Washington University in St. Louis

INFORMED CONSENT DOCUMENT

Project Title: **Closed Loop Acoustic Stimulation during Sedation with Dexmedetomidine (CLASS-D)**

Principal Investigator: **Ben Palanca, MD PhD**

Research Team Contact: **Christian Guay, MD (314-599-2922)**

This consent form describes the research study and helps you decide if you want to participate. It provides important information about what you will be asked to do during the study, about the risks and benefits of the study, and about your rights and responsibilities as a research participant. By signing this form you are agreeing to participate in this study.

- You should read and understand the information in this document including the procedures, risks and potential benefits.
- If you have questions about anything in this form, you should ask the research team for more information before you agree to participate.
- You may also wish to talk to your family or friends about your participation in this study.
- Do not agree to participate in this study unless the research team has answered your questions and you decide that you want to be part of this study.

WHAT IS THE PURPOSE OF THIS STUDY?

This is a research study. We invite you to participate in this research study because you are a healthy adult.

The purpose of this study is to find out how acoustic stimulation (also called Pink Noise) along with use of the sedative dexmedetomidine affects a person's brain waves as measured by an electroencephalogram (EEG).

To administer dexmedetomidine, we will use a target-controlled infusion using the Rugloop II software. Rugloop II is considered investigational, which means that it has not been approved by the U.S. Food and Drug Administration.

You will be asked to squeeze a ball while the dose of dexmedetomidine is increased to a level that produces certain brain wave patterns in your EEG.

Dexmedetomidine is approved by the U.S. Food and Drug Administration to provide sedation.

We may use the DREEM device which is a lightweight headband sleep-monitor device, designed to record your brain waves and heart rate. In addition, we may use an actigraphy watch to acquire data. Neither device is approved by the U.S. Food and Drug Administration for clinical purposes.

WHAT WILL HAPPEN DURING THIS STUDY?

The study procedures will be performed in Barnes-Jewish Hospital, within clinical areas typically used for sedation prior to surgical procedures.

Pregnancy test results will be disclosed. Other data can be given to you based on your request but will not be useable for clinical diagnoses.

After you sign the consent, your participation will begin and you will have the following procedures:

- Sleep questionnaires (in light of COVID-19 concerns, we may email or text you a link to complete our surveys electronically via REDCap, which is a secure database system for collecting research answers)
- Home sleep studies
- Administration of a FDA-approved sedative called dexmedetomidine
- Blood draws
- An electroencephalogram (EEG)
- Vital signs taken
- Acoustic stimulation
- Quantitative Sensory Testing (QST) using a Thermal Sensory Analyzer (TSA)

Visit 1

Visit one is expected to last approximately two hours. At this visit we will ask you to complete questionnaires about your sleep. You are free to skip any questions of the questionnaires that you would prefer not to answer. We will also perform baseline Quantitative Sensory Testing (QST) using a Thermal Sensory Analyzer (TSA). This involves applying gradually increasing amounts of heat to your forearm until you press a button when you feel pain. The amount of heat that can be applied by the TSA is much lower than the amount required to injure your skin. We will also provide instructions for completing multiple home sleep studies using a DREEM device, which is a consumer-grade sleep-monitor device designed to record your brain waves and heart rate. The DREEM device was also designed to deliver small amounts of acoustic stimulation to enhance natural sleep. This feature may be used during multiple home sleep studies. We will also provide you with an actigraphy watch to record sleep duration during the nights preceding and following your sedation session.
Alternate Operations Due to COVID-19: The research team will send a lightweight headband to your home. We will email or text you a link to an instructional video to show you how to use the device and a link to complete our surveys electronically. Before going to sleep, you will be asked to stay awake with your eyes open for 4 minutes followed by eyes closed for 4 minutes while wearing the headband. We will contact you before and after each day of recording to assist you in this process. Depending on your convenience, we will ask you to bring the DREEM back on the day of your first visit or ship the device back to us using a prepaid shipping package.

Visit 2

Visit two is expected to last approximately 4 – 8 hours and is the day we administer dexmedetomidine via an intravenous (IV) line, introduce intermittent bursts of pink noise (broadband sound, similar to

white noise) and measure the effects of both using EEG measurements. We will also start a second IV line so that we may obtain blood samples at two time points during the visit. Each blood sample will equal 5 ml, which is approximately one teaspoon.

There are six phases of this visit.

- Phase 1: We will start the EEG to track your brain waves, start administering dexmedetomidine, and ask you to squeeze a ball when you breathe in and release it when you breathe out.

- Phase 2**:** We will continue administering dexmedetomidine as you squeeze the ball.. Additionally, we will start delivering intermittent pink noise.

- Phase 3: We will increase the dexmedetomidine infusion until you stop squeezing the ball.

- Phase 4: We will continue tracking your brain waves and continue the administration of dexmedetomidine. Additionally, we will resume delivering intermittent pink noise. If you hear the noise, resume the task of squeezing the ball.

- Phase 5: We will continue tracking your brain waves, administering dexmedetomidine, and intermittently delivering pink noise. Additionally, we will wake you up three times using small heat to your forearm using the Thermal Sensory Analyzer (TSA) in the same manner as we did during baseline (visit 1) quantitative sensory testing (QST). Immediately after we wake you up, we will ask you to report any memories and to rate your pain on a visual analog scale. When you are woken up in this way, you will resume the task of squeezing the ball.

- Phase 6: We will stop administering dexmedetomidine and continue tracking your brain waves as you naturally wake up. We may also intermittently deliver pink noise as you wake up. When you wake up, you will resume the task of squeezing the ball. We will then ask you to complete another set of sleep questionnaires.

Because you are being given sedation, you will have recovery time in either the Post-Anesthesia Care Unit (PACU) or the Clinical Translational Research Unit (CTRU) and will not be discharged until your vital signs are stable. You will also be required to have a family member/relative or friend drive you home. You will not be able to drive for 24 hours as you may feel a little drowsy, and perhaps dizzy for several hours after the visit.

Visit 3

Visit three is for a subset of participants who will be invited to complete a non-contrast brain MRI at a later date.

An MRI scanner takes pictures of the inside of your body by sending out a magnetic field and radio waves. Because the MRI scanner contains a very strong magnet, you may not be able to have the MRI if you have certain kinds of metal in your body (for example, from medical devices or a metal plate). Someone will ask you questions about this before you have the MRI.

The MRI scanner is a large machine that contains a hollow tube. You will be asked to lie on your back on a special table that slides into the tube. The sides of the tube will be fairly close to your body and the scanner makes a loud hammering noise while you are inside.

As part of this study, we are obtaining data on your sleep quality, brain signals, brain structure, and blood levels of dexmedetomidine. These may be used for commercial profit (even if we remove your identifiable information.) There are no plans to provide financial compensation to you should this occur. By allowing us to use your blood samples, body signals, brain signals and images, you give up any property rights you may have in the blood samples, body signals, brain signals and images.

Will you save my research information [and/or biospecimens to use in future research studies?

We would like to use the data and blood samples we are obtaining in this study for studies going on right now as well as studies that are conducted in the future. These studies may provide additional information that will be helpful in understanding sedation and acoustic stimulation, or other diseases or conditions, including research to develop investigational tests, treatments, drugs or devices that are not yet approved by the U.S. Food and Drug Administration. It is unlikely that what we learn from these studies will have a direct benefit to you. There are no plans to provide financial compensation to you should this occur. By allowing us to use your data and blood samples you give up any property rights you may have in the data and blood samples.

We might remove identifiers from your private information and your data and blood samples and then use the information and your data and blood samples for future research studies or share them with other researchers for their future research. If this occurs we will not ask you for additional consent for these uses of your information or data and blood samples.

We will share your blood drug levels, brain signals, brain images, and body signals with other researchers. They may be doing research in areas similar to this research or in other unrelated areas. These researchers may be at Washington University, at other research centers and institutions, or industry sponsors of research. We may also share your research data with large data repositories (a repository is a database of information) for broad sharing with the research community. If your individual research data is placed in one of these repositories only qualified researchers, who have received prior approval from individuals that monitor the use of the data, will be able to look at your information.

Your data and blood samples will be stored without your name or any other kind of link that would enable us to identify which sample(s) or data are yours. Therefore, it will be available for use in future research studies indefinitely and cannot be removed.

Audio Recording/Video Recording/Photographs

One aspect of this study involves making video recordings of you during the six phases of visit 2. These video recordings will allow the research team to determine precisely the times at which you become sedated and wake up during the experiment. Only members of the research team will have access to these videos. The videos will be stored on a physical hard drive and kept in a secured location accessible only via key by research personal. The videos will not be destroyed.

HOW MANY PEOPLE WILL PARTICIPATE?

Approximately 30 people will take part in this study conducted by investigators at Washington University.

HOW LONG WILL I BE IN THIS STUDY?

You will have up to 3 visits in this study and your participation may last up to 3 months. Study visit one will last approximately 1-2 hours. Three days later, study visit two will last approximately 4-8 hours. The third visit is a non-contrast brain MRI that will be offered to a subset of participants. If you are not asked to do the brain MRI, your participation is expected to last 4 days.

WHAT ARE THE RISKS OF THIS STUDY?

You may experience one or more of the risks indicated below from being in this study. In addition to these, there may be other unknown risks, or risks that we did not anticipate, associated with being in this study.

EEG

Less Likely: small skin abrasions at the site of electrodes. Care will be taken to minimize pressure at the electrode sites.

Rare: inflammatory reaction of skin to electrode gel.

Dexmedetomidine

Less Likely: high blood pressure, low blood pressure, high heart rate, low heart rate, prolonged recovery time. These vitals signs are continuously monitored and medications are ready to be administered to reverse them, as is standard during sedation and procedures in the hospital.

Rare: allergic reaction, decreased breathing rate. You will be attended by an anesthesia provider during sedation, with all standard sedation and airway management equipment available should any adverse events occur. Abnormal heart rhythm, which in rare instances may cause death; difficulty breathing; fever, abnormal liver , kidney function tests or alterations in blood electrolyte levels; abdominal pain or upset; dizziness, headache, nerve pain, speech disorder, seizure, changes in mental status; sweating, abnormal vision, anemia.

Acoustic Stimulation

Less Likely: sore ears from prolonged wearing of ear phones.

Rare: hearing damage as a result of high intensity sounds delivered during sedation. To reduce this risk, a maximal volume of 80 decibels will be pre-set on the sound delivery device, which is equivalent to a standard ringing telephone.

Blood Draws

Less Likely: Pain or bruising at site of blood draw if performed by needle stick.

Rare: Risk of contamination involved with the catheter method of obtaining blood. Occasionally some people experience dizziness or feel faint. Infection.

Quantitative Sensory Testing (QST) / Thermal Sensory Analyzer (TSA)

Less Likely: irritation or small abrasions at the thermode site.

Rare: superficial skin damage. The levels of thermal energy required to induce skin injury are reported to be one thousand times higher than the maximum amount of energy that can be delivered by the TSA.

Women Capable of Becoming Pregnant
If you are a woman capable of becoming pregnant, we will ask you to have a pregnancy test before beginning this study. You must use effective birth control methods and try not to become pregnant while participating in this study. If you become pregnant, there may be unknown risks to your unborn child, or risks to your unborn child that we did not anticipate. There may be long-term effects of the treatment being studied that could increase the risk of harm to an unborn child. You must tell the doctor if your birth control method fails while you are on the study. If you believe or know you have become pregnant while participating in this research study, please contact the research team member identified at the top of this document as soon as possible. Please discuss with the research team how long you need to wait before becoming pregnant after completing the treatment or procedures on this study.

MRI scans

Common risks:

- discomfort inside the MRI scanner if you do not like to be in closed spaces ("claustrophobia")
- muscle stiffness from lying still
- muscle cramping caused by nerve stimulation
- tissue heating which may cause you to feel very warm

Rare risks:

- hearing loss due to the loud hammering noise from the MRI scanner
- sensation of flashing lights while in the MRI scanner
- burns that could be serious

During the procedure, you will be able to talk with the MRI staff through a speaker system. You will be given earplugs to reduce the risk of hearing loss. If you experience any of these symptoms and do not wish to continue, you can ask that the scan be stopped immediately.

Devices
If you have a device such as a pacemaker, bone hardware, cardiac stent, or device placed in your uterus there may be additional risks. We will review what device you have and inform you of these risks. In general, these risks could be:

- heating or movement of the device
- device malfunction
- damage to the tissue that surrounds the device.

Breach of Confidentiality

One risk of participating in this study is that confidential information about you may be accidentally disclosed. We will use our best efforts to keep the information about you secure. Please see the section in this consent form titled *"How will you keep my information confidential?"* for more information.

WHAT ARE THE BENEFITS OF THIS STUDY?

You will not benefit from being in this study.

However, we hope that, in the future, other people might benefit from this study because we will know if the use of auditory stimuli can enhance slow waves and their physiological effects during sedation.

WILL IT COST ME ANYTHING TO BE IN THIS STUDY?

You will not have any costs for being in this research study.

WILL I BE PAID FOR PARTICIPATING?

You will be paid for being in this research study. You will need to provide your social security number (SSN) in order for us to pay you. You may choose to participate without being paid if you do not wish to provide your social security number (SSN) for this purpose. You will also need to provide your address so that we can mail a check to you. You can expect payment approximately one month after completion of your participation in the study. If your social security number is obtained for payment purposes only, it will not be retained for research purposes.

Compensation is broken down as follows:

- $180 for Visit 2
- $20 for the home sleep studies
- $50 for the MRI scan
- **$250 for completion of all study procedures**

WHO IS FUNDING THIS STUDY?

The University and the research team are not receiving payment from other agencies, organizations, or companies to conduct this research study.

WHAT IF I AM INJURED AS A RESULT OF THIS STUDY?

Washington University investigators and staff will try to reduce, control, and treat any complications from this research. If you feel you are injured because of the study, please contact Dr. Ben Palanca at 314-273-9076 or Dr. Christian Guay at 314-599-2922 and/or the Human Research Protection Office at 1-(800)-438-0445.

Decisions about whether payment for medical treatment for injuries relating to your participation in research will be made by Washington University. If you need to seek medical care for a research-related injury, please notify the investigator as soon as possible.

HOW WILL YOU KEEP MY INFORMATION CONFIDENTIAL?

Other people such as those indicated below may become aware of your participation in this study and may inspect and copy records pertaining to this research. Some of these records could contain information that personally identifies you. We will keep your participation in this research study confidential to the extent permitted by law.

- Government representatives (including the Office for Human Research Protections) to complete federal or state responsibilities
- The U.S. Food and Drug Administration
- Hospital or University representatives to complete Hospital or University responsibilities
- Information about your participation in this study may be documented in your health care records and will be available to anyone with access to your health care record, including your health insurance company. This information may also be released as part of a release of information request.
- The last four digits of your social security number may be used in hospital or University systems to track billing information for research procedures.
- Washington University's Institutional Review Board (a committee that oversees the conduct of research involving human participants) and the Human Research Protection Office. The Institutional Review Board has reviewed and approved this study.
- Any report or article that we write will not include information that can directly identify you. The journals that publish these reports or articles require that we share your information that was collected for this study with others to make sure the results of this study are correct and help develop new ideas for research. Your information will be shared in a way that cannot directly identify you.

To help protect your confidentiality, you will be assigned a study ID number and we will use that ID to manage all your study related information and blood samples. Additionally, the key to the ID code linking code numbers to names will be kept in a password-protected file, behind the university's firewall, and only the research team will have access to it. We will destroy the link between your ID and your identifiers at the end of the study. If we write a report or article about this study or share the study data set with others, we will do so in such a way that you cannot be directly identified.

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.

We will disclose to the proper authorities information shared with us or activities we observe concerning abuse, neglect or harm to others or yourself.

Are there additional protections for my health information?

Protected Health Information (PHI) is health information that identifies you. PHI is protected by federal law under HIPAA (the Health Insurance Portability and Accountability Act). To take part in this research, you must give the research team permission to use and disclose (share) your PHI for the study as explained in this consent form. The research team will follow state and federal laws and may share your health information with the agencies and people listed under the previous section titled, "How will you keep my information confidential?"

Once your health information is shared with someone outside of the research team, it may no longer be protected by HIPAA.

The research team will only use and share your information as talked about in this form or as permitted or required by law. When possible, the research team will make sure information cannot be linked to you (de-identified). Once information is de-identified, it may be used and shared for other purposes not discussed in this consent form. If you have questions or concerns about your privacy and the use of your PHI, please contact the University's Privacy Officer at 866-747-4975.

Although you will not be allowed to see the study information, you may be given access to your health care records by contacting your health care provider.

If you decide not to sign this form, it will not affect

your treatment or the care given by your health provider.
your insurance payment or enrollment in any health plans.
any benefits to which you are entitled.
However, it will not be possible for you to take part in the study.

If you sign this form:

- You authorize the use of your PHI for this research
- This authorization does not expire.

You may later change your mind and not let the research team use or share your information (you may revoke your authorization).

- To revoke your authorization, complete the withdrawal letter, found in the Participant section of the Human Research Protection Office website at https://hrpo.wustl.edu/participants/withdrawing-from-a-study/ or you may request that the investigator send you a copy of the letter.
    - **If you revoke your authorization:**
        - The research team may only use and share information already collected for the study.
        - Your information may still be used and shared as necessary to maintain the integrity of the research, for example, to account for a participant's withdrawal from the research study or for safety reasons.

- You will not be allowed to continue to participate in the study.

Can we contact you by email?
We would like to contact you by email for the purposes listed below. Some of these emails may contain health information that identifies you.

- To send study questionnaires that you may complete electronically
- To schedule telephone follow-up appointments
- To send reminders about scheduled follow-up appointments

Only the research team will have access to your email communications. We will only communicate by email to send you the information listed above. If you have any questions or need to contact us for an urgent or emergent situation, please contact the research team member identified at the top of this document.

You should be aware that there are risks associated with sending your health information via email.

- There is always a risk that the message could be intercepted or sent to the wrong email address. To avoid sending messages to the wrong email address, the first email we send you will be a test message to ensure we have the correct email address.
- When using any computer you should be careful to protect your username and password. Make sure you log-out before getting up from the computer.
- If you share a home computer with other family members, and do not want them to know you are participating in this study make sure you provide an email address that only you can access.
- Your employer will have access to any email communications sent or received on any electronic devices used for work or through a work server.

The following privacy protections will be enacted for all email communications involving PHI: 1) a test email will be sent to you to verify your identity (confirm correct recipient) and this email will be sent in a secure manner (i.e., [secure] in subject line); 2) The body of the email will instruct you to send all information as a response and to not remove the "[secure]" from the subject line; 3) we will document your agreement to provide information over email in your research record.

Do you agree to allow us to send your health information via email?

_____ Yes **_____ No**
Initials **Initials**

IS BEING IN THIS STUDY VOLUNTARY?

Taking part in this research study is completely voluntary. You may choose not to take part at all. If you decide to be in this study, you may stop participating at any time. Any data that was collected as part of your participation in the study will remain as part of the study records and cannot be removed.

If you decide not to be in this study, or if you stop participating at any time, you won't be penalized or lose any benefits for which you otherwise qualify.

What if I decide to withdraw from the study?

You may withdraw by telling the study team you are no longer interested in participating in the study or you may send in a withdrawal letter. A sample withdrawal letter can be found at https://hrpo.wustl.edu/participants/withdrawing-from-a-study/ under Withdrawing from a Research Study.

Will I receive new information about the study while participating?

If we obtain any new information during this study that might affect your willingness to continue participating in the study, we'll promptly provide you with that information.

Can someone else end my participation in this study?

Under certain circumstances, the investigator might decide to end your participation in this research study earlier than planned. This might happen for no reason or because in our judgment it would not be safe for you to continue.

WHAT IF I HAVE QUESTIONS?

We encourage you to ask questions. If you have any questions about the research study itself, please contact Dr. Ben Palanca at 314-273-9076 or Dr. Christian Guay at 314-599-2922.

If you have questions, concerns, or complaints about your rights as a research participant, please contact the Human Research Protection Office 1-(800)-438-0445, or email hrpo@wustl.edu. General information about being a research participant can be found on the Human Research Protection Office web site, http://hrpo.wustl.edu. To offer input about your experiences as a research participant or to speak to someone other than the research staff, call the Human Research Protection Office at the number above.

This consent form is not a contract. It is a written explanation of what will happen during the study if you decide to participate. You are not waiving any legal rights by agreeing to participate in this study. As a participant you have rights and responsibilities as described in this document and including:

- To be given enough time before signing below to weigh the risks and potential benefits and decide if you want to participate without any pressure from the research team or others.
- To understand all of the information included in the document, have your questions answered, and receive an explanation of anything you do not understand.
- To follow the procedures described in this document and the instructions of the research team to the best of your ability unless you choose to stop your participation in the research study.
- To give the research team accurate and complete information.
- To tell the research team promptly about any problems you have related to your participation, or if you are unable to continue and wish to stop participating in the research study.

Your signature indicates that this research study has been explained to you, that your questions have been answered, and that you agree to take part in this study. You will receive a signed and dated copy of this form.

Do not sign this form if today's date is after EXPIRATION DATE: 05/22/24.

_____ _____
(Signature of Participant) (Date)

_____
(Participant's name – printed)

Statement of Person Who Obtained Consent

The information in this document has been discussed with the participant or, where appropriate, with the participant's legally authorized representative. The participant has indicated that they understand the risks, benefits, and procedures involved with participation in this research study.

_____ _____
(Signature of Person who Obtained Consent) (Date)

_____
(Name of Person who Obtained Consent - printed)