Underlying mechanisms of obesity-induced obstructive sleep apnea

The traditional risk factors for obstructive sleep apnea (OSA) are weight and age. Individuals with sleep apnea may experience periods of time where their breathing is reduced or completely stops due to closure of the upper airway. Untreated OSA is associated with major neurocognitive and cardiovascular issues. Obesity is a major risk factor for OSA, however, it is unclear how obesity may cause or be contributing to OSA. Given the rising prevalence of obesity and lack of effective therapies for sleep apnea patients, it is important to understand the relationship between the two. The study will examine upper airway functionality and other traits associated with OSA in bariatric surgery patients. OSA patients and people without OSA will be enrolled.

University of California, San Diego
Consent to Act as a Research Subject

Underlying mechanisms of obesity-induced obstructive sleep apnea

Introduction

Dr. Atul Malhotra and associates are conducting this research and asking for your consent to participate. This section provides a summary of important information. The rest of the form provides additional details.

- Research is voluntary - whether or not you join is your decision. You can discuss your decision with others (such as family and friends).
- You can say yes but change your mind later.
- If you say no, we will not hold your decision against you.
- Your decision will not affect your health care or any other benefits you may be entitled to.
- You can say no even if the person inviting you is part of your healthcare team.
- Please ask questions or mention concerns before, during or after the research.

The study is being conducted to investigate the relationship between obesity and obstructive sleep apnea, which may lead to alternative treatment options for this patient population. Participation in the study may or may not benefit you directly, and may result in new knowledge that may help others.

If you agree to be in this study, the following will happen to you:

1) A standard overnight sleep study (Overnight Visit #1) to assess obstructive sleep apnea severity and a blood draw will be completed. You will have a basic health exam and report on your health status. You will also complete questionnaires, heart and lung function assessments, and a computerized reaction assessment.
2) A research sleep study (Overnight Visit #2) to measure the traits the affect OSA, and
3) An MRI of your upper airway (MRI Visit #1) during the day or evening.

You will be asked to participate in a 6-month follow-up where you repeat the three visits, after your bariatric surgery. You will undergo:

4) A standard sleep study (Overnight Visit #4)
5) A research sleep study (Overnight Visit #5)
6) An MRI of your upper airway (MRI Visit #2)

You will be asked to arrive at the UCSD Sleep Laboratory at approximately 8pm in order to go through an orientation process and to start the procedures of the sleep study. The following procedures will be performed at the Altman Clinical Translational Research Institute Clinic, 9452 Medical Center Dr, La Jolla, CA 92037. All overnight sleep studies will be hosted at this location.

Overnight Visit #1:

Before sleep, you will complete a basic health exam – height, weight, neck/hip/waist circumference, and vitals will be taken. You will complete questionnaires related to your sleep and general quality of life. You will take part in a non-invasive measure of blood vessel function, which involves siting with a blood pressure cuff on your arm for a few minutes. You will then complete a lung function assessment where you are asked to breath in and out through a mouthpiece. You will also complete a 5-minute computerized reaction assessment.

To prepare you for the sleep study, you will have sensors pasted on your scalp, face, chest, and legs that will help determine when you are asleep or awake. A microphone will be placed on your neck to monitor snoring. A small vital sign monitor will be taped to your finger to read additional vital signs. An adhesive body position sensor will be placed on your body to monitor what position you are sleeping in, and the volume of your chest while breathing. Almost all of this equipment is standard for a diagnostic sleep study and should not be uncomfortable.

We will also take 2-3 teaspoons of blood. Please note that this blood will be separated into serum and plasma for analysis to find links between other diseases. We will not be using this blood sample for DNA analysis.

If you consent to giving blood or tissue specimens as part of this study, these specimens will become the property of the University of California. The blood samples will not be shared with other researchers/institutions outside of University of California, San Diego,

The study will end at approximately 6AM, all the monitoring equipment will be removed, and you will be allowed to go home. A member of the research team will assess your level of sleepiness before you leave.

Overnight Visit #2:

You will return to the UCSD sleep laboratory. A nasal mask will be placed over your nose and secured.

A nasal mask will be placed over your nose and secured. Attached to the mask will be a flow meter for measurement of air flow as you breath. Your mouth will be either gently taped closed or a chin strap applied to ensure you breathe through your nose. Mask pressure and carbon dioxide will be continuously analyzed from the air you breathe. A modified continuous positive airway pressure (CPAP) device that delivers both positive and negative airway pressure will be connected to the mask. The CPAP device is commonly used to treat obstructive sleep apnea in the home setting. After you go to sleep, the CPAP pressure will be increased and decreased throughout the night so to measure your upper airway response to the different CPAP pressures. A second machine, a standard CPAP machine, will also be used to make the same measurements. A small vital sign monitor will be taped to your finger. After the pressure measurements are completed, the CPAP will be either returned to the beginning pressure or stopped and the mask removed. You will be allowed to continue sleeping. Of note, for the majority of the night your CPAP will be at your therapeutic pressure.

The study will end at approximately 4AM, at which time all the monitoring equipment will be removed, and you will be allowed to go home. A member of the research team will assess your level of sleepiness before you leave.

In some cases, the quality of your sleep may not allow us to get all the data we need. In these cases, you may be invited back for an additional overnight stay. However, you are under no obligation to participate in the extra overnight study.

Are you willing to be contacted for the extra overnight visits, if needed? You will be compensated for the additional study night ($100).

☐ Yes ☐ No Initials _____

The following procedure will be performed after the overnight sleep study #1 at the Radiology Imaging Laboratory at 3510 Dunhill Street, San Diego, CA 92121:

MRI Visit #1

You will be asked to have a magnetic resonance scan performed at the Radiology Imaging Laboratory (RIL). No anesthesia will be used for this procedure. The scan will involve you lying inside the center of a large, doughnut shaped magnet for approximately an hour. Magnetic resonance imaging scans (MRI's) are simply pictures of the upper airways that can be obtained by the use of a magnetic field and radio frequencies around the head and upper torso. Data about the structure of your upper airways will be collected. Before scanning, headphones and a face mask will be placed on you. Paste-on electrodes (pads with wires attached) will be applied to your scalp and face to monitor your wakefulness and sleep during the scan. Your head will be placed in a special, helmet-like head coil with which signals will be collected. Pneumatic belts will be placed around your abdomen, and you will be covered with a weighted blanket for warmth and motion reduction. You will hear loud knocking sounds as images are being made. You will be asked to rest relaxed in the scanner for 60 to 90 minutes. You will be able to communicate with the research personnel operating the machine at all times, for a microphone is present in the scanner room.

We will ask you to arrive for your scheduled appointment between 8AM-6PM. We ask you to refrain from napping or caffeine that day prior to your visit.

Are you willing to be contacted for MRI visits, if needed? You will be compensated for the additional visit ($100).

☐ Yes ☐ No Initials _____

We will schedule the three visits above before your bariatric surgery. Six months after you complete the surgery, you will complete a repeat of the three visits ─ a standard overnight sleep

study (overnight study #3), research sleep study (overnight study #4), and MRI visit (MRI visit #2).

The most commonly expected risks of the study are feeling sleepy the next morning after your overnight sleep studies, having nasal dryness from use of the CPAP mask during the research sleep study, and having temporary discomfort after your blood draw.

The most serious risks of the study may include feeling claustrophobic or anxiety in the MRI, allergic skin reactions from placement of the sensors and electrodes, and infection from venipuncture (blood draw).

Additional detailed information about this research is provided below. Please feel free to ask questions before signing this consent.

Why have you been asked to participate, how you were selected, and what is the approximate number of participants in the study?
You have been asked to participate in this study because you are scheduled for bariatric surgery. There will be approximately 110 participants enrolled in this study at UCSD.

What will happen to you in this study and which procedures are standard of care and which are experimental?
The overnight sleep studies and MRI visits are voluntary study activities and separate from your standard of care. Your bariatric surgery is part of your standard of care, but not completed by our research personnel. If you choose not to undergo bariatric surgery, you will be withdrawn from remaining study activities.

How much time will each study procedure take and how long will the study last?

1) Overnight Visit #1 will last 10 hours (mostly sleeping)
2) Overnight Visit #2 will last 8 hours (mostly sleeping)
3) MRI Visit #1 will approximately 5 hours

The final three visits will be completed 6-months after your bariatric surgery:

4) Overnight Visit #3 will last 10 hours (mostly sleeping)
5) Overnight Visit #4 will last 8 hours (mostly sleeping)
6) MRI Visit #2 will be approximately 5 hours

What risks are associated with this study?
Participation in this study may involve some added risks or discomforts. In addition to the risks described at the beginning of this form,

Risks of Sleep Studies: During the sleep studies, there may be discomfort at the electrodes or monitors sites that can develop; a localized skin irritation/allergy can occur due to application of the skin surface electrodes for EEG, EKG, and EMG recordings. Similarly, the CPAP mask can cause temporary skin irritation, nasal congestion, and/or nasal dryness.

Short periods of apnea during the study might occur when the CPAP pressure is turned down. However, these would not be expected to cause side effects, other than the possibility of awakening from sleep.

You might be sleepy the next morning after participating in the study. After the end of the sleep study, you will have the option of sleeping without equipment for as long as you would like before leaving. If you do not feel rested and safe to drive home, you will be provided with a cab voucher. Consider asking someone to drive you to and from the studies.

Risks of a blood draw/blood pressure test: You may have temporary pain or discomfort during the blood draw or endothelial function test.

Risks of the breathing tests: You may feel short of breath or lightheaded during breathing responses testing. More serious reactions, including seizure or respiratory distress have been reported but are extremely rare, and you will be carefully monitored.

Risks of MRI: The imager makes a loud, banging noise while it is taking pictures. You will be given a set of ear plugs to help with the noise. You may experience feelings of claustrophobia or anxiety. You may also experience some discomfort and tiredness from lying still in a confined space during the imaging. There are no known effects from exposure to magnetic fields (MRI). However, some subjects undergoing this procedure become anxious. If this happens to you, you can stop the procedure at any time. If you have metal clips or plates in your body or a pacemaker, you should tell your doctor about it. MRI may not be appropriate under some of the following conditions: a cardiac pacemaker; metal fragments in eyes, skin, or body; heart valve replacement; brain clips; venous umbrella; being a sheet-metal worker or welder; aneurysm surgery; intracranial bypass; renal or aortic clips; prosthetic devices such as middle ear, eye, joint, or penile implants; joint replacements; hearing aid; neurostimulator; insulin pump; I.U.D.; being pregnant or trying to become pregnant; shunts/stents; metal mesh/coil implants; metal plate/pin/screws/wires, or any other metal implants; and permanent eyeliner and/or eyebrows.

Risks of an Incidental Finding: The MRI scan protocol has been designed for research purposes, not for clinical diagnostic purposes. All analysis will be done only by research staff for the purposes of our research study only. The scans will not be reviewed by a radiologist. However, it is possible that an abnormality may be identified. In that case, a written report of the abnormality will be share with you and you may be recommended to seek appropriate evaluation with your primary care doctor.

Risks of Loss of Confidentiality: Even with all of the study procedure precautions that will be taken to protect confidentiality, there is a still a risk of loss of confidentiality associated with this study. Research records will be kept confidential to the extent allowed by law. The study personnel are well trained in securing and safely storing all your data.

Unknown Risks: Because this is a research study, there may be some unknown risks that are currently unforeseeable. You will be informed of any significant new findings.

Are there risks to the reproductive system or a developing fetus?

Stress or anxiety potentially experienced during the MRI or any research procedures may pose a risk on a developing fetus. For this reason, if you become pregnant, we will not be able to participate in this study. After you have been enrolled in this study and during the research, pregnancy testing will be performed. If you have a positive pregnancy test, we may withdraw you from the study. If you become pregnant or if there is any chance of pregnancy (e.g., late menstrual period), please contact the study personnel immediately so that we may provide medical assistance and counseling.

What are the alternatives to participating in this study?
The alternatives to participation in this study are not to participate in the study.

What benefits can be reasonably expected?
There is no direct benefit to you for participating in this study. Benefits of this study are principally to science and future patients, in that we may be able to identify traits associated with obstructive sleep apnea in obese patients as well as a new and clinically useful treatment methods. This information may be useful to clinicians.

What happens if you change your mind about participating?
If you decide that you no longer wish to continue in this study, you will be requested to reach out to a member of our research team. We will terminate any of your remaining study activities.

Can you be withdrawn from the study without your consent?

You may be withdrawn from the study for the following reasons:

- You become ill,
- Are required to use medications that are known to disrupt sleep,
- Become injured and cannot get around without assistance.

You may also be withdrawn from the study if you do not follow the instructions given you by the study personnel.

Will you be compensated for participating in this study?
In compensation for your time and travel, you will receive $600 for participating in this research.

- Overnight Visit #1: $100
- Overnight Visit #2: $100
- MRI Visit #1: $100
- 6 Month Follow up Overnight PSG: $100
- 6 month Follow up Research overnight: $100
- 6 Month Follow up MRI: $100
- If data is inconclusive and an additional polysomnogram night or MRI visit is required, you will be paid $100.

Personal information about you, including your name, address, and social security number, will be released to the UCSD Accounting Office for the purpose of payment and for tax reporting to the Internal Revenue Service (IRS).

Parking will be available free of charge and participants will also be reimbursed for minor out of pocket expenses including meal vouchers, public transportation or taxi vouchers. If the subject terminates the study early, they will receive an amount based on the visits that have been completed. If any of the visits are missed, the subject will not be compensated for those visits.

Are there any costs associated with participating in this study?
There will be no cost to you for participating in this study. Parking expenses at UCSD study sites will be covered.

What if you are injured as a direct result of being in this study?
If you are injured as a direct result of participation in this research, the University of California will provide any medical care you need to treat those injuries. The University will not provide any other form of compensation to you if you are injured. You may call the Human Research Protections Program Office at (858) 246-4777 for more information about this, to inquire about your rights as a research subject or to report research-related problems.

What about your confidentiality?
Research records will be kept confidential to the extent allowed by law. To guard your confidentiality, you will be assigned a unique identifying number to label all your data collection sheets. All personal information will be kept strictly confidential by the investigators. All study forms, and data collected will be kept locked in a secure location. All your data forms will only list your unique study ID number. All research staffs are trained in the protection of subject privacy and confidentiality. Research records may be reviewed by the UCSD Institutional Review Board, or the study Sponsor, the National Institute of Health (NIH). .

Because of the need to release information to these parties, absolute confidentiality cannot be guaranteed. The results of this research study may be presented at meetings or in publications; however, your identity will not be disclosed in those presentations.

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.

Biospecimens (such as blood) collected from you for this study and/or information obtained from your biospecimens may be used in this research or other research. You will not share in any commercial value or profit derived from the use of your biospecimens and/or information obtained from them.

Will you receive any results from participating in this study?
Letters summarizing the results of your overnight sleep studies will be provided. If any clinical relevant research results are found during the sleep studies or MRI visits, a written report of the abnormality will be share with you and you may be recommended to seek appropriate evaluation

with your primary care doctor.

Who can you call if you have questions?
This study has been explained to you and your questions have been answered. If you have other questions or research-related problems, you may reach Dr. Atul Malhotra and his research study coordinators at (858) 246-2154.

You may call the Human Research Protections Program Office at 858-246-HRPP (858-246-4777) to inquire about your rights as a research subject or to report research-related problems.

Your Signature and Consent
You have received a copy of this consent document and a copy of the "Experimental Subject's Bill of Rights" to keep.

You agree to participate.

_____ _____
Subject's signature Date

_____ _____
Signature of the person conducting the informed consent discussion Date