Intranasal Vasopressin Treatment in Children With Autism

Informed Consent Form

NCT03204786

December 12, 2023

IRB Use Only
Approval Date: December 12, 2023
Expiration Date: December 12, 2024

STANFORD UNIVERSITY

Consent to act as a participant in the Stanford University Study: Intranasal Vasopressin Treatment in Children with Autism

___You are the parent or guardian granting permission for a child in this study.

Print child's full name and date of birth here:

Name:_____ Date of birth:_____

Protocol Director: **Antonio Hardan, MD**

Address: **Stanford University**
401 Quarry Road
Stanford, CA 94305-5719

Telephone: **(650) 736-1235**

Is your child participating in any other research studies? _____ yes _____no

PURPOSE OF RESEARCH

Your child is invited to participate in a research study to investigate the effectiveness of vasopressin nasal spray for treating symptoms associated with autism. Vasopressin is a hormone that is produced naturally within the body and has been implicated in regulating social behaviors. It has been proposed that administration of the hormone may also help improve social functioning in individuals with autism.

Your child was selected as a possible participant in this study because your child has an autism spectrum disorder.

If you decide to terminate your participation in this study, you should notify the research staff at (650) 736-1235.

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This research study is looking for 110 children with an autism spectrum disorder, who currently reside in the United States, and are between the ages of 6 and 17 years to enroll as research participants at Stanford University. Stanford University expects to enroll 110 research study participants.

VOLUNTARY PARTICIPATION

Your participation in this study is entirely voluntary. Your decision not to participate will not have any negative effect on you or your medical care. You can decide to participate now, but withdraw your consent later and stop being in the study without any loss of benefits or medical care to which you are entitled.

DURATION OF STUDY INVOLVEMENT

This research study is expected to take no longer than 14 weeks, with 6 to 8 visits at Stanford University.

PROCEDURES

If you and your child choose to participate, Dr. Antonio Hardan and his research study staff will perform the following procedures after signing the informed consent and authorization form regarding the confidentiality of your child's personal health information.

Your child will be in the study for a maximum of 14 weeks. This requires a minimum of 6 visits to Dr. Hardan's office and the research facilities. The procedure for each visit is outlined in the chart below. Between visits, families will be contacted weekly by phone to monitor protocol adherence and to inquire about side effects. Additionally, research staff will call families four weeks after trial completion for a follow-up to ask them to complete the SRS-2.

The participants will be divided into three groups: 1) drug-drug, in which participants will be on active vasopressin for the entire 8-week dosing period, 2) placebo-drug, in which participants will be on placebo for four weeks and then switch to active vasopressin for the remaining four weeks, and 3) placebo-placebo, in which participants will be on placebo for the entire 8-week dosing period. At the end of visit 6, participants in the placebo-placebo group will be given the option to switch to active vasopressin for a four-week dosing period, which would require two additional visits to Dr. Hardan's office and the research facilities. The ratio of participants in the three groups is 1:2:2 (drug-drug: placebo-drug: placebo: placebo).

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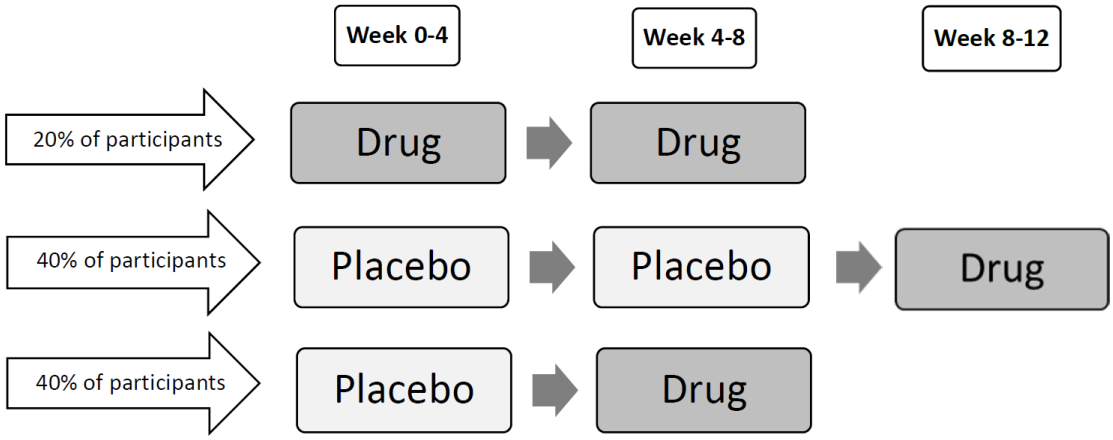

Schedule of Events:

	Visit 1 (Screening)	Visit 2 (Baseline)	Visit 3 (Week 2)	Visit 4 (Week 4)	Visit 5 (Week 6)	Visit 6 (Week 8)
Informed Consent	X					
Family and Medical History	X					
Parent Interview	X					
Neuropsychological testing	X	X		X		X
Computer tasks		X		X		X
Blood and urine collection	X			X		X
Saliva and buccal cell samples	X			X		X
Electroencephalogram (EEG)		X		X		X

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Electrocardiogram (ECG)	X			X		X
Assessments with Doctor	X	X	X	X	X	X
Blood Pressure and Temperature	X	X	X	X	X	X
Parent Questionnaires	X	X	X	X	X	X

Visit 1 (Screening): The screening procedures will take approximately 4-6 hours and can be split into two shorter visits if desired.

1. Dr. Hardan and his research team will review your child's psychiatric and medical history. They will also perform diagnostic evaluations and clinical assessments.
2. Neuropsychological testing will be administered.
3. Your child's vital signs (heart rate, blood pressure, and temperature) will be measured, as well as his/her height and weight.
4. A blood sample of up to 30mL (about six teaspoons) of blood will be drawn for laboratory testing. Peripheral blood mononuclear cells (PBMCs) may be collected from these blood samples and will be reprogrammed to induced pluripotent stem cell (iPSC) lines to further study the molecular and cellular mechanisms of ASD.
5. A urine sample will be collected.
6. Saliva samples and buccal cell samples will be collected. Your child should fast one hour prior to saliva and buccal cell sample collection. Your child will also be instructed to rinse his or her mouth prior to saliva and buccal cell collection. Up to 4 mL of saliva will be collected.
7. Female participants of childbearing age (12.5 years and older) or females with a history of menstruating will undergo urine pregnancy testing.
8. Your child will have an electrocardiogram (ECG) to measure heart function.
9. You will complete the Social Responsiveness Scale 2 (SRS-2), a questionnaire regarding your child's behavior.
10. Inclusion and exclusion criteria will be assessed.

Visit 2 (Baseline): Approximately 2-3 hours.

1. Your child's vital signs and height and weight will be measured.

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2. The research team will perform an optional high density electroencephalogram (EEG) to detect electrical activity in your child's brain.
3. You will complete a series of questionnaires regarding your child's behavior.
4. Dr. Hardan and his research team will perform clinical assessments.
5. Your child will be asked to complete a series of behavioral laboratory tasks and neuropsychological tests.
6. You will be provided with a dosing log and four-weeks supply of vasopressin or placebo and will be provided with instructions on following the dose schedule at home.

Visit 3 (week-two nasal spray treatment): Approximately 1 hour.

1. Your child's vital signs and height and weight will be measured.
2. You will complete the SRS-2, a questionnaire regarding your child's behavior.
3. Dr. Hardan and his research team will perform clinical assessments.

Visit 4 (week-four nasal spray treatment): Approximately 2-3 hours.

1. Your child's vital signs and height and weight will be measured.
2. You will complete a series of questionnaires regarding your child's behavior.
3. A blood sample of up to 30mL (about six teaspoons) of blood will be drawn for laboratory testing. Peripheral blood mononuclear cells (PBMCs) may be collected from these blood samples and will be reprogrammed to induced pluripotent stem cell (iPSC) lines to further study the molecular and cellular mechanisms of ASD.
4. A urine sample will be collected.
5. Saliva samples and buccal cell samples will be collected. Your child should fast one hour prior to saliva and buccal cell sample collection. Your child will also be instructed to rinse his or her mouth prior to saliva and buccal cell collection. Up to 4 mL of saliva will be collected.
6. You child will undergo an ECG to measure heart function.
7. The research team will perform an optional high density electroencephalogram (EEG) to detect electrical activity in your child's brain.
8. Dr. Hardan and his research team will perform clinical assessments.
9. Your child will be asked to complete a series of behavioral laboratory tasks and neuropsychological tests.

At visit 4, participants who were on active vasopressin will continue taking active vasopressin for the remainder of the study. If your child was on placebo, he or she will either switch to active vasopressin or continue on the placebo.

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Visit 5 (week-six nasal spray treatment): Approximately 1 hour.

1. Your child's vital signs and height and weight will be measured.
2. You will complete the SRS-2, a questionnaire regarding your child's behavior.
3. Dr. Hardan and his research team will perform clinical assessments.

Visit 6 (week-eight nasal spray treatment): Approximately 2-3 hours.

1. Your child's vital signs and height and weight will be measured.
2. You will complete a series of questionnaires regarding your child's behavior.
3. A blood sample of up to 30mL (about six teaspoons) of blood will be drawn for laboratory testing. Peripheral blood mononuclear cells (PBMCs) may be collected from these blood samples and will be reprogrammed to induced pluripotent stem cell (iPSC) lines to further study the molecular and cellular mechanisms of ASD.
4. A urine sample will be collected.
5. Saliva samples and buccal cell samples will be collected. Your child should fast one hour prior to saliva and buccal cell sample collection. Your child will also be instructed to rinse his or her mouth prior to saliva and buccal cell collection. Up to 4 mL of saliva will be collected.
6. Your child will undergo an ECG to measure heart function.
7. The research team will perform an optional high density electroencephalogram (EEG) to detect electrical activity in your child's brain.
8. Dr. Hardan and his research team will perform clinical assessments.
9. Your child will be asked to complete a series of behavioral laboratory tasks and neuropsychological tests.

At the end of Visit 6 if your child was in the placebo-placebo group, you and your child will be given the option to participate in a 4 week treatment period where your child will be given the active vasopressin nasal spray and you will be provided with a dosing log and four-weeks supply of the active vasopressin. If your child was on the drug-drug or placebo-drug group then they will end the study at visit 6. If you decide to participate in the optional extension study, you and your child would be required to complete Visits 7 and 8 as outlined below.

Visit 7 (week-ten nasal spray treatment): Approximately 1 hour.

1. Your child's vital signs and height and weight will be measured.
2. You will complete the SRS-2, a questionnaire regarding your child's behavior.
3. Dr. Hardan and his research team will perform clinical assessments.

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Visit 8 (week-twelve nasal spray treatment): Approximately 2-3 hours.

1. Your child's vital signs and height and weight will be measured.
2. You will complete a series of questionnaires regarding your child's behavior.
3. A blood sample of up to 30mL (about six teaspoons) of blood will be drawn for laboratory testing.
4. A urine sample will be collected.
5. Saliva samples and buccal cell samples will be collected. Your child should fast one hour prior to saliva and buccal cell sample collection. Your child will also be instructed to rinse his or her mouth prior to saliva and buccal cell collection. Up to 4 mL of saliva will be collected.
6. Your child will undergo an ECG to measure heart function.
7. The research team will perform an optional high density electroencephalogram (EEG) to detect electrical activity in your child's brain.
8. Dr. Hardan and his research team will perform clinical assessments.
9. Your child will be asked to complete a series of behavioral laboratory tasks and neuropsychological tests.

Any of your samples which are used in research may result in new products, tests or discoveries. In some instances, these may have potential commercial value and may be developed and owned by the Investigators, Stanford University and/or others. However, donors of samples do not retain any property rights to the materials. Therefore, you would not share in any financial benefits from these products, tests or discoveries.

Optional Electroencephalogram (EEG)
This study involves an optional resting-state EEG that detects brain activity while your child focuses straight ahead and breathes normally. Brain waves will be recorded from sensors that will be applied to the surface of the scalp. Placing the sensors on the head requires 10-15 minutes. The sensors are held in place by a stretchy cap and have been disinfected before use. The actual recording time involved will be approximately 5 minutes.

_____ I consent to the resting-state EEG for my child.

_____ I do not consent to the resting-state EEG for my child.

Women of Childbearing Potential
If your child is a female who is able to become pregnant, it is expected that she will use an effective method of birth control to prevent exposing a fetus to a potentially dangerous agent with unknown risk. If your child is pregnant or

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currently breast feeding, she may not participate in this study. You understand that if your child is pregnant, if she becomes pregnant, or if she is breast-feeding during this study, your child may be exposed to an unknown risk.

To confirm to the extent medically possible that your child is not pregnant, your child must have a negative pregnancy test at the screening visit before beginning this research study. Your child must agree to avoid sexual intercourse or use a birth control method judged to be effective by the investigator and which will not interfere with the proposed investigation. Your child must accept the risk that pregnancy could still result despite the responsible use of reliable method of birth control. You agree to notify the investigator as soon as possible of any failure of proper use of your child's birth control method, or if your child becomes pregnant, either of which may result in your child being withdrawn from the study.

If your child is a male participating in this study, he and his partner must use adequate contraception while he is participating in the study. Your child's doctor will discuss with your child what methods of birth control are considered adequate. He should inform the study doctor if his partner becomes pregnant.

As part of this study, pregnancy testing will be performed. The results of pregnancy tests for those under 18 are confidential according to California Minor Consent Laws. If you are a parent whose child is participating in this study, results will be given to your child by one of the study nurses or doctors in private. Every effort will be made to maintain confidentiality regarding positive pregnancy test results. Although we will not typically tell parent(s) or guardian(s) without your child's permission, under certain circumstances, we might be compelled to reveal this information. For example, if your child's life or someone else's life is at risk or if abuse is suspected, it may be necessary to inform you as parent(s) or guardian(s) of a positive pregnancy test. If we believe it's necessary to tell a parent or guardian of a positive pregnancy test without your child's permission, we will meet with your child first in private to discuss our concerns before divulging any information regarding pregnancy. During research, if your child has a positive pregnancy test, we may withdraw your child from the study. This means that even if we do not reveal the results, you may suspect that your child is pregnant despite our best efforts to maintain confidentiality. If your child becomes pregnant or if there is any chance that your child is pregnant (late menstrual period), please contact the study personnel immediately so that we may provide medical assistance and counseling.

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DESCRIPTION OF STEM CELL RESEARCH

Peripheral blood mononuclear cells (PBMCs) will be collected from the blood samples obtained during blood draws. Collected PBMCs will be reprogrammed towards induced pluripotent stem cell (iPSC) lines using established protocols for iPSCs derivation from PBMCs in collaboration with Stanford Stem Cell Core facility. iPSCs lines will be maintained for research purposes and differentiated towards neural cells for further analysis and characterization. These will include analysis such as RNA-Seq for gene expression of neural progenitors and differentiated neurons at different time points. Additionally, we will be analyzing cell morphology, synapse formation and epigenetic states of derived cells. The cell phenotype will be back crossed to results of the vasopressin treatment, in order study the molecular/cellular mechanisms that might be involved in vasopressin signaling.

Combining molecular investigation of patient-derived neurons differentiated from the iPSCs with clinical data collected during the vasopressin treatment trial will facilitate research into ASD disease biology, molecular mechanisms of vasopressin action, and, ultimately, the ability to determine which patients stand to benefit the most from vasopressin treatment.
You should be aware that your child's tissues, cells or other materials derived from these tissues may be kept for many years and may be used by researchers at Stanford or by researchers at entities outside of Stanford in future studies, which are not foreseeable now. They may include research that involves genetic manipulation.

Your child's samples may be sent outside of Stanford for analysis or other purposes.

It is possible that derived cells or cell products may be placed into humans or animals. There can be no restrictions placed on the ultimate recipients of these derived cells or cell products, except in the case where donation is intended for autologous transplantation (when your child, the donor, would also be the recipient).

The results of the study of your child's samples will be used for research purposes and tissue derivatives may also be used in human therapies.

You have the right to refuse to allow your child's tissues to be studied now or saved for future study; however you cannot withdraw derivatives and other

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products made from cells isolated from that tissue once they have been distributed, reprogrammed or incorporated into other cells or cellular materials.

If you agree to participate, investigators in this study may wish to re-contact you in the future to ask about your child's health status, in order to include that information with your child's tissue.

I consent to being re-contacted in the future should the investigators wish to ask for additional health information.

Initials _____ Date _____

I ***do not*** consent to being re-contacted in the future should the investigators wish to ask for additional health information.

Initials _____ Date _____

You must be given the opportunity to impose restrictions on future uses of donated materials. However, researchers may choose to use materials only from donors who agree to all future uses without restriction.

_____ I consent to my child's samples (PBMCs) being saved for future research.

_____ No restrictions.

_____ Restrictions (Please specify):_____

_____ I do not consent to my child's samples being saved for future research.

If we cannot collect enough blood for the PBMCs at Visit 1, can we collect additional blood at either Visit 3 or 5 for PBMCs?

Please initial: _____ Yes _____No

Tissue Sampling for Research

Research using tissues is an important way to try to understand human disease. You have been given this information because the investigators want to include your child's tissues (i.e., blood, urine, saliva, and buccal cell samples) in a

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research project and because they want to save the samples for future research. There are several things you should know before allowing your child's tissues to be studied.

Your child's tissues will be stored in a -80˚C freezers and will be labeled with code numbers linked to your child's research records at Stanford University.

Your samples may be sent outside of Stanford for analysis or other purposes.

You have the right to refuse to allow your tissues to be studied now or saved for future study. You may withdraw from this study at any time. The investigators might retain the identified samples, e.g., as part of your routine clinical care, but not for additional research.

You will be told the results of tests that are part of your clinical care, but you will not be told the results of the research tests, including any future research tests.

_____ I consent to my child's samples being saved for future research.

_____ I do not consent to my child's samples being saved for future research.

Tissue Sampling for Genetic Testing

As part of the analysis on your child's samples, the investigators may do genetic testing. Genetic research is research that studies genes, including gene characteristics and gene versions that are transmitted by parents to children. Genetic research may include looking at information, such as personal appearance and biochemistry, gene sequences, genetic landmarks, individual and family medical histories, reactions to medications and responses to treatment. Genetic research raises certain questions about informing you of any results. Possible risks of knowing results include: anxiety; other psychological distress; and the possibility of insurance and job discrimination. A possible risk of not knowing includes being unaware of the need for treatment. These risks can change depending on the results of the research and whether there is a treatment or cure for a particular disease.

Sometimes patients have been required to furnish information from genetic testing for health insurance, life insurance, and/or a job. A Federal law, the Genetic Information Nondiscrimination Act of 2008 (GINA), generally makes it

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illegal for health insurance companies, group health plans, and employers with 15 or more employees to discriminate against you based on your genetic information.

The results of the study of your samples from this project will be used for research purposes only, and you will not be told the results of the tests.

VIDEO AND AUDIO RECORDINGS

Video and/or audio recording will occur in a private room at 401 Quarry Road. Recorded data will be analyzed for reliability of the diagnostic assessments and for the purposes of the outcome research. Recordings will be kept in a locked cabinet at 401 Quarry Road and will be securely disposed of seven years after the completion of the study.

1. I give consent for my child and I to be videotaped during this study:

Please initial: _____ Yes _____No

2. Audio and/or video recording(s) can be analyzed for research and the results of these analyses can be shared for scientific purposes.

Please initial: _____ Yes _____No

3. The recording(s) can be shown in classrooms to students for educational purposes.

Please initial: _____ Yes _____No

4. The recording(s) can be shown in public presentations to non-scientific groups.

Please initial: _____ Yes _____No

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5. Please be aware that public presentations to scientific and non-scientific groups are often videotaped for public distribution by the group. Do you consent to have your recording used in a presentation that may be videotaped and publicly distributed (e.g., posted on a website, made available for purchase on DVD)?

Please initial: _____ Yes _____No

NATIONAL DATABASE FOR AUTISM RESEARCH

Data from this study may be submitted to the National Institute of Mental Health Data Archive (NDA). NDA is a data repository run by the National Institute of Mental Health (NIMH) that allows researchers studying mental illness to collect and share deidentified information with each other. A data repository is a large database where information from many studies is stored and managed. Deidentified information means that all personal information about research participants such as name, address, and phone number is removed and replaced with a code number. With an easier way to share, researchers hope to learn new and important things about mental illnesses more quickly than before.

During and after the study, the researchers will send deidentified information about your health and behavior and in some cases, your genetic information, to NDA. Other researchers nationwide can then file an application with the NIMH to obtain access to your deidentified study data for research purposes. Experts at the NIMH who know how to protect health and science information will look at every request carefully to minimize risks to your privacy.

You may not benefit directly from allowing your information to be shared with NDA. The information provided to NDA may help researchers around the world treat future children and adults with mental illnesses so that they have better outcomes. NIMH will also report to Congress and on its web site about the different studies that researchers are conducting using NDA data. However, you will not be contacted directly about the data you contributed to NDA.

You may decide now or later that you do not want to share your information using NDA. If so, contact the researchers who conducted this study, and they will tell NDA, which can stop sharing the research information. However, NDA cannot take back information that was shared before you changed your mind. If you would like more information about NDA, this is available on-line at http://data-archive.nimh.gov.

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SIMONS FOUNDATION POWERING AUTISM RESEARCH FOR KNOWLEDGE (SPARK)

Are you a SPARK participant? _____Yes _____ No

For those individuals who participated in the SPARK study, we are asking your consent for the SPARK study, hosted by the Simons Foundation, to share with Stanford University the clinical, demographic and genetic data collected during your participation in SPARK. This information will be shared using your linked research ID number and using a secure transfer system. We are also asking for your consent to share the data we collect during this study here at Stanford University with SPARK in order to add to the information that was collected during your participation in SPARK. Please note that because you are a participant in both studies, SPARK and this study will be able to share and link your identifying information as well as any future data you may contribute to either project.

If you are a participant in the SPARK study, your child's coded blood samples and /or induced pluripotent stem cells (iPSCs) may be provided to the Simons Foundation for storage in a designated repository and distribution to qualified investigators, at Stanford University and other institutions, for future research not specified in this consent. The Simons Foundation funds innovative research and provides coded data and sample access (coded means your identifying information is removed) to qualified researchers. Researchers can file an application with the Simons Foundation, which includes Institutional Review Board approval or exemption from their institution, to obtain access to your study data and/or samples for research purposes. Experts at the Simons Foundation who protect health and science information will look at every request carefully to minimize risks to your privacy.

Can we share your child's blood and/or iPSC samples with the Simons Foundation?

Please initial: _____ Yes _____ No

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PARTICIPANT RESPONSIBILITIES

As a participant, your responsibilities include:

- Follow the instructions of the Protocol Director and study staff.
- Take the study drug as instructed
- Keep your study appointments. If it is necessary to miss an appointment, please contact the Protocol Director or research study staff to reschedule as soon as you know you will miss the appointment.
- Tell the Protocol Director or research study staff about any side effects, doctor visits, or hospitalizations that you may have.
- Tell the Protocol Director or research staff if you believe you might be pregnant or gotten your partner pregnant.
- Keep the study drug in a safe place, away from children and for your use only.
- Complete your questionnaires as instructed.
- Ask questions as you think of them.
- Tell the Protocol Director or research staff if you change your mind about staying in the study.

WITHDRAWAL FROM STUDY

If you first agree to participate and then you, or your child, change your mind, you and your child are free to withdraw your/his/her consent and discontinue his/her participation at any time. This decision will not affect your child's ability to receive medical care and your child will not lose any benefits to which he/she would otherwise be entitled.

If you decide to withdraw your consent to participate in this study, you should notify Antonio Hardan at (650) 736-1235.

If you withdraw from the study, or the study medication is stopped for any reason, please do come in for an early termination visit, which would include an assessment of your child's vital signs and response to the drug. This is for your child's safety.

The Protocol Director may also withdraw your child from the study and the study medication may be stopped, without your consent for one or more of the following reasons:

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- Failure to follow the instructions of the Protocol Director and study staff.
- The Protocol Director decides that continuing your participation could be harmful to you.
- Pregnancy
- You need treatment not allowed in the study.
- The study is cancelled.
- Other administrative reasons.
- Unanticipated circumstances.

POSSIBLE RISKS, DISCOMFORTS, AND INCONVENIENCES

There are risks, discomforts, and inconveniences associated with any research study. These deserve careful thought. You should talk with the Protocol Director if you have any questions.

The drug formulation we will use in this study is a synthetic version of vasopressin manufactured by PAR Pharmaceutical, an Endo International Company. This drug and a matched placebo solution will be transferred to nasal spray applicators. Studies that have already been done using vasopressin have shown that the drug is generally well tolerated and safe, but there may be other serious or potentially fatal risks with using it in this clinical trial. In some cases, local or systemic allergic reactions may occur in hypersensitive individuals.

The following side effects have been reported following **intranasal** administration of vasopressin, which is the route of administration used in this study:

- Relaxation/tiredness
- Headache
- Dizziness
- Increased blood pressure
- Stinging in nose
- Bad taste in mouth

In our pilot intranasal trial at Stanford, minimal side effects were reported, including:

- Fever
- Cough
- Body aches
- Excitement/agitation
- Increased motor activity
- Insomnia

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- Headache
- Decreased motor activity
- Sense of restlessness
- Depressive affect
- Drowsiness
- Head banging
- Nasal congestion
- Blurred vision
- Dry mouth
- Decreased appetite/anorexia
- Nausea/vomiting
- Constipation
- Increased urination
- Bed wetting
- Skin rash
- Bug bite
- Lethargy/tiredness
- Feeling emotional
- Bloody nose
- Stinging sensation in nose
- Burning sensation in throat

In our current trial at Stanford, sneezing, gagging, sore throat, increased appetite, irritability, snoring, touching of private parts, stomach ache, soreness in nostril, diarrhea, impulsivity, pain on urination, mimicking, anxiety, and eye redness have also been reported.

A number of side effects have also been reported following intravenous, intramuscular, and subcutaneous **injections** of vasopressin. These include the following:

- Upset stomach
- Feeling sick or vomiting
- Shakiness or dizziness
- Headache
- Strep throat
- Sweating
- Skin rash or infection
- Heart problems
- Difficulty breathing
- Water intoxication (possibly resulting in seizure or coma)

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Based on animal studies there is also a theoretical risk for increased aggression following vasopressin treatment. The US Food and Drug Administration (FDA) do not currently approve vasopressin for the treatment of cognitive and behavioral problems associated with autism. This is the first study to investigate the effects of intranasal vasopressin treatment for cognitive and behavioral problems associated with autism in children. So, there might be some unknown side effects that have not been listed above.

Potential side effects will be monitored closely throughout the study. If your child experiences any of the symptoms listed above, or other symptoms, during the study, contact the research team at 650-736-1235 during business hours, and through the Stanford page operator (650-723-6661; page # 23552) after hours and during weekends/holidays.

If your child receives the placebo (inactive nasal spray), then the behavioral issues associated with autism that your child might be experiencing, would go untreated for the length of the study.

Obtaining blood can hurt briefly and can cause bruising. The volume of blood we collect will be below the Lucile Packard phlebotomy clinics recommended maximum amount. The amount of blood we will collect will be below 2% of your child's total blood volume.

Allergic reactions are possible with any drug or supplement.

Allergic Reaction Risks: As with taking any drug, there is a risk of allergic reaction. If your child has a very serious allergic reaction, your child may be at risk of death. Some symptoms of allergic reactions are: rash, difficulty breathing, wheezing, sudden drop in blood pressure, swelling around the mouth, throat or eyes, a fast pulse, and sweating. Please seek treatment and alert the study doctor and study staff immediately if your child has any of these symptoms, or any other side effects, during the study.

There will be multiple questionnaires to fill out during the visits, which may be frustrating at times. The study physician will also ask questions relating to suicide and self-harm, which may be uncomfortable for you or your child to discuss. Some of the eye-tracking and computer equipment might also be frustrating, as they require that your child sit very still during the tests.

Another risk of research studies is a breach of confidentiality.

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It is possible that researchers may learn information from this study that may make them concerned about your child's health and/or safety or the health and/or safety of others; in such a case, the researchers may tell you or someone else about it.

INFORMATION REGARDING COVID-19

It is important that you disclose to us any indication of having been exposed to COVID-19, or whether you have experienced any signs or symptoms associated with COVID-19 diseases before attending any visits at Stanford University. We will ask that you not attend in person sessions if you exhibit any of the following symptoms.

Symptoms of COVID-19 Include

- Fever
- Chills
- New cough
- New shortness of breath
- New severe fatigue or muscle aches
- Sore throat
- Loss of smell and/or taste
- Runny nose/congestion
- Sneezing
- Headache
- Diarrhea
- Nausea
- Vomiting

If you are coming in-person to research visits, you are required to be fully vaccinated—2 doses (1 for Johnson and Johnson), 2 weeks out and to provide proof of your vaccination (e.g., CDC COVID-19 Vaccination Card, e-Health record, etc.) to the researcher prior to study participation. Alternately, you can provide a negative COVID test within 72 hours of your visit.

Additionally, even if you are fully vaccinated, we may ask you and/or your child for a negative rapid COVID test within 24 hours (ideally on the day of the visit) or a negative PCR COVID test within 72 hours of your in-person visit.

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POTENTIAL BENEFITS

Intranasal vasopressin can potentially lead to an improvement in social and communication deficits and possibly in other symptom domains. Participants might also benefit indirectly through the information learned in their cognitive and behavioral evaluation.

Although participation in this research project may be of no direct benefit to your child, it is likely that the knowledge that may be gained from this study will contribute to better therapy for autism and its related behavioral issues. It is possible that there will be an improvement in your child's behavior but we cannot guarantee this outcome.

We cannot and do not guarantee or promise that you will receive any benefits from this study.

ALTERNATIVES

The alternative to participation in this study is not to participate. You do not have to participate in the study in order to receive treatment for your child's autism. You can also discuss with your physician or with Dr. Hardan the different therapeutic strategies that are available for your child.

PARTICIPANT'S RIGHTS

You should not feel obligated to agree to participate. Your questions should be answered clearly and to your satisfaction. If you decide not to participate, tell the Protocol Director.

You will be told of any important new information that is learned during the course of this research study, which might affect your condition or your willingness to continue participation in this study.

ClinicalTrials.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.

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CONFIDENTIALITY

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 except as authorized by you or as required by law**.** However, there is always some risk that even de-identified information might be re-identified.

Patient 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.

The purpose of this research study is to obtain data or information on the safety and effectiveness of vasopressin treatment in children with autism; the results will be provided to the sponsor, the Food and Drug Administration and other federal and regulatory agencies as required.

If information is revealed about child abuse or neglect, elder or dependent abuse or neglect, or potentially dangerous future behavior to others or yourself, the law requires that this information be reported to the proper authorities.

STANFORD DATA SHARING

If you have previously participated in other research studies at Stanford University that used the same behavioral tests as this study, we would like access to your testing data in order to avoid having you and your child repeat these assessments.

Can we access your child's research data and past behavioral testing from those other studies at Stanford University?

Please initial: _____ Yes _____No

We may also want to share your child's research data and behavioral testing data from this study with other research studies at Stanford University. This may help your child avoid repeating assessments if you and your child choose to participate in other future studies.

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Can we share your child's research data and behavioral testing data with other Stanford studies that you are participating in?

Please initial: _____ Yes _____No

CERTIFICATE OF CONFIDENTIALITY

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation by the National Institute of Child Health and Development (NICHD) which is funding this project or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law of child abuse or neglect, elder abuse or neglect, or potentially dangerous future behavior to others or yourself.

The Certificate of Confidentiality will not be used to prevent disclosure for any purpose you have consented to in this informed consent document.

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Authorization To Use Your Health Information For Research Purposes

Because information about you and your health is personal and private, it generally cannot be used in this research study without your written authorization. If you sign this form, it will provide that authorization. The form is intended to inform you about how your health information will be used or disclosed in the study. Your information will only be used in accordance with this authorization form and the informed consent form and as required or allowed by law. Please read it carefully before signing it.

What is the purpose of this research study and how will my health information be utilized in the study?

The purpose of this study is to see if vasopressin can help lessen behavioral problems and other symptoms in children with autism. We hope that by studying the effects of vasopressin treatment in more detail, we can design better ways to treat individuals with this condition. This study is meant to test the tolerability of vasopressin and its effectiveness in the treatment of behavioral difficulties in children with autism. It will also examine the possible benefit of this agent in improving the core deficits in autism such as social deficits. Your child's health information may be used in scientific publications and discussed at scientific meetings. Results from this study will be provided to the sponsor, National Institute of Child Health and Development, the Food and Drug Administration and other federal and regulatory agencies as required.

Do I have to sign this authorization form?

You do not have to sign this authorization form. But if you do not, you will not be able to participate in this research study, including receiving any research-related treatment.
Signing the form is not a condition for receiving any medical care outside the study.

If I sign, can I revoke it or withdraw from the research later?

If you decide to participate, you are free to withdraw your authorization regarding the use and disclosure of your health information (and to discontinue any other participation in the study) at any time. After any revocation, your health information will no longer be used or disclosed in the study, except to the extent that the law allows us to continue using your information (e.g., necessary to maintain integrity of research). If you wish to revoke your authorization for the research use or disclosure of your health information in this study, you must write to: Dr. Antonio Hardan at the following address: 401 Quarry Road, Stanford CA, 94305.

What Personal Information Will Be Obtained, Used or Disclosed?

Your child's health information related to this study, may be used or disclosed in connection with this research study, including, but not limited to, name, date of birth, social security number (for payment purposes only), telephone number, e-mail address, and mailing address. The records that will be collected, used, and shared for this study may include your child's research record, supporting information from your child's medical record number, medical records, results of laboratory, diagnostic or other tests, results of tests on samples (blood or urine) that have been stored, and clinical and research observations and video recordings made during your child's participation in the research study.

Who May Use or Disclose the Information?

The following parties are authorized to use and/or disclose your health information in connection with this research study:

- The Protocol Director Dr. Antonio Hardan
- The Stanford University Administrative Panel on Human Subjects in Medical Research and any other unit of Stanford University as necessary
- Research Staff

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Who May Receive or Use the Information?

The parties listed in the preceding paragraph may disclose your health information to the following persons and organizations for their use in connection with this research study:

- The Office for Human Research Protections in the U.S. Department of Health and Human Services
- National Institute of Child Health and Development (NICHD)
- The Food and Drug Administration
- The National Database for Autism Research (NDAR).
- Mariner Advanced Pharmacy Corp.
- Pearson Clinical
- Other Research Studies at Stanford University
- Simons Foundation Powering Autism Research for Knowledge (SPARK)

Your information may be re-disclosed by the recipients described above, if they are not required by law to protect the privacy of the information.

When will my authorization expire?

Your authorization for the use and/or disclosure of your health information will end on December 31, 2045 or when the research project ends, whichever is earlier.

Will access to my medical record be limited during the study?

To maintain the integrity of this research study, you may not have access to any health information developed as part of this study until it is completed. At that point, you would have access to such health information if it was used to make a medical or billing decision about you (e.g., if included in your official medical record).

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_____ _____
Signature of Legally Authorized Representative (LAR) Date
(e.g., parent, guardian or conservator)

_____
Print Name of LAR

_____
LAR's Authority to Act for Participant
(e.g., parent, guardian or conservator)

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FINANCIAL CONSIDERATIONS

Payment

You will be provided a payment of 60 dollars for the first visit and 30 dollars for each additional completed visit. The total payment for completing the study could be up to 210 dollars for participation in the 8-week trial and 270 dollars if you also end up participating in the open-label extension phase.

Payments may only be made to U.S. citizens, legal resident aliens, and those who have a work eligible visa. You may need to provide your social security number to receive payment.

Costs

If you participate in this study, the study will pay for those services, supplies, procedures, and care associated with the study that are not a part of your routine medical care. However, there may be additional costs to you. These include basic expenses like transportation and the personal time it will take to come to the study visits. You and/or your health insurance must pay for services, supplies, procedures, and care that are required during this study for routine medical care. **You will also be responsible for any co-payments and/or deductibles as required by your insurance.** Participation in this study is not a substitute for health insurance.

Sponsor

The National Institute of Child Health and Human Development (NICHD) is providing financial support for this study.

The National Institutes of Health are providing some financial support for the facility and staff where part or all of the study is taking place.

COMPENSATION for Research-Related Injury

All forms of medical diagnosis and treatment – whether routine or experimental – involve some risk of injury. In spite of all precautions, you might develop medical complications from participating in this study. If such complications arise, the Protocol Director and the research study staff will assist you in obtaining appropriate medical treatment. In the event that you have an injury or illness that is directly caused by your participation in this study, reimbursement for all related costs of care first will be sought from your insurer, managed care

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plan, or other benefits program. **You will be responsible for any associated co-payments or deductibles as required by your insurance.**

If costs of care related to such an injury are not covered by your insurer, managed care plan or other benefits program, you may be responsible for these costs. If you are unable to pay for such costs, the Protocol Director will assist you in applying for supplemental benefits and explain how to apply for patient financial assistance from the hospital.

You do not waive any liability rights for personal injury by signing this form.

CONTACT INFORMATION

Questions, Concerns, or Complaints: If you have any questions, concerns or complaints about this research study, its procedures, risks and benefits, or alternative courses of treatment, you should ask the Protocol Director, Dr. Antonio Hardan. You may contact him now or later at 650-736-1235.

Injury Notification: If you feel you have been hurt by being a part of this study, please contact the Protocol Director, Dr. Antonio Hardan at 650-736-1235.

Independent Contact: If you are not satisfied with how this study is being conducted, or if you have any concerns, complaints, or general questions about the research or your rights as a participant, please contact the Stanford Institutional Review Board (IRB) to speak to someone independent of the research team at 650-723-5244 or toll free at 1-866-680-2906. You can also write to the Stanford IRB, Stanford University, 1705 El Camino Real, Palo Alto, CA 94306.

Appointment Contact: If you need to change your appointment, please contact the research study staff at 650-736-1235.

Alternate Contact: If you cannot reach the Protocol Director, please contact the outpatient clinic of the Child Psychiatry Division at 650-723-5511 at any time of the day or night and ask to speak to the physician on call.

EXPERIMENTAL SUBJECT'S BILL OF RIGHTS

As a research participant you have the following rights. These rights include but are not limited to the participant's right to:

- be informed of the nature and purpose of the experiment;

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- be given an explanation of the procedures to be followed in the medical experiment, and any drug or device to be utilized;
- be given a description of any attendant discomforts and risks reasonably to be expected;
- be given an explanation of any benefits to the subject reasonably to be expected, if applicable;
- be given a disclosure of any appropriate alternatives, drugs or devices that might be advantageous to the subject, their relative risks and benefits;
- be informed of the avenues of medical treatment, if any available to the subject after the experiment if complications should arise;
- be given an opportunity to ask questions concerning the experiment or the procedures involved;
- be instructed that consent to participate in the medical experiment may be withdrawn at any time and the subject may discontinue participation without prejudice;
- be given a copy of the signed and dated consent form; and
- be given the opportunity to decide to consent or not to consent to a medical experiment without the intervention of any element of force, fraud, deceit, duress, coercion or undue influence on the subject's decision.

May we contact you about future studies that may be of interest to you?
____ Yes ____ No

Signing your name means you agree to be in this study and that you will receive a copy of this signed and dated consent form.

_____
Print Name of Participant

_____ _____
Signature of Legally Authorized Representative (LAR) Date
(e.g., parent, guardian or conservator)

_____
Print Name of LAR

_____
LAR's Authority to Act for Participant
(e.g., parent, guardian or conservator)

The IRB determined that the permission of two parents is recommended in accordance with 21 CFR 50.55 unless one parent is deceased, unknown, incompetent, not reasonably available, or only one parent has legal responsibility for the care and custody of the child. *Not reasonably available* means that the other parent is not present during the consenting process, or will not be available prior to the start of research procedures.

_____ _____
(If available) Signature of Other Parent or Guardian Date

_____
Print Name of Other Parent or Guardian

_____
Authority to Act for Participant

_____ _____
Signature of Person Obtaining Consent Date

_____
Print Name of Person Obtaining Consent