ The videotapes of me can be kept for use in future studies provided they are kept secure and any future study will be reviewed by an IRB. I understand that I will not be able to inspect, review or approve their future use.

How Long Will I Be in the Study?

You will be in the study for 2 visits.
We will call you at days 1 and 7 after your study visits and ask about any events you experience after the study.

You can stop participating at any time. If you decide to stop participating in the study we encourage you to talk to the investigators or study staff first to learn about any potential health or safety consequences.

What Are the Risks of the Study?

Being in this study involves some risk to you. You should discuss the risk of being in this study with the study staff. Risks and side effects related to the oxytocin we are studying include:

Oxytocin
Oxytocin is approved by the Food and Drug Administration (FDA) for use in the dose and route of administration we are using. We will monitor you for many theoretical problems such as changes in your blood pressure, how fast your heart is beating, and your urge to breathe.
There is the possibility of a feeling of being flushed (warm feeling), headache and increased heart rate with no significant change in blood pressure during or immediately after the injection. These events have been reported by participants in a previous study of oxytocin given by intravenous administration. The events were short lived, lasting approximately 12-15 minutes.

Pupillometry
The use of infrared video camera will not expose you to a greater amount of light than expected in normal use of an infrared camera.

In addition, there is a slight risk of a breach of confidentiality. We will do our best to protect your confidential information. There also may be other side effects that we cannot predict. You should tell the research staff about all the medications, vitamins and supplements you take and any medical conditions you have. This may help avoid side effects, interactions and other risks.

Intramuscular injection
The intramuscular injection may be uncomfortable and cause a stinging sensation. You may have a small bruise at the injection site.

Placebo
There is no risk associated with the placebo injection.

Taking part in this research study may involve providing information that you consider confidential or private. Efforts, such as coding research records, keeping research records secure and allowing only authorized people to have access to research records, will be made to keep your information safe.

Reproductive Risks and other Issues to Participating in Research

Due to unknown risks and potential harm to the unborn fetus, sexually active women of childbearing potential must use a reliable method of birth control while participating in this study. Reliable methods of birth control are: abstinence (not having sex), oral contraceptives, intrauterine device (IUD), DepoProvera, tubal ligation, or vasectomy of the partner (with confirmed negative sperm counts) in a monogamous relationship (same partner). An acceptable, although less reliable, method involves the careful use of condoms and spermicidal foam or gel and/or a cervical cap or sponge. We encourage you to discuss this issue further with your physicians if you have any questions.

Pregnant women are excluded from participation in this study. Because some methods of birth control are not 100% reliable, a pregnancy test is required at least 10 days from your last normal menstrual period, if you are a sexually active woman of childbearing potential.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

You are not expected to receive any direct benefit from taking part in this research study. We hope the information learned from this study will benefit other people in the future.

WHAT OTHER CHOICES ARE THERE?

This is not a treatment study. Your alternative is to not participate in this study.

WHAT ARE THE COSTS?

All study costs, including any study medications and procedures related directly to the study, will be paid for by the study. Costs for your regular medical care, which are not related to this study, will be your own responsibility.

WILL YOUR RESEARCH RECORDS BE CONFIDENTIAL?

The results of this research study may be presented at scientific or medical meetings or published in scientific journals. Your identity and/or your personal health information will not be disclosed unless it is authorized by you, required by law, or necessary to protect the safety of yourself or others. There is always some risk that even de-identified information might be re-identified.

Participant information may be provided to Federal and other regulatory agencies as required. The Food and Drug Administration (FDA), for example, may inspect research records and learn your identity if this study falls within its jurisdiction.

WILL YOU BE PAID FOR PARTICIPATING?

You will be paid $200 if you complete all the scheduled study visits. If you withdraw for any reason from the study before completion you will be paid as follows:

Completion of study visit 1: $50
Completion of study visit 2: $150

To receive payment, you must provide your social security number, name and address so that we can comply with IRS (Internal Revenue Service) reporting requirements. When payments are reported to the IRS we do not let them know what the payment is for, only that you have been paid. If you do not wish to provide this information you can still take part in this study but you will not be paid.

The findings from this research may result in the future development of products that are of commercial value. There are no plans to provide you with financial compensation or for you to share in any profits if this should occur.

WHO IS SPONSORING THIS STUDY?

This study is being sponsored by the Department of Anesthesiology at Wake Forest School of Medicine. The sponsor is providing money or other support to Wake Forest University Health Sciences to help conduct this study. The researchers do not, however, hold a direct financial interest in the sponsor or the product being studied.

WHAT HAPPENS IF YOU EXPERIENCE AN INJURY OR ILLNESS AS A RESULT OF PARTICIPATING IN THIS STUDY?

Should you experience a physical injury or illness as a direct result of your participation in this study, Wake Forest University School of Medicine maintains limited research insurance coverage for the usual and customary medical fees for reasonable and necessary treatment of such injuries or illnesses. To the extent research insurance coverage is available under this policy the reasonable costs of these necessary medical services will be paid, up to a maximum of $25,000. Wake Forest University Baptist Medical Center holds the insurance policy for this coverage. It provides a maximum of $25,000 coverage for each claim and is limited to a total of $250,000 for all claims in any one year. The Wake Forest University School of Medicine, and

the North Carolina Baptist Hospitals, Incorporated do not assume responsibility to pay for these medical services or to provide any other compensation for such injury or illness. Additional information may be obtained from the Medical Center's Director of Risk and Insurance Management, at [redacted].

If you are injured, the insurer may require information such as your name, social security number, and date of birth in order to pay for your care. This is because the insurer is required by law to report any payments made to cover the care of any persons who are members of a government insurance plan to the Department of Health and Human Services.

You do not give up any legal rights as a research participant by signing this consent form. For more information on medical treatment for research related injuries or to report a study related illness, adverse event, or injury you should call James Eisenach at [redacted] or after hours you should call the study coordinator at [redacted]

WHAT ABOUT MY HEALTH INFORMATION?

In this research study, any new information we collect from you about your health or behaviors is considered Protected Health Information. The information we will collect for this research study includes**:** medical history and medication history.

If this research study involves the diagnosis or treatment of a medical condition, then Protected Health Information collected from you during this study may be placed in your medical record, and may be used to help treat you, arrange payment for your care, or assist with Medical Center operations.

We will make every effort to keep your Protected Health Information private. We will store records of your Protected Health Information in a cabinet in a locked office or on a password protected computer.

Your personal health information and information that identifies you ("your health information") may be given to others during and after the study. This is for reasons such as to carry out the study, to determine the results of the study, to make sure the study is being done correctly, to provide required reports and to get approval for new products.

Some of the people, agencies and businesses that may receive and use your health information are the research sponsor; representatives of the sponsor assisting with the research; investigators at other sites who are assisting with the research; central laboratories, reading centers or analysis centers; the Institutional Review Board; representatives of Wake Forest University Health Sciences and North Carolina Baptist Hospital; representatives from government agencies such as the Food and Drug Administration (FDA) or the Office of Human Research Protections (OHRP), the Department of Health and Human Services (DHHS) and similar agencies in other countries.

Some of these people, agencies and businesses may further disclose your health information. If disclosed by them, your health information may no longer be covered by federal or state privacy regulations. Your health information may be disclosed if required by law. Your health

information may be used to create information that does not directly identify you. This information may be used by other researchers. You will not be directly identified in any publication or presentation that may result from this study unless there are photographs or recorded media which are identifiable.

Any Protected Health Information collected from you in this study that is maintained in the research records will be kept for an indeterminate period of time. This authorization does not expire. You will not be able to obtain a copy of your Protected Health Information in the research records until all activities in the study are completely finished.

You can tell Dr. James C. Eisenach that you want to take away your permission to use and share your Protected Health Information at any time by sending a letter to this address:

James C. Eisenach, M.D.
[redacted]

However, if you take away permission to use your Protected Health Information you will not be able to be in the study any longer. We will stop collecting any more information about you, but any information we have already collected can still be used for the purposes of the research study.

By signing this form you give us permission to use your Protected Health Information for this study.

If you choose to participate in this study, your medical record at Wake Forest University Baptist Medical Center will indicate that you are enrolled in a clinical trial. Information about the research and any medications or devices you are being given as a participant may also be included in your medical record. This part of the medical record will only be available to people who have authorized access to your medical record. If you are not a patient at this Medical Center, a medical record will be created for you anyway to ensure that this important information is available to doctors in case of an emergency.

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

A North Carolina Baptist Hospital (NCBH) medical record will be created for all study participants. Information about your participation in the study will be placed in the NCBH medical record, along with any routine medical test results that were obtained at NCBH as part of this study.

WHAT ARE MY RIGHTS AS A RESEARCH STUDY PARTICIPANT?

Taking part in this study is voluntary. You may choose not to take part or you may leave the study at any time. Refusing to participate or leaving the study will not result in any penalty or loss of benefits to which you are entitled. If you decide to stop participating in the study we encourage you to talk to the investigators or study staff first to learn about any potential health or safety consequences. The investigators also have the right to stop your participation in the study at any time. This could be because new information becomes available, you had an unexpected reaction, you failed to follow instructions, or because the entire study has been stopped.

Information that identifies you may be removed from the data or specimens that are collected as part of this study and could be used for future research or shared with others without additional consent.

You will be given any new information we become aware of that would affect your willingness to continue to participate in the study.

This study will be enrolling students from the Wake Forest University Medical Center campus. In addition to your rights as a research participant noted in the previous section, as a student, you are under no obligation to participate in this study. You may refuse to participate or withdraw from the study at any time and for any reason without affecting your grades, performance evaluations, or assignments. You will not be pressured into participating in this research study by any statements or implied statements that your grades, performance evaluations or assignments will be affected by your willingness to enroll in the study. Your medical records/information will not be used by the faculty, administration or study staff to make decisions regarding the status of your medical benefits. If you have questions regarding your enrollment in the study and your status as a medical student, please contact the Office of Student Services for additional information.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

For questions about the study or in the event of a research-related injury, contact the study investigator, Dr. James Eisenach at [redacted] or after hours you should call the study coordinator by calling [redacted].

The Institutional Review Board (IRB) is a group of people who review the research to protect your rights. If you have a question about your rights as a research participant, or you would like to discuss problems or concerns, have questions or want to offer input, or you want to obtain additional information, you should contact the Chairman of the IRB at [redacted] or the Research Subject Advocate at [redacted].

You will be given a copy of this signed consent form.

SIGNATURES

I agree to take part in this study. I authorize the use and disclosure of my health information as described in this consent and authorization form. If I have not already received a copy of the Privacy Notice, I may request one or one will be made available to me. I have had a chance to ask questions about being in this study and have those questions answered. By signing this consent and authorization form, I am not releasing or agreeing to release the investigator, the sponsor, the institution or its agents from liability for negligence.

Subject Name (Printed):_____

Subject Signature: _____ Date: _____Time:_____ am pm

Person Obtaining Consent (Printed):_____

Person Obtaining Consent: _____

Date: _____Time:_____ am pm