Enhancing Prolonged Exposure Therapy for PTSD with Oxytocin

NCT04228289

September 4, 2024

Subject's Name: **Date:**

Principal Investigator: Julianne Flanagan, Ph.D.

Study Title: Enhancing Prolonged Exposure Therapy for PTSD with Oxytocin

SUMMARY
- You are being asked to participate in a research study. Participation is voluntary; however, you must be enrolled at Ralph H. Johnson VA Health Care System (RHJVAHCS) or be eligible for care at the RHJVAHCS (verification is required). You have the option to complete visits in our research offices or through telemedicine visits.
- The purpose(s) of the research is to test a new medication for Veterans experiencing posttraumatic stress disorder (PTSD). The study consists of 10 weekly therapy sessions. Once per week before each therapy session, you will take an intranasal dose of investigational medication. The study also involves a 3 and 6 month follow up appointment. You will be asked to complete weekly surveys to assess how you are feeling.
- You may experience side effects such as: nasal irritation, runny nose, and tearing of the eyes.
- There is no direct and guaranteed benefit to you for participating in this study.
- If you decide not to participate, you will be provided with referrals for other treatment.

A. PURPOSE OF THE RESEARCH

You are being asked to volunteer for a research study. In order to participate in this research study, you must be either enrolled in the RHJVAHCS or eligible for care there (verification is required). The purpose of this study includes evaluation of both the safety and effectiveness of the study drug.

The purpose of this study is to test the ability of a medication (oxytocin) to improve a form of talk therapy (Prolonged Exposure therapy, or PE) for Veterans with Posttraumatic Stress Disorder (PTSD). PE is a widely used form of counseling or talk therapy for PTSD. In order to accomplish this goal, we are conducting a clinical trial. The study consists of 10 weekly therapy sessions. If you are enrolled, once per week before each therapy session, you will take an intranasal dose of investigational medication. This study has the potential to improve patient care practices, advance the science in this area, and decrease public health costs.

The investigational medication we are testing is called oxytocin. Oxytocin is currently approved by the Food and Drug Administration (FDA) to be given to women who are pregnant in order to speed up the labor process. However, oxytocin is considered "investigational use" in this study, meaning that the FDA has not approved it for the treatment of PTSD.

Please read this consent form carefully and take your time making your decision. As your study doctor or study staff discusses this consent form with you, please ask him/her to explain any words or information that you do not clearly understand. You are being asked to participate in this study

Subject's Name: **Date:**

Principal Investigator: Julianne Flanagan, Ph.D.

Study Title: Enhancing Prolonged Exposure Therapy for PTSD with Oxytocin

because you are at Veteran eligible for care at the RHJVAHCS, at least 18 years of age and you may meet criteria for PTSD. The study is sponsored by the Veterans Affairs (VA). The investigator in charge of this study at the Ralph H. Johnson VA Health Care System is Dr. Julianne Flanagan. The study is being done at two sites. Approximately 210 people will take part study-wide and 105 will take part at this institution.

A. PROCEDURES

All procedures will take place at the Ralph H. Johnson VA Health Care System (or through home- based telemedicine).

If you agree to be in this study, the following will happen:

1. You will be asked to attend an initial appointment where we will ask you questions to see if you are eligible for participation in the study. You will be asked to provide verification that you are receiving care or enrolled at the RHJVAHCS.
2. During the first visit, you will be asked to complete questionnaires about topics such as your age, employment, and education. You will also be asked to complete questionnaires to assess your symptoms of PTSD and other conditions, such as depression and alcohol/drug problems, in order to determine eligibility for study participation. These assessments will take place while you are physically located at the RHJVAHCS or via home-based telemedicine.
3. A history and physical (H&P) exam will be conducted. H&P exams will include a physical and neurological examination; blood pressure and pulse measurements; and weight and body mass index (BMI) calculation. If you are a female, you will be given a pregnancy test. If you are pregnant, you will not be able to participate in the study. Instead, clinical referrals will be provided for you. The assessment visit will last approximately 2-3 hours.
4. If the physical examination and test results show that you are eligible for the study, you will be randomly assigned to one of two groups. The two groups are Group A (dose of oxytocin) and Group B (placebo, an inactive substance). This means that you have a 50/50 chance (like flipping a coin) of being in either group. Neither the researchers nor you will make the choice to which group you are assigned.

Subject's Name: **Date:**

Principal Investigator: Julianne Flanagan, Ph.D.

Study Title: Enhancing Prolonged Exposure Therapy for PTSD with Oxytocin

1. After you are assigned to your treatment group, you will start the treatment phase, where you will be scheduled to meet with a therapist to receive 10 sessions of Prolonged Exposure (PE) therapy. The therapy sessions will last 60-90 minutes each and generally be held once a week. Prior to each therapy session, you will take a dose of the study medication intranasally.
2. Female participants will take a pregnancy test prior to receiving the weekly dose of medication.
3. All sessions will be in individual therapy format (not group) and delivered by a trained clinical psychologist.
4. All therapy sessions will be recorded. These recordings are important for you to complete your homework assignments in treatment, ensure treatment fidelity and for associated research procedures. Homework includes things like worksheets or interactive exercises related to your PTSD. As part of your homework, you will be asked to review these recordings between your weekly therapy sessions.
5. At each of your therapy visits (either in-person or through telemedicine visits), you will be asked to complete some assessments about your PTSD and other mental health symptoms (such as sleep, depression, and how well you are functioning in your relationships and other areas of life). Your heart rate and skin conductance will be measured continuously throughout each therapy session. You will also be asked to complete additional assessments during your week 5 and 10 visits. The weekly visits will last about 2-3 hours.
6. After the treatment phase, you will enter the follow-up phase where you will be asked to complete 3- and 6-month follow-up visits (either in office or through telehealth visits). During these appointments, you will be asked to complete similar assessments. The follow- up visits will last about 1.5 hours.
7. If you indicate during the assessment interviews (in person or via telemedicine) or on the questionnaires that you are having thoughts about harming yourself or someone else, we will ask you to sign a "safety plan". This safety plan is a promise you make to us that you will call Dr. Flanagan, your study therapist, or an emergency number we give you or 911, and that you agree to refrain from hurting yourself or someone else. The numbers to call will be on the safety plan contract. We will also give you a list of local treatment referrals.

Subject's Name: **Date:**

Principal Investigator: Julianne Flanagan, Ph.D.

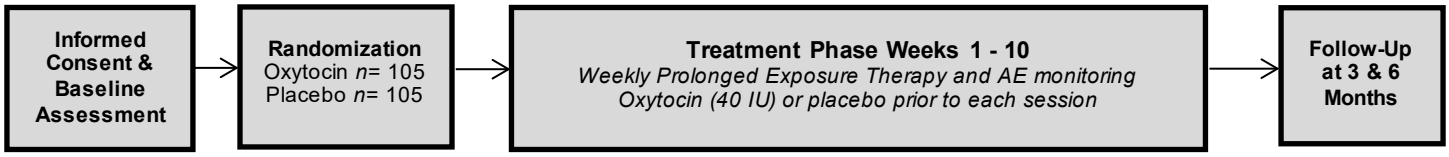
Study Title: Enhancing Prolonged Exposure Therapy for PTSD with Oxytocin

8. If you are a woman of childbearing potential and/or a man capable of fathering a child before, during, and/or after participation precaution should be taken. Examples of acceptable methods of birth control for participants involved in the study includes birth control pills, patch, IUD, implant, ring, condom, sponge, diaphragm with spermicide, or avoiding sexual activity that could cause you to become pregnant.

While participating in this research study, do not take part in any other research project without approval from the investigators. This is to protect you from possible injury from things such as extra blood drawing, extra X-rays, or potential drug interactions. Taking part in other research studies without first discussing it with the investigators of this study may invalidate the results of this study, as well as that of the other studies.

B. DURATION

Participation in the study will take about 13 visits over a period of 12 months.



C. RISKS AND DISCOMFORTS

Oxytocin: The FDA has approved oxytocin for use among women during labor. When used to induce labor, adverse effects associated with oxytocin have included mental disturbances, nausea, vomiting, irregular heartbeat, high blood pressure, seizures, and unexpected bleeding or contraction of the uterus in a small number of women. When used as a nasal spray, other side effects may include nasal irritation, runny nose, and tearing of the eyes. However, several studies have been conducted in humans with the same intranasal dose as this study, and no adverse side effects have been reported. Oxytocin may have unknown side effects. The researchers will let you know if they learn anything that might make you change your mind about participating in the study.

Interviews: Because this study involves answering questions about and discussing topics of a personal and sensitive nature, you may become upset. You may also experience some physical or emotional distress during the interviews or therapy sessions. If you feel significant distress at any time, you may stop filling out the questionnaires or decide to stop the interview or visit.

Subject's Name: **Date:**

Principal Investigator: Julianne Flanagan, Ph.D.

Study Title: Enhancing Prolonged Exposure Therapy for PTSD with Oxytocin

You do not have to answer any questions on the questionnaires or during the interview that you do not want to answer.

Risks to pregnant women: If you are a woman of childbearing potential, you will receive a pregnancy test, and if pregnant, you will not be allowed to participate in the study as oxytocin can induce labor. If you are capable of becoming pregnant, you must be using a medically approved method of birth control (such as abstinence, surgical sterilization, contraceptive pills, diaphragms, or other forms of barrier contraceptives) and you must continue to do so during the course of the study.

Confidentiality: Your personal identifiers (e.g., name, date of birth) are kept separate from your assessment materials. All assessments are kept in a locked filing cabinet in a locked office suite and/or on a password protected server. Thus, it would be very difficult for someone to match personal identifiers with the information you provide during the assessment and during treatment. Every effort will be made to keep your information confidential and protected from third parties.

However, there still remains a risk of a loss of confidentiality of your personal information as a result of participation in this study.

Randomization Risk: You will be assigned to the study medication by chance. The study medication you receive may prove to be less effective or to have more side effects than the other study medication or other available treatments

Placebo Risk: If you are in the group that receives placebo (saline), your condition will go without active medication treatment for 10 weeks. However, everyone who participates in the study will receive PE therapy with a trained therapist.

Limits of Confidentiality: Suspected or known abuse or neglect of a child, disabled or elder abuse, or threatened violence to self or others may be reported to appropriate authorities. There is always a chance that any procedure can harm you. The procedures in this study are no different. In addition to the risks described above, you may experience a previously unknown risk or side effect.

Risks of the usual care you receive are not risks of this study. Those risks are not included in this consent form. You should talk with your healthcare providers if you have any questions about the risks of usual care.

Subject's Name: **Date:**

Principal Investigator: Julianne Flanagan, Ph.D.

Study Title: Enhancing Prolonged Exposure Therapy for PTSD with Oxytocin

D. MEDICAL RECORDS and/or CERTIFICATE OF CONFIDENTIALITY

Since you are a RHJVAHCS patient – or are enrolled at the RHJVAHCS, you have a VA medical record. If you have never been a Ralph H. Johnson VA Medical Center patient, a VA medical record will be created for the purposes of this study. Results of research tests or procedures will be included in your VA medical record. All information within your medical record can be viewed by individuals authorized to access the record. We will make every effort to keep confidential all research information in the medical record that identify you to the extent allowed by law.

E. BENEFITS

The potential benefit to you is that the treatment you receive may prove to be more effective than the other study treatment or than other available treatments, although this cannot be guaranteed. However, it is hoped that the information gained from the study will help in the treatment of future patients with PTSD and will help the researcher learn more about how to best treat other Veterans.

F. COSTS

You will not be charged for any treatments or procedures that are part of this study. If you usually pay co-payments for VA care and medications, you will still pay these copayments for VA care and medications that are not part of this study.

G. PAYMENT TO PARTICIPANTS

In return for your time, effort, and travel expenses, you will be paid up to $600. The VA will either directly deposit the compensation into your bank account, or if you do not have a bank account, you will be issued a direct deposit Debit Mastercard, provided by the Ralph H. Johnson VAHCS. Ink signatures from participants are required for both options prior to payment submission. Direct deposit will be available within 3-5 days of submission. Funds for the Debit Mastercard will be available within 10 business days of submission. If you do complete the study, you will receive $50 for the baseline assessment visit, $25 for each weekly PE session and study assessment, $50 each for week 5 and week 10 sessions, and $100 for each follow- up visit. The IRS requires a tax form be filed if your compensation exceeds $600.00/year.

Subject's Name: **Date:**

Principal Investigator: Julianne Flanagan, Ph.D.

Study Title: Enhancing Prolonged Exposure Therapy for PTSD with Oxytocin

H. ALTERNATIVES

If you choose not to participate in this study, you could receive other treatments for PTSD. These treatments include both pharmaceutical (involving a medication) and/or non-pharmaceutical approaches. If you choose not to participate, it will not affect your relationship with any current treatment providers you may have or your right to health care or any other services to which you are otherwise entitled.

Withdrawal from the Study: Your participation in this study is voluntary. You may refuse to take part in or stop taking part in this study at any time. You should talk with the investigator in charge of this study if you decide to do this. Your decision not to take part in the study will not affect your current or future medical care or any benefits to which you are entitled. The investigators and/or the sponsor may stop your participation in this study at any time if they decide it is in your best interest. They may also do this if you do not follow the investigator's instructions. If your participation is ended for medical reasons, you will be referred to a doctor or other health professional for care. You will be responsible for the cost of these services.

I. DATA SHARING

Some data related to the assessments completed via telemedicine will be available to staff members located at the SFVAMC. However, information about you (including your identifiable private information and/or any identifiable biospecimens) may have all of your identifiers removed and used for future research studies or distributed to other researchers for future research without additional informed consent from you or your legally authorized representative.

J. DISCLOSURE OF RESULTS

Research results, including individual research results, will not be disclosed to subjects.

K. PHOTOGRAPHS, VOICE AND/OR VIDEO RECORDING

Participation in this study includes recording your therapy sessions, as these recordings are important for you to complete your homework assignments in treatment, ensure treatment fidelity and for other associated study measures. Homework includes things like worksheets or interactive exercises related to your PTSD. As part of your homework, you will be asked to review these recordings between your weekly therapy sessions. This could pose a risk to confidentiality and we will take every step possible to ensure that all recordings are stored securely and any risks minimized. However, there is a risk is that you could be identified, including information regarding alcohol and drug

Subject's Name: **Date:**

Principal Investigator: Julianne Flanagan, Ph.D.

Study Title: Enhancing Prolonged Exposure Therapy for PTSD with Oxytocin

use, or other criminal behavior. To minimize any risk, all recordings will be kept in a locked file cabinet or on a secure and encrypted server and only the project staff and Principal Investigator will have access to the recordings. They will be destroyed after the study has been completed. Do you authorize the research team to record your therapy sessions?

Please indicate by your choice:

____Yes, I agree to be recorded

____No, I do not agree to be recorded

L. SIGNIFICANT NEW FINDINGS

If there are significant new findings during the course of the study, you will be notified.

M. STUDENT PARTICIPATION

Your participation or discontinuance will not constitute an element of your academic performance, nor will it be a part of your academic record at this Institution.

N. EMPLOYEE PARTICIPATION

Your participation or discontinuance will not constitute an element of your job performance or evaluation, nor will it be a part of your personnel record at this Institution.

O. CLINICAL TRIALS.GOV

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.

P. COLLECTION OF SPECIMENS

Urine samples will be collected at each visit for female participants only. The sample will be collected to test for pregnancy. The sample will not be stored.

Subject's Name: **Date:**

Principal Investigator: Julianne Flanagan, Ph.D.

Study Title: Enhancing Prolonged Exposure Therapy for PTSD with Oxytocin

Q. FUTURE CONTACT

The researcher in charge of this study might like to contact you in the future about other research opportunities. Please initial by your choice below.

Please indicate by your choice below:

____Yes, I agree to be contacted

____No, I do not agree to be contacted

You have the option of receiving appointment reminders and link to study surveys through text messages or electronically (via email or secure message). Should you elect to receive text messages, normal cellular data usage and rates will apply. Please indicate your choice below.

Please indicate by your choice below:

____Yes, I agree to be contacted via text/secure message

____No, I do not agree to be contacted via text/secure message

CONSENT

Your privacy is very important to us, and the researchers will make every effort to protect it. Results of this research will be used for the purposes described in this study. These results may be published, but you will not be identified.

The investigators associated with this study, the sponsor, and the MUSC Institutional Review Board for Human Research will have access to identifying information. Information that is obtained concerning this research that can be identified with you will remain confidential to the extent possible within State and Federal law. There are times when we may have to show your records to other people from Federal agencies that oversee our research such as the Department of Health and Human

Subject's Name: **Date:**

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Study Title: Enhancing Prolonged Exposure Therapy for PTSD with Oxytocin

Service's Office of Human Research Protections (OHRP), the Food and Drug Administration (for FDA regulated research only), the Government Accountability Office (GAO), the VA Office of the Inspector General (OIG), the VA Office of Research Oversight (ORO), our local VA Research and Development Committee, and other study monitors may look at or copy portions of records that identify you. Also, all records in South Carolina are subject to subpoena by a court of law. Any information shared with these outside groups may no longer be protected under federal law.

The VA will provide necessary medical treatment to a research subject injured by participation in a research project. This requirement does not apply to treatment for injuries that result from non-compliance by a research subject with study procedures. If you sustain an injury as a direct result of your study participation, medical care will be provided by the Ralph H. Johnson VA Medical Center. Financial compensation is not available for such things as lost wages, disability or discomfort due to an injury.

Your participation in this study is voluntary. You may refuse to take part in or stop taking part in this study at any time. You should call the investigator in charge of this study if you decide to do this. Your decision not to take part in the study will not affect your current or future medical care or any benefits to which you are entitled.

The investigators and/or the sponsor may stop your participation in this study at any time if they decide it is in your best interest. They may also do this if you do not follow the investigator's instructions.

VOLUNTEER STATEMENT

This research has been explained to me. I have been told of the risks or discomforts and possible benefits of the study. I have been told of other choices of treatment available to me. I have been given the chance to ask questions and obtain answers.

If I have any more questions about my participation in this study or study related injury, or if I have comments, concerns or complaints, I may contact: **Julianne Flanagan, Ph.D. at 843-792-5569**.

If I have questions about my rights as a study participant, or I want to make sure this is a valid VA study, I may contact the Medical University of South Carolina's Institutional Review Board (IRB). This is the Board that is responsible for overseeing the safety of human participants in this study. I may call the MUSC IRB (843) 792-4148, or the Ralph H. Johnson VA Medical Center's Research Compliance Officer at (843) 789-7399, if I have questions, complaints, or concerns about the study or if I would like to obtain information or offer input.

Subject's Name: **Date:**

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Study Title: Enhancing Prolonged Exposure Therapy for PTSD with Oxytocin

By signing this document below, I voluntarily consent to participate in this study. I also confirm that I have read this consent, or it has been read to me. I will receive a copy of this consent after I sign it. A copy of this signed consent will also be put in my medical record.

I agree to participate in this research study as has been explained in this document.		
Participant's Name	Participant's Signature	Date
Name of person obtaining consent	Signature of person obtaining consent	Date