Introduction

The purpose of this form is to provide you with information about taking part in a research study. Please read this form carefully. Your child is invited to take part in a research study investigating the effects of a novel intonation-based therapy, Auditory-Motor-Mapping-Training (AMMT), compared to a non-intonation-based speech therapy, Speech Repetition Therapy (SRT) in helping children with autism develop speech. If you have any questions about the research or any portion of this form, please ask us. If you decide to take part in this research study with your child we will ask you to sign this form. We will give you a copy of the signed form.

The person in charge of this study is Dr. Helen Tager-Flusberg. Dr. Helen Tager-Flusberg can be reached at 617-358-5919 or via email at htagerf@bu.edu. We will refer to this person as the “researcher” throughout this form.

Why is this study being done?

The purpose of this research is to learn why some children with Autism Spectrum Disorder (ASD) do not acquire spoken language. It is hard to evaluate these children with standardized language measures. In this study we investigate the effects of an intonation-based speech therapy, AMMT, versus a non-intonation-based speech therapy, SRT, in helping children with ASD who have limited verbal abilities to produce speech sounds. We will also examine any changes in brain activity due to the therapy. This research may contribute to improvements in future clinical evaluations and interventions for these children.

We are asking for your child to take part in this study because s/he is between the ages of 5 and 10 years, and is diagnosed with ASD.

About 150 children will take part in this research study at Boston University (BU), Beth Israel Deaconess Medical Center (BIDMC) and Massachusetts General Hospital (MGH).

This research is funded by the National Institutes of Health.
How long will I take part in this research study?

We expect that your child will be enrolled in this research study for approximately one year. The study activities will take place at BU, MGH and BIDMC. The study activities are divided into 5 phases referred to as: 1. Pre-therapy behavioral and electrophysiology (EEG) assessments at BU. 2. Pre-therapy MRI scans at MGH. 3. Therapy sessions (either AMMT or SRT) at BIDMC, over a five-week period. 4. Post-therapy behavioral and EEG assessments at BU and 5. Post-therapy MRI scans at MGH. Details of participation in each phase are summarized below:

1. Participation in the study starts at BU, where we will ask you to make between 3 - 8 study visits lasting up to 3 hours per visit including breaks, depending on child compliance. The initial assessments consist of standardized tests, clinical diagnostic evaluations and an EEG session. We will refer to these initial visits at BU as pre-therapy clinical-core assessments. The pre-therapy clinical-core visits will be scheduled over a 2-5 week period or longer, depending on the participant’s family scheduling preferences.

2. The next phase of the study involves 1- 2 visits to MGH, where your child will take part in a mock fMRI scan session for practice, followed by an MRI scan referred to as baseline (pre-therapy) MRI scan. Behavioral training to acclimate the participant to the scanning environment will be provided as needed for each child prior to the mock scanning session, which is required for all participants. Either during the same visit or on a separate visit scheduled within the following 1-2 weeks the participant will have an MRI scan to assess the existing connections between the brain regions involved in language comprehension and speech.

3. The therapy sessions will take place at BIDMC over a period of 5 or 8 weeks and will consist of 25 sessions of either AMMT or SRT. Each therapy session will last about 45 minutes.

4. The therapy sessions will be followed by 2 post- therapy assessments at 4 weeks and at 8 weeks from the end of the intervention. The behavioral and EEG post-therapy assessments will take place at BU.

5. After the completion of all therapy sessions the participant will return to MGH for a set of post-therapy MRI scans similar to the baseline (pre-therapy) MRI scans, to investigate possible changes in brain connections resulting from therapy. The MRI scan sessions will take about 1 hour.

Overall children are expected to participate in the study for about 16 -18 weeks, including all assessments and therapy sessions, for up to 38 visits over the course of one year.

What will happen if I take part in this research study?

If you agree to take part in this study, we will ask you to sign the consent form before we do any study procedures.

Prior to the study you will have been asked to complete a telephone interview. To prepare your child for participating in the research, you will receive a picture booklet (a Family visit guide) showing photographs of the buildings in which the labs are located, the lab rooms, people whom the child will meet, and a schedule of activities for each visit. You will be asked to look through the book with your child before your first lab visit to help your child prepare for the visit.

All research activities will begin with training. Each testing session will last around 1-3 hours depending on

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how your child responds to the activities involved. Assessments will be conducted across several testing
days, scheduled at your convenience. We may need up to 5 sessions to give your child a chance to get used
to the environment and our testing. Breaks and reinforcers will be included as needed.

All children will be administered the pre-therapy assessments consisting of standardized evaluations,
electrophysiological assessments of electrical brain activity (EEG) and brain imaging (MRI), before starting
the therapy sessions. Then, some children will receive an AMMT therapy and others will receive a SRT
therapy. Children will be randomly assigned to each of the therapies. You cannot choose which therapy your
child will receive. After completing the therapy sessions, children will be given the same types of
assessments as in the pre-therapy phase.

The design of the study is fairly complex and combines several components broken down as follows:

1. Clinical Assessments:

The first study visits will take place at Boston University and will involve standardized assessments and
EEG. The standardized assessments are conducted to get a measure of cognitive ability (IQ) and language.
During these lab visits your child will be given several behavioral tests by trained staff, which will involve
looking at books or a computer monitor and playing some games with the researchers. The behavioral tests
should take a total of 3-5 hours and may need to be split over multiple visits. The EEG assessment is done
to measure brain electrical activity when listening to sounds. We plan to conduct a comprehensive clinical
assessment following procedures and guidelines developed by the National Institute of Health (NIH)
Working Group on Assessing Minimally Verbal School-aged Children with ASD. During this time we will
also evaluate your child’s capacity for participation in the rest of the study.

Assessment time will alternate with breaks, snacks, visits with parents etc. On entry into this program you
will be assigned to a specific member of staff who will be primarily responsible for conducting all
assessments and your child will be tested in a room in close proximity to you; often you will have the option
to observe the testing through a one way mirror. An observer will watch your child via a video camera
throughout the session and you may stay with your child during the testing session if you wish to do so. If
your child becomes anxious or frustrated, we will stop the session. If, at any point, you wish to stop the
testing for any reason, please feel free to ask us to stop.

Children who are not testable on standardized tests may require additional visits, during which they
will be tested via eye-tracking (a non-invasive method of recording your child’s eye movements as they
watch different scenes on a computer screen, while listening to speech). This is a method to test your
child’s comprehension of words and sentences that does not require a behavioral response from the
child. The eye-tracking based assessments take about 20 minutes to complete, depending on the child’s
attention to the computer screen.

As the parent/guardian, you will be asked to complete a set of questionnaires and an interview with one
of the team clinicians. You can complete the questionnaires during the visits to our lab with your child
or take them home to complete and bring back to us at the child’s next study visit.
You will also be asked to provide a copy of your child’s medical record to be inspected by one of the study PIs who is a MD, in order to determine whether or not your child may have contraindications to having an MRI scan or has a history of neurological abnormalities that may impact the study results.

We will also ask you to record your child’s vocalizations at home over a period of 24 hours using a LENA device provided by us, prior to starting the therapy, as well as later, post-therapy, at a time specified by us. The LENA system involves a small battery-powered recorder weighing only 2.5 oz that can be put into a chest pocket of the children’s clothing to record the child’s vocalization throughout the day in completely naturalistic environments. The LENA data provide an important measure of spoken language use in varied contexts and allow for comparisons between vocal output prior to the start of therapy and post-therapy across similar contexts (e.g., home) and timeframes.

2. Electrophysiology Assessment (EEG)

Children will also be tested by measuring their brain’s electrical activity (electroencephalogram or EEG) as they are presented with visual and audio stimuli. To record your child’s brain electrical activity we use recording electrodes. The electrodes are inside of small sponges, which are held together in a cap made of stretchable material. The sponges are placed in salt water with a small amount of baby shampoo to get them wet, and the cap is then placed on your child’s head. There is a wire attached to each sensor. The wires connect to a computer and the computer records the brain's electrical activity on the screen, as children are presented with auditory stimuli played through speakers and videos. We will also look at their ability to understand speech and non-speech sounds by recording the brain’s electrical activity while listening to sounds. These measures will be collected at BU and should take about 45–50 minutes, including cap placement and breaks.

If needed, you will be given a “practice cap” to take home so that the child gets used to wearing it before the testing study visits. At the first study visit at BU we will demonstrate to you how to place the practice cap on your child’s head. You may practice placing the practice cap on a foam head at our BU lab prior to taking the net home. If the child refuses to wear the cap, you may start by having the child touch the cap, then touch the child’s top of the head with the cap for a few moments, then gradually increase the time you keep the cap on the top of child’s head, before expanding it appropriately over the child’s head and tightening the straps under the chin. If helpful, you may gradually try to place the practice cap on your child’s head at home several times, and let the child wear the practice cap for up to 30 minutes at a time, to get used to the feeling of wearing the cap. In past research we have found that these preparations make a large difference in the child's comfort level and increase the likelihood of cooperation.

The electrophysiology testing can be completed in one study visit, but may be split over 2 visits if the child is not comfortable wearing the cap for the entire assessment session.

We expect that about 3-8 visits to BU will be required to complete the Clinical behavioral assessments, scheduled over a 2 – 5 week period.
3. Brain Imaging Assessment (MRI)

A Magnetic Resonance Imaging (MRI) machine is a scanner that contains a large magnet, which allows us to look at your child’s brain. During the MRI, we will ask your child to lie still on a table that slides into a tunnel-shaped machine. To help your child get accustomed to lying in an MRI machine, he/she will practice in a “mock scanner”, that looks and feels just like the real MRI scanner.

The MRI machine makes loud noises as it take pictures and your child will be given earplugs to reduce the noise. Your child will be able to hear and speak to the research staff at all times during the MRI procedures. The researcher will be able to hear your child at all times and you will be free to stop the procedure at any time. The machine is very safe, but if your child becomes anxious or decides that they don’t like lying in the machine, we will take them out immediately. The experience in the mock scanner will imitate that of a real MRI machine. It looks like and sounds like the real MRI machine. This will help your child to become used to lying down inside of the tube-like magnet and to hearing the noises made by the magnet when brain scanning takes place. The mock scanner training is also used to help your child learn to stay as still as possible while lying in the scanner. When your child is ready to go into the scanner, they will be asked to put in earplugs while they watch a DVD. Overall the MRI part of the study will take about 55-60 minutes including the preparation time and breaks, and will take place at MGH. A study staff familiar with your child will remain in the scanner suite for the duration of the scanning for reassurance and to monitor your child’s well-being.

For the MRI part of the study additional screening will take place at MGH. You will be given a separate consent form to read and to sign at MGH. This will give you further details on MRI’s and the risks/benefits involved, before your child partakes in this part of the study.

The brain imaging assessments can be completed in one visit, but may be split over 2-3 visits if the child needs repeated practice in the mock scanner or shorter scanning sessions.

4. Auditory Motor Mapping Training Therapy or Speech Repetition Therapy

Auditory Motor Mapping Training is based on the observation that children with autism often respond positively to music. The AMMT therapy consists of observing the child’s response to music while the therapist softly taps two drums. We are testing the efficacy of this intervention compared to a SRT intervention, which consists of observing the child’s response to speech presented without the singing intonation and tapping of drums. We are doing the AMMT and SRT interventions in this study to answer research questions, not to give medical care. All therapy sessions will take place at BIDMC.

Children will receive a total of 25 therapy sessions of 45 minutes each spread over a 5 to 8-week period. Prior to the therapy sessions children will be randomly assigned to the AMMT or the SRT conditions. The sessions will be administered one-on-one as interactive games in a quiet room with a speech therapist at BIDMC. If a child is assigned to the SRT condition they will be offered to participate in a full trial of the AMMT therapy after the SRT phase is completely done.
You will be required to sign a separate consent form, provided by Beth Israel Deaconess Medical Center, which will give further details on AMMT and SRT therapies and the risks/benefits involved, before your child partakes in this part of the study.

5. Post Therapy Assessments

After the completion of the intervention sessions your child will undergo behavioral follow up, including LENA recordings, brain imaging and electrophysiology assessments, as described above for the pre-intervention assessments. The same procedures will be followed in the post-interventions assessments, which will take place at 4 and 8 weeks after the intervention is completed, and may take 2 to 5 study visits.

Videotaping

We would like to videotape your child during this study. If your child is videotaped it may be possible to identify them in the video. We will store these tapes in a locked cabinet and only approved study staff will be able to see the tapes. We will label these tapes with a code instead of your child’s name. The key to the code connects your child’s name to their videotape. The researchers will keep the key to the code in a password-protected computer/locked file and they will be stored for five years following the end of the study.

Do you agree to let us videotape you during this study?

___YES  ________NO  __________INITIALS

Storing Study Information for Future Use

We would like to store your child’s study information for future research related to minimally verbal children with ASD. We will label all of the study information with a code instead of your child’s name. The key to the code connects your child’s name to their study information. The researchers will keep the code in a password-protected computer/locked file.

Do you agree to let us store your child’s study information for future research related to minimally verbal children with ASD?

___YES  ________NO  __________INITIALS

Sending Study Information to Research Collaborators Outside Boston University

Due to the size of the funding received for this study we are collaborating with institutions outside of Boston University. We will send your child’s study information to research collaborators at outside sites. We will label all study information with a code instead of your child’s name. The key to the code that connects your

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child’s name to the study information will only be accessible to the primary investigators at Boston University and their primary research collaborators at Beth Israel Deaconess Medical Center and Massachusetts General Hospital. Nobody outside of these three study sites will know which study information is yours. Data without identifiers (de-identified) from this research study will also be sent to the National Database for Autism Research (NDAR), as required by our funding and research agreements.

**How Will You Keep My Study Records Confidential?**

We will keep the records of this study confidential, as all study documents will be identified by a unique study ID. The unique study ID will be linked to the subject via a mastercode. Access to the mastercode will be limited to the PIs and primary research staff from the three study sites and the key to the mastercode will be stored separately from the study data in a secure password protected database. We will make every effort to keep your records confidential. However, there are times when federal or state law requires the disclosure of your records.

We will store your child’s study records for 7 years following the end of the study.

As part of this study, you will be asked to provide information from your child’s medical record. This information may be shared with the primary investigators from the three study sites.

The following people or groups may review your study records for purposes such as quality control or safety:

- The Researcher and any member of his/her research team
- The Institutional Review Board at Boston University. The Institutional Review Board is a group of people who review human research studies for safety and protection of people who take part in the studies.
- The sponsor or funding agency for this study, the National Institutes of Health
- Federal and state agencies that oversee or review research
- If some law or court requires us to share the information, we would have to follow that law final ruling.

The results of this research study may be published or used for teaching. We will not put identifiable information on data that are used for these purposes.

**Study Participation and Early Withdrawal**

It is your choice as to whether your child takes part in this study. You are free to decide you do not want your child to take part and you are free to withdraw at any time for any reason. No matter what you decide, there will be no penalty or loss of benefit to which you are entitled.

If you decide to withdraw from this study, the information that you have already provided will be kept confidential.
The researcher may take you out of this study without your permission. This may happen because:
- Your child does not meet all the inclusion criteria to move onto the next phase of the study
- The researcher thinks it is in your child’s best interest
- You can’t make the required study visits
- Other administrative reasons

**Future Contact**

We may like to contact you in the future either to follow-up to this study or to see if you are interested in other studies taking place at Boston University.

Do you agree to let us contact you in the future?

______YES ______NO __________INITIALS

**What are the risks of taking part in this research study?**

There are minimal physical or psychological risks to the children associated with participation in this study.

**Risks of Completing Tasks**

Your child may get tired during the tasks and they can rest at any time. We will provide your child with regular breaks during the testing to avoid tiredness. If your child becomes tired or finds the research activities frustrating or discomforting, the activities will be stopped immediately.

All testers have been trained to minimize any anxiety or distress to you and your child by giving encouragement and maintaining a supportive and non-stressful environment. Every effort will be made to make our participants comfortable and relaxed in the testing and intervention sessions.

**MRI Risks**

There are no known harmful effects from the strong magnetic field used for MRI. But the magnet is very powerful. The magnet may affect pacemakers, artificial limbs, and other medical devices that contain iron. The magnet will stop a watch that is close to the magnet. Any loose metal object has the risk of causing damage or injury if it gets pulled toward the strong magnet.

An MRI should not take place if the child has claustrophobia (fear of small spaces). The top and sides of the machine will be very close to the body. Because of this, the child may feel anxious while inside the MRI machine. If you feel the child is in distress during the procedure you can request to stop the MRI at any
time. If the participant feels anxious during the procedure, they can request to stop the MRI at any time.

We are doing the MRI in this study to answer research questions, not to give medical care. This MRI is not the same as one that your own doctor would order. It may or may not show problems that would be found on a regular MRI. If we do see something that looks like a medical problem, we will ask a radiologist (a doctor who specializes in looking at MRI scans results) to review the results. If the radiologist thinks there might be a problem, we will tell you and help you get follow-up care.

If the radiologist thinks that there may be a medical problem, but it turns out that there is not, we may have caused you to worry unnecessarily.

Electrophysiology Assessment Risks

There are no known or foreseeable physical risks associated with collecting electrophysiology measures. All features of the EEG system to be used in the proposed study have been approved by the FDA and will be operated using parameters accepted by the FDA. The only potential risk for children would be the risk of psychological discomfort if a participant were uncomfortable with the electrode cap. However, all potential children will undergo extensive training to ensure they can tolerate the cap. Children who fail to acclimate to the electrode cap will not be included in the study. Thus, these procedures will exclude children with any foreseeable risk. If during the experiments a child becomes agitated, a sign of distress, the research team will immediately stop the experiment and remove the electrode cap.

Loss of Confidentiality

The main risk of allowing us to use and store your information for research is a potential loss of privacy. We will protect your privacy by labeling your information with a code and keeping the key to the code in a password-protected database. Information from your child’s medical record may become available to the primary researchers at the three study sites; However all these investigators are obligated to protect your privacy and they will not share this information with anyone else.

Due to the need for videotaping the activities, there is a minimal risk of identification. However, no records (video, audio or in databases or print form) will ever identify your child by name and the only identifier will be a number. All appropriate methods will be taken to ensure there is no loss of confidentiality.

Are there any benefits from being in this research study?

There is no guarantee that every child enrolled in the study will benefit from the therapy part of the study. However, after the completion of the study, the AMMT therapy will be available to all participants, if requested. Therefore if the AMMT therapy is beneficial in helping children with ASD develop speech, there is the potential for improvement in their lives as a result of acquiring some spoken language skills.

In the long term, the information gathered by this study will help us to understand why some children with...
ASD fail to acquire spoken language and will provide evidence for the efficacy and impact of a novel therapy. Ultimately, we expect this information to contribute to changes in clinical practice and advances in treatment for children with ASD, especially those who are minimally verbal.

The risks of the research are minimal; overall the potential short- and long-term benefits of the research outweigh the risks involved.

What alternatives are available?

You may choose not to take part in this research study.

Taking part in this research is your choice. If you decide to take part in this study, you may leave/stop the study at any time. There will be no penalty to you. If you would like to stop taking part in this research you should let us know.

Will I get paid for taking part in this research study?

We will pay for your parking while you are taking part in this study. At the end of each visit your child will receive $15 in the form of gift certificates. In addition, participants’ parents will receive $50 for the completion of the pre- and post-intervention assessment at BU. For participating in the MRI portion of the study you will receive $25 for the mock-scan and $50 for a real scan at MGH. You will also receive $25 per assessment visit at BIDMC, but you will not be compensated for therapy sessions. If your child is unable to complete the whole study they will receive partial compensation averaging $15 for each visit they complete.

What will it cost me to take part in this research study?

There are no costs to you for taking part in this research study.

What happens if I am injured as a result of participating in this research study?

If you are injured as a result of taking part in this research study, we will assist you in getting medical treatment. However, your insurance company will be responsible for the cost. Boston University does not provide any other form of compensation for injury.

If I have any questions or concerns about this research study, whom can I talk to?

You can call us with any concerns or questions. You may contact the Project Principal Investigator, Dr. Helen Tager-Flusberg, at 617-358-5919 or htagerf@bu.edu.

If you have questions about your rights as a research subject or want to speak with someone independent of the research team, you may contact the Boston University IRB directly at 617-358-6115.

Statement of Consent
I have read the information in this consent form including risks and possible benefits. I have been given the chance to ask questions. My questions have been answered to my satisfaction, and I agree to participate in the study. I have been given a copy of this form.

SIGNATURE

Name of Subject
________________________________________________________________________

Name of Parent/Guardian
________________________________________________________________________

Signature of Parent
________________________________________________________________________
Date

I have explained the research to the subject and answered all his/her questions. I will give a copy of the signed consent form to the subject.

Name of Person Obtaining Consent
________________________________________________________________________

Signature of Person Obtaining Consent
________________________________________________________________________
Date

Please do not sign this form. We will go over it with you at your first visit.

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