Official title: Integrated Oxytocin and Nonverbal, Emotion Recognition, and Theory of Mind Training for Children With Autism Spectrum Disorder

NCT number: NCT02918864

Document date: 2/8/2021

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Protocol Title: Integrated Oxytocin & NETT in ASD (ION-ASD)

Sponsor(s): National Institute of Child Health and Human Development
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RUSH

Subject Information Sheet and Consent Form

Note: If you are a parent, guardian, or legal representative of a minor or person who is not able to consent for themselves, the terms "you" or "your" refer to the research participant.

Key Information:

You are being invited to participate in a research study. Research studies answer important questions that might help change or improve the way we do things in the future.

This consent form will give you information about the study to help you decide whether you want to participate. Please read this form, and ask any questions you have, before agreeing to be in the study.

Taking part in this research study is voluntary. You do not have to participate in this study and may choose to leave the study at any time. If you decide not to participate in this study or leave the study at a later time, your health care, benefits, or relationship with Rush University Medical Center will not change or be affected.

The purpose of this study is to evaluate two models of social skills group therapies for children with autism: 1) a facilitated play group and 2) a combination behavioral-medication treatment (social cognitive skills therapy group with intranasal [through the nose] oxytocin). In the facilitated play group, therapists will encourage children to play and engage in appropriate social activities using topics and activities chosen by the children. The combination behavioral-medication treatment will consist of a social cognitive skills therapy group and intranasal oxytocin (Syntocinon®). Oxytocin is a hormone (a substance made by a gland in the body that regulates another part of the body) produced in the brain. Previous research conducted suggests oxytocin may enhance social learning in individuals with autism spectrum disorder (ASD). The study aims to assess the feasibility, safety, tolerability, preliminary effectiveness, and maintenance of treatment effects from both interventions. We do not yet know if the group therapies help children with autism. The Food and Drug Administration (FDA) has not approved use of oxytocin for ASD or for the use in children.

If you agree to participate in this study, your participation may last up to 30 weeks and you will be asked to complete 16-20 study visits: 1) screening/baseline (2-4 visits), 2) Groups (12 visits), 3) follow-up evaluations: endpoint (1-2 visits), week 16 (1 visit), week 24 (1 visit).

During these visits, you will be asked to complete several assessments, questionnaires, parent interviews, laboratory procedures, and health check-ins. For a detailed description of study procedures, please see the "*What are the activities you will be doing if you participate in this study?*" section of this consent form.

There are risks to you for participating in research. In this study, there is a risk of stress or anxiety associated with participating in testing and social interactions particularly with unfamiliar adults and peers during evaluation and group sessions. For participants receiving intranasal oxytocin, nasal irritation, itchy and runny nose and watery eyes associated with use of a nasal spray may occur; and potential restlessness, increased energy, increased irritability and mild decrease in appetite have been reported in both intranasal oxytocin and placebo conditions in autism studies. With all health care procedures including those in this study, there may be a risk of loss of confidentiality of medical information. Several precautions are taken to minimize these behavioral, health, and confidentiality risks. For a detailed list of risks you should know about, please see the "*What are the risks and discomforts of participating in this study*?" section of this consent form (pg. 8).

You may not directly benefit from taking part in this study. A possible benefit is that your condition may improve as a result of either intervention. Intranasal oxytocin has been reported to make people feel good after using the nasal spray. There may also be some benefit for you via the psychiatric and medical evaluation provided in the study. The information collected from the study may increase knowledge about the processes that will help select better treatments for individual patients and for particular subgroups of patients. This study may help other children with ASD in the future if the research team finds a new treatment option through this study and/or learns more about why some children do well with study medication and others do not.

There are other options available to you if you decide not to participate in this study. You may choose another form of treatment or care without being in a study such as:

- Other forms of group psychotherapy as well as individual psychotherapy have been utilized to treat autism; however, they have not been scientifically proven to be helpful.

- Although there is currently no medication approved to effectively treat autism, some medications such as fluoxetine (Prozac), paroxetine (Paxil), divalproex sodium (Depakote) and risperidone (Risperdal) have been helpful in improving some of the symptoms of this disorder.

Detailed Information: Please review the rest of this document for details about the above topics and additional information you should know before making a decision about whether or not you will participate in this study.

Why are you being invited to participate in this study?
You are being asked to take part in this study because you are between the ages of 8 and 11, inclusive, and have been diagnosed with autism spectrum disorder (ASD). You are also eligible for this study because you and your parent/caregiver are interested in participating in social skills group therapy types.

How many participants will take part in the study?
Approximately 90 people are expected to take part in this research study at Rush University Medical Center.

What are the activities you will be doing if you participate in this study?
If you are eligible for the study, your full participation would last approximately 30 weeks from screening to the last follow-up visit.

If you agree to participate in this research study, your involvement will include the following:

Screening Visit(s)
First you will have some assessments performed so that the study team can determine if you have any medical illnesses or other conditions that would interfere with the study. The assessments may take anywhere from 4-6 hours, and can be split between 2 site visits and combined with baseline visits (see next section). If the study assessments show that you are not eligible to continue in this study, your participation will end.

- You will have an intake evaluation assessing your developmental, medical, and psychiatric history, and to make sure you may not have conditions that would interfere with your participation in this study.
- One of the tests that will be performed during screening (**Autism Diagnostic Observation Schedule-2**) will be video recorded. The recording will be used for the study staff to view and check scoring; this is to make sure that all of the people who do the testing do it the same way. The recording will be labeled with a code number, stored electronically on the encrypted Rush computer network in a password protected folder and destroyed when the study is completed.
    - **Childhood Autism Rating Scale, Second Edition** (CARS2) (Optional, alternative to ADOS2). The CARS2 is a well-validated, clinician completed rating form developed to assist in identifying individuals with autism spectrum disorders and distinguish them from individuals with other diagnoses. It includes two versions, the CARS2-Standard Version (CARS2-ST) and the CARS2-High-Functioning Version (CARS-HF). The version rated by the clinician is determined by the child's cognitive level and age. The CARS2 requires the clinician to rate 15 areas of behavior in terms of frequency, intensity, peculiarity, and duration,

and yields a quantitative score reflecting a continuum of behavior problems related to autism that can be used in making comparative judgments regarding the level of autism-related behaviors present in a given individual or group. The CARS2 will be administered if in-person testing with the ADOS2 is compromised because of masking restrictions related to COVID-19 precautions.

- A member of our research team will ask you or another member of the family questions regarding possible past or present emotional or developmental problems (**Autism Diagnostic Interview-Revised**). This interview will be conducted at Rush University Medical Center and will take approximately three hours to complete.
    - If needed, this interview can be completed via a HIPAA compliant platform (i.e. Zoom)

- To determine IQ, your child will be assessed on one of the following measures:
    - **The Wechsler Intelligence Scale for Children (WISC-V):** The WISC-V is an IQ test that measures how you learn. The test questions individuals on how they perform different activities related to thinking and memory. The WISC-V takes approximately 1.5 hours to administer.
    - **The Wechsler Abbreviated Scale of Intelligence-II (WASI-II):** The WASI-II is an IQ test that measures how you learn. The test questions individuals on how they perform different activities related to thinking and memory. The WASI-II takes approximately 30 minutes to administer.
- We will also ask you to complete assessments. You will be given tasks that involve solving puzzles and social problems, remembering lists, and defining words.
- You will have a full physical exam including height, weight, temperature, and vital signs (blood pressure, heart rate and breathing rate).
- An electrocardiogram (ECG) will be administered. Sticky patches are placed on your chest. These patches are connected to a machine which shows the electrical activity of your heart.
- You will go to the outpatient laboratory at Rush University Medical Center and have the following tests:
    - You will have urine collected for safety laboratory tests
    - You will have blood collected (about 1 teaspoon) as part of the general medical evaluation to look for any signs in the blood that may mean you should not participate in this study.
    - A pregnancy test will be completed if applicable.

Baseline Visit(s)

Participants entering the study will undergo the baseline assessments, which are anticipated to take approximately 6-10 hours to complete no more than 21 days from the last screening visit. The baseline visit can be split into as many as three visits if this is better for the participant. You will be given tasks that involve problem solving, thinking and memory games, looking at images and making judgements about them, and listening to sounds and words and answering questions about them. Some of the tasks will be presented on a computer screen. Additionally some of these assessments will be video recorded. The recording will be labeled with a code number, stored electronically on the encrypted Rush computer network in a password protected folder and destroyed when the study is completed.

Your parents will also be asked to complete interviews and questionnaires about your current functioning, daily living habits, and behavior. You will have a physical exam including height, weight, temperature, and vital signs.

- If needed, some of the interviews can be completed via phone or virtually on a HIPAA compliant platform (i.e. Zoom).

At the baseline visit, you will also be randomized to receive either:

1. The facilitated play group

OR

2. The combination behavioral-medication treatment (social cognitive skills therapy group with intranasal oxytocin).

The treatment you receive will be chosen by chance, like flipping a coin. You will have an equal chance of being selected for the facilitated play group or the social cognitive skills therapy group with intranasal oxytocin. You will be told which group you are in. The medication in the combination group is intranasal oxytocin (Syntocinon®), which is a nasal spray.

Interventions

Once the study doctors agree that you are able to participate in this study, you will be assigned to the facilitated play group or the combination treatment group (the social cognitive skills therapy group with intranasal oxytocin), as stated above. You and your parent/caregiver will attend weekly groups with up to 12 other children and their parents. Social skills groups will consist of 12 weekly sessions, each lasting 90 minutes. Each group will be run by one primary leader with additional staff helping. For both types of groups, there will be a parent group that meets at the same time as the child group. During this meeting, child progress and difficulties will be discussed. Homework may be assigned for both you and your parent. For children assigned to the combination treatment group, the medication should be taken three times before homework assignments, and one time before the social skills group therapy sessions. At least one parent/caregiver must be able and willing to participate in the weekly parent group. The social skills group will be video recorded. The recording will be labeled with a code number, stored electronically on the encrypted Rush network in a password protected folder and destroyed when the study is completed.

1. **Social Cognitive Skills Therapy Group (combination treatment with intranasal oxytocin)**

   Those in the combination treatment condition will be provided with a one week supply of oxytocin at each visit. You will take 24 units (3 sprays into each nostril) of the medication spray in your nose 4 times per week. During each week, you will take the medication one time before the weekly social skills group, and 3 times before your homework assignments. You will receive training on how to administer the medication from the study team, and a diary to record all doses of the medication. You will take the first dose at the first study visit so that the study team can demonstrate how to properly administer the study medication.

   Each child group session will follow a consistent written schedule, which includes 1) Circle time/greeting period, 2) Skill review, 3) Introduction of target skill, 4) Free Play, and 5) Snack and Prizes. Structured teaching includes defining skills, breaking them down into simple, concrete steps, modeling the skill through role-play, and introducing a game or activity to practice the target skill. Tokens will be used to help reinforce participation, maintain newly learned skills, and increase motivation. Tokens can be exchanged for prizes at the end of each session.

2. **Facilitated Play Group**

Each child group session will follow a written schedule similar to the combination treatment group which includes: 1) Circle/Greeting time, 2) Game-Activity-Talk Time, 3) Free Play, and 4) Snack and Prizes. Group leaders will follow subjects' interests and suggestions for games. They will facilitate play, verbally praise appropriate behavior, and provide an enjoyable atmosphere and opportunities for social interaction. In addition, a small prize (such as stickers, small toy) will be given to children at the end of each session.

Please note, in the event that meeting in person is not recommended, groups will take place virtually via a HIPAA compliant platform (i.e. Zoom). Additionally, medication will be mailed to participant. Medication compliance logs and homework will be available online via Google Classroom to accommodate for virtual transition.

Weekly Visits (1-11)
You and your parent/caregiver will be asked to come to Rush for two hours each week. Time will be spent in a homework group, meeting with the study doctor, and participating in the social skills group (with or without the intranasal oxytocin depending on which group you have been randomized to) and parent education group. You will meet with the treating physician at week 1, week 3, week 5, week 7, week 9, and week 11 (or biweekly schedule depending on group start day/date) to talk about any new symptoms or issues, if you have taken any new medications, and if you have shown any changes in behavior. Additionally vital signs and temperature will be taken at this time. You will see study clinicians at each visit and you may be asked social questions, such as about your friendships and how you are doing. Some of these assessments will be video recorded. The recording will be labeled with a code number, stored electronically on the encrypted Rush computer network in a password protected folder and destroyed when the study is completed.

Check-ins with the treating physician and study clinicians can be completed virtually via a HIPAA compliant platform (i.e. Zoom) if needed.

Week 6
At week 6 your parents will also be asked to complete questionnaires about your current functioning and behavior and meet with the treating physician blinded to the study condition.

Week 12 (Endpoint)
The end of treatment visit occurs at Week 12 (to take place within ± 7 days from the target date). At these visits, blood work, urine collection, vital signs, height, weight, temperature, and an ECG will be completed. In addition, participants will undergo a series of assessments, which are anticipated to take approximately 4-6 hours to complete. The visit can be split into as many as three visits if this is better for the participant. You will be given tasks that involve problem solving, thinking and memory games, looking at images and making judgments about them, and listening to sounds and words and answering questions about them. Some of the tasks will be presented on a computer screen. Additionally some of these assessments will be video recorded. The recording will be labeled with a code number, stored electronically on the encrypted Rush computer network in a password protected folder and destroyed when the study is completed.

An electrocardiogram (ECG) will be administered. Sticky patches are placed on your chest. These patches are connected to a machine which shows the electrical activity of your heart.

Your will be go to the outpatient laboratory at Rush University Medical Center and have the following tests:

- Urine collected for safety laboratory tests
- Blood collected (about 1 teaspoon) as part of the general medical evaluation to look for any signs in the blood that may mean that you should not participate in this study.
- A pregnancy test will be completed (if applicable).

Your parents will also be asked to complete interviews and questionnaires about your current functioning and daily living skills and behavior. Some of the tasks will be presented on a computer screen.

Note: Electrocardiogram (ECG) and Safety labs will be optional at Week 12 **only** for participants in social play condition, i.e. non-medication arm.

Week 16 & Week 24 (Maintenance visits 1 & 2)
There will be an additional follow-up appointment 4 weeks and 12 weeks (± 7 days) after the participant stops taking the study drug. This visit is primarily to examine safety of OXT (oxytocin) discontinuation, and look for possible maintenance of any favorable effects of oxytocin and longer term safety. The assessments completed during this visit are identical to the Week 12/end of treatment visit except no safety labs or electrocardiogram will be required.

Missed Visits and Visit Windows
Subjects that miss a weekly group meeting will be asked to come in +/-2 days from the scheduled day to complete safety assessments. In the event the subject is unable to come in, we will ask the family to follow up with the study physician via phone to complete safety assessments.

Unplanned Visits
Unplanned visits will be permitted if there are any concerns or new symptoms.

Other Medications/Therapy
You will not be eligible to participate if you plan to start or change medications, educational settings, and/or other therapies during the course of this study. No changes in dosing or prescribed medications are allowed for 1 month prior to screening for most medications. If you are prescribed drugs involved in serotonergic transmission, such as fluoxetine (Prozac), fluvoxamine (Luvox), and citalopram (Celexa), you must have stable dosing and medications for 6 months prior to screening. Examples of drugs in this category include. Non-pharmacologic educational, behavioral, or dietary interventions must be stable for 3 months prior to screening.

Will you be contacted about participating in future research?
If you agree, we may contact you after your participation in this study about participating in future research. Please initial and date one of the following options:

_____ _____ Yes, I agree to be contacted about future research.
Initials Date

_____ _____ No, I do NOT agree to be contacted about future research.
Initials Date

What are the risks and discomforts of participating in this study?

The potential risks involved with participation in social skills groups are minimal but may include increased stress and anxiety associated with engaging in social interaction and/or potential conflict and aggression related to peer interactions. These potential risks are minimized with high therapist to child ratios, use of visual supports to provide reminders for behavioral expectations, and visual schedules to structure and frame both groups.

In both the social skills treatment group and the facilitated play group, potential risks may include increased stress related to additional schedule and homework demands placed on your family related to group activities.

If you are enrolled in the combination treatment group, you may experience side effects associated with the four times/weekly dose of intranasal Syntocinon®. All study medications may cause some side effects or other reactions. The common side effects of Syntocinon® (occurring in more than 10% of adults) include nasal irritation, itchy and/or runny nose or watering of the eyes. Other side effects reported in studies in ASD include restlessness, increased energy, increased irritability and mild decrease in appetite.

Rare and potentially more severe side effects of Syntocinon® (occurring in less than 1% of adults) include unusual bleeding, seizures, cramps in females, nausea (feeling like you are going to throw up) and headache, as well as feeling anxious, tired, or sad. Recent studies have also shown that nausea, increased allergies, and possibly shortness of breath may occur at a greater frequency. Sleep disturbance has been reported in cases in which dosing occurred in the late afternoon. No serious side effects have been reported in previous Syntocinon® studies.

Although ***you will not be given an injection***, rare side effects have been associated with oxytocin when delivered through the vein. The rare side-effects are skin rashes, shortness of breath, swelling, some heart problems including the heart beating too fast or too slow (arrhythmia), or increase or decrease blood pressure. More commonly, injections may make people feel bloated. As far as we know, these side effects are temporary and reversible. ***Once again, you will not be getting any injections.***

Allergic reactions can happen with any medication. Common allergy symptoms may include a skin rash, itching, or hives. A severe and possibly life-threatening allergic reaction can happen, although this is rare. Symptoms of a severe allergic reaction include trouble breathing or unexplained swelling. **If you have a severe allergic reaction, you need to go to your nearest emergency room.**

Drawing blood by placing a needle in a vein may cause pain, lightheadedness, fainting, bleeding, bruising, or swelling at the puncture site. Infection is a rare possibility. Numbing cream may be used on the skin to decrease the discomfort if needed. Skin irritation or an allergic reaction is possible following the use of the numbing cream.

It is possible that you could feel upset when answering questions about your diagnosis or medical treatment. You don't have to answer any of the questions that you find upsetting or that you do not want to answer. The study staff will be available to discuss this with you further.

There may be other risks of being in this study that are not known at this time. A study staff member will discuss with you any new information that is found during the course of the study that might affect your health, or that may pose any additional risks to either you or your parents as soon as possible.

What about pregnancy?
It is not known if Syntocinon® affects an unborn baby or sperm, but it may induce a miscarriage. You should not become pregnant or father a child while in this study. If you are female and able to get pregnant, a pregnancy test will be done at the screening visit. If the test is positive, you will not be able to enter the study. The results of the pregnancy test are confidential and will be given to you by one of the study nurses or doctors in private. Study physicians may inform your parent/caregiver if s/he decides sharing the results is in your best interest.

You must call the study staff right away if you think you may be pregnant. Your participation in the study will be changed if you become pregnant. This includes the possibility that Syntocinon® will not be given anymore. This will be discussed between you and the study doctor.

What if there is new information that may affect your decision to participate in this study?
During this study, you will be told about important findings (either good or bad), such as changes in the risks or benefits of participation in the study or new choices to participation that might cause you to change your mind about being in the study. If new information is shared with you, you may be asked to sign a revised consent form in order to continue participating in this study.

Will you receive your individual results from the study?
Generally, activities performed for research purposes are not meant to provide clinical information. We may learn things about you from this study which could be important to your health or treatment. If this happens, this information will be shared with you. Families will be provided a summary of testing results from standardized clinical assessments including: autism diagnostic testing, cognitive testing, and adaptive behavior measures as well as a behavioral evaluation of their progress in group in a testing summary at the end of their study participation. Reports will be distributed by encrypted email by the study coordinator. You may need to meet with experts to follow up on recommendations from the study evaluations. The study will not cover the costs of additional clinical follow-up actions outside of the study.

Can you leave or be removed from this study?
You have the right to leave a study at any time without penalty. For your safety, however, you should consider the study doctor's advice about how to leave this study. If you leave this study before the final study visit, the study doctor may ask you to complete the final steps. Every effort will be made to obtain information on subjects who withdraw. Subjects who discontinue oxytocin prematurely will be asked to return to the clinic and complete all end of study safety lab work (week 12 blood work). Subjects will also be asked to complete all endpoint study procedures on their final visit before withdrawal to allow for true intent to treat analysis.

The researchers and Sponsor also have the right to stop your participation in this study without your consent if:

- They believe it is in your best interests;
- You do not follow the instructions;
- The study is cancelled for any reason.

What about confidentiality of your medical information?

This authorization is voluntary. Rush University Medical Center and its affiliates ("Rush") will not withhold or refuse your treatment, payment, enrollment, or eligibility for benefits if you do not sign this authorization. You do not have to sign this authorization, but that means that you cannot be in the study or receive study-related treatment.

By signing this document, you voluntarily authorize (give permission to) Dr. Soorya and her study team, and other Rush personnel involved with the conduct and review of this study (which may include off-site personnel) to use or disclose (release) health information that identifies you for the study described in this document.

During the study, Dr. Soorya and her study team will collect Protected Health Information (PHI) about you for the purposes of this research. PHI is your health information that includes your medical history and new information obtained as a result of this study. Some of this information will come from your medical record. The health information that Rush may use or disclose for this research includes:

- Taking a medical history (includes current and past medications or therapies, illnesses, conditions or symptoms, family medical history, allergies, etc.)
- Doing a physical examination that generally includes blood pressure reading, heart rate, and temperature
- Completing the tests, procedures, questionnaires and interviews explained in the description section of this consent
- Reviewing mental health records

Dr. Soorya and her study team may share your health information and the results of your study-related procedures and tests with people outside of Rush who assist with the conduct and review of this study. The persons who receive your health information may not be required by Federal privacy laws to protect it and may share your information with others without your permission, but only if permitted by the laws governing them. Your health information described above may be used or disclosed to:

- To the Researchers
    - Dale Smith, PhD at Olivet Nazarene University, a study statistician
    - Don Hedeker, PhD at University of Chicago, a study statistician
    - Edwin Cook, MD at University of Illinois at Chicago, a clinical co-investigator
    - Andras Lorincz, PhD at Eotvos Lorand University in Budapest Hungary, who is studying digital markers of social behaviors collected during computerized neurocognitive and ADOS2 evaluations
    - Molly Losh, PhD at Northwestern University who is studying gaze and language patterns observed during computerized neurocognitive testing.
- The study Sponsor, The Brinson Foundation, The Brain and Behavior Foundation, and National Institute of Child Health and Human Development (NICHD), and its representatives National Database for Autism Research (NDAR).

  - Data from the study will be submitted to the National Database for Autism Research (NDAR). NDAR is a computer system run by the National Institutes of Health that allows researchers studying autism to collect and share information with each other. With an easier way to share, researchers hope to learn new and important things about autism more quickly than before. During and after the study, the researchers will send information about your health and behavior, to NDAR. Before they send it to NDAR, however they will remove information such as name, address, and phone number, and replace that information with a code number. Other researchers nationwide can then file an application with the National Institutes of Health who protect health and science information will look at every request carefully to minimize risks to your privacy.
- Simons Foundation Autism Research Initiative (SFARI)
  - Data from this study will be submitted to the Simons Foundation Autism Research Initiative (SFARI). SFARI funds innovative research that aims to improve the understanding, diagnosis, and treatment of autism spectrum disorders. During and after the study, the researchers will send information about your health and behavior to SFARI. Before they send it to SFARI, however, they will remove information such as name, address, and phone number, and replace that information with a code number. Other researchers can then file an application with the SFARI to obtain access to your study data for research purposes. Experts at the SFARI who protect health and science information will look at every request carefully to minimize risks to your privacy

    If you participate in SPARK, which is hosted by SFARI, please note that because you are participating in both studies, SPARK and this study will be able to share and link your identifying information to the current and future data you may contribute to either project.
- Monitoring agencies such as the Food and Drug Administration (FDA), the National Institutes of Health and the Rush Institutional Review Board (IRB).
- Data Safety Monitoring Committee (DSMC): internal Rush committee overseeing study progress and patient safety matters in the trial.

While you participate in the study you will have access to your medical record, but Dr. Soorya is not required to release to you study information that is not part of your medical record. Rush is required by law to protect your health information, and study records that identify you will be kept confidential. The results of study tests/procedures performed as part of this study may become part of your medical record. Any study information in your medical record will be kept indefinitely. Your identity will not be revealed on any report, publication, or at scientific meetings. All audio/video tapes recorded during the study will be labeled with a code number, stored electronically on the encrypted Rush network in a password protected folder and destroyed when the study is completed.

You have a right to inspect and copy the information to be disclosed with this authorization and you may obtain a copy of the information by contacting the office listed below.

If you no longer want to be in the study and do not want your future health information to be used, you may change your mind and revoke (take back) this authorization at any time by writing to Dr. Soorya at 1645 W. Jackson Blvd. Suite 603 Chicago, IL 60612. If the authorization is revoked, you will no longer be allowed to participate in the study and previously authorized

individuals/entities may still use or disclose health information that they have already obtained about you as necessary to maintain the integrity or reliability of the current study.

This authorization is valid for the entirety of this research study. It will expire upon completion of the study or if you revoke (take back) the authorization.

If you withdraw from this study, the data already collected from you may not be removed from the study records. The study doctor and/or study team may ask you whether they can continue to collect follow-up data on you. If follow-up information will be requested, you will be asked to sign a separate consent form before this information can be collected.

Records of participation in this study will be maintained and kept confidential as required by law. In all disclosures outside of Rush University, you will not be identified by name, social security number, address, telephone number, or any other direct personal identifier unless disclosure of the direct identifies is required by law. Some records and information disclosed may be identified with a unique code number. The Principal Investigator will ensure that the key to the code will be kept in a locked file, or will be securely stored electronically. The code will not be used to link the information back to you without your permission, unless the Institutional Review Board allows it after determining that there would be minimal risk to privacy. Even if those records are identifiable when inspected, the information leaving the institution will be stripped of direct identifiers. Therefore, our collaborators will only have access to de-identified data. By signing this document you are authorizing this access.

The Rush Institutional Review Board (IRB) will have access to your files as they pertain to this research study. The IRB is a special committee that reviews new and ongoing human research studies to check that the rules and regulations are followed regarding the protection of the rights and welfare of human participants.

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. This research study can be found by searching for the following Clinical Trial Registry Number (NCT#): 02918864.

If you disclose actual or suspected abuse, neglect, or exploitation of a child, or disabled or elderly adult, the researcher or any member of the study staff must, and will, report this to Child Protective Services (such as the Department of Family and Human Services), Adult Protective Services, and/or the nearest law enforcement agency.

What are the costs to participate in this study?

.All costs for the required study visits, examinations, laboratory procedures and study medication (Syntocinon®) will be paid for and at no cost to you.

You or your insurance will be responsible for paying for the cost of any routine medical care that you would receive whether you participate in this study or not, unless you are told that such item or services will be supplied at no cost. If you have health insurance, the insurance may or may not pay for the costs associated with your participation in this study. You will have to pay for any co-payments, deductibles or co-insurance amounts that your insurance coverage requires. Before you decided to be in this study, you should contact your insurance provider to verify

coverage.

Will you be paid for your participation in this study?

You will be paid $25 or $15 for each completed study visit. If you do not finish this study, you will be paid for the study visits you have completed. You will be paid in cash at the end of each completed appointment. If you complete the study you will receive a total $140.

- Screening - $25
- Baseline - $25
- Week 6 (Midpoint) - $15
- Week 12 (Endpoint) - $25
- Week 16 (1 month follow up) - $25
- Week 24 (3 month follow up) - $25

We may need to collect your social security number or Taxpayer Identification Number (TIN) in order to pay you and for tax reporting purposes to the United States Internal Revenue Service (IRS).

Your participation in this study may contribute to the development of commercial products from which the Sponsor company or others may derive financial benefit. There are no plans to pay you for any of these developments.

What happens if you experience a research related injury?

If you get ill or injured from being in the study, Rush University Medical Center will help you get medical treatment. You should let the study doctor know right away that you are ill or injured. If you believe you have become ill or injured from this study, you should contact Dr. Soorya at telephone number (312) 942-3767 or if after hours, page (312) 942-6000 pager #9078 to reach Dr. Adrienne Adams, MD.

You should let any health care provider who treats you know that you are in this study. If you do seek medical treatment, please take a copy of this document with you because it may help the doctors where you seek treatment to treat you. It will also provide the doctors where you seek treatment with information they may need if they want to contact your study doctor.

You or your health insurance plan will be billed. No money has been set aside to pay the costs of this treatment. Health insurance plans may or may not cover costs of research-related injury or illness. You should check with your insurance company before deciding to participate in this research study. Costs not covered by insurance could be substantial.

Rush University Medical Center has no program for financial compensation or other forms of compensation for injuries which you may incur as a result of participation in this study.

By signing this form, you are not giving up any legal rights to seek compensation of injury.

What other information should you know about?

Investigator Financial Disclosure

Argus Cognitive, Inc. has developed software to analyze video-based and eye-tracking outcome measures. Dr. Soorya and Dr. Pollack (investigators on this study) own a stake (financial value) in Argus Cognitive, Inc. They also make decisions for Argus Cognitive, Inc. Their relationship with Argus Cognitive, Inc. is external to their Rush activities. The stake/ financial value of this

investment might be affected by the results of this study. This means Drs. Soorya and Pollack could gain or lose money depending on the results of outcomes analyzed using Argus software. It was determined by a conflict committee that the relationship was considered unlikely to affect your safety and/or the scientific quality of the study. This decision was given to the IRB for its review and approval of the study. If you would like more information, please contact Drs. Soorya and Pollack.

Who can you contact for more information about this study?
Questions are encouraged. If you have further questions about this study, you may call Dr. Soorya at (312) 942-3767.

Who can you contact if you have concerns about your rights as a study participant?
Questions about the rights of research participants may be addressed to the Rush University Medical Center Office of Research Affairs at 1-800-876-0772.

What are your rights as a study participant?
Taking part in this study is voluntary. If you choose not to participate in this study or to leave the study at any time, your health care, benefits or relationship at Rush University Medical Center will not change or be affected.

If you choose to leave this study and you do not want any of your information to be used, you must inform Dr. Soorya in writing at the address on the first page. Dr. Soorya may still use your information that was collected prior to your written notice.

SIGNATURE BY THE PARTICIPANT OR THE PARTICIPANT'S LEGAL REPRESENTATIVE:

By signing below, you are consenting to participate in this research study. You have read the information given or someone has read it to you. You have had the opportunity to ask questions, which have been answered satisfactorily to you by the study staff. You do not waive any of your legal rights by signing this consent/authorization form. You will be given a signed copy of this document.

_____

Name of Participant

_____

Parent, Guardian or Legal Representative's Signature Date of Signature

SIGNATURE BY THE INVESTIGATOR/INDIVIDUAL OBTAINING CONSENT:

I attest that all the elements of informed consent described in this consent document have been discussed fully in non-technical terms with the participant or the participant's legally authorized representative. I further attest that all questions asked by the participant or the participant's legal representative were answered to the best of my knowledge.

_____ _____

Signature of Individual Obtaining Consent Date of Signature

SIGNATURE BY WITNESS/INTERPRETER:

I observed the signing of this consent document and attest that, to the best of my knowledge, the person signing the consent form is the participant or the participant's legally authorized representative and the person signing the form has done so voluntarily.

_____

Name of Witness/Interpreter

_____ _____

Signature of Witness/Interpreter Date of Signature

SIGNATURE OF THE PRINCIPAL INVESTIGATOR:

I attest that I am aware of the enrollment of this subject in the study discussed in this consent document.

_____ _____

Signature of the Principal Investigator Date of Signature