UNIVERSITY OF WISCONSIN-MADISON

Subject CONSENT to Participate in Research
And
AUTHORIZATION to Use and/or Disclose Identifiable Health information for Research

Title of the Study: UNderstanding CONSciousness Connectedness and Intraoperative Unresponsiveness Study (UN-CONSCIOUS)

Principal Investigator: Dr. Robert Pearce, .MD, PHD 608-263-4558.

Mailing Address: B6/319 Clinical Science Center, 600 Highland Avenue, Madison, WI 53792

INVITATION

You are invited to participate in this research study about changes in consciousness that happen during anesthesia. You are invited to take part because you are a male and/or female, in good health, between 18 and 40 years old. Up to 80 people will participate in the UN-CONSCIOUS study here at the UW-Madison.

Your participation in this research study is voluntary. If you decide not to participate, the health care provided to you by the University of Wisconsin-Madison (UW-Madison) and its affiliates (the University of Wisconsin Hospital and Clinics and the University of Wisconsin Medical Foundation) will not be affected in any way.

A. WHAT IS THE PURPOSE OF THIS STUDY?

The purpose of this study is to see how the brain functions during sedation and awaking from sedation. We will study four different drugs that can be used to put people to sleep under anesthesia. These four drugs are commonly used but each work differently. The changes in consciousness (how awake or aware a person is, or how the body responds) between the four drugs will be compared. We will collect data on how the electrical activity in the brain changes during changes in consciousness associated with anesthesia. This may help us understand the ways that consciousness may be altered. This may lead to changes in how anesthesia is used and to improved knowledge about consciousness itself.

B. WHAT WILL MY PARTICIPATION INVOLVE?

Screening Visits:

If you agree to participate, you will meet with an anesthesiologist to review whether or not you are eligible for the study by asking you about your medical history and perform a basic examination to determine if you are healthy enough to participate in the study. This examination will be the same as one you would receive if you were having anesthesia for any medical purpose, in which the anesthesiology will review your medical history, listen to your heart and lungs and assess your airway by looking in your throat.

Sleep Visit:

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ClinicalTrials.gov: NCT03284307

We will collect EEG data of your natural sleep during a separate study visit conducted in a sleep laboratory at the University of Wisconsin Department of Psychiatry. You will be fitted with the HD-EEG cap within 30 minutes of your usual bedtime and allowed to fall asleep. We will collect 2-3 hours of EEG data while you are sleeping. We will then wake you up every 15-30 minutes thereafter to ask you questions about your dreams.

Since you may not be used to sleeping with this HD-EEG cap on your head, you can undergo an “accommodation” night in the sleep lab or will be able to use a “demo” HD-EEG cap at home prior to the sleep lab recording.

This procedure is comparable to clinical polysomnography (PSG) but should not be considered to be a substitute for a clinical study ordered by your physician. However, you will be informed of any identified sleep disorders that are determined by a supervising board-certified Sleep Medicine Specialist supervising the sleep study.

Sedation Visit(s):

The sedation visit involves the use of a single, FDA approved sedative (a type of drug) to put you into an unconscious (sleep-like) state so that we can perform tests to better understand experiences during sedation. A total of 4 different sedatives will be used in this study, but only one sedative is used at each sedation visit. You will participate in a single sedation visit and can agree to come back for additional sedation visits. The sedation visits will be at least 28 days apart.

The sedatives used in this study are dexmedetomidine, ketamine, propofol, and midazolam. We plan to study 20 subjects using each sedative. The sedative that you receive will depend on how many subjects we have previously enrolled in the study and drug availability. The staff anesthesiologist will tell you what sedative will be using before the procedure and you will be informed of the drugs individual risks before consenting to the procedure. All four of the drugs are administered into a vein.

You will be asked to fast from food and non-clear liquids including milk for at least 6 hours before the sedation visit, and to abstain from drinking water for at least 2 hours before the sedation visit.

The sedation visit will take place at the Clinical Research Unit at the University of Wisconsin Hospital and Clinics. It will begin with a meeting with a study anesthesiologist to review eligibility criteria and prepare you for the sedation visit. This includes a basic pre-anesthesia exam and answering any questions you may have. The anesthesiologist will also confirm that you are fasting for this visit.

At the beginning of the sedation session you will be informed which sedation drug will be used. The sedation session will involve placement of up to two IV lines, depending on the sedative drug being used. You will also be set up with standard anesthetic monitors and safety equipment in the clinical environment. You will then be brought into an examination room where you will lie down on a table and one of the four sedatives will be administered by the anesthesiologist.

The drugs, dexmedetomidine, propofol, ketamine or midazolam will be administered through the

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IV line via slow infusion.

We will start by lightly sedating you so that you are awake enough to respond to verbal commands. While you are in this state, we will ask you to respond to what you see in a series of visual illusions and auditory-visual association tasks. We will then wake you up at approximately one minute intervals to ask questions about what was going through your mind.

Once this initial round of testing is done, we will then deepen the anesthetic so you are sedated and do not wake to verbal commands. We may then repeat auditory sensory testing. We may also perform tetanic stimulus during this deep sedation period. Tetanic stimulus involves using a nerve stimulator to contract a forearm muscle. This is often performed clinically under anesthesia to test nerve-muscle function. We may perform this test to see if you are arousable at this deeper level of sedation. The deep sedation period will last about 1 hour.

While you are sedated we will take two blood samples from the IV line to measure the amounts of the drugs in your blood. About a teaspoon of blood (5 mL) is taken at each blood draw for a total of 2 teaspoons (10 mL). We will take these blood samples twice during the sedation session, one set during the light sedation and one set during the deep sedation periods, for a total of 20 mL of blood taken during the session. These samples will be used to assess the amount of the drugs in your blood during the testing.

Before, during, and after sedation, you will be asked to complete some cognitive tasks. We will use the results of these games to see how you think at baseline, while sedated, and after recovering. These tests will not increase the amount of time you are sedated or recovering in the CRU. The tests will include a card sorting test of decision making, a task of attention, and a task testing your ability to associate sounds and images.

Once all of the testing procedures are done, the sedation drug will be stopped and you will be allowed to wake up as the drugs wear off. A drug called Zofran (Ondansetron) may be administered before you wake up to reduce the risk of nausea and vomiting when you wake. During the time while you wake up your vital signs will be monitored. The total amount of time that you are sedated will be 4 hours.

The sedation visit will take about 8 hours total, although it may be shorter or longer depending on how fast you wake up. Before you are able to leave an anesthesiologist will make sure it is safe for you to go home. You must be accompanied by someone who will take you home and stay with you overnight. The study team will contact you the next day to ask about how you are feeling. You will also be asked to email a brief reflection of your experience to the study team following your sedation visit.

We will also collect the following information about you for this research study:

From you:

- Age, phone number, race, height, weight, general health information

From your medical records kept by the UWHC and/or other providers:

- Vital sign measurements
- Study drug totals after sedation

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From medical tests or other procedures done for this study:

- Vital sign measurements
- Female patients will require a pregnancy test on the day of sedation to confirm lack of pregnancy.

Costs

There are no costs to you to participate in this study.

C. ARE THERE ANY BENEFITS TO ME?

You are not expected to benefit directly from participating in this study. Your participation may help you or other people who need anesthesia in the future through enhanced understanding of anesthesia and consciousness. In particular, it remains unclear how anesthesia impairs consciousness. Enhanced understanding of this would not only help reduces awareness of surgery under anesthesia but aid the understanding of consciousness in other disciplines.

Society may benefit from the possible development of a new diagnostic technique (i.e., a monitor of sedation and anesthesia), and because information may be obtained regarding the mechanisms of conscious experience. These potential benefits go beyond anesthesiology and may inform diverse fields from the disorders of consciousness (such as coma or delirium) to sleep.

D. WILL I BE PAID FOR MY PARTICIPATION?

You will be paid for being in this study. You will be paid an additional $50 for participating in the baseline sleep study.

You will be paid an additional $200 for each sedation visit that you complete. Payments will be provided after each sedation visit. If you participate in all 4 sedation visits, you would receive a total of $800 for the sedation visits.

E. ARE THERE ANY SIDE EFFECTS OR RISKS TO ME?

Intravenous catheters will be placed by the attending anesthesiologist using local anesthesia before needle placement. There may be some discomfort from the IV placement and there is a slight risk of bruising and swelling after removal. In normal subjects these are very rare complications, and are easily managed with warm packs and oral analgesics.

Study Drugs

Common risks include residual 'hangover' after administration of an anesthetic, such as sleepiness and nausea. We will administer the drug ondansetron to reduce the risk of nausea from the anesthetic drugs, which might give you a headache or cause constipation. The sedation drugs can impair your ability to think, drive and perform normal tasks. These effects may continue into the next day.

Serious risks of the study drugs include respiratory depression and pulmonary aspiration. Respiratory depression frequently occurs under anesthesia, and is readily managed by an

anesthesiologist. Pulmonary aspiration is uncommon, but rarely it can result in death. The risk of death from anesthesia/sedation is rare. In patients the attributable mortality to anesthesia and sedation is between 1:100,000 to 1:1,000,000. However given that no surgical procedure is being performed and we are conducting this in study in an approved clinical environment and only recruiting healthy subjects, we expect our study will be significantly safer than these statistics.

Allergies to propofol, ketamine, dexmedetomidine and midazolam administration are extremely rare. While a number of side effects have been report with acute and chronic use, they are very uncommon.

Common Side Effects of the Drugs Administered

Bicitra
Bicitra may cause diarrhea, nausea and vomiting, and convulsions.

Ondansetron
Ondansetron can cause constipation, diarrhea, and headache.

Propofol
Propofol can cause depressed breathing and loss of airway reflexes resulting in airway obstruction. Propofol may also cause low blood pressure, high blood pressure, difficulty breathing, decreased oxygen levels, irregular heartbeat, stinging at injection site, rash and itching. Allergy to propofol has been reported but is rare.

Ketamine
Short-lived confusion may occur upon awakening from ketamine anesthesia. Other common side effects may include low blood pressure, change in heart rhythm, difficulty breathing, double-vision, rapid eye movement, increased eye pressure, and difficulty breathing.

Dexmedetomidine
Dexmedetomidine may often cause low heart rate, dry mouth, and low blood pressure.

Midazolam
Common side effects of midazolam include hiccoughs, headache, nausea, vomiting, coughing and drowsiness. Rare, but serious, side effects include depressed breathing and loss of airway reflexes resulting in airway obstruction if given too rapidly.

You may see the informational handouts on each of these drugs if you wish.

Intravenous Catheter Placement and Blood Draws

There is a small chance of pain, or bruising at the site where the catheter is placed and your blood is drawn; in less than 1% infection may occur. There is also a slight chance of lightheadedness or fainting when your blood is drawn.

Other Risks

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The cognitive testing and questionnaires might cause you to become tired or anxious. The tetanic stimulus can cause pain and, if used, will only be administered after you become unconscious, though it may wake you up. Muscle aches may occur following the stimulus though these are often short lived.

There is a risk that your study information could become known to someone who is not involved in performing or monitoring of this study, which might make you uncomfortable, but the chance that this could happen is very small.

This study may involve risks to the subject which are currently unforeseeable. We will inform subjects as soon as possible if we discover any information that may affect the subject's health, welfare, or decision to be in this study.

H. WILL THERE BE COMPENSATION IF I AM INJURED?

In the event that you are physically injured as a result of participating in this research, emergency care will be available. You will, however, be responsible for the charges for the emergency care. There is no commitment to provide any compensation for research-related injury. You should realize, however, that you have not released this institution from liability for negligence. Please contact the investigator, Dr. Robert Pearce at 608-265-0588 if you are injured or for further information.

I. HOW WILL MY PRIVACY BE PROTECTED AND WHO WILL USE MY HEALTH INFORMATION?

All information obtained during this study will be kept private and confidential. A code number and initials will be used instead of directly identifiable information to label the study data. All information collected in this research study will be stored on secure servers or in locked cabinets at the University of Wisconsin-Madison Anesthesiology Clinical Research Program. The study results may be published, however, results used in publications or presentations will not identify individuals.

The information collected from you during this study will be used by the researchers and research staff of the UW-Madison and its affiliates (the University of Wisconsin Hospital and Clinics and the University of Wisconsin Medical Foundation). It may also be shared with others at the UW-Madison and outside the UW-Madison as noted above.

Others at UW-Madison and its affiliates who may need to use your health information in the course of this research:

- UW-Madison regulatory and research oversight boards and offices
- Accounting and billing personnel at the UW-Madison

Others outside of UW-Madison and UW Health who may need to receive your health information in the course of this research: NONE

People outside of UW- Madison and its affiliates who receive your health information may not be covered by privacy laws and may be able to share your health information with others without your permission. This study, however, does not involve sharing any of your health information

with individuals outside of the UW-Madison and UW Health.

An electronic research record, much like your electronic medical record, will also be created any time you participate in a clinical research study at the UW. Information as described above pertaining to the research study will also be placed in your electronic research record, including demographic information which may come from your medical record.

J. IS MY PERMISSION VOLUNTARY AND MAY I CHANGE MY MIND?

Your decision to participate in this research is entirely voluntary. You may choose not to participate. If you do decide to participate, you may change your mind at any time without penalty or loss of benefits that you had prior to the study. You will be told of any new and significant findings which may affect your willingness to continue. Your decision of whether or not to participate in this study will not affect the quality of your medical care at this institution.

K. HOW LONG WILL MY PERMISSION TO USE MY HEALTH INFORMATION LAST?

By signing this form you are giving permission for your health information to be used by and shared with the individuals, companies, or institutions described in this form. Unless you withdraw your permission in writing to stop the use of your health information, there is no end date for its use for this research study. You may withdraw your permission at any time by writing to the person whose name is listed below:

Dr. Robert Pearce, MD, PHD.
B6/319 Clinical Science Center
600 Highland Avenue
Madison, WI 53792

Beginning on the date you withdraw your permission, no new information about you will be used. Any information that was shared before you withdrew your permission will continue to be used. If you withdraw your permission, you can no longer actively take part in this research study.

L. WHO SHOULD I CONTACT IF I HAVE QUESTIONS?

Please take as much time as you need to think over whether or not you wish to participate. If you have any questions about this study at any time, contact the Principal Investigator Dr. Robert Pearce at 608-265-0588.

If you are not satisfied with the response of the research team, have more questions, or want to talk with someone about your rights as a research participant, contact the UWHC Patient Relations Representative at 608-263-8009.

Video Recording

As part of the study we will collect video recordings of you during each sedation visit.
The video is being collected to record your verbal and behavioral responses and to record exact timing of events that occur throughout the day. A written copy of the recordings will be made for use in the research.

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Video recordings will be kept indefinitely (banked), meaning we have no plan to destroy the recordings. The video recordings may be used in the future for future research. When the recordings are used in the future we will edit them whenever possible so that you cannot be directly identified.

Optional:

I would like to receive drug informational handouts YES NO

I have received informational handouts on the following drugs:

_____

Participant name (Please Print): _____

_____ _____

Participant Signature Date

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AGREEMENT TO PARTICIPATE IN THIS STUDY
AND
PERMISSION TO USE AND/OR DISCLOSE MY HEALTH INFORMATION

I have read this consent and authorization form describing the research study procedures, risks, and benefits, what health information will be used, and how my health information will be used. I have had a chance to ask questions about the research study, including the use of my health information, and I have received answers to my questions. I agree to participate in this research study, and permit the researcher to use my health information as described above.

Participant Name (please print): _____

_____ _____
Participant Signature Date

YOU WILL RECEIVE A COPY OF THIS FORM AFTER SIGNING IT.

Signature of person obtaining consent and authorization:

_____ _____
Signature Date

*****Please answer these questions VERBALLY with the research staff before signing this consent form*****

Can you describe the main study procedures?

What are the main risks of this study?

What are the expected benefits of the study?

Do you have to participate in this study and when are you allowed to withdraw from the study?

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