Investigations of Amygdala Function Using Neurophysiological Recording and Stimulation

Informed Consent Form

NCT03958903

November 30, 2021

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Are you participating in any other research studies? _____ Yes _____No

SUMMARY

Your consent or reconsent is being sought for a research study and your participation is entirely voluntary. Not all of these procedures/tasks described below will be completed with each consent or reconsent.

This study aims to study changes in Brain signals in reaction to emotional images and different sensations. We also want to observe how electrical stimulation produced by the RNS® System by NeuroPace, Inc. affects your brain signals.

This study will occur over 4-6 hours over 2 days duration.

You will begin with a Psychodiagnostic interview with a Neuropsychiatrist. You will have interviews and will be asked to perform cognitive tests and fill out surveys.

You will then be taken to a room where you will be seated in a chair and fitted with an EEG cap, this looks like a swim cap with wires. We will apply gel in your scalp for the EEG recording. We will attach leads to your hand and your face to monitor your physiological responses. Afterwards, NeuroPace tools will be placed over your implanted RNS system to collect brain signals. You may be asked to wear a backpack (with legs) that is used to hold the tools and accessories.

You will be asked to perform several tasks throughout which your brain signals will be recorded. Some of these tasks will require you to wear a VR headset and/or eye-tracker. Within certain tasks you will be stimulated through the RNS device. The stimulations will not be different than the ones you will normally receive from your NeuroPace RNS. The only difference is that we will be controlling when it stimulates your brain during the study.

You will be asked to look at images, words, faces and asked to respond to the content presented while occasional bursts of sound are delivered through headphones. You may be administered a non-painful, mild electrical shock adjusted to your comfort level.

You may be asked to look at pleasant/neutral/unpleasant slides while recording your brain activity, skin conductance, heart rate and or respiration.

You will be asked to press down on two triggers, paired with stimulus- either rewarding(juice) or aversive (mild electric shock)

You will be asked to press buttons to deliver milkshake or a tasteless solution to your mouth via tubing.

You will be asked to make decisions on trials based on known outcomes. You are given rewards in the form of points and punishment in the form of aversive picture paired with noise.

You will react to a cue on a computer screen that signal whether money will be earned or lost. Depending on the cue, you can either win money or avoid losing money based on your reaction time. A practice run will always be provided, and you will not lose any money.

You might experience fatigue or discomfort from wearing the EEG cap, VR or eye-tracking headset for extended periods of time. Some of the images will have emotional content and might be upsetting to some individuals. The mild electric shock may possibly cause immediate and mild discomfort to you. Sensitivity to dairy may cause discomfort with one of the tasks.

By participating in this study, there is no direct benefit to you. The general benefit in participating in this study consists of adding to the knowledge regarding brain signals.

The alternative to participating in this study is not participating. You are free to withdraw your consent at any time.

PURPOSE OF RESEARCH

You are invited to participate in a research study of brain function. We hope to better understand what signals your brain produces in reaction to emotional images and different sensations. We also want to observe how electrical stimulation produced by the RNS® System by NeuroPace, Inc. affects your brain signals. You were selected as a possible participant in this study because you have received the RNS® System for treatment of epilepsy.

This research study seeks to enroll people with the RNS® System. Enrollment will occur throughout Northern California. Stanford University expects to enroll a total of 30 research study participants for this study.

VOLUNTARY PARTICIPATION

Your participation in this study is entirely voluntary. Your decision not to participate will not have any negative effect on you or your medical care. You can decide to participate now but withdraw your consent later and stop being in the study without any loss of benefits or medical care to which you are entitled.

If you decide to terminate your participation in this study, you should notify Dr. Mahendra Bhati at (650) 498-2577.

DURATION OF STUDY INVOLVEMENT

Your participation in this research study is expected to take place over 4-6 hours over 2 days.

PROCEDURES

If you choose to participate, Dr. Mahendra Bhati and his research study staff ask you to undergo the following procedures. You will likely be asked to undergo only a subset of these procedures. You may be asked to repeat some procedures if the original data collected is not useable for some reason. The majority of procedures will take place at Stanford University. There is the possibility for visits to occur remotely via phone or videoconference. This will be determined at the discretion of the research team and will depend on your comfort with remote visits, as well as your access to the tools and privacy needed for remote visits. Neuropace technical staff may be present in the room during the study.

1. Psychodiagnostic Interviews, Medical History, and Neurocognitive Assessments for Screening:

This procedure involves an assessment of anxiety or mood symptoms, eating behavior, medical history, and tests about how you think and feel. The session typically lasts no longer than 2 hours. The assessment will be done by a licensed physician and will involve interviews, review of your medical records, completing questionnaires, and doing computer and/or pen and paper evaluations. Your eligibility to participate in the study is conditional on passing the screening clinical assessment. Some surveys may be administered by a trained research team member under direct supervision of a licensed physician.

Risks: Answering questions on some of the questionnaires and interviews used in this study may provoke mild feelings of frustration, fatigue, sadness, or anxiety. You have the right to refuse to answer any particular questions that make you feel uncomfortable on any of the questionnaires or interviews. Information you provide will remain anonymous and will be used only for the

purpose of the research study. However, it is possible that, based on the information gained from this study, the researchers may be required to report information (e.g., information relating to suicide, physical or sexual abuse) to the appropriate authorities.

We will keep your study data as confidential as possible, with the exception of certain information that we must report for legal or ethical reasons, such as suspected child abuse or neglect, suspected elder abuse or neglect, or intent to harm yourself or others.

2. Behavioral testing:

You will be shown images of things, such as simple letters, words, or pictures that will be displayed on a monitor. You may be asked simple questions relating to these letters, words, or pictures. Your responses to these questions will be recorded.

3. Electroencephalogram (EEG) and Psychophysiological Assessment:

EEG is a test that measures and records the electrical activity of the brain. To collect this information, we will ask you to wear a cap on your head that is like a swimming cap. The cap has special sensors attached to it and it hooked by wires to a computer. The computer will then record your brain's electrical activity on the computer screen as wavy lines. We may also put the sensors on your face with a sticky paste to record facial movements and eye-blinking. Electrodes will be attached to your face to measure eye-blinks, heart-rate, and facial muscles which are associated with frowning and smiling. Finger sensors measuring how much you sweat will be attached to your left index and middle fingers. The test causes no discomfort. The electrodes only record activity and do not produce any sensation.

Risks: There are very minimal risks associated with EEG and it does not cause any pain. You may experience fatigue or discomfort from wearing the EEG cap for extended periods of time.

4. Recording and Stimulation with the RNS® System:

After your RNS® System is implanted, we will be recording the electrical signals produced by your brain during in-clinic tasks as well as real-world ambulatory recordings. During some of the in-clinic tasks, we will stimulate your brain using the device. The stimulations will not be different than the ones you will normally receive. The only difference is that we will be controlling when it stimulates your

brain during the study. For ambulatory recordings, we will ask you to swipe your NeuroPace magnet over the RNS system during reward-seeking behavior (e.g. craving for food/drinks, gambling). We will also ask that you keep a diary with the time you swiped your magnet for specific behavior, and report the time-stamps to the study coordinator.

Risks: There will be no additional risks associated with the RNS® System other than the ones you were already informed of when you agreed to receive the device.

5. Learned Fear and Extinction Experiments:

For this task, you will be asked to do simple mental tasks or make predictions about upcoming visual information presented. You will be asked to look at a series of words, pictures, or faces and asked to respond to the content of these materials while occasional bursts of noise or sound are delivered through headphones on particular trials. You may be administered non-painful, mild electrical shock pulses at slightly different durations on the skin of your inner ankle. The shock levels are adjusted to your comfort level. In some cases, you will be informed about the type of symbol that predicts an upcoming mild electrical shock pulse. In other cases, you will only know that a particular trial *may* include a mild electrical shock pulse but you will not know exactly when the shock pulse will or will not occur. Monitors attached to your skin will provide information on your eye-blink muscles and other related responses to tasks and stimuli presented.

Risks: Some of the images, words, and sounds presented will have an emotional content and so could be mildly upsetting to some individuals. Also, the surprising nature of the sound could be unpleasant for some individuals. The mild electrical shock pulse may possible provide immediate and brief mild discomfort to you.

6. Emotional Evocation with Images:

During the experiment, you may also be asked to watch pleasant and/or neutral and/or unpleasant slides and/or films and/or text. Some of these stimuli might bring up intense emotions. You may be asked questions about your feelings and appraisals.

In addition to measuring brain activity during the experiment, other physiological measures may be recorded. These include heart rate, skin conductance, and/or respiration. If obtained, these measurements will be taken using non-invasive techniques that pose minimal risk.

7. Approach-Avoidance Task:

For this task you will have two triggers which you press down on. They are paired with two stimuli shown on the screen, either a rewarding stimulus (juice) or a punishment stimulus (mild electric shock).

Risks: The mild electrical shock pulse may possibly provide immediate and brief mild discomfort to you.

7. Milkshake Task:

Before beginning this task, you may be asked to fill out a questionnaire regarding your liking of milkshakes. There will be two syringes filled with milkshake and tasteless solutions connected via Tygon tubing to a manifold and placed in your mouth. You will then be asked to press a button as fast as you can in response to visual cues. The images signal that a milkshake or tasteless solution *may* or *may not* be delivered through the tubes. After you have completed the task you may be asked, again, to fill out a questionnaire.

Risks: sensitivity to dairy may cause discomfort with this task.

8. AAC Task:

For this task you will be making decisions on a given trial based on known outcomes. You are given rewards in the form of points and punishments in the form of negative, aversive pictures paired with a sound. On each trial you make the decision if the reward is worth the aversive picture. Once you have completed all the trials, you may be asked to fill out a post-task survey.

Risks: Some of the images and sounds presented may be unpleasant for some individuals.

8.Monetary Incentive Delay task
In this task, you will react to a cue on a computer screen that signal whether money will be earned or lost. Depending on the cue, you can either win money or avoid losing money based on his or your reaction time. A practice run will be provided and you will not lose any of your own money.
You can make anywhere from 0-60$ for this task which will be paid at the end of the task.

CLINICALTRIALS.GOV

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.

PARTICIPANT RESPONSIBILITIES

As a participant, your responsibilities include:

- Follow the instructions of the Protocol Director and study staff.
- Keep your study appointments. If it is necessary to miss an appointment, please contact the Protocol Director or research study staff to reschedule as soon as you know you will miss the appointment.
- Tell the Protocol Director or research study staff about any side effects, doctor visits, or hospitalizations that you may have.
- Tell the Protocol Director or research staff if you believe you might be pregnant or gotten your partner pregnant.
- Complete your questionnaires as instructed.
- Ask questions as you think of them.
- Tell the Protocol Director or research staff if you change your mind about staying in the study.

While participating in this study, you should not take part in any other research project without approval from all of the investigators. This is to protect you from possible injury arising from such things as extra blood drawing, interaction of research drugs, or similar hazards.

WITHDRAWAL FROM STUDY

If you first agree to participate and then you change your mind**, you are free to withdraw** your consent and discontinue your participation at any time. Your decision will not affect your ability to receive medical care for your disease and you will not lose any benefits to which you would otherwise be entitled, and your decision will not affect your ability to receive medical care for your condition.

If you decide to withdraw your consent to participate in this study, you should notify Dr. Mahendra Bhati at (650) 498-2577. There are no anticipated consequences to withdrawal from the research study.

The Protocol Director may also withdraw you from the study without your consent for one or more of the following reasons:

- Failure to follow the instructions of the Protocol Director and study staff.
- The Protocol Director decides that continuing your participation could be harmful to you.
- Pregnancy
- You need treatment not allowed in the study.
- The study is cancelled.
- Other administrative reasons.
- Unanticipated circumstances.

POSSIBLE RISKS, DISCOMFORTS, AND INCONVENIENCES

There are risks, discomforts, and inconveniences associated with any research study. These deserve careful thought. You should talk with the Protocol Director if you have any questions. The specific risks associated with each procedure are described above in the Procedures section.

Women of Childbearing Potential

If you are a woman who is able to become pregnant, it is expected that you will use an effective method of birth control to prevent exposing a fetus to a potentially dangerous agent with an unknown risk. If you are pregnant or currently breast feeding, you may not participate in this study. You understand that if you are pregnant, if you become pregnant, or if you are breast-feeding during this study, you or your child may be exposed to an unknown risk.

To confirm you agree to have a pregnancy test done before the beginning of this research study. You must agree to avoid sexual intercourse or use a birth control method judged to be effective by the investigator and which will not interfere with the proposed investigation. You must accept the risk that pregnancy could still result despite the responsible use of a reliable method of birth control. You agree to notify the investigator as soon as possible of any failure or proper use of your birth control method, or if you become pregnant, either of which may result in your being withdrawn from the study.

POTENTIAL BENEFITS

There is no direct benefit for you. The possible general benefit for science resulting from participating in this study consists of adding to the knowledge regarding brain signals. We cannot and do not guarantee or promise that you will receive any benefits from this study.

ALTERNATIVES

The only alternative to participating in this study is not participating in this study.

PARTICIPANT'S RIGHTS

You should not feel obligated to agree to participate. Your questions should be answered clearly and to your satisfaction. If you decide not to participate, tell the Protocol Director.

You will be told of any important new information that is learned during the course of this research study, which might affect your condition or your willingness to continue participation in this study.

CONFIDENTIALITY

The results of this research study may be presented at scientific or medical meetings or published in scientific journals. Your identity and/or your personal health information will not be disclosed except as authorized by you or as required by law**.** However, there is always some risk that even de-identified information might be re-identified.

Identifiers might be removed from identifiable private information and/or identifiable specimens and, after such removal, the information and/or specimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from you.

Patient information may be provided to Federal and other regulatory agencies as required. The Food and Drug Administration (FDA), for example, may inspect research records and learn your identity if this study falls within its authority.

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.

The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation by National Institute of Health (NIH) which is funding this project or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA).

You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law. If information is revealed about child abuse or neglect, elder or dependent abuse or neglect, or potentially dangerous future behavior to others or yourself.

The Certificate of Confidentiality will not be used to prevent disclosure for any purpose you have consented to in this informed consent document, such as: the results of this research study may be presented at scientific or medical meetings or published in scientific journals.

Authorization To Use Your Health Information For Research Purposes

Because information about you and your health is personal and private, it generally cannot be used in this research study without your written authorization. If you sign this form, it will provide that authorization. The form is intended to inform you about how your health information will be used or disclosed in the study. Your information will only be used in accordance with this authorization form and the informed consent form and as required or allowed by law. Please read it carefully before signing it.

What is the purpose of this research study and how will my health information be utilized in the study?

The purpose of this study is to learn more about what brain signals your brain produces when you reacts to certain emotional stimuli. We also want to observe how stimulation with the RNS® System by NeuroPace, Inc. affects your brain signals. Knowledge gained from this study may further our understanding of how the brain works and how the RNS® System may help patients with other neurological and psychiatric disorders. Your health information will be kept in secure settings so that only Stanford researchers will have access to any identifying information. This allows us to be certain that your identifying information is linked to the data acquired from you in this study. If this research leads to scientific publications, any and all identifying information will be removed.

Do I have to sign this authorization form?

You do not have to sign this authorization form. But if you do not, you will not be able to participate in this research study. Signing the form is not a condition for receiving any medical care outside the study.

If I sign, can I revoke it or withdraw from the research later?

If you decide to participate, you are free to withdraw your authorization regarding the use and disclosure of your health information (and to discontinue any other participation in the study) at any time. After any revocation, your health information will no longer be used or disclosed in the study, except to the extent that the law allows us to continue using your information (e.g., necessary to maintain integrity of research). If you wish to revoke your authorization for the research use or disclosure of your health information in this study, you must write to: Dr. Mahendra Bhati, 401 Quarry Rd, Stanford, CA 94305.

What Personal Information Will Be Obtained, Used or Disclosed?

Your health information related to this study, may be used or disclosed in connection with this research study, including, but not limited to the following types of data collected:

> Psychology and mental health records, clinical records, brain images, demographics, names, prescriptions and medications, phone numbers, addresses, birthdates, emails, medical record numbers, and RNS® System identifiers, serial numbers, and recordings.

Who May Use or Disclose the Information?

The following parties are authorized to use and/or disclose your health information in connection with this research study:

- The Protocol Director, Dr. Mahendra Bhati, MD
- The Stanford University Administrative Panel on Human Subjects in Medical Research and any other unit of Stanford University as necessary
- Research Staff

Who May Receive or Use the Information?

The parties listed in the preceding paragraph may disclose your health information to the following persons and organizations for their use in connection with this research study:

- NeuroPace, Inc.

- The Office for Human Research Protections in the U.S. Department of Health and Human Services
- The Food and Drug Administration
- National Institute of Health

Your information may be re-disclosed by the recipients described above, if they are not required by law to protect the privacy of the information.

When will my authorization expire?
Your authorization for the use and/or disclosure of your health information will end on December 31, 2025 or when the research project ends, whichever is earlier.

_____ _____
Signature of Adult Participant Date

_____
Print Name of Adult Participant

FINANCIAL CONSIDERATIONS

Payment
Research subjects will be offered $25 per hour up to a maximum of $150 for their participation in this study.

A maximum of $60 will be awarded to you according to your performance in the monetary incentive delay task. The payment ranges from $0 to $60

You will be reimbursed for gas at the rate of 55.5 cents per mile. Meals will be reimbursed as follows: $15 for breakfast, $16 for lunch, and $28 for dinner. Under certain circumstances, you will be reimbursed for rideshare service to and from the study site.

A hotel room will be provided for you for the night.

Payments may only be made to U.S. citizens, legal resident aliens, and those who have a work eligible visa. You may need to provide your social security number to receive payment.

Costs
There is no cost to you for participating in this study, other than basic expenses like transportation and the personal time it will take to come to all of the study visits.

Sponsor
The Department of Psychiatry at the Stanford School of Medicine is providing financial support and/or material for this study.

The National Institute of Health is also providing financial support for this study.

COMPENSATION for Research-Related Injury

All forms of medical diagnosis and treatment – whether routine or experimental – involve some risk of injury. In spite of all precautions, you might develop medical complications from participating in this study. If such complications arise, the Protocol Director and the research study staff will assist you in obtaining appropriate medical treatment. In the event that you have an injury or illness that is directly caused by your participation in this study, reimbursement for all related costs of care first will be sought from your insurer, managed care

plan, or other benefits program. **You will be responsible for any associated co-payments or deductibles as required by your insurance.**

If costs of care related to such an injury are not covered by your insurer, managed care plan or other benefits program, you may be responsible for these costs. If you are unable to pay for such costs, the Protocol Director will assist you in applying for supplemental benefits and explain how to apply for patient financial assistance from the hospital.

You do not waive any liability rights for personal injury by signing this form.

CONTACT INFORMATION

Questions, Concerns, or Complaints: If you have any questions, concerns or complaints about this research study, its procedures, risks and benefits, or alternative courses of treatment, you should ask the Protocol Director, Dr. Mahendra Bhati at (650) 498-2577. You should also contact him at any time if you feel you have been hurt by being a part of this study.

Independent Contact: If you are not satisfied with how this study is being conducted, or if you have any concerns, complaints, or general questions about the research or your rights as a participant, please contact the Stanford Institutional Review Board (IRB) to speak to someone independent of the research team at (650)-723-5244 or toll free at 1-866-680-2906. You can also write to the Stanford IRB, Stanford University, 1705 El Camino Real, Palo Alto, CA 94306.

Appointment Contact: If you need to change your appointment, please contact Noriah Johnson at (650) 254-6824.

EXPERIMENTAL SUBJECT'S BILL OF RIGHTS

As a research participant you have the following rights. These rights include but are not limited to the participant's right to:

- be informed of the nature and purpose of the experiment;
- be given an explanation of the procedures to be followed in the medical experiment, and any drug or device to be utilized;
- be given a description of any attendant discomforts and risks reasonably to be expected;
- be given an explanation of any benefits to the subject reasonably to be expected, if applicable;

- be given a disclosure of any appropriate alternatives, drugs or devices that might be advantageous to the subject, their relative risks and benefits;
- be informed of the avenues of medical treatment, if any available to the subject after the experiment if complications should arise;
- be given an opportunity to ask questions concerning the experiment or the procedures involved;
- be instructed that consent to participate in the medical experiment may be withdrawn at any time and the subject may discontinue participation without prejudice;
- be given a copy of the signed and dated consent form; and
- be given the opportunity to decide to consent or not to consent to a medical experiment without the intervention of any element of force, fraud, deceit, duress, coercion or undue influence on the subject's decision.

May we contact you about future studies that may be of interest to you?
____ Yes ____ No

Signing your name means you agree to be in this study and that you will receive a copy of this signed and dated consent form.

_____ _____
Signature of Adult Participant Date

_____
Print Name of Adult Participant

_____ _____
Signature of Person Obtaining Consent Date

_____
Print Name of Person Obtaining Consent