Cerebellar Neuromodulation to Enhance Fear Extinction And Predict Response to Exposure Therapy

November 2, 2017

APPROVED
AS MODIFIED
Mar 14, 2018
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Laureate Institute for Brain Research, Inc., Tulsa, OK, United States

RESEARCH SUBJECT INFORMATION AND CONSENT FORM	
TITLE:	*Predicting treatment response to Exposure Therapy using a carbon dioxide habituation paradigm (CHP) in patients with high levels of anxiety sensitivity*

This consent form contains important information to help you decide whether to participate in a research study.

The study staff will explain this study to you. Ask questions about anything that is not clear at any time. You may take home an unsigned copy of this consent form to think about and discuss with family or friends.

- **Being in a study is voluntary – <u>your choice</u>.**
- **If you join this study, you can still <u>stop at any time</u>.**
- **<u>No</u> one can <u>promise</u> that a study will help you.**
- **Do not join this study unless all of your <u>questions</u> are <u>answered</u>.**

After reading and discussing the information in this consent form you should know:

- Why this research study is being done;
- What will happen during the study;
- Any possible benefits to you;
- The possible risks to you;
- Other options you could choose instead of being in this study;
- How your personal health information will be treated during the study and after the study is over;
- Whether being in this study could involve any cost to you; and
- What to do if you have problems or questions about this study.

Please read this consent form carefully.

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RESEARCH SUBJECT INFORMATION AND CONSENT FORM

TITLE:	Predicting treatment response to Exposure Therapy using a carbon dioxide habituation paradigm (CHP) in patients with high levels of anxiety sensitivity
PROTOCOL NO.:	2017-006-00 WIRB® Protocol #20171583
SPONSOR:	Laureate Institute for Brain Research (LIBR)
INVESTIGATOR:	Justin Feinstein, PhD 6655 S Yale Ave Tulsa, Oklahoma 74136 United States
STUDY-RELATED PHONE NUMBER(S):	Justin Feinstein, PhD 918-502-5169 918-481-4000 (24 hours)

This consent form describes a research study. Research studies involve only individuals who choose to participate. Please take your time to make your decision about participating in the study.

This consent form may contain words that you do not understand. Please ask the Principal Investigator or the study staff to explain any words or information that you do not clearly understand. You may take home an unsigned copy of this consent form to think about or discuss with family or friends before making your decision.

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.

Why Have You Been Asked To Participate In This Study?
You are being asked to take part in this study because:

- you are in good health
  or
- you have a mental health condition with elevated levels of anxiety

Why Is This Study Being Done?
This study is being done to better understand the factors that could predict the outcome for Exposure Therapy, a common treatment for anxiety. In this study, we will be examining a range of different factors, including your body's response to carbon dioxide (CO_2), and your brain's response during functional Magnetic Resonance Imaging (fMRI).

What Devices Are Involved In This Study?
A Magnetic Resonance Imaging (MRI) scanner is used to look at brain function and anatomy. An MRI scan does not emit any radiation, and it does not require any injections. A physiological recording system built by Hans Rudolph will be used to monitor bodily responses such as changes in heart rate and breathing, while you breathe through an air mask. A spirometer will be used to measure how much air you have in your lungs.

How Many Subjects Will Take Part In The Study?
About 100 subjects will take part in this study at the Laureate Institute for Brain Research.

What Is Involved In The Study?
If you take part in this study, you may have the following tests and procedures at the Laureate Institute for Brain Research:

Interviews & Questionnaires
You will be asked to complete a number of different questionnaires and interviews. These questionnaires will measure your mental and physical state. The interviews will be with a member of the research staff, where you will be asked a series of questions about your mental and physical health, and symptoms you may have experienced during your lifetime.

CO_2 Habituation Paradigm (CHP)
During the CHP, you will be fitted with an air mask that you can take on and off. You will be asked to take several vital capacity breaths at your own pace, where you empty your lungs of all air and take as big of a breath as you can. We will video record you while taking these breaths, which will allow us to measure your behavioral response, and you will also be providing ratings of how you are feeling. The video will only be viewed by the research team and will be destroyed when the study is completed. You will also be asked to provide some saliva samples at the beginning and end of testing.

Magnetic Resonance Imaging (MRI)
Before the MRI, you will be given a brief medical history questionnaire and screening form to complete. Undesirable medical findings may arise during the interview, screening, or MRI scanning. If so, these findings will remain confidential and will be discussed with you by a researcher of this study.

The MRI scanner rapidly takes pictures of your brain. The MRI scanner is a metal tube surrounded by a strong magnetic field. During the MRI, you will lie on a table that can slide in and out of the tube. Earplugs and headphones will be provided to lessen the loud “knocking” sounds that the scanner makes while it is imaging your brain.

Before MRI scanning, you will learn tasks that will involve (a) responding to potential rewards or losses, and (b) paying attention to sensations in your body like your heartbeat or breath. You will be responding to these various tasks using button presses. Training for the MRI tasks will last approximately 10 minutes. You will then be placed in the MRI scanner and asked to try your best to remain still during scanning.

During the scan, you will be fitted with a cuff around your finger tip to monitor how fast your heart is beating (heart rate) and a strap around your chest to monitor the number of breaths you take per minute (breathing rate). First, you will receive a series of short scans that allow us to know where your head is inside the tube. You will then receive a scan lasting about 20 minutes that gives us more detailed pictures of your brain. Finally, you will undergo a series of scans lasting about 40 minutes during which you will perform the tasks you practiced or asked to rest with your eyes open. Your total time in the scanner will be about 1 hour.

If you are a female, a urine pregnancy test will be completed just prior to any MRI scanning. You will not be allowed to participate in the study if the pregnancy test reads positive.

Physical Measurements
We will measure your heart rate, breathing rate, the amount of sweat on your skin (skin conductance), and amount of oxygen and carbon dioxide in your lungs.

You may be asked to provide a breath sample to test for recent alcohol use and a urine drug test. These results are confidential, however, if you are under the influence of alcohol or illicit drugs, you may be excluded from the study or from participating that day.

Treatment Visits
You will be asked to participate in 10 weekly group sessions that will last about 1½ hours each. All therapy sessions will be led by a licensed Clinical Social Worker, licensed Clinical Psychologist, and/or a clinical psychology Doctoral Student. The type of Behavior Therapy being utilized is called Exposure Therapy, which has been shown by previous research to reduce symptoms of anxiety for some people. This therapy will ask you to face situations or things in life you may want to avoid due to anxiety in order to promote emotional health and learning.

Each therapy session will be video and audio recorded and may be reviewed by the research team and/or affiliated consultants that are experts in the treatment being provided. The recording(s) will be stored on secure servers that are password protected. Access to files will be limited to research staff and affiliates, and all recordings will be destroyed at the end of the study.

In addition to the in-person therapy sessions, you will be provided between-session assignments to complete as part of that therapy. You may also be contacted by clinicians or research staff in between sessions for scheduling purposes or to check in regarding therapy assignments.

If you withdraw from the study prior to finishing therapy, you will also be asked to complete a set of assessments via phone or online, estimated to take approximately 10-15 minutes.

How Long Will You Be In The Study?
You will receive Exposure Therapy treatment once a week for 10 weeks. You will also have pre- and post-treatment study visits. The Pre-Treatment Visits 1-3 will occur in the weeks prior to starting Exposure Therapy. Post-Treatment Visits 15-17 will occur 1 week, 6 weeks, and 6 months after completing Exposure Therapy. See the Visit and Payment Schedule Table for an estimate of the amount of time it will take to complete each visit. Your total participation may take up to 14 months.

There may be circumstances under which your participation in the study may be stopped by the investigator without your consent. This could include instances in which you are unable to comply with study procedures, treatment, or your symptoms require more intensive treatment than the study can provide.

You may stop participating in this study at any time.

What Are The Risks Of The Study?
The study may involve the risks described in this section.

It is possible that your participation in this study might reveal unanticipated medical or psychiatric findings. You have the right to refuse answering any question that you do not wish to answer and to withdraw from participating in the study at any time.

It is possible that medical or psychiatric problems may arise or be identified during the screening process, for which we may not be able to provide treatment. It is important that you understand that treatment for medical or psychiatric conditions other than anxiety will not be offered in this study.

If unanticipated findings occur, we will provide you with all results of screening tests and will assist you in communicating these results to your primary physician or other health care provider, so long as you provide written consent for us to do so.

The risks of the study procedures are listed and discussed below.

Risks Associated with the Questionnaires & Interviews
The interviews and questionnaires about your health, mood, and behavior are not physically harmful but may be stressful to complete and may discuss sensitive information. We ask only that you try to answer honestly. You may stop at any time.

Risks of CHP
There are no serious risks that have been associated with taking single vital capacity breaths of 20% CO_2 or 35% CO_2. The CO_2 may cause brief periods where it feels difficult to breath and you might feel anxious. These brief periods typically resolve within 1-2 minutes following a vital capacity breath.

Risks of MRI Scanning
People are at risk for injury from the MRI magnet if they have any of the following metal implants or fragments:

- pacemakers or other implanted electronic devices
- brain stimulators
- dental implants
- aneurysm clips (metal clips on the wall of a large artery)
- metallic prostheses (including metal pins and rods, heart valves, and cochlear implants)
- permanent eyeliner
- implanted delivery pump
- shrapnel fragments

You will be asked to complete an MRI screening form for the MRI scan. You will be screened for these implants or metal fragments before the study, and if you have any of them, you will not receive an MRI scan and cannot be in the study. Tell the study doctor if you are uncertain whether you have any metal objects in your body. In addition, all magnetic objects (for example, watches, coins, jewelry, and credit cards) must be removed before entering the MRI scanner room.

Welders and metal workers are also at risk for injury because they may be unaware of small metal fragments in the eye. There are no known long-term risks or consequences of MRI scans. However, you may become uncomfortable because you will be lying in a small space. Some people are bothered by the loud noises made by the scanner. You will wear earplugs to reduce the noise and increase your comfort during scanning. LIBR study staff will closely and continuously monitor you throughout the scanning procedure. You will be able to use an emergency call button at all times during the scan. You will be removed from the scanner immediately if you request to be removed.

Risks For Females
If you are a female, you must not be pregnant while participating in this study. A urine-based pregnancy test will be obtained prior to any MRI scanning.

Risks For Group Therapy Sessions
There is minimal risk in participating in the group therapy sessions. However, your anxiety could increase over time in the study. You will be monitored weekly for a change in your symptoms by researchers. A clinical psychologist and psychiatrist are part of the research team.

Are There Benefits To Taking Part In The Study?
The type of Behavior Therapy being utilized in this study (Exposure Therapy) has been shown by previous research to reduce anxiety symptoms for some people. Therefore, there is a possibility that you will benefit from this treatment. In addition, your participation should help us understand what behaviors and brain responses may predict how individuals respond to this treatment. Understanding what predicts therapy response could help us improve the outcome and develop new treatments for anxiety which may benefit others in the future.

What Are The Costs Of Participating In The Study?
Neither you nor your health insurance will be charged for any of the study tests, procedures, or activities.

If you need to be hospitalized, voluntarily or involuntarily, Laureate Institute for Brain Research does not intend to provide payment for this, and you or your insurance provider will be billed for these costs.

Will You Be Paid For Participating In This Study?
For the interviews, questionnaires, and the CHP, you will be paid $20 each time you complete them. When you are in the MRI scanner, you will be paid $50 per hour. You may earn an additional $0-30 based on your participation in the reward task during the MRI. If you withdraw from the study prior to completing treatment, you will be asked to complete a set of questionnaires via phone or online, taking approximately 10-15 minutes to complete, for which you will be compensated $10. You will not be paid for Exposure Therapy, but will receive a bonus of $50 if you complete the study that will be paid at the end of the study. In total, you will be compensated up to $310 for participating.

Visit & Payment Schedule	Pre-Treatment Visit 1	Pre-Treatment Visit 2	Pre-Treatment Visit 3	Weekly Treatment Visit 4-14	Post-Treatment Visit 15	6-week Follow Up Visit 16	6-month Follow Up Visit 17
Questionnaires & Interviews	3 hrs: $20	1 hr: $20	--------	--------	3 hrs: $40	1 hr: $20	1 hr: $20
MRI Scan	--------	1 hr: $50	--------	--------	--------	--------	--------
CHP Session	--------	1 hr: $20	1 hr: $20	--------	1 hr: $20	1 hr: $20	--------
Exposure Therapy	--------	--------	--------	1.5hrs/visit	--------	--------	Bonus: $50
Reward task	--------	$0-30	--------	--------	--------	--------	--------

You will be paid through a ClinCard (similar to a debit card) that may be used 48 hours after the visit. The compensation will be provided within 48 hours after completion of each visit.

What Other Options Are There?
This study is for research purposes only, so your other option is not to participate in the study. While the treatments being provided as part of this study have been found to reduce anxiety symptoms, there are other options to obtain treatment. Your options may include receiving the approved medications, as well as the same or different behavioral therapies, than are used in the current study. Information concerning community clinics and treatment resources will be provided to you as requested.

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Confidentiality
What information may be used and given to others?
The study doctor will get your personal and medical information. For example:

- Research records
- Records about phone calls made as part of this research
- Records about your study visits

Only de-identified information may be used or given to others. We assign your case a unique number that ensures no one can identify who you are.

Who may use and give out information about you?
The study investigator, the study staff, and study collaborators.

Who might get this information?
The sponsor of this research. "Sponsor" means any persons or companies that are:

- working for or with the sponsor, or
- owned by the sponsor.

Your information <u>may</u> be given to:

- The U.S. Food and Drug Administration (FDA)
- Department of Health and Human Services (DHHS) agencies
- Western Institutional Review Board® (WIRB®)

Why will this information be used and/or given to others?

- to do the research,
- to study the results, and
- to make sure that the research was done right.

If the results of this study are made public, information that identifies you will not be used.

What if I decide not to give permission to use and give out my health information?
Then you will not be able to be in this research study.

May I review or copy my information?
Yes, but only after the research is over.

May I withdraw or revoke (cancel) my permission?
Yes, but this permission will not stop automatically.

You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the study doctor. If you withdraw your permission, you will not be able to stay in this study.

When you withdraw your permission, no new health information identifying you will be gathered after that date. Information that has already been gathered may still be used and given to others.

Is my health information protected after it has been given to others?
The information you provide as part of this study will be kept confidential within Laureate Institute for Brain Research, within the limits of the law. However, there is always a risk that your information will be given to others without your permission and may no longer be protected.

If you have any questions or concerns about your privacy rights, you should contact the LIBR Privacy Officer at 918-502-5155 or via email at privacy@laureateinstitute.org.

You have the right to access the medical information that has been collected about you as a part of this research study. However, you may not have access to this medical information until the entire research study is finished.

What If You Are Injured While Participating In This Study?
If you get hurt or sick from participating in this study, emergency medical treatment is available. In an emergency, call 911. Be sure to tell the emergency staff and other healthcare providers of your participation in this study. Contact Justin Feinstein, PhD, as soon as possible at 918-502-5169 or 918-481-4000 (24 hours) if you think you have a research-related injury or illness. You or your health insurance provider will be billed to cover the cost of the medical or emergency services provided. No funds have been set aside by the Laureate Institute for Brain Research to compensate you if you are hurt or get sick. However, you still have the right to bring a law suit if you think you were harmed and deserve compensation.

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

Who Will Provide Funding For The Study?
Funding for this research study will be provided by the Laureate Institute for Brain Research and through a grant from the National Institute of General Medical Sciences.

What Are Your Rights As A Participant?
Taking part in this study is voluntary. You may choose not to participate. Refusal to participate will involve no penalty or loss of benefits to which you are otherwise entitled.

If you agree to participate and then decide against it, you can withdraw for any reason and leave the study at any time without penalty or loss of benefits to which you are otherwise entitled.

Your participation in this study may be stopped at any time by the study doctor or the sponsor without your consent for any reason, including the following:

- if it is in your best interest
- if you do not consent to continue in the study after being told of changes in the research that may affect you

What If There Are New Findings?
We will provide you with any significant new findings developed during the research study that may affect your health, welfare, or willingness to continue your participation in this study.

Who Should You Call If You Have Questions Or Problems?
If you have questions, about your participation in this study, concerns, or complaints about the study, or have a research-related injury, contact the study investigator Justin Feinstein PhD, at 918-502-5169 or 918-481-4000 (24 hours). For emergencies, call 911.

If you have questions about your rights as a research subject or if you have questions, concerns, input, or complaints about the research, you may contact:

Western Institutional Review Board® (WIRB®)
1019 39th Avenue SE Suite 120
Puyallup, Washington 98374-2115
Telephone: 1-800-562-4789 or 360-252-2500
E-mail: Help@wirb.com

WIRB is a group of people who perform independent review of research.

WIRB will not be able to answer some study-specific questions, such as questions about appointment times. However, you may contact WIRB if the research staff cannot be reached or if you wish to talk to someone other than the research staff.

Do not sign this consent form unless you have had a chance to ask questions and have received satisfactory answers to all of your questions. If you agree to be in this study, you will be given a signed and dated copy of this consent form.

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Signature
I have read the information in this consent form. I have been given an opportunity to ask questions. All my questions about the study and my participation in it have been answered.

I Agree To Participate In This Study
I authorize the use and disclosure of my health information to the parties listed in the authorization section of this consent for the purposes described above.

_____
PRINTED NAME OF PARTICIPANT

Consent Signature

_____ _____
PARTICIPANT SIGNATURE (18 years and older) Date

_____
PRINTED NAME OF PERSON CONDUCTING INFORMED CONSENT

_____ _____
SIGNATURE OF PERSON CONDUCTING INFORMED CONSENT Date