R01 FX ENTRAIN: Perturbation of Neurodynamics Underlying Sensory Hyperarousal and Statistical Learning in Youth with FXS

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KEY INFORMATION

We are asking you to be in a research study so that we can learn new information that may help others. If you decide not to be in this study, we will still take good care of you. If you decide to be in this study, you may change your mind at any time during the study and you can stop being in the study. Take all the time you need to make your choice. Ask us any questions you have. It is also okay to ask more questions after you decide to be in the study. You can ask questions at any time.

Parents/Guardians: You have the option of having your child or teen join this research study. This is a parental permission form. It explains this research study. If you decide that your child can be in this study, you will sign this form to show that you agree. If you sign this form, you will receive a signed copy for your records.

COMBINED Parental Permission/Assent: If you are a parent or legal guardian of a child who may take part in this study, permission from you is required. The assent (agreement) of your child may also be required. When we say "you" in this form, we mean you or your child; "we" means the study doctor and other staff.

The word **"you" or "I"** in this form refers to your child/teen.

REASON FOR THE STUDY

The main reason for this research study is to learn more about brain and behavioral problems associated with Fragile X Syndrome (FXS) and related disorders. Specifically, this study has two aims: 1) understand how individual differences in the brains of individuals with FXS affect cognition (ability to learn) and behavior, and 2) determine if alpha auditory entrainment (AAE) can improve cognition and reduce sensory hyperarousal in this disorder.

You are being asked to take part in this study because you are an individual with FXS, an individual with ASD, or an individual who does not have either disorder who we recruit for comparison purposes.

PROCEDURES

If you qualify and decide you want to be in the study, you will come to Cincinnati Children's Hospital Medical Center (CCHMC) 4 separate times lasting approximately 3-4 hours each if necessary, for a total of approximately 16 hours of involvement. This study can be completed over the course of up to two years. Visits 1 and 2 can be completed up to three months apart. Visits 3 and 4 must be completed at least 1 week, and up to three months, apart.

If you agree to be in the study, the following things may happen:

Initial visit: Before any study procedures take place, you will be asked to carefully read this informed consent form. A member of the research team will explain the study to you and answer any questions you may have. If you would like to participate, you will be asked to sign this form.

- *Medical Evaluation:* You will be asked to complete questionnaires regarding your family medical history and your medical and developmental history, including medications you have taken or are taking. We may perform a standard non-invasive medical evaluation, which includes your height, weight, head measurements, and vision and hearing tests.
- *Cognitive testing:* Intelligence, cognitive, developmental, and/or language tests may be complete by the study staff. If this has been clinically completed, the test may not need to be repeated. The cognitive testing may occur after your initial visit to the clinic.
- An interview about your adaptive functioning skills may be completed with a member of the research team. If you prefer, the interview can be completed over the phone or video.
- An interview to assess for mental disorders will be completed by a trained clinician.
- *Neuropsychological Testing:* You may engage in a computer program that assesses ability to learn, attentional performance, motor skills, and cognition tasks.
- *Autism Diagnostic Observation Schedule (ADOS):* This is a developmental evaluation that may be performed by a member of the study staff. The ADOS involves interaction and observation according to specific procedures. If this assessment has been clinically completed, it may not need to be repeated. This assessment takes approximately 45-60 minutes. The ADOS may occur after your initial visit to the clinic.
- *Questionnaires and Checklists:* As part of the study, you may be asked to complete several questionnaires about your child, including a demographics form. The rating scales and behavior checklists will collect information about you/your child's development and you/your family's quality of life. Some of these assessments may be completed over the phone, dropped off, mailed to the clinic, or remotely via web link.
- *Eye Tracking Assessment:* We may use an eye-tracking system that uses a monitor with cameras or a camera-based system that track your eye movements and pupil responses. During the procedure, you are asked to look at a computer monitor to view a series of pictures of faces and objects while the computer measures eye movements and pupil size. You may receive a small token at the completion of the eye-tracking assessment.
- *EEG:* We may have you wear an electroencephalography (EEG) headset to monitor how your brain responds to certain stimuli. The sensors pick up the electrical activity of your brain, "listening" to your brain communication. The study team may use a program to take a picture of the electrode placement on the participant's head. The study team may record video or take photos during the EEG. This helps the study team analyze the EEG data.

- *Auditory Stimuli/AAE:* During the EEG and neuropsychological testing sessions, you may be asked to wear headphones and listen to some sounds so we can see how your brain responds to them.

If you have previously had any genetic testing, behavioral or neuropsychological testing, routine blood tests, imaging, electroencephalograms (EEG), vital signs and/or medication management at CCHMC, data from these records may also be used from your medical record as part of the study.

If you participate in another study conducted by the Neurobehavioral research group, the use of questionnaires and assessments may be used for this study. The study staff will let you know which assessments can be used for more than one study.

Data collection and sample access:

A secure database at CCHMC will include the results of the tests, questionnaires, and assessments that have been completed with your child. Access to all identifiable information will be restricted to the study staff members. Results from validated tests performed on study may be provided to you if requested at the discretion of the study physician.

BENEFITS TO PARTICIPATE

Being in this study may not help you right now. When we finish the study, we hope that we will know more about developmental disorders (DDs). This may help others with DDs later on.

RISKS TO PARTICIPATE

We will take all necessary precautions to minimize the risks stated below:

- The completion of the assessments, (e.g., IQ or ADOS) may cause mild nervousness or tiredness. During assessments we will provide breaks, behavioral support, and encouragement. If you get very upset during an assessment, we will stop the testing.
- There may be a risk for loss of confidentiality during study-related procedures. To protect your privacy in this research study we will ensure that all subject data be de-identified using a non-identifying subject code, locked storage, and password protected databases.
- There may be risks associated with the study that are not currently known. If we discover any new risks during your participation in the study, we will inform you.

If you experience any problems related to the study, you should contact Dr. Pedapati (the study doctor) immediately.

OTHER OPTIONS

Participation in research is completely voluntary. Your decision to participate or not to participate will not affect the care you receive.

Your alternative to participating in this research study is to not participate.

COST TO PARTICIPATE

There are no direct costs for taking part in this study.

PAYMENT

You (your child) will be compensated for your time and effort while you are in this research study. You will be paid $50 per completed study visit, for a total of up to $200. If you are not able to complete any study visits or your participation in the study is terminated prior to completing any study visits, you will be compensated at a rate of $15/hour for the time you have given. Families traveling significant distance to our clinic may be reimbursed for travel costs at the discretion of the PI.

We will give you your payment in the form of a reloadable debit card (ClinCard) and you will receive a handout that will explain how to use the card. We will provide you with a card and we will load money onto your card after each visit you complete. Because you (your child) are being paid for your participation, Cincinnati Children's is required by the Internal Revenue Service (IRS) to collect and use your (your child's) social security number (SSN) or taxpayer identification number (TIN) to track the amount of money that we pay. You will need to complete a Federal W-9 form for this income tax reporting. This form requires your child's Social Security number. This form will be given to the Cincinnati Children's business office. It will not be kept as part of your child's study chart. If you move, you will need to complete another W-9 with an updated address.

Additional Study Information:

The following is more detailed information about this study in addition to the Key Information.

If I have Questions or would like to know about:

Who to talk to…	**You can call …**	**At …**
• Emergencies • General study questions • Research-related injuries • Any research concerns or complaints	**PI Name** Ernest Pedapati, MD	Phone: 513-636-6553
• Emergencies • General study questions • Research-related injuries • Any research concerns or complaints	**Lead Study Coordinator** Elizabeth Blank	Phone: 513-803-8635
• Your child's rights as a research participant	**Institutional Review Board** This is a group of scientists and community members who make sure research meets legal and ethical standards.	Phone: (513) 636-8039

CHANGE OF MIND/STUDY WITHDRAWAL:

You can choose to leave the research at any time; it will not be held against you. A withdrawal of your permission to use and share your PHI would also include a withdrawal from participation in the research study. If you wish to withdraw your permission to use and share PHI you need to notify the study doctor, listed on the first page of this document, in writing. Your request will be effective immediately and no new PHI about you will be used or shared. The only exceptions are (1) any use or sharing of PHI that has already occurred or was in process prior to you withdrawing your permission and (2) any use or sharing that is needed to maintain the integrity of the research. If you stop being in the research, data already collected may not be removed from the study database.

The person in charge of the research study or the sponsor can remove you from the research study without your approval. Possible reasons for removal could include failure to continue to meet inclusion criteria or inability to tolerate the procedures.

PRIVACY:

Efforts will be made to limit the use and disclosure of your personal information, including research study and medical records, to people who have a need to review this information. We cannot promise complete privacy. Organizations that may inspect and copy your information include the IRB, other representatives of this organization, and the National Institutes of Health (NIH).

Your personal information may be disclosed if required by law, such as if abuse or neglect is uncovered during research procedures.

Because this research study involves payment for participation, we are required by federal Internal Revenue Service (IRS) rules to collect and use your social security or tax ID number (SSN) in order to track the amount of money that we pay you. We will only use your SSN to keep track of how much money we pay you and your SSN will not be used as part of this research.

The sponsor, monitors, auditors, the IRB, the Food and Drug Administration will be granted direct access to your medical records to conduct and oversee the research. By signing this document, you are authorizing this access. We may publish the results of this research. However, we will keep your name and other identifying information confidential.

Other researchers on our team may access your data from this study for research purposes. You may not benefit directly from allowing your information to be shared with other studies. The information provided to other studies may help researchers treat future children with developmental disabilities so that they have better outcomes.

Some of your data may be submitted to the National Database for Autism Research (NDAR). NDAR is a computer system run by the NIH that allows researchers to collect and share research information with each other. With an easier way to share, researchers hope to learn new and important things more quickly than before. Before information is sent to NDAR, we will remove information such as name and birthplace city and replace that information with a

code number. Other researchers nationwide can then file an application with the NIH to obtain access to your study data for research purposes. Experts at the NIH 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 NDAR. The information provided to NDAR might help researchers around the world treat future children and adults with different developmental disorders so that they have better outcomes. NDAR will report to Congress and on the NDAR website about the different studies that researchers are conducting using NDAR data; however, NDAR will not be able to identify you individually or contact you about specific studies. You may decide now or later that you do not want to share your information using NDAR. If so, contact the study doctor and he/she will tell NDAR to stop sharing the research information. However, NDAR cannot take back information that was shared before you changed your mind. If you would like more information about NDAR, this is available on-line at http://ndar.nih.gov.

All future researchers will be given the least amount of information needed to meet the goals of their research project. Researchers that use these samples and information must agree to never try to re-identify a participant from a coded dataset. Researchers will only be allowed to use the provided samples and information for approved research purposes. Any researchers planning to do research with information that may identify you will need to have extra review and approval by the Cincinnati Children's Institutional Review Board (IRB).

RETURN OF RESULTS:

Most tests done on samples or images obtained in research studies are only for research and have no clear meaning for healthcare. If the research with your information gives results that do have meaning for your health, the researchers will contact you and ask you if you would like to know what they have found. You can say No to hearing about the results at that time if you desire.

AUTHORIZATION FOR USE/DISCLOSURE OF HEALTH INFORMATION FOR RESEARCH

To be in this research study you must also give your permission (or authorization) to use and disclose (or share) your "protected health information" (called PHI for short).

What protected health information will be used and shared during this study?

CCHMC will need to use and share your PHI as part of this study. This PHI will come from:

- Your CCHMC medical records
- Your research records

The types of information that will be used and shared from these records include:

- Laboratory test results, diagnosis, and medications
- Reports and notes from clinical and research observations
- Imaging (like CT scans, MRI scans, x-rays, etc.) studies and reports
- If applicable, information concerning drug or alcohol abuse, drug-related conditions, alcoholism, and/or psychiatric/psychological conditions (but not psychotherapy notes).

Who will share, receive and/or use your protected health information in this study?

- Staff at the research study site
- Personnel who provide services to you as part of this study
- Other individuals and organizations that need to use your PHI in connection with the research, including people at the sponsor and organizations that the sponsor may use to oversee or conduct the study.
- The members of the Cincinnati Children's Institutional Review Board and staff of the Office of Research Compliance and Regulatory Affairs.

How will you know that your PHI is not misused?

People that receive your PHI as part of the research are generally limited in how they can use your PHI. In addition, most people who receive your PHI are also required by federal privacy laws to protect your PHI. However, some people that may receive your PHI may not be required to protect it and may share the information with others without your permission, if permitted by the laws that apply to them.

Will this permission expire?

Since this study involves the creation of a repository for storing data, your permission will never expire.

Will your child's other medical care be impacted?

By signing this document, you / your child agree to participate in this research study and give permission to Cincinnati Children's to use and share you/your child's PHI for the purpose of this research study. If you refuse to sign this document you/your child will not be able to participate in the study. However, you/your child's rights concerning treatment not related to this study, payment for services, enrollment in a health plan or eligibility of benefits will not be affected.

While you/your child are participating in this research study you may not be able to access some of your/your child's health information that is related to the study. Any request for this information can be fulfilled once the study is completed.

RESEARCH REPORT AND MEDICAL RECORD OPTION

All subjects may receive a report containing testing information after the participant's study activities are complete upon request. You have the option of having this report uploaded into the participant's medical record at CCHMC. This upload is optional and declining will not affect your participation in the study.

RESEARCH REPORT

_____ Yes, I want the study team to provide me with a research report

_____ No, I do not want the study team to provide me with a research report

_____ N/A, I will not be completing testing through this research study

REPORT IN MEDICAL RECORD (DEVELOPMENTAL DISABILITIES ONLY)

_____ Yes, I want the study team to upload the research report into my medical record

_____ No, I do not want the study team to upload the research report into the my medical record

_____ N/A, I will not be completing testing through this research study or I don't not qualify to have the research report uploaded to my medical record

SIGNATURES

The research team has discussed this study with you and answered all of your questions. Like any research, the researchers cannot predict exactly what will happen. Once you have had enough time to consider whether you/your child should participate in this research, you will document your permission by signature below.

You will receive a copy of this signed document for your records.

_____
Printed Name of Research Participant

_____ _____
Signature of Research Participant Indicating Assent Date

_____ _____
Signature of Parent or Legally Authorized Representative* Date

_____
* If signed by a legally authorized representative, a description of such representative's authority must be provided

_____ _____
Signature of Individual Obtaining Consent Date