COMPOUND AUTHORIZATION AND CONSENT FOR PARTICIPATION IN A RESEARCH PROJECT
200 FR. 4 (2016-2)

YALE UNIVERSITY SCHOOL OF MEDICINE – YALE CHILD STUDY CENTER & YALE DEPARTMENT OF PSYCHOLOGY

Study Title: Brain response associated with parent-based treatment for childhood anxiety disorders
Principal Investigator: Eli Lebowitz, Ph.D.
Funding Source: Anxiety & Mood Disorders Program, Yale Child Study Center; National Institute of Mental Health (NIMH)

Invitation to Participate and Description of Project

We are inviting you and your child to participate in a research study designed to investigate and compare two treatments for childhood anxiety: Supportive Parenting for Anxious Childhood Emotions (SPACE) and Cognitive Behavioral Therapy (CBT). We are also examining the effect of each treatment on child brain functioning. You and your child have been asked to participate because you contacted the Anxiety and Mood Disorders Program indicating your child is experiencing anxiety and/or fear. This study will enroll a total of 226 children and their mothers.

In order to decide whether or not you wish to be a part of this research study you should know enough about its risks and benefits to make an informed decision. This consent form gives you detailed information about the study, which a member of the research team will discuss with you. This discussion should go over all aspects of this research: its purpose, the procedures that will be performed, any risks of the procedures, possible benefits and possible alternative treatments. Once you understand the study, you will be asked if you wish for you and your child to participate; if so, you will be asked to sign this form.

Description of Procedures

Before your child can participate in this study, you and your child will be asked to complete an initial evaluation to determine if your child is eligible for this study. This initial evaluation will involve separate interviews with you and your child, completion of questionnaires and behavioral tasks, cognitive testing, a videotaped interaction, and blood and saliva samples. This initial evaluation appointment will last approximately 4 hours. Eligible participants will then undergo neuroimaging using fMRI and be assigned to treatment as described below.

Interviews and Questionnaires:

You and your child will be asked to answer a number of questions. Many of these will focus on symptoms of anxiety and others will deal with other aspects of behavior, feelings or thoughts. Some of the questions will be asked in ‘interview form’ with a clinician writing down your answers while others will be written scales and questionnaires that are administered on paper forms or electronically. All the measures in this study are well established measures that are commonly in used in research and treatment settings.

Videotaped Interaction
You and your child will be asked to participate in two conversations and we would like to videotape both of you while you do this. We will tell you what we would like you to talk about and make a recording of you having that conversation. Each conversation will not last longer than 7 minutes.

Blood Sample
You and your child will be asked to provide us with a small blood sample for our research at the initial appointment, and again at the 6-month follow up appointment. The total amount drawn will be less than one ounce each time. An experienced and qualified professional will draw the blood from a vein near the elbow. This is a very standard procedure, like many blood samples you may have already given in the past.

We are also asking for your permission to store blood samples for future research projects we may initiate. If you agree the blood will be stored in a safe place without personal identification and retained for future research purposes.

Saliva Sample
To collect a sample of saliva we will ask you and your child to chew on a small cotton swab for about one minute. You will then spit it out into a special sterile container. That is all that is required for the saliva sample.

Behavioral Task
You and your child will be asked to play brief computer games lasting a few minutes each. During one game you or your child will stand in front of a TV screen and play the game by walking to the right or to the left to catch things that fall on the screen. You will see images appearing on the screen. The images will include everyday things such as faces or pictures of animals or insects. During the other game, you and your child will be provided a laptop and mouse. You will see pictures of faces on the screen as well as arrows indicating which mouse button to click. You will be able to stop playing at any time if you wish.

MRI Simulation
Your child will have a chance to practice what the MRI (magnetic resonance imaging) scan is by using a mock MRI scanner. Your child will hear the sounds that the real scanner makes, see similar images, and experience what it feels like to lie in the scanner. This practice session can help your child to feel comfortable during the real MRI scan. We will explain the scanning procedures to you and your child, and you and your child can ask any questions that you might have.

After it has been determined your child is eligible to participate in this study the following things will occur:

1. MRI visit:
   Your child will participate in an MRI scan and play computer games during the MRI scan. This visit will take place at Yale's Brain Imaging Center. A member of the research team will accompany your child to Yale's Brain Imaging Center and stay for the duration of the scanning session. The computer tasks will consist of the presentations of visual and auditory stimuli. Your child will be instructed to press different buttons depending on what he/she sees on the screen or what he/she hears through the headphones, or just to listen and or look at the stimuli as they are presented without making any response. During the scan your

child's physiological responding will be measured, such as heart rate, breathing, and galvanic skin response (a measure of sweating).

We will show your child the MRI scanner prior to the scan and explain the procedure in detail. During the scan we will ask your child to lie as still as possible so that the pictures of his/her brain can be taken clearly. The researchers will place padding around your child's head to help him/her feel comfortable. A headset and screen will allow your child to watch movies and play the computer games while lying down and keeping his/her head still. During scanning a thumping sound can be heard. This is the switching of the magnetic field in use. We provide ear plugs and headphones for your child to soften the noise level. The scanner has a microphone and speakers, so that your child and the researchers can communicate at all times. Your child will have several breaks of 1-2 minutes between the collection of each set of pictures while we set up the scanner for the next set of pictures. During part of the MRI scan, we will invite you to join your child in the scanner room to participate in one of the games.

Your child will be in the scanner for approximately 60-90 minutes. If your child finds the scanning environment to be uncomfortable or feels nervous, he/she can take longer breaks or choose to stop the scan. Your child will be able to communicate with the researchers at all times and may be removed from the scanner at any time upon his/her request. Your child will be compensated for your participation regardless, without any worry of bias because of his/her level of participation.

If your child is taking a stimulant medication for Attention Deficit Hyperactivity Disorder, we will arrange the MRI scans, with your permission and consultation from the prescriber, on a day your child is not taking this medication.

2. Your child will initially be randomly assigned to either the CBT or SPACE treatment. CBT will focus on helping your child change his/her anxious and fearful thoughts and to learn gradually how to approach or deal with anxiety producing objects or events. In CBT children will be introduced to and discuss the presenting problem, review treatment rationale and goals, work with the therapist to devise an anxiety hierarchy, and participate in in-session and out-of-session exposure tasks. Additionally, children will be introduced to the cognitive component of treatment by identifying faulty cognitions and generating incompatible self-statements, and exploring alternatives. SPACE is an entirely parent-based treatment where you will be provided helpful information on the role of parents as it relates to childhood anxiety. Through role-play, rehearsal with feedback, practice, and simulation you will learn to respond to your child's anxiety in supportive manners and to identify and reduce the ways you may be accommodating your child's anxiety symptoms. Both CBT and SPACE consist of 12 weekly sessions of approximately 60 minutes each. Parents of children in the CBT group will meet briefly with your child's therapist to inform you of your child's progress and to answer questions three times throughout the course of treatment. Treatment sessions for both CBT and SPACE can occur either in person at the Yale Child Study Center or over secure video-link using software called Zoom. You and your child may choose to have sessions at either the Yale Child Study Center or over Zoom and or may choose to have some in person and some over Zoom.

3. After 6 weeks of sessions, there will be a mid-point re-assessment including many of the

same procedures done at the first assessment.

4. After all 12 weeks of sessions are complete, you and your child will be asked to complete a post-treatment evaluation including the same procedures done at the first assessment. This post-treatment evaluation appointment will last approximately 4 hours. After the treatment is complete your child will also participate in another MRI visit, which will be the same as the first one.

5. Time of participation in study: 12 weeks.

6. After treatment has ended we will contact you by phone to conduct follow-up assessments with you and your child. This will occur 3, 6, and 12 months after the end of treatment. At each of these three times we will ask you to respond to brief questionnaires and each conversation should not take longer than 30 minutes.

7. After 6 months from your initial appointment, a member of the research team will contact you by phone to invite you to participate in a follow-up visit. At this visit we will ask you and your child to complete questionnaires, play a video game, and provide a blood sample. Families will be compensated during this 6-month follow up visit.

Participating in Future Research Studies

We would like to contact you in the future to see if you would be interested in participating in another research study. Please indicate below if you are willing to be contacted about any future research studies.

_____Yes, I agree to be contacted about future research studies.
_____No, I do not want to be contacted about future research studies.

Risks and Inconveniences

Although the treatments (CBT and SPACE) have been found to be effective for reducing childhood anxiety and fears, the success of treatment cannot be guaranteed for any particular individual. If any new findings that may affect your child's willingness to continue to be in this study are developed during the time that he/she is in this study, you will be informed as soon as possible.

Risks associated with the treatments are:
CBT:

- Your child may experience some discomfort or anxiety when discussing anxiety-related topics or when practicing coping strategies during treatment sessions or as out-of-session assignments between treatment sessions.
- Some children could get worse, but the deterioration may or may not be related to CBT.

SPACE:

- -Your child may become uncomfortable when you are less accommodating of anxiety symptoms. In some cases, a child may become angry or upset.
- -Some children could get worse over treatment. The deterioration may or may not be related to SPACE.

There is little risk involved in the computer tasks other than boredom or some frustration if your

child finds the tasks difficult. You and your child will be asked to answer a variety of personal questions during the study. You and your child are not required to answer questions during interviews or on questionnaires that you find distressing. If a problem is uncovered, you will be offered a referral for further evaluation and treatment for your child if you so desire.

The PI does not believe that scheduling MRI scans on days the child is not taking stimulant medication for Attention Deficit Hyperacuity Disorder will increase risks.
As part of the screening for the MRI, we will ask your child (females only) if she may be pregnant. No pregnancy test will be administered. If she reports that she may be pregnant, she will not be able to participate in this study. We will notify you and the authorities of the pregnancy. If your child is of any age, and in immediate danger of hurting him/herself or someone else, then we will notify you and refer your child for an evaluation. If you or your child is uncomfortable with discussing possible pregnancy, then we would recommend that your child does not participate in this study.

Risks and Inconveniences associated with MRI

Magnetic resonance imaging (MRI) uses magnetic fields and radio waves to take pictures of the body. MRI is very safe, with no known long-term ill-effects. Hundreds of millions of people have safely had MRI scans.
MRI uses a strong magnet, which can pull strongly on some metals. These metals must not be brought into the scan room. They could be pulled towards the magnet and cause serious injuries if they hit you. People entering the scan room must remove all metal from their body, clothing and pockets. This includes jewelry, hearing aids, watches, cell phones, keys, coins, and wallets.

We will ask you to fill out an MRI safety form for yourself and for your child to check if you or your child has anything in the body which might be dangerous in the MRI. **It is very important that you fill out these forms accurately and ask if you are unsure about anything**. Some metal objects could also heat up during the MRI, burning you. Electrical devices such as pacemakers could go wrong or stop working.

You must also tell us if you or your child is wearing anything that could contain metal. For example, some medication patches have a metal backing. Some clothing can contain metal fibers that could also heat up during the MRI. We will provide you clothes to change into if needed.

During the MRI scan, your child may feel uncomfortable or worried. When the MRI scanner is making pictures, it makes loud tapping, buzzing, and beeping noises. Without protection, this could damage your child's hearing. We will give your child earplugs and/or headphones to reduce the sound to a safe level. While the scanner is making noises, we will not be able to hear your child. We will give your child a squeeze bulb for them to contact us.

The MRI scan is intended for research and not to find disease. The researchers are not qualified to medically interpret your child's scan. If we do see something that may be a concern, we will let you know. You can then decide if you want to discuss this with your doctor. The investigators and Yale University are not responsible for any treatment that your child receives based on these findings. The pictures collected in this study are not a healthcare MRI exam and will not be made available for healthcare purposes.

Benefits

1. Treatment may help your child overcome or reduce problems with anxiety
2. The treatment may result in positive side effects in other areas of your child's life that may not be directly related to the main problem of anxiety.
3. This research has the potential for developing treatments tailored to meet the specific needs of children and adolescents with anxiety and/or fears.

Economic Considerations

Participants will be compensated $50 for the first MRI visit (which is expected to take approximately 2-2.5 hours) or a tablet of equal value. Participants will be compensated $100 for the second MRI visit (which is expected to take approximately 2-2.5 hours) or tablets of equal value. Participants can choose whether to receive the cash or the tablet(s) of equal value. Participants are compensated regardless whether they finish the MRI scan so that participants who feel uncomfortable with the scan can discontinue without concern about compensation. Participants who complete all components of the appointment will receive an additional $50 at each visit.

Participants that participate in the 6-month follow up appointment will receive an additional $100 or tablet(s) of equal value. The payment will be given to the parent participant who will provide it to the child participant at their discretion. There are no other payments to participants.

According to the rules of the Internal Revenue Service (IRS), payments that are made to you as a result of your participation in a study may be considered taxable income.

You will not have to pay for the study. Costs for any further examination or treatment, if referred, are the responsibility of you and your insurance company and not Yale University, its researchers, or any affiliates of this study.

Treatment Alternatives/Alternatives

Evidence based treatments may be provided as standard of care to youth not participating in this study at the Yale Child Study Center.

Confidentiality and Privacy

Any identifiable information that is obtained in connection with this study will remain confidential and will be disclosed only with your permission or as permitted by U.S. or State law. Examples of information that we are legally required to disclose include abuse of a child or elderly person, or certain reportable diseases. When the results of the research are published or discussed in conferences, no information will be included that would reveal your child's identity unless your specific permission for this activity is obtained.

We understand that information about you and your child obtained in connection with your child's health is personal, and we are committed to protecting the privacy of that information. If you decide you want to enroll your child in this study, the researcher will get information that identifies your and your child's personal health information. This may include information that might directly identify you and your child, such as name, age, home address etc. as well as the clinical data we will be collecting. This information will be de-identified at the earliest reasonable time after we receive it, meaning we will replace your identifying information with a code that does not directly identify your child. The principal investigator will keep a link that identifies your child to your

child's coded information, and this link will be kept secure and available only to the PI or selected members of the research team. Any information that can identify your child will remain confidential. With respect to the video-recordings, only research

staff members will observe tapes for coding. The tapes will be destroyed seven years after recording. Biological samples (blood and saliva) will likewise be stored in de-identified fashion. Electronic data will be kept on a password protected encrypted computer and paper data will be stored in a secure filing cabinet in a locked office. The research team will only give this coded information to others to carry out this research study. The link to your personal information will be kept for seven years after which time the link will be destroyed and the data will become anonymous. The data will be kept in this anonymous form indefinitely.

The information about your child's health that will be collected in this study includes:

- Information about phone calls that were made as part of this research
- Diagnoses made during the study
- Research study records such as your and your child's answers to questionnaires and interviews
- Records about the medication your child received
- Records about your child's progress in treatment

Information about you and your child's health which might identify you and/or your child may be used by or given to:

- Representatives from Yale University and the Human Investigation Committee (the committee that reviews, approves, and monitors research on human subjects), who are responsible for ensuring research compliance. These individuals are required to keep all information confidential.
- The Principal Investigator – Eli R. Lebowitz, Ph.D.
- Co-Investigators and other investigators associated with this study.
- Study Coordinator and Members of the Research Team.

By signing this form, you authorize the use and/or disclosure of the information described above for this research study. The purpose for the uses and disclosures you are authorizing is to ensure that the information relating to this research is available to all parties who may need it for research purposes.

All health care providers subject to HIPAA (Health Insurance Portability and Accountability Act) are required to protect the privacy of your information. The research staff at the Yale School of Medicine and Child Study Center are required to comply with HIPAA and to ensure the confidentiality of your information.

You have the right to review and copy your health information in your medical record in accordance with institutional medical records policies.

This authorization to use and disclose your health information collected during your participation in this study will never expire.

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

Sharing of Anonymous Data

This study will share research data through data-sharing efforts such as the 1000 Functional Connectomes Project and its International Neuroimaging Data-sharing Initiative (INDI), which provides research laboratories (e.g. medical centers, universities, private research groups) with access to data contributed by neuroimaging sites around the world. Data will be stored in repositories such as the Neuroimaging Informatics Tools and Resources Clearinghouse (NITRC), supported by the NIH. Genetic data will not be included in the data sharing.

Prior to sharing, we will remove all identifiers from the data obtained from you or your child. We are doing this so that the information cannot be linked back to you or your child. Each dataset will be assigned an identification number and the relationship between the anonymized code and original subject identifier will be destroyed. In spite of all of the safety measures that we will use to protect your child's privacy and yours, we cannot guarantee that your child's identity or yours will never become known. However, the procedures described above make this risk very low.

Such anonymous data sharing is beneficial as it reinforces open scientific inquiry, encourages diversity of analysis and opinion and permits the creation of new, large, demographically diverse data sets by combining data from multiple sources. The information released for the research study will be kept in confidential, de-identified and encrypted databases.

Withdrawing from the Study

Participating in this study is voluntary. You are free to choose not to take part in this study. Refusing to participate will involve no penalty or loss of benefits to which you are otherwise entitled (such as your health care outside the study, the payment for your health care, and your health care benefits). However, you will not be able to enroll in this research study and will not receive study procedures as a study participant if you do not allow use of your information as part of this study. You do not give up your legal rights by signing this form.

If you decide to take part in this study, and then change your mind, you can always stop and withdraw from this study at any time during its course. To stop your participation in the study, you can call a member of the research team at any time and tell them that you no longer want

to take part. This will cancel any future appointments (if applicable). Even if you stop participating in the study, the researchers will still be able to use the information that has already been collected about you. That information could also be given to others until the end of the research study, to make sure that the study produces valid results.

Withdrawing from the study will involve no penalty or loss of benefits to which you are otherwise entitled. If you choose not to participate or if you withdraw it will not harm your relationship with your own doctors or with Yale Child Study Center. We would still treat you with standard therapy or, at your request, refer you to a clinic or doctor who can offer this treatment.

Withdrawing your Authorization to Use and Share Your Health Information

If you do not want researchers to use and disclose your health information as described in the Confidentiality section, you need to tell a member of the study staff or send a written notice to Dr. Eli R. Lebowitz a t 230 S. Frontage Rd. New Haven, CT 06520. It is called 'withdrawal of your authorization'. When you do that, no new health information identifying you will be collected after that date. Again, the investigators will be able to use the information that they already collected about you to finish the study.

If you withdraw your authorization, you will not be able to stay in this study.

You do not give up any of your legal rights by signing this form.

Optional Specimens for Future Storage/Genetic Testing

You are invited to allow some of you and your child's samples (called specimens) and related information to be stored (banked) for future research. This may help researchers in the future learn more about how to prevent, diagnose, and treat anxiety.

Your specimens would be stored for an unlimited time and may be used to make a cell line that will live indefinitely. Future research may look at your genes, which are the units of inheritance that are passed down from generation to generation. Genes are responsible for many things about you such as eye color, hair color, blood type and hundreds of other traits. Future genetic analysis may possibly include finding out the details of how your DNA is put together.

When your specimens and information are stored, we are careful to try to protect your identity from discovery by others. Your samples and information will receive a unique code. Other researchers will only receive coded samples and information and will not be able to link the code to you. Strict security safeguards are in place to reduce the chance of misuse or unplanned release of information.

Using your specimens for research will probably not help you or your child. We do hope the research results will help families in the future.

There is a risk that your information could be misused, for example becoming identified. The chance of this happening is very small. We have protections in place to lower this risk such as oversight by Institutional Review Boards, de-identification of samples, secure storage locations etc. There can also be a risk in uncovering genetic information. New health information about inherited traits that might affect you or your blood relatives could be found during a research study. Very rarely, health or genetic information could be misused by employers, health insurance companies, and others. There is a federal law called the Genetic Information Nondiscrimination Act (GINA) that, in general, makes it illegal for health insurance companies, group health plans, and most employers (except those with fewer than 15 employees) to discriminate against you based on your genetic information. However, it does not protect you against discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

You and your child's specimens and information will only be used for research and will not be sold. There is a possibility that this research may lead to development of products that will be commercialized. If this happens, there is no plan to share any financial gain with you.

Research results will not be returned to you or your doctor. If research results are published, your name and other personal information will not be given.

The choice to take part is up to you. You may choose not to let us store and use your samples, and your care will not be affected by this decision. You may take part in the rest of the study even if you do not choose to let us store and use your samples. If you decide that your samples can be kept, you may change your mind at any time. Contact the study staff at 203- 785-7905 to let them know you do not want your samples used any longer. Your samples will either be destroyed or made anonymous (the code linking them to you will be destroyed) as you prefer. You must follow up this request with a written request, mailed to Eli Lebowitz, PhD at 230 S. Frontage Rd., New Haven, CT 06520.

I agree to allow my samples and information to be stored and used for future research as described above: (initial your choice)

_____YES_____NO

Questions

We have used some technical terms in this form. Please feel free to ask about anything you don't understand and to consider this research and the consent form carefully – as long as you feel is necessary – before you make a decision.

Authorization and Permission

I have read (or someone has read to me) this form and have decided to participate in the project described above with my child. Its general purposes, the particulars of my involvement and possible hazards and inconveniences have been explained to my satisfaction. My signature also indicates that I have received a copy of this consent form.

By signing this form, I give permission to the researchers to use [and give out] information about me for the purposes described in this form. By refusing to give permission, I understand that I will not be able to be in this research.

Name of Child: _____

_____ _____

Parent Signature Date

_____ _____

Signature of Person Obtaining Permission Date

If after you have signed this form you have any questions about your privacy rights, please contact the Yale Privacy Officer at 203/432-5919.

If you have further questions about this project or if you have a research-related problem, you may contact the Principal Investigator Eli R. Lebowitz PhD., 203-785-7905. If you would like to talk

with someone other than the researchers to discuss problems, concerns, and questions you may have concerning this research, or to discuss your rights as a research subject, you may contact the Yale Human Investigation Committee at (203) 785-4688.