Consent Form for Adult Participant

Study Title: Single Dose Intranasal Oxytocin (IN-OT) Versus Placebo in Autism: Examining Cognitive Effects

Study #: N/A

Sponsor: N/A

Study Doctor: Suma Jacob, PhD
University of Minnesota
717 Delaware St. SE, Rm. 346, Minneapolis, MN 55455

Telephone Number: (612) 625-8448

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You are invited to participate in a research study investigating the effects of intranasal oxytocin on social behavior and cognitive inflexibility in people with autism. The study will investigate the way people with autism think, act in different situations, and how their body reacts with resulting changes in their blood, urine, and saliva.

The study is being conducted by Suma Jacob, MD, PhD at the University of Minnesota. You are being selected as a possible participant because you have a research diagnosis of autism or autism spectrum disorder (ASD).

Before deciding if you want to participate in this study, it is important that you read this consent form. This form may contain words that you do not understand. Please ask one of the study team members to explain any information that is not clear. You may take as much time as you wish to make up your mind about whether or not to participate. If desired or needed, you may take home an unsigned copy of this consent form to think about or discuss with family or friends or anyone you choose before making your decision.

This research is being funded by the University of Minnesota Clinical and Translational Science Institute.

When reading this form, please note that the words “you” and “your” refer to the person in the study rather than to a legally authorized representative who might sign this form on behalf of the person in the study.

Why is this study being done?

This research is being done to better understand if the social, language, and cognitive thought processes of individuals with autism can become more flexible. We are looking into new approaches such as intranasal oxytocin that may increase their brain’s ability to learn by being less rigid and more flexible.

A hormone is a substance made by a gland in the body that regulates another part of the body. In this study we will be using a hormone called oxytocin, which is produced in the brain. Oxytocin is known to be involved in both repetitive and social behavior. Some children with ASD have uncommon oxytocin levels. Also, taking oxytocin has been shown to increase social

behavior and decrease repetitive behavior in small samples of people with ASD. However, it is unclear whether every person with ASD has abnormal oxytocin levels, or whether oxytocin affects repetitive/rigid behavior or social behavior differently. We aim to determine whether oxytocin dosing affects social thought and flexibility. This is why we are studying it in people with ASD. In addition, this study will compare oxytocin with a placebo to see if taking oxytocin is better than taking a placebo. The placebo is a substance that looks like a drug but has no drug in it.

It is planned that about 30 people with ASD will be in this study.

Oxytocin can also be found in a drug called Pitocin. Pitocin given as an injection or shot is used to help women when they are giving birth or after giving birth. Pitocin at low doses also has effects on the brain and social behavior in men and women.

In this study oxytocin will be delivered as a spray through the nose.

Be aware that this form refers to oxytocin and placebo as “study drug.”

How long will the study last?

If you agree to participate in this research study, you will first be screened to check that it is safe for you to be in the study and check that you meet the requirements for the study. During screening, we will assess symptoms of autism and check you can do the tasks given in the study. Your IQ may be tested (if you have not had an IQ test in the last 2 years), and your vital signs will be checked (blood pressure, pulse, height, and weight). We will also check you do not have any sicknesses that will make it unsafe for you to participate in the study. The screening visit can be split into two visits if necessary. In addition, the screening visit and study visit 1 may be combined into one visit.

If the study doctor says you can be in the study, after the screening visit(s), you will need to come to the study site up to 2 more times, about 2 weeks apart. In addition, you will receive a follow-up telephone call from the study staff within a week of each study visit. Each study visit will take approximately 3-4 hours.

What is involved in the study?

Intranasal oxytocin is investigational in this study, which means that it is being tested and has not been approved for sale in the United States by the United States Food and Drug Administration (FDA). We will not be using oxytocin to treat you. You will be receiving a single dose of the drug so that we may better understand how it may act on symptoms of autism. The dose of oxytocin you receive will be based on a weight calculation, and will be 0.6 IU (International Units)/kg.

If you qualify to continue in this study based on your results of the screening process, you will be randomly assigned by chance (like the flip of a coin) to receive either oxytocin or placebo during the first study visit. You have an equal chance of receiving either oxytocin or placebo at this visit. At the second study visit, you will receive the other substance. For example, if you receive oxytocin at the first visit, you will receive placebo at the second visit. Neither you nor the study doctor or study staff will be able to pick the order you receive oxytocin or placebo. This is a double-blind study, which means neither you nor the study doctor or study staff will know

which order you received oxytocin or placebo at the study visits. In case of an emergency however, the study doctor can get this information.

Before any study-related tests and procedures are conducted, you will be asked to read and sign this consent document and we will check there have not been any changes in your medical history that prevent you from participating. We will ask you about the medications you have taken and if there have been any recent changes in your medications.

During each study visit, you will be given a nasal spray of either oxytocin or placebo. You will then be given several tasks that involve problem solving, looking at images and making judgments about them, and listening to sounds and words and answering questions about them. These tests will measure mental abilities such as cognitive flexibility and social recognition. During some of the tasks, we will attach electrodes (in the form of "stickers") on your chest to collect heart rate data, which may help us learn more about how you feel as you perform the various study tasks. This is called Autonomic Nervous System (ANS) testing and uses a type of electrocardiogram (EKG). You will be asked to relax and sit as still as possible for 2 minutes several times during the study visits to get a good measurement of your heart rate at rest. We will also record how your eyes move when they look at items presented on the computer screen.

Samples of your blood will be taken for laboratory testing through your vein 4 times throughout the study (2 times at each of the study visits). Each blood sample will be about 6 teaspoons. It will take about 10 minutes to collect a blood sample. You will also have urine and saliva samples collected for laboratory tests 2 times at each of the study visits. If you are a woman who is able to have children, your urine will also be tested to see if you are pregnant. You can read more about pregnancy testing later in this form.

Your samples will always be identified by a code number. The code number will be linked to your identifying information and the research team will be the only ones who will know what code number goes with your name. The master list that contains this information will be stored in a secure database that is password protected and accessible only to the research team. If you have consented to participate in previous studies we have conducted, we may also use that data including blood samples and DNA in this study.

After each of the study visits, we will follow up with a phone call to see if you notice any physical changes or symptoms after you left our testing center. We will also ask you if you notice any changes in your body after taking the study drug.

If any new information is found while we are doing this study that may change your mind about taking part, we will tell you about it as soon as possible and ask you again if you still want to participate in the study.

While you are in the study, you must:

- Follow the instructions you are given.
- Come to the study center for all visits with the study doctor or study staff.
- Tell the study doctor or study staff if you want to stop being in the study at any time.

Genetic Testing

Another component of this study is the collection of DNA samples (material that makes up your genes). DNA is in your cells, and it is what makes you different from everyone else. DNA

controls things like the color of your hair or eyes. DNA might make you more likely to get certain diseases or affect whether a drug helps you and/or gives you side effects.

DNA samples may be extracted from your blood samples collected during the study, in addition to the testing described above. This collection of DNA samples is optional, which means you can agree or disagree to the collection of these samples without affecting your participation in the main study. These samples will be used to determine whether the social behaviors and thinking profiles we identify about you may relate to the genes involved in autism. If you agree, your blood sample will be stored at the University of Minnesota for use in this genetic study.

You can indicate your choice about the collection of these samples at the end of this form.

The results of the genetic tests are for research only. You will not receive the results of the genetic tests. The results will not be added to your regular medical record.

What else should you know about biological samples?

You should ask the study doctor or study staff about how long your blood, urine, and saliva samples might be kept.

If you change your mind later about being in the study, be aware that your samples may or may not be withdrawn from the research, depending on the study center's policies. You can ask the study doctor or study staff about this.

Schedule of Study Procedures

Procedure	Screening Visit	Study Visit 1	Study Visit 2
Obtain consent	X	X	
Diagnostic Assessments	X		
IQ test	X		
Medical history review and past medications	X	X	
Vitals (blood pressure, pulse, height, weight)	X	X	X
Review current medications	X	X	X
Blood draw		X	X
Urine collection		X	X
Pregnancy Test		X	X
Saliva Collection		X	X

Receive study drug		X	X
ANS measures/EKG		X	X
Behavioral outcomes		X	X
Eye-tracking		X	X
Monitor side effects		X	X
Post follow up phone call		X	X

The screening visit can be split into two visits if necessary. In addition, the screening visit and study visit 1 may be combined into one visit.

What are the possible risks?

There may be risks from the study that are not known at this time, which could include your health getting worse.

Ask the study doctor if you have questions about the signs or symptoms of any side effects that you read about in this consent form.

Common side effects (unpleasant effects) of intranasal oxytocin may include:

- headache,
- itchy and runny nose, or
- nausea (feeling like you are going to vomit),
- watering eyes.

Rare/uncommon and potentially more severe side effects include:

- unusual bleeding, seizures, and cramps in women,
- severe allergic reaction,
- drowsiness,
- anxiety, and
- sad mood.

When oxytocin is given by injection, through the vein, some of the more serious side-effects are:

- skin rashes,
- shortness of breath,
- swelling, and
- some heart problems including :
    - the heart beating too fast or too slow (arrhythmia), or
    - increase or decrease in blood pressure.

Sometimes, injections may make people feel bloated.

It is possible that taking intranasal oxytocin may change how your regular medications, vaccines, or supplements work. It is very important that you tell the study doctor about any medications, supplements, or vaccines before you take them during the study.

If you have an allergic reaction, what are the risks?

Sometimes people have allergic reactions to drugs. If you have a very bad allergic reaction, you could die. Some things that happen during an allergic reaction that could be a sign or symptom of a life-threatening allergic reaction (anaphylaxis) are:

- a rash
- a fast pulse
- sweating
- a feeling of dread
- swelling around the eyes and mouth
- swelling of the throat
- wheezing
- having a hard time breathing
- a sudden drop in blood pressure (making you feel dizzy or lightheaded)
- inability to breathe without assistance

You should get medical help and contact the study doctor or study staff if you have any of these or any other side effects during the study.

Please tell the study doctor or study staff right away if you have any side effects. Please tell them if you have any other problems with your health or the way you feel during the study, whether or not you think these problems are related to the study drug.

The length of time required for interviewing and testing may produce fatigue and tiredness. In addition, answering the study doctor or study staff's questions could lead you to feel uncomfortable or upset. If you feel fatigued, tired, uncomfortable, or in any way upset during any of the sessions, you can ask for a rest or to have the testing stopped. You have the right to refuse to answer any questions.

You may experience some pain associated with having blood collected. Discomfort, bruising, and/or bleeding or infection at the site where the needle is inserted may occur. Sometimes, people feel dizzy and faint when blood is drawn. A trained professional will perform the blood draws to help minimize your stress.

There is a risk of loss of confidentiality of your information. You will read more about the protection of your information later in this form. Please ask the study doctor or study staff if you would like to know more about how your information will be protected while you are in this study.

The risks to you and your family from genetic research are low. Your samples will be identified only with your study code number. In the event of an unexpected breach of confidentiality, a recent federal law (Genetic Information Non-Discrimination Act, GINA) will help protect you from health insurance or employment discrimination based on genetic information obtained about you through research such as this. However, GINA does not protect you against discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. If you have questions about GINA or the risks of research on genetic information, please ask study staff.

What are the reproductive risks?

Oxytocin is known to have effects on the uterus such as abnormal contractions. It is not known if intranasal oxytocin has any direct effects on sperm. You should not become pregnant or father a child while in this study. Pregnant or nursing females are not eligible to participate in this study, as there may be risks to an unborn baby or nursing child. Sexually active males and females must agree to use contraception for the duration of the study.

If you are female and able to get pregnant, a pregnancy test will be done at study visit one and two. If the test is positive, you will not be able to enter or continue in the study. The results of the pregnancy test are confidential.

We also do not know the interactions between oxytocin and the hormones in birth control, therefore any female on the birth control pill, Depo-Provera (birth control shot) or an intra-uterine device (IUD) is not eligible to participate in this study.

We strongly encourage all individuals to abstain from sexual activity during this study and for at least 30 days after taking the last dose of study drug. If you are female and of childbearing potential, and sexually active during participation in this study, you are required to use two methods of birth control that do not include hormones, such as 'barrier methods' including condoms, diaphragm or the sponge. You must call the study doctor or study staff right away if you think you may be pregnant. Your participation in the study will be changed if you become pregnant during this study. This will be discussed between you and the study doctor.

If you are a man, there may be risks to an unborn baby you father during or after the study. Nobody knows what all of these risks are right now. The study doctor or study staff will talk to you about the birth control options you must use during the study. If you think your partner is pregnant during the study, you must tell the study doctor or study staff immediately.

Are there any potential benefits?

The study drug may help your ASD, but there is no guarantee that being in this study will help you. You may or may not receive any direct benefit from participating in this study. The information that we collect in the study may increase the knowledge about autism, which may help individuals with autism in the future.

What other options are there?

There are no other alternatives to participating in this study. The other option is not to participate in this study. Currently, there are no drugs proven to work for the social difficulties and rigid behaviors in autism.

Will you have to pay for any tests and procedures to be in this study?

There will be no cost to you/your health care payer/insurer. During the study, the study drug (oxytocin and placebo) will be provided to you without charge.

Is there compensation available for participating in this study?

You will receive a $10 gift card for each visit, for a total of $40 if you complete all visits. If you do not finish the study, you will be compensated for the visits you have completed. You will also have free parking during your visits to this facility for your sessions.

What will happen if there is a research-related injury?

You should tell the study doctor or study staff as soon as possible if you experience an unpleasant side effect from the study drug or the procedures that are part of the study, or if you have any changes in your health or the way you feel. The study doctor can be reached at the number on the first page of this form. Call 911 or go to the nearest emergency department if there is an emergency. If you require emergency care, be sure to tell the emergency care provider about your participation in this study.

In the event that this research activity results in an injury, treatment will be available, including first aid, emergency treatment and follow-up care as needed. Care for such injuries will be billed in the ordinary manner, to you or your insurance company. If you think that you have suffered a research related injury, let the study doctor or study staff know right away.

You do not give up any of your legal rights by signing this form.

Be aware that your health care payer/insurer might not cover the costs of study-related injuries or illnesses.

How will personal information be protected?

The records of this study will be kept private. In any publications or presentations, we will not include any information that will make it possible to identify you as a subject. Your record for the study may, however, be reviewed by the National Institutes of Health (NIH) or a representative of the Food and Drug Administration, Quorum Review (a group of people who review research studies to protect the rights and welfare of research participants), and by departments at the University with appropriate regulatory oversight. Study data will be encrypted according to current University policy for protection of confidentiality.

Your information may also be transmitted and/or reviewed by University of Minnesota (UM), University of Minnesota Physicians (UMP) and University of Minnesota Medical Center, Fairview personnel who monitor research and UM, UMP and Medical Center personnel who need access to the information to complete the clinical study. These organizations and people must keep the information private, as required by law.

Your information will only be shared with the groups above. The study doctor, study staff or regular health care providers may need to look at your entire medical chart to get a complete medical history. In addition, the FDA and Quorum Review may look at your medical records.

Your protected health information created or received for the purposes of this study is protected under the federal law known as the HIPAA Privacy Rule. This means that we must keep your medical information private and confidential to the greatest extent possible. Your protected health information includes your contact information or any identifying information about you. You will be asked to review and sign a separate HIPAA authorization concerning the use of this information.

To these extents, confidentiality is not absolute.

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.

What are your rights as a research subject?

Participation in this study is voluntary. Your decision whether or not to participate in this study will not affect your current or future relations with the University. If you decide to participate, you are free to withdraw at any time without affecting those relationships. No matter what you decide, there will be no penalty to you, and you won't lose any benefits.

What if I work for the study center or sponsor? What if I am a family member of someone who works for the study center or sponsor?

Study center/sponsor employees and their family members do not have to be in this study. No one should influence or pressure you to be in this study. An employee's or his/her family member's decision to be in the study, or to leave the study early, will not affect the employee's job or job benefits.

Will my regular doctor find out if I am in this study?

We would like for you to tell your primary care doctor (if you have one) that you are in this research study. This is done so care can be taken in prescribing other drugs and looking at any unexplained symptoms that may occur. You can indicate your decision about your regular doctor being informed of your participation in this study at the end of this form.

When is the study over? Can you leave the study before it ends?

The study doctor or the study funder can stop your participation in the study at any time without your consent for any reason, such as if the study doctor or study staff believes it is best for you to stop being in the study, or if you do not follow directions about the study. You also have the right to withdraw from the study **at any time**, even after signing the consent form, without giving a reason.

If you withdraw voluntarily from the study or are taken out of the study by the study doctor/study funder, you may be asked questions about your experience with the study drug.

If you leave the study, the study doctor and study staff will still be able to use your information that they have already collected.

What if new information becomes available about the study?

The study doctor will notify you if there are new findings that might affect your willingness to continue to be in the study, or that could affect your health either during or after the study. You may be asked to sign a new consent form if this occurs. You may contact the study doctor at

any time after your participation ends to find out if any new information about this study has become available.

Who can you call if you have questions about the study?

You can ask questions about the study at any time. You can call the study doctor or study staff at any time if you have any concerns or complaints. You should call the study doctor or study staff at the phone number listed on page 1 of this form if you have questions about the study procedures, study costs (if any), study payment (if any), or if you get hurt or sick during the study.

Quorum Review reviewed this study. Quorum Review is a group of people who review research studies to protect the rights and welfare of research participants. Review by Quorum Review does not mean that the study is without risks. If you have questions about your rights as a research participant, if you are not able to resolve your concerns with the study doctor or study staff, if you have a complaint, or if you have general questions about what it means to be in a research study, you can call Quorum Review or visit the Quorum Review website at www.quorumreview.com.

Quorum Review is located in Seattle, Washington.
Office hours are 8:00 AM to 5:00 PM Pacific Time, Monday through Friday.
Ask to speak with a Research Participant Liaison at 888-776-9115 (toll free).

You will be given a signed copy of this form to keep for your records.

Statement of Consent

I have read the above information. I have asked the study doctor and study staff questions and have received answers. I voluntarily consent to participate in the study.

By signing this form, I do not give up any of my legal rights. I will get a signed copy of this consent form.

_____

Printed Name of Participant

_____ _____

Signature of Participant Date

I am the legally authorized representative of the participant named above and I consent to his/her participation in this research study.

_____

Printed Name of Legally Authorized Representative

_____ _____

Signature of Legally Authorized Representative Date

I attest that the individual providing consent had enough time to consider this information, had an opportunity to ask questions, and voluntarily agreed to participation in this study.

_____

Printed Name of Person Explaining Consent

_____ _____

Signature of Person Explaining Consent Date

OPTIONAL CONSENT

Please complete the section below and return it to our study staff.

Optional Genetic Blood work Consent

The study doctor and study staff want to collect DNA samples from your blood for genetic testing. Information about this testing is included earlier in the form. If you later change your mind about this optional genetic testing, tell the study doctor or study staff.

Please **initial** one of the choices below:

_____ I give you permission to take blood to study oxytocin and related genes

_____ I **do not** give you permission to take blood to study oxytocin and related genes. I can still be in the rest of the study.

_____ _____ _____

PERSON GIVING CONSENT (Print Name) SIGNATURE DATE
Participant/ Legally Authorized Representative

Notification of Primary Care Physician

Please **initial** one of the choices below:

_____ I give you permission to contact my primary care doctor to inform them about my participation in this study

_____ I do not give you permission to contact my primary care doctor to inform them about my participation in this study

_____ I do not have a primary care doctor

_____ _____ _____

PERSON GIVING CONSENT (Print Name) SIGNATURE DATE
Participant/Legally Authorized Representative