Researchers at the Mount Sinai School of Medicine are studying

ESSENTIAL TREMOR OF VOICE
SPASMODIC DYSPHONIA

Purpose of this research study:
Investigate effects of a novel drug, sodium oxybate, Xyrem®, on symptoms and brain changes in patients with essential tremor of voice and spasmodic dysphonia compared to healthy subjects

You may qualify if
• You have essential tremor of voice and/or spasmodic dysphonia or you are a healthy volunteer
• Your symptoms are relieved after alcohol intake
• You wish to participate in the brain functional magnetic resonance imaging (fMRI) study
• You are 21 through 80 years of age

You may not qualify if
• You have a history of other neurological, psychiatric or voice problems

Place and Time
The outpatient research study will be conducted at the Mount Sinai Hospital in New York, NY, and may last up to 3 hours

Cost
There is no cost for the participation in the study or any tests associated with this research. You will be reimbursed for your time in amount of $50, which you will receive in form of a check. If you are an out-of-town patient, your travel costs to the Mount Sinai Hospital for this study may be reimbursed.

This study is funded by the National Institute on Deafness and other Communication Disorders of the National Institutes of Health (NIDCD/NIH) under Award Number R01DC012545. This study was approved by the Institutional Review Board of the Mount Sinai School of Medicine on 06/28/2012.

For more information, please contact our research team at
(212) 241-2635 or dystonia.research@gmail.com
TITLE OF RESEARCH STUDY:

Voice tremor in spasmodic dysphonia: central mechanisms and treatment response

PRINCIPAL INVESTIGATOR (HEAD RESEARCHER) NAME AND CONTACT INFORMATION:

Name: Kristina Simonyan, M.D., Ph.D.
Address and Phone: 1 Gustave L. Levy Place, Annenberg 2-210C, New York, NY 10029, Tel.: (212) 241-0656

WHAT IS A RESEARCH STUDY?

A research study is when scientists try to answer a question about something that we don't know enough about. Participating may not help you or others.

People volunteer to be in a research study. The decision about whether or not to take part is totally up to you. You can also agree to take part now and later change your mind. Whatever you decide is okay. It will not affect your ability to get medical care at Mount Sinai.

Someone will explain this research study to you. Feel free to ask all the questions you want before you decide. Any new information that develops during this research study, which might make you change your mind about participating, will be given to you promptly.

PURPOSE OF THIS RESEARCH STUDY:

The purpose of this study is to better understand the brain changes in patients with spasmodic dysphonia and vocal tremor and how these brain changes can be improved with treatment with sodium oxybate, Xyrem®.

You may qualify to take part in this research study because
  ▪ You are 21 through 80 years of age.
  ▪ You have essential tremor of voice, spasmodic dysphonia or you are a healthy volunteer.
  ▪ You have no laryngological, other neurological, psychiatric problems, past or present history of suicidal ideation or attempt, alcohol or substance abuse, neuroleptic exposure, ferromagnetic objects in your body that cannot be removed before MRI, selective ramisectomy or deep brain stimulation, treatment with botulinum toxin less than 3 month ago, inability to abstain from all alcohol use for one week prior to the trial and throughout the study.

Funds for conducting this research are provided by Mount Sinai School of Medicine.

This Consent Document is approved for use by Mount Sinai’s Institutional Review Board (IRB)
Form Approval Date: 7/28/12
DO NOT SIGN AFTER THIS DATE → 7/27/13
Rev. 2/1/2011
IRB Form HRP-502a
LENGTH OF TIME AND NUMBER OF PEOPLE EXPECTED TO PARTICIPATE

Participation in this study is expected to last up to 1 hour for screening examination and up to 1.5 hours for functional magnetic resonance imaging (fMRI) of your brain. If you are a patient, you may have up to 3 fMRI scans performed, one before treatment, one after treatment with sodium oxybate and one after combined treatment with sodium oxybate and botulinum toxin. All research procedures will be conducted at the Mount Sinai Hospital. You will receive the sodium oxybate treatment as part of your clinical care at the Department of Neurology of the Mount Sinai Hospital. You will receive botulinum toxin as part of your clinical care by your otolaryngologist or neurologist. We will not perform botulinum toxin injections as part of this research study. If you are a healthy volunteer, you will have only one fMRI scan performed and you will not receive any treatment.

There will be four groups of subjects: 1) Healthy subjects 2) Patients with vocal tremor 3) Spasmodic dysphonia patients without vocal tremor 4) Spasmodic dysphonia patients with vocal tremor. The total number of people expected to take part in this research study is 95.

DESCRIPTION OF WHAT'S INVOLVED:

If you agree to participate in this research study, the following information describes what may be involved.

All research procedures, including history and physical examination and functional magnetic resonance imaging, will be conducted at the Mount Sinai Hospital. You will receive treatment with sodium oxybate, Xyrem®, as part of your clinical care at the Movement Disorders Clinic of the Department of Neurology, Mount Sinai Hospital. You will receive botulinum toxin injections at the office of your otolaryngologist or neurologist as part of clinical care, after which we will ask you to return to the Mount Sinai Hospital for the follow up fMRI study to assess the combined effects of botulinum toxin and sodium oxybate.

If you choose to participate, the following procedures (detailed below) will be performed.

1) History and Physical Examination
During the screening visit, we will explain the study to you. We will ask you about your medical history, including past and present medical problems, and specifically we will ask you about the when and how your voice disorder started. We will perform a physical examination, such as listening to your heart and lungs, to see if you are eligible to participate in the study. We will also record and videotape your voice and speech, unless you are a healthy volunteer. Your audio and video recorded voice and speech samples will not be identifiable, that is your name will be removed and replaces by a unique study code. Your digitally recorded audio and video files will not be discarded when this research study is completed. They will be saved on the password-secured computer located in the PI's office indefinitely. The recorded audio and video files will be shared between the investigators using password-secured encrypted disks dedicated to this protocol.

Would you agree to have your voice and speech recoded and videotaped?  Yes  No
Your voice and video recordings will be kept after the study is complete so that they can be used to review and publish in the future. They may also be used for long-term comparisons of how well the treatment works in the same patients. If you decide to withdraw from the study, you can request your recordings to be destroyed.

If you are a woman of childbearing potential, we will ask you to provide urine sample for a pregnancy test within 24 hours prior the MRI scan. The pregnancy test must be negative before proceeding with brain imaging.

2) Magnetic Resonance Imaging
MRI uses a strong magnetic field and radio waves instead of X-rays to obtain images of body organs and tissues. This technique is more sensitive than X-rays in some circumstances. There is no radiation exposure because X-rays are not used. The MRI scanner is a metal cylinder surrounded by a strong magnetic field. During the MRI, we will place you on a table that can slide in and out of the cylinder. In the scanner, you will hear loud knocking noise and you will wear earplugs to muffle the sound. You will be able to communicate with the MRI staff at times during your scan. We will conduct MRI for research purposes only. In this study, we will use the MRI machine to take a picture of your brain while you are simply lying still in the machine and performing some vocal tasks, such as producing syllables and short sentences. We will also perform high-resolution MRI to obtain anatomical images of your brain. You may have light meal prior to the MRI scanning.

If you are a healthy volunteer, you will have only one fMRI scan. If you are a patient, you will have two fMRI scans: one before and one after the treatment with sodium oxybate.

YOUR RESPONSIBILITIES IF YOU TAKE PART IN THIS RESEARCH:

If you decide to take part in this research study you will be responsible for the following things: taking the medication, sodium oxybate, as prescribed by Dr. Frucht at Mount Sinai Hospital, and participation in MRI research sessions.

COSTS OR PAYMENTS THAT MAY RESULT FROM PARTICIPATION:

If you agree to take part in this research study, we will pay you $50 for your time and effort at the completion of the study. Checks require some time to be prepared and will be given to you as available.

Tax law may require the Mount Sinai Finance Department to report the amount of payment you receive from Mount Sinai to the Internal Revenue Service (IRS) or other agencies, as applicable. Generally this reporting would take place if you receive payments that equal $600 or more from Mount Sinai in a calendar year. You would be responsible for the payment of any tax that may be due.

POSSIBLE BENEFITS:

This Section For IRB Official Use Only

This Consent Document is approved for use by Mount Sinai's Institutional Review Board (IRB)

Form Approval Date: 7/28/12  DO NOT SIGN AFTER THIS DATE ➔ 7/27/13

Rev. 2/1/2011

IRB Form HRP-502a
It is important to know that you may not get any benefit from taking part in this research. Others may not benefit either. However, possible benefits may include learning about how sodium oxybate might help improve patients' symptoms by positively affecting their brain. It is possible that other patients might benefit from participation in this research study, if sodium oxybate is developed as a symptomatic treatment for spasmodic dysphonia and vocal tremor.

**REASONABLY FORESEEABLE RISKS AND DISCOMFORTS:**

**MRI**
There are no known long-term risks or consequences of MRI scans. However, there might be possible risks and discomfort associated with MRI if you have either metal in your body, are pregnant, or fear of confined spaces.
1. People are at risk for injury from the MRI magnet if they have pacemakers or other implanted electrical 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, or shrapnel fragments. Welders and metal workers are also at risk for injury because of possible small metal fragments in the eye of which they may be unaware. We will screen you for these conditions prior to the study. If you have any, you will not receive an MRI scan. If you have a question about any metal objects being present in your body, you should inform the physician. In addition, all magnetic objects (for example, watches, coins, jewelry, and credit cards) must be removed before entering the MRI scanning room.
2. Women, who are pregnant, may not undergo a research MRI. Therefore, all women of childbearing potential will have a pregnancy test performed. This test must be negative, before proceeding. There are no known risks during pregnancy to having an MRI. There may be risks that are unknown.
3. Individuals with a fear of confined spaces may become anxious during an MRI.

**Loss of confidentiality**
There always exists the potential for loss of private information; however there are procedures in place to minimize this risk. In order to protect your privacy and confidentiality, we will replace your personal information, such as your name, with a code and will store the images of your brain and your data securely so that only members of the research team will see your information.

**OTHER POSSIBLE OPTIONS TO CONSIDER:**

You may decide not to take part in this research study without any penalty. The choice is totally up to you. The alternative to participate is not to participate.

**IN CASE OF INJURY DURING THIS RESEARCH STUDY:**

If you believe that you have suffered an injury related to this research as a participant in this study, you should contact the Principal Investigator.
ENDING PARTICIPATION IN THE RESEARCH STUDY:

You may stop taking part in this research study at any time without any penalty. This will not affect your ability to receive medical care at Mount Sinai or to receive any benefits to which you are otherwise entitled.

If you decide to stop being in the research study, please contact the Principal Investigator or the research staff.

You may also withdraw your permission for the use and disclosure of any of your protected information for research, but you must do so in writing to the Principal Investigator at the address on the first page. Even if you withdraw your permission, the Principal Investigator for the research study may still use the information that was already collected if that information is necessary to complete the research study. Your health information may still be used or shared after you withdraw your authorization if you should have an adverse event (a bad effect) from participating in the research study.

Withdrawal without your consent: The study doctor, the sponsor or the institution may stop your involvement in this research study at any time without your consent. This may be because the research study is being stopped, the instructions of the study team have not been followed, the investigator believes it is in your best interest, or for any other reason. If specimens or data have been stored as part of the research study, they too can be destroyed without your consent.

CONTACT PERSON(S):

If you have any questions, concerns, or complaints at any time about this research, or you think the research has hurt you, please contact the office of the research team and/or the Principal Investigator at phone number 212-241-0656.

This research has been reviewed and approved by an Institutional Review Board. You may reach a representative of the Program for Protection of Human Subjects at Mount Sinai School of Medicine at telephone number (212) 824-8200 during standard work hours for any of the following reasons:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You are not comfortable talking to the research team.
- You have questions about your rights as a research subject.
- You want to get information or provide input about this research.

DISCLOSURE OF FINANCIAL INTERESTS:

None.
MAINTAINING CONFIDENTIALITY – HIPAA AUTHORIZATION:

As you take part in this research project it will be necessary for the research team and others to use and share some of your private protected health information. Consistent with the federal Health Insurance Portability and Accountability Act (HIPAA), we are asking your permission to receive, use and share that information.

What protected health information is collected and used in this study, and might also be disclosed (shared) with others?

As part of this research project, the researchers will collect your Name, Address, Date of Birth, Telephone number and E-mail address. The researchers will also get information from your medical record from your private doctor about your health status.

During the study the researchers will gather information by:

- taking a medical history (includes current and past medications or therapies, illnesses, conditions or symptoms, family medical history, allergies, etc.)
- doing a physical examination that generally also includes blood pressure reading, heart rate, breathing rate and temperature
- completing the tests and procedures explained in the description section of this consent
- recording and videotaping your voice and speech.

The researchers will also get information from your medical record at Mount Sinai Hospital or from your private doctor.

During the study the researchers will gather information by:

- taking a medical history (includes current and past medications or therapies, illnesses, conditions or symptoms, family medical history, allergies, etc.)
- doing a physical examination that generally also includes blood pressure reading, heart rate, breathing rate and temperature
- completing the tests, procedures, questionnaires and interviews explained in the description section of this consent.

Why is your protected health information being used?

Your personal contact information is important to be able to contact you during the study. Your health information and the results of any tests and procedures being collected as part of this research study will be used for the purpose of this study as explained earlier in this consent form. The results of this study could be published or presented at scientific meetings, lectures, or other events, but would not include any information that would let others know who you are, unless you give separate permission to do so.

The research team and other authorized members of The Mount Sinai Hospital and Mount Sinai School of Medicine (together, “Mount Sinai”) workforce may use and share your information to ensure that the research meets legal, institutional or accreditation requirements. For example, the Mount Sinai School of Medicine Program for the Protection of Human Subjects is responsible for overseeing research on human subjects, and may need to see your information. If you receive any payments for taking part in this study, the Mount Sinai Medical Center Finance Department may need your name,
address, social security number, payment amount, and related information for tax reporting purposes. If the research team uncovers abuse, neglect, or reportable diseases, this information may be disclosed to appropriate authorities.

Who, outside Mount Sinai, might receive your protected health information?

As part of the study, the Principal Investigator, study team and others in the Mount Sinai workforce may disclose your protected health information, including the results of the research study tests and procedures, to the following people or organizations: (It is possible that there may be changes to the list during this research study; you may request an up-to-date list at any time by contacting the Principal Investigator.)

- The United States Food and Drug Administration
- The United States Department of Health and Human Services and the Office of Human Research Protection.
- Others: the Office of Human Research Protection

In all disclosures outside of Mount Sinai, you will not be identified by name, social security number, address, telephone number, or email unless disclosure of the direct identifier is required by law. Some records and information disclosed may be identified with a unique code number. The Principal Investigator will ensure that the key to the code will be kept in a locked file, or will be securely stored electronically. The code will not be used to link the information back to you without your permission, unless the law requires it, or rarely if the Institutional Review Board allows it after determining that there would be minimal risk to your privacy. It is possible that a sponsor or their representatives, a data coordinating office, a contract research organization, will come to inspect your records. Even if those records are identifiable when inspected, the information leaving the institution will be stripped of direct identifiers. Additionally, the monitors, auditors, the IRB, the Food and Drug Administration will be granted direct access to your medical records for verification of the research procedures and data. By signing this document you are authorizing this access. We may publish the results of this research. However, we will keep your name and other identifying information confidential.

For how long will Mount Sinai be able to use or disclose your protected health information? Your authorization for use of your protected health information for this specific study does not expire.

Will you be able to access your records?

During your participation in this study, you will have access to your medical record and any study information that is part of that record. The investigator is not required to release to you research information that is not part of your medical record.

Do you need to give us permission to obtain, use or share your health information?

NO! If you decide not to let us obtain, use or share your health information you should not sign this form, and you will not be allowed to volunteer in the research study. If you do not sign, it will not affect your treatment, payment or enrollment in any health plans or affect your eligibility for benefits.

Can you change your mind?

You may withdraw your permission for the use and disclosure of any of your protected information for research, but you must do so in writing to the Principal Investigator at the address on the first page.

This Section For IRB Official Use Only

This Consent Document is approved for use by Mount Sinai's Institutional Review Board (IRB)

Form Approval Date: 7/28/12

DO NOT SIGN AFTER THIS DATE \rightarrow 7/27/13

Rev. 2/1/2011

IRB Form HRP-502a
Even if you withdraw your permission, the Principal Investigator for the research study may still use your protected information that was already collected if that information is necessary to complete the study. Your health information may still be used or shared after you withdraw your authorization if you should have an adverse event (a bad effect) from being in the study. If you withdraw your permission to use your protected health information for research that means you will also be withdrawn from the research study, but standard medical care and any other benefits to which you are entitled will not be affected. You can also tell us you want to withdraw from the research study at any time without canceling the Authorization to use your data.

It is important for you to understand that once information is disclosed to others outside Mount Sinai, the information may be re-disclosed and will no longer be covered by the federal privacy protection regulations. However, even if your information will no longer be protected by federal regulations, where possible, Mount Sinai has entered into agreements with those who will receive your information to continue to protect your confidentiality.

If as part of this research project your medical records are being reviewed, or a medical history is being taken, it is possible that HIV-related information may be revealed to the researchers. If that is the case, the information in the following box concerns you. If this research does not involve any review of medical records or questions about your medical history or conditions, then the following section may be ignored.

---

Notice Concerning HIV-Related Information

If you are authorizing the release of HIV-related information, you should be aware that the recipient(s) is (are) prohibited from re-disclosing any HIV-related information without your authorization unless permitted to do so under federal or state law. You also have a right to request a list of people who may receive or use your HIV-related information without authorization. If you experience discrimination because of the release or disclosure of HIV-related information, you may contact the New York State Division of Human Rights at (212) 460-2522 or the New York City Commission of Human Rights at (212) 306-5070. These agencies are responsible for protecting your rights.
Signature Block for Capable Adult
Your signature below documents your permission to take part in this research and to the use and disclosure of your protected health information. A signed and dated copy will be given to you.

DO NOT SIGN THIS FORM AFTER THIS DATE → 7/27/13

Signature of subject

Date and Time

Printed name of subject

Person Explaining Study and Obtaining Consent

Signature of person obtaining consent

Date and Time

Printed name of person obtaining consent

If the individual cannot read, a witness is required to observe the consent process and document below:
My signature below documents that the information in the consent document and any other written information was accurately explained to, and apparently understood by, the subject, and that consent was freely given by the subject.

Signature of witness to consent process

Date and Time

Printed name of person witnessing consent process

This Section For IRB Official Use Only
This Consent Document is approved for use by Mount Sinai’s Institutional Review Board (IRB)
Form Approval Date: DO NOT SIGN AFTER THIS DATE → 7/27/13
Rev. 2/1/2011
IRB Form HRP-502a