University of Nebraska Medical Center

DEPARTMENT OF PSYCHIATRY

Re: NCT 02824627

Please see the attached IRB approved informed consent document (approval date 12/20/2021) for study **IRB#321-16-FB: Investigating the impact of oxytocin on irritability/emotional dysregulation in children and adolescents with disruptive behavior and mood disorders, and the possible mediating role of amygdala activity.**

Sincerely,

Brigette Vaughan MSN, APRN
Lead Research Coordinator
UNMC Department of Psychiatry

985575 Nebraska Medical Center / Omaha, NE 68198-5575
402-559-6002 / FAX 402-559-6248 / www.unmc.edu/psychiatry

PARENTAL CONSENT - CLINICAL BIOMEDICAL

Title of this Research Study

Invitation
You are invited to allow your child to take part in this research study. You have a copy of the following, which is meant to help you decide whether or not to allow your child to take part:

- Informed consent form
- "What Do I need to Know Before Being in a Research Study?"
- The Rights of Research Subjects

Why is your child being asked to be in this research study?
Your child is being asked to be in this research study because he or she has a significant level of irritability and difficulty controlling his or her emotions and behavior.

If your child is pregnant, nursing an infant, or plans to become pregnant during this study, she may not be in this study.

What is the reason for doing this research study?
This study is being done to see if Oxytocin, a hormone known to increase social behavior, can be helpful for reducing irritability and emotional problems in children.

What will be done during this research study?
Initial assessment session
The initial assessment session will occur at the outpatient clinic at the UNMC Department of Psychiatry. It will take between 2 and 4 hours to complete. Your child will meet with either a child and adolescent psychiatrist or a psychiatric nurse practitioner to confirm his/her psychiatric diagnosis. You and your child will be asked to fill out five rating scales about your child's symptoms and behavior.

Your child will do a urine drug screen test to make sure your child does not have substance use. If the drug screen turns out to be positive, we will inform you and your child of the result. In this case, your child will not be allowed to participate in the study.

Your child will also have the inside of his/ her cheek rubbed 10-20 times with a small

brush to collect some cells for genetic testing. This will allow us to look at the gene for oxytocin. The sample is collected by gently scraping the inside of your child's mouth, 10-20 times with a small brush.

Collection of this sample of cheek cells is not required in order to participate in the study. You and your child can opt out (not participate) in this study procedure.

Visit 1

Visit 1 will occur within a week of the initial assessment session. It may also occur that same day of the initial assessment session. Your child will be asked to perform a few tests on the computer that will require him/her to respond to pictures or make simple decisions. Sometimes your child will be asked to just lie still and do nothing. During this time, we will be using the fMRI and MEG scans to take pictures of your child's brain. The fMRI scan will happen at the Boys Town National Research Hospital, and MEG will happen at the MEG center of the University of Nebraska Medical Center. We will try to coordinate these two scans on the same day, but if your schedule wouldn't allow it, we will do them on separate dates (as close as possible to each other). Before the fMRI and MEG scans, if your child is a girl, we will do an urine test to make sure that your child is not pregnant. If the pregnancy test is positive, we will inform you and your child about this, and your child will not be allowed to participate in the study, due to unknown risk related to use of oxytocin and fMRI/MEG during pregnancy.

Functional MRI (fMRI) and MEG use magnetic fields and radio waves to take pictures of your child's brain. These scans allow us to see what parts of the brain are active when your child does specific tasks. In the fMRI scanner, a helmet will be placed over your child's head. The MEG scanner uses electrodes attached to the skin surface of your child's skull. Before the scan, your child will be told about the task and have the opportunity to practice. A computer screen will show your child information about the task while he or she is in the scanner.

The fMRI procedure will take about 60 minutes, though they are only in the scanner about 30 minutes. While in the scanners your child will hear knocking noises (somewhat louder in the fMRI scanner than MEG). Your child will be fitted with earplugs to muffle the sounds. Your child will be able to communicate with the MRI and MEG staff at all times and he or she may ask to be moved out of the machines at any time.

If you and your child prefer, you are welcome to stay with your child during the MRI

and MEG scans.

Visit one will last approximately 4 and half hours (2 and half hours at the Boys Town National Research Center, and one and half hours at the MEG center of the University of Nebraska Medical Center, and half an hour of transporting between two places).

Oxytocin/Placebo Treatment

After the first visit, your child will be started on a nasal spray which will contain either Oxytocin or placebo (inactive solution). Your child will be randomly assigned to either oxytocin treatment or placebo treatment, just like flipping a coin. You and your child and the study team will not know which treatment your child is getting. If your child weighs more than 88 pounds, your child will take 2 puffs to each nostril once a day, and only 1 puff to each nostril daily if less than 88 pounds. You and your child will be given instructions for how to use the nasal spray by the study doctor or staff. You will be given enough study medication for 3 weeks of use, though your child's participation may not last that long.

You and your child will be seen after 1 week of being on the study medication. The study doctor and staff will talk with you and your child about his or her symptoms and any problems with the study medication, including side effects. If your child's symptoms require treatment with other interventions, he or she may be removed from the study at that time.

Visit 2

After at least 14 days but no later than 21 days of oxytocin or placebo treatment, your child will return to Boys Town and UNMC for a second fMRI and MEG scan to see if there are any changes in brain activity following study treatment. The scan procedures will be exactly the same as those done at visit 1. If your child is a girl, we will repeat urine pregnancy test to make sure that your child is not pregnant.

The rating scales used during the initial assessment will be completed again by you and your child, allowing us to determine if there have been changes in his or her symptoms following study medication treatment.

What are the possible risks of being in this research study?

MRI

People are at risk for injury from the MRI magnet if they have pacemakers or other implanted electrical devices, brain stimulators, some types of dental implants, aneurysm clips (metal clips on the wall of a large artery), metallic prostheses

(including metal pins and rods, heart valves, and cochlear implants), permanent eyeliner, implanted delivery pump, or shrapnel fragments. Welders and metal workers are also at risk for injury because of possible small metal fragments in the eye of which they may be unaware. Your child will be screened for these conditions before having any scan, and if he/she has any of these, they will not be scanned. If you have a question about any metal objects being present in your child's body, you should inform the staff. In addition, all magnetic objects (for example, watches, coins, jewelry, piercings, and credit cards) must be removed before entering the MRI scan room.

It is not known if MRI is completely safe for a developing fetus. Therefore, if your child is a girl and old enough to become pregnant, we will do a pregnancy test. Girls who are pregnant may not take part in this study. If the pregnancy test is positive, we will inform you and your child. If your daughter objects to having this required pregnancy test, she should not participate in this study.

People with a fear of confined spaces may become anxious during an MRI. Those with back problems may have back pain or discomfort from lying in the scanner. The noise from the scanner is loud enough to damage hearing, especially in people who already have hearing loss. Everyone having a research MRI scan will be fitted with hearing protection. If the hearing protection comes loose during the scan, your child should let us know right away. Please notify the investigators if your child has hearing or ear problems. You will be asked to complete an MRI screening form for your child for each MRI scan your child has. There are no known long-term risks of MRI scans.

An additional risk of MRI is that the MRI pictures may reveal an abnormality in your child's brain. These findings may be benign (mild anatomical variation) or serious (brain tumor). If there is any abnormal finding in the MRI of your child, we will contact you immediately to inform you and to discuss further steps necessary to be taken. This may include referral to your child's primary care provider, or if requested, to an appropriate department of the University of Nebraska Medical Center.

MEG

Your child may experience discomfort from the paste and tape that is used to attach the electrodes and head helmet to the skin surface. Such discomfort may include skin irritation or accidental hair removal.

Your child will be closely observed at all times by staff who will stop the MEG scan if your child appears distressed by the experience. You will be asked to complete an MEG screening form for your child for each MEG scan your child has. There are no

know long-term risks of MEG scans.

Oxytocin

Potential side effects of oxytocin nasal spray include: light-headedness/vertigo, drowsiness/sleepiness, dry throat/mouth, nasal irritation, runny nose, abdominal discomfort, anxiety, elevation of mood, and headache. According to previous studies, these side effects occur at the same rate as they did in patients who received placebo. Use of a nasal spray may result in irritation of the inside of the nose, and nose-bleeding, post-nasal drip, and experiencing an unpleasant taste or smell. Side effects are mostly minor and transient. The relatively short treatment period (14-21 days) may lower the risk of side effects.

Collection of the Buccal Cell Sample

The possible risk of collecting the cheek swab includes mild irritation of the inside of the cheek, minor bleeding of mucosa, and an uncomfortable sensation and taste of the brush.

Genetic testing of oxytocin receptor

The possible risk of genetic testing for the oxytocin receptor is minimal. It doesn't include any information that can be used for personal identification. This information will not be stored for future studies.

Pregnancy testing

The risk of pregnancy test is finding out that your child is indeed pregnant. Girls who are pregnant may not take part in this study. If your child is pregnant, we will inform you and your child. If your child objects to having this required pregnancy test, she should not participate in this study.

Urine drug screen

The risk of urine drug screening is finding out that your child has used a potentially illegal substance that could have mood and behavior-altering effects. We will inform you and your child if the test result is positive, thus your child is not eligible for participating in the study.

Interviews and assessments

Questions regarding mood and behavior symptoms may be upsetting or stressful for you and your child. The study doctor and staff are experienced in child psychiatry and will perform the interviews and assessments in a sensitive and professional manner.

It is possible that other rare side effects could occur which are not described in this consent form. It is also possible that your child could have a side effect that has not occurred before.

What are the possible benefits to your child?
Your child will receive a comprehensive psychiatric assessment and evaluation, including symptom severity measurements. Your child also will receive an anatomical MRI scan of his or her brain, which may rule out any possible anatomical abnormality or deviation. Your child may show improvement in his/her level of irritability and difficulty with emotional and behavioral regulation. This benefit may be transient due to the relatively short duration of action of Oxytocin.

Your child may not get any benefit from being in this research study.

What are the possible benefits to other people?
This study may lead to a better understanding of the areas of the brain involved in irritability and emotional dysregulation, and the possible effects of treatment by oxytocin on these. This may improve our understanding of irritability and emotional dysregulation in children and adolescents.

What are the alternatives to being in this research study?
Instead of being in this research study you can choose not to allow your child to participate. The alternative to this study is to not participate. Psychiatric evaluation and treatment, with behavioral intervention is available at UNMC as well as other agencies in the community.

The investigators will discuss with you the risks and benefits of each of the alternatives described above.

What will allowing your child to be in this research study cost you?
There is no charge to you for participating in the study. You will be responsible for any costs associated with the follow up of an abnormal MRI scan. You will be responsible for any applicable insurance deductibles and co-payments related to your child's normal care. If you wish to speak with a financial counselor about your child's insurance coverage and benefits, let the investigator or other study personnel know. A contact for personal assistance will be made available for you.

Will you or your child be paid for being in this research study?
Your child will be paid for being in this research study.
$20.00 per visit to your child

$20.00 per visit to you as parent

A check will be issued to the parent/guardian (unless otherwise requested) at the end of your child's study participation. You will only be paid for those visits that have been completed.

For the payment to be processed, we will ask your social security number, to process and mail the check of payment. If you don't want to provide your social security number, your child still can participant in the research, but no payment will be made.

Who is paying for this research?
This research is being paid for by grant funds from the Department of Psychiatry at the University of Nebraska Medical Center.

What should you do if your child is injured or has a medical problem during this research study?
Your child's welfare is the main concern of every member of the research team. If he/she is injured or has a medical problem or some other kind of problem as a direct result of being in this study, you should immediately contact one of the people listed at the end of this consent form. Emergency medical treatment for this injury or problem will be available at the Nebraska Medical Center. If there is not sufficient time, you should seek care for your child from a local health care provider.

The Institution has no plans to pay for any required treatment or provide other compensation.
Agreeing to this does not mean you have given up any of you or your child's legal rights.

How will information about your child be protected?
Your child has rights regarding the protection and privacy of his/her medical information collected before and during this research. This medical information is called "protected health information" (PHI). PHI used in this study may include his/her medical record number, address, birth date, medical history, the results of physical exams, blood tests, x-rays as well as the results of other diagnostic medical or research procedures. Only the minimum amount of PHI will be collected for this research. Your child's research and medical records will be maintained in a secure manner.

Who will have access to information about your child?
By signing this consent form, you are allowing the research team to have access to

your child's PHI. The research team includes the investigators listed on this consent form and other personnel involved in this specific study at the Institution.

Your child's PHI will be used only for the purpose(s) described in the section "What is the reason for doing this research study?"

You are also allowing the research team to share his/her PHI, as necessary, with other people or groups listed below:

- The UNMC Institutional Review Board (IRB)
- Institutional officials designated by the UNMC IRB
- Federal law requires that the subject's information may be shared with these groups:
    - The HHS Office of Human Research Protections (OHRP)
- The HIPAA Privacy Rule requires the following groups to protect the subject's PHI:
    - Researchers at Boys Town National Research Hospital.

You are authorizing us to use and disclose your child's PHI for as long as the research study is being conducted.

You may cancel your authorization for further collection of your child's PHI for use in this research at any time by contacting the principal investigator. However, the PHI which is included in the research data obtained to date may still be used. If you cancel this authorization, your child will no longer be able to participate in this research.

How will results of the research be made available to you during and after the study is finished?

Information obtained in the course of the research that will not be shared with you or your child is whether or not your child is taking oxytocin or the placebo and the results of the oxytocin genetic testing. By signing this authorization, you are temporarily giving up the right to see this research-related information while the research is going on. You will be able to see this information if you wish after the research is completed.

In most cases, the results of the research can be made available to you when the study is completed, and all the results are analyzed by the investigator or the sponsor of the research.

The information from this study may be published in scientific journals or presented at

scientific meetings, but your child's identity will be kept strictly confidential.

If you want the results of the study, contact the Principal Investigator at the phone number given at the end of this form or by writing to the Principal Investigator, Dr. Soonjo Hwang, at the following address: 985578 Nebraska Medical Center, Omaha, NE 68198-5578

If you want the results of the study, contact the Principal Investigator at the phone number given at the end of this form or by writing to the Principal Investigator at the following address: 985578 Nebraska Medical Center | Omaha, NE 68198-5578

What will happen if you decide not to give permission for your child to be in this research study?
You can decide not to give permission for your child to be in this research study. Deciding not to be in this research will not affect your child's medical care or his/her relationship with the investigator or the Institution. Your child's doctor will still take care of him/her. Your child will not lose any benefits to which he/she is entitled.

What will happen if you decide to stop your child's participation once it starts?
You can stop your child's participation in this research (withdraw) at any time by contacting the Principal Investigator or any of the research staff.

Deciding to withdraw will otherwise not affect your child's care or relationship with the investigator or this institution. Your child will not lose any benefits to which he/she is entitled.

For the safety of your child, please talk to the research team before you have the him/her stop taking any study drugs or stop other related procedures. They will advise you how to withdraw your child safely. If you withdraw your child, you may be asked to allow your child to undergo some additional tests. You do NOT have to agree to have your child undergo these tests.

Your child may be taken off the study if he/she doesn't follow instructions of the investigator or the research team.

Any research data obtained to date may still be used in the research.

Any tissue (e.g., cheek swab) obtained to date may also be used in the research. Should you wish to have any leftover tissue samples withdrawn from use in future research, a request must be made to the Principal Investigator.

Will you be given any important information during the study?
You will be informed promptly if the research team gets any new information during this research study that may affect whether you would want your child to continue being in the study.

What should you do if you have any questions about the study?
You have been given a copy of *"What Do I Need to Know Before Being in a Research Study?"* If you have any questions at any time about this study, you should contact the Principal Investigator or any of the study personnel listed on this consent form or any other documents that you have been given.

What are your child's rights as a research subject?
Your child has rights as a research subject. These rights have been explained in this consent form and in The Rights of Research Subjects that you have been given. If you have any questions concerning his/her rights or complaints about the research, you can contact any of the following:

- The investigator or other study personnel
- Institutional Review Board (IRB)
    - Telephone: (402) 559-6463.
    - Email: IRBORA@unmc.edu
    - Mail: UNMC Institutional Review Board, 987830 Nebraska Medical Center, Omaha, NE 68198-7830
- Research Subject Advocate
    - Telephone: (402) 559-6941
    - Email: unmcrsa@unmc.edu

Documentation of informed consent
You are freely making a decision whether to give permission for your child to be in this research study. Signing this form means that:

- You have read and understood this consent form.
- You have had the consent form explained to you.
- You have been given a copy of The Rights of Research Subjects
- You have had your questions answered.
- You have decided to permit your child to be in the research study.
- If you have any questions during the study, you have been directed to talk to one of the investigators listed below on this consent form.
- You will be given a signed and dated copy of this consent form to keep.

Signature of Parent/Guardian _____

Date _____

You are agreeing to be in this research study. You have had someone explain the study to you, and answer your questions.

Signature of Subject _____
Date _____

My signature certifies that all the elements of informed consent described on this consent form have been explained fully to the parent(s)/guardian(s) of the subject. In my judgment, the parent(s)/guardian(s) possesses the legal capacity to give informed consent for the subject to participate in this research and is voluntarily and knowingly giving informed consent.

Signature of Person obtaining consent _____
Date _____

Authorized Study Personnel
Principal
* Hwang, Soonjo
phone: 405-552-6002
alt #: 402-552-6351
degree: MD

Lead Coordinator
* Soltis-Vaughan, Brigette
phone: 402-552-6239
alt #: 402-552-6239
degree: APRN