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Nov 02, 2017
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Laureate Institute for Brain Research, Inc., Tulsa, OK, United State

RESEARCH SUBJECT INFORMATION AND CONSENT FORM	
TITLE:	Neural basis of interoceptive dysfunction and anxiety in anorexia nervosa

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: Neural basis of interoceptive dysfunction and anxiety in anorexia nervosa

PROTOCOL NO.: 2015-004-04
WIRB® Protocol #20150986

SPONSOR: Laureate Institute for Brain Research

INVESTIGATOR: Sahib Khalsa, MD, PhD
6655 S Yale Ave
Tulsa, Oklahoma 74136
United States

STUDY-RELATED PHONE NUMBER(S): Sahib Khalsa, MD, PhD
918-502-5155
918-481-4000 (24 hours)

This consent form describes a clinical trial 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 been diagnosed with Major Depressive Disorder, Generalized Anxiety Disorder, Panic Disorder, Anorexia Nervosa or Brain Injury.

Why Is This Study Being Done?

This project seeks to discover how conditions such as depression, anxiety, eating disorders, and brain injury affect body sensation and emotional experience and how they can be better understood and treated.

What Devices Are Involved In This Study?

The Magnetic Resonance Imaging (MRI - use of a magnetic field to produce an image) scanner is used to look at brain function and anatomy. The LIBR is using the MRI scanner in a research (experimental) mode. U.S. Food and Drug Administration (FDA) approval has not been obtained for the particular ways that information about inter-personal interaction from the MRI may be used in this research; however, the MRI scanner will not be used for purposes outside its intended application.

A physiological recording system will also be used to monitor heart rate and breathing.

How Many Subjects Will Take Part In The Study?

About 410 subjects will take part in this study at the Laureate Institute for Brain Research.

What Is Involved In The Study?

The study may involve:

- Questionnaires
- Physical Measurements
- Urine tests
- Isoproterenol and saline infusion
- Topical anesthetic application
- MRI scanning
- Electrocardiogram (EKG)
- Electroencephalogram (EEG)

Questionnaires

These tests and questionnaires about your health, mood, and personality will measure your mental and physical states.

Physical Measurements

Your weight, height, blood pressure, pulse, electrocardiogram (EKG) and other like measurements may be obtained for research purposes.

Urine Tests

You will have urine tests. A urine drug test will be performed prior to any infusions. If you are female, you will also receive an over the counter pregnancy test prior to any MRI scanning or infusions. You will not be allowed to participate in the study if either of the tests read positive.

Isoproterenol and Saline Infusion

You will be asked to rate your experience of body sensations and emotions during and after receiving isoproterenol and saline infusions. Isoproterenol is a medicine that is similar to adrenaline, a hormone naturally released by the body. During the study you will receive the isoproterenol infusions through an intravenous line (IV) or you will receive saline. The saline infusions are intended as a placebo, that is, they will not have an effect on heartbeat or breathing sensations. This is opposite the isoproterenol infusions, which will have an effect on heartbeat and breathing sensations. At different points during the study you will receive isoproterenol or saline. However, neither you nor your study doctor will know when you will receive the isoproterenol or saline.

Body sensation assessment

Your experience of different body sensations, such as heartbeat and breathing sensations will be measured during several challenges. You will be asked to: 1) hold your breath, after you exhale, for as long as you can tolerate while wearing a nose clip, 2) tap a response box along with your heartbeat or with a series of tones heard through headphones with your eyes closed, and 3) put one of your hands in a pool of cold water for as long as you can tolerate.

Autonomic assessment

Your heart rate and breathing response will be measured during several conditions. You will be asked to: 1) squeeze a handgrip for up to two minutes, 2) perform a mental arithmetic task by counting backwards for up to five minutes, and 3) hold your breath and bear down for up to 30 seconds on two occasions.

MRI Scanning

You may be asked to participate in the MRI scanning. For your safety, you will be given a brief pre-screening form to complete. It will tell us if you have any metal inside your body. The pre-screening form may identify some unanticipated medical findings that prevent you from participating in the MRI scan. If so, these findings will remain as confidential as possible, and will be discussed with you by a researcher involved in this study.

Prior to your scan, you will be taught some tasks for use in the scanner.

The MRI scanner rapidly takes pictures of your brain without exposure to radiation. The MRI scanner is a metal cylinder surrounded by a strong magnetic field. During the MRI, you will lie on a table that can slide in and out of the cylinder. You will be asked to lie still during scanning by remaining as relaxed as possible. While in the scanner you will hear loud knocking noises, and you will be fitted with earplugs to muffle the sound. You will be able to communicate with the MRI staff at all times during your scan, and you may ask to be moved out of the machine at any time. We will also monitor your heart rate and respiration using a device on your finger and a rubber belt that fits loosely around your chest using the built-in scanner equipment.

The study will use anatomical MRI and functional Magnetic Resonance Imaging (fMRI). During the fMRI, the MRI scanner measures changes in blood oxygen levels in different brain regions while you perform mental tasks. The tasks involve attending to body sensations and making ratings about them. Some of the tasks will involve receiving isoproterenol and saline infusions while inside of the scanner. Some of the tasks do not involve isoproterenol and saline infusions. This procedure will provide us with information about which brain areas become more active (that is, receive more blood oxygen) while you are performing the tasks.

If you are asked to participate in the MRI scanning, there may be two brain-scanning visits. The time in the scanner per visit will be approximately 2 hours. If you are not asked to participate in the MRI scanning, there may be two visits occurring outside of the scanner. You may be asked to participate in two remote follow up visits approximately 1 hour per visit.

EKG

An electrocardiogram (EKG) is a test that checks for problems with the electrical activity of your heart. An EKG will be conducted by a trained technician. You will be in a private exam room and modesty drapes will be provided if indicated.

EEG

You may also be asked to have an EEG outside the MRI scanner and/or during MRI. An EEG monitors brain activity. After you are familiarized with the equipment, a cap consisting of multiple MRI-compatible EEG electrodes with gel in them will be placed on your scalp and a few electrodes with gel in them will be placed on your back. The electrodes will be connected to a data collection system and EEG signals will be collected and stored onto the computer of the recording system.

Topical anesthetic application

At some point during the study we may apply a topical anesthetic cream to your skin (LMX 4, which contains 4% lidocaine), on several regions of your body. Applying this cream to a specific area of your body will result in a loss of skin sensation in that area only. Body areas will be defined based on your responses during the infusions, but may will be

repeated after the cream has been applied. Each area will be cleansed and then the cream will be placed with the help of the experimenter or a nurse. The cream will not be applied to the groin region, buttocks or thighs of any male or female. If the cream needs to be applied to the chest of any female (e.g., upper chest near the sternum), it will either be placed by yourself, or with help of a female experimenter. All sensitive regions of the chest (e.g., nipple), or any other region of the body that you deem sensitive, will be avoided. The total area will be about the size of a postcard.

Visit Schedule Summary:

	Visit 1 Screen	**Visit 2 Infusion**	**Visit 3 Infusion**	**6 Month Follow Up**	**1 Year Follow Up**
Consent and Assessment, EKG	2 hours				
Drug & Pregnancy test					
Questionnaires	2 hours			1 hour	1 hour
Out of Scanner Visit					
• Drug & Pregnancy test					
• Isoproterenol or saline infusion		3 hours	3 hours		
• Body sensation & autonomic assessment		0.5 hours	0.5 hours		
• Meal		1 hour	1 hour		
In Scanner Visit					
• Drug & Pregnancy test					
• Prep for MRI/EEG		1 hours	1 hours		
• Isoproterenol or saline infusion					
• MRI or MRI with EEG		2 hours	2 hours		
• EEG cap removal and debriefing		0.5 hours	0.5 hours		
• Meal		1 hour	1 hour		
Total Study Visit Time	**4 hours**	**5 hours**	**5 hours**	**1 hour**	**1 hour**

All times are approximate. Visit 2 and 3 may be either MRI scanner only, outside of the scanner only, or both. There may only be one visit after the assessment. Follow up visits will be done remotely.

How Long Will You Be In The Study?

We expect you will be in this study until completion of your study visits. This may take approximately one year.

There may be circumstances under which your participation in the study may be stopped by the investigator without your consent. Functional MRI is dependent upon measuring very small changes in blood flow in the brain. Therefore, there may be times in which the information collected will be unusable due either to a scanner malfunction or from you moving your head too much. Under these circumstances your participation may be stopped without your consent.

You may stop participating in this study at any time. You may also refuse to be contacted again in the future about participating in the study again.

What Are The Risks Of The Study?

Questionnaires

There is no medical risk associated with the questionnaires. You may experience temporary discomfort, including anxiety and sadness, when recalling particularly negative memories. Members of the research staff are trained to help you if you have an unusually strong reaction to these memories. You can also stop the procedure at any time. Also, if you show a strong reaction, such as extreme sadness, to any part of the study, researchers will stop the procedure and help you relax before leaving the LIBR.

Physical Measurements

There are no risks in measuring your physical measurements.

Urine Testing

Testing your urine for drugs and/or pregnancy offers no risks. If either test is positive, that information will be kept confidential.

Intravenous line (IV)

The placement of the intravenous needle/cannula will be performed by an RN or MD using sterile technique. You may have some discomfort and bruising at the site of needle/cannula entry. There is a very small risk of fainting or infection in the area of the needle/cannula insertion.

Isoproterenol Infusion

If you receive the isoproterenol, you will receive a standard dose that is approved for use. It is possible that the isoproterenol could cause some side effects such as:

- Palpitations
- Shortness of breath
- Tremors
- Flushing (redness of the skin)
- Nausea
- Headache
- Low or high blood pressure
- Heart rhythm changes
- Elevated heart rate
- Dizziness
- Anxiety
- Allergic reaction

Anesthetic cream
If you receive the anesthetic cream, you will receive a standard dose that is approved for use. It is likely that you will experience numbness of the skin after the cream is applied. It is possible that you may notice some side effects such as:

- Skin redness or whitening after removal
- Dizziness
- Headache
- Fatigue
- Allergic reaction

Interactions between isoproterenol and anesthetic cream

It is possible that the administration of isoproterenol and the anesthetic cream together may increase the amount of side effects of each drug. This includes any of the side effects mentioned above, such as:

- Skin vasodilation
- Dizziness
- Headache
- Shaking
- Confusion
- Chest pain
- Seizure
- Abnormal heart rhythm
- Methemoglobinemia

However, these interactions are rarely seen.

A Physician and a Registered Nurse will be available during the study visit to monitor you for any problems. Your heart rate, respirations, and blood pressure will be closely and continually monitored during the infusion part of this study. You will be removed from the study immediately if the study staff determines that you are at increased risk from the infusions.

Brain MRI

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

Welders and metal workers are also at risk for injury because they may be unaware of small metal fragments in the eye.

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.

You will be asked to complete an MRI screening form and to sign a separate MRI screening form for each MRI scan.

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 thumping 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 removed from the scanner immediately if you request to be removed.

EKG

There is no risk associated with obtaining an EKG.

EEG

There are no significant risks expected in the stand alone EEG or MRI compatible EEG. However, there may be minor discomfort from wearing an EEG cap, which is similar to wearing a tight hat. You may feel local pressure points and minor skin irritation from the electrode patches. This will be minimized by the use of gel in each electrode and foam pads placed under and surrounding your head.

Body sensation assessment

Holding your hand in cold water may make you physically uncomfortable, however, it is not harmful. Holding your breath may make you feel anxious or uncomfortable and like you cannot breathe. You can stop at any time or take a break and remove the nose clip. Breathing through your mouth can make it feel dry. You will be given water to drink as needed. The nose clip can feel uncomfortable, however, you should tell the researcher and the clip will be adjusted.

Autonomic assessment

Squeezing a handgrip, counting backwards, and holding your breath may make you physically uncomfortable or slightly anxious, however, it is not harmful. You can stop or take a break at any time.

There may be other risks from study participation that currently are unknown.

Are There Benefits To Taking Part In The Study?

There is no direct medical benefit anticipated for you in this study. Information learned from this study may benefit other people 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 Visit 1, you will receive $50. For Visit 2 & 3, you will receive $150 for each visit. If you participate in the MRI scanning portion of the study, you will receive $100 for each visit. You will receive $20 for the 6 month and the 1 year follow up.

You will be paid with a ClinCard (similar to a debit card) that may be used 24 hours after each visit.

What Other Options Are There?

This is not a treatment study. The alternative to participating in this study is not to participate.

Confidentiality

What information may be used and given to others?

The study doctor will get your personal and medical information. For example:

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

Who may use and give out information about you?

The study doctor and the study staff.

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?

There is 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.

Certificate of Confidentiality:

We will do everything we can to keep others from learning about your participation in this study. To further help us protect your privacy, we have obtained a Certificate of Confidentiality from the United States Department of Health and Human Services (DHHS). With this Certificate, we cannot be forced (for example by court order or subpoena) to disclose information that may identify you in any federal, state, local, civil, criminal, legislative, administrative, or other proceedings. The researchers will use the Certificate to resist any demands for information that would identify you, except to prevent serious harm to you or others, and as explained below.

You should understand that a Certificate of Confidentiality does not prevent you, or a member of your family, from voluntarily releasing information about yourself, or your involvement in this study.

If an insurer or employer learns about your participation, and obtains your consent to receive research information, then we may not use the Certificate of Confidentiality to withhold this information. This means that you and your family must also actively protect your own privacy. Disclosure will be necessary, however, upon request of DHHS for the purpose of audit or evaluation, and is limited only to DHHS employees involved in the review.

You should understand that we will in all cases, take the necessary action, including reporting to authorities, to prevent serious harm to yourself, children, or others. An example of a reportable incident would be child abuse or neglect.

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 the Principal Investigator of this study, Sahib Khalsa, MD, PhD, as soon as possible at 918-502-5155 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.

Whom Should You Call If You Have Questions Or Problems?

Your contact person for this study is Sahib Khalsa, MD, PhD. He can be reached during business hours at 918-502-5155.

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 doctor, Sahib Khalsa, MD, PhD, at 918-502-5155 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.

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.

By signing this consent form, I have not given up any of my legal rights.

Consent:

_____
Subject Name (printed)

CONSENT SIGNATURE:

_____ _____
Signature of Subject (18 years and older) Date

_____ _____
Signature of Person Conducting Informed Consent Discussion Date

I confirm that the research study was thoroughly explained to the subject. I reviewed the consent form with the subject and answered the subject's questions. The subject appeared to have understood the information and was able to answer the following questions correctly:

1. What is the purpose of this study?
2. If you decide to be in the study, what will you be asked to do?
3. What is the possible benefit of participating in this study?
4. What are the possible risks of participating in this study?
5. If you decide not to participate in this study, what options do you have?
6. Will participating in this study cost you anything? If so, what will you have to pay for?
7. Do you have to be in this study?
8. If you decide to be in the study, can you leave the study when you want to?

Printed Name of Person Conducting the Informed Consent Discussion	Position
Signature of Person Conducting the Informed Consent Discussion	Date