

**UNderstanding CONSciousness Connectedness and Intraoperative Unresponsiveness Study-3**

**PARTICIPANT INFORMATION SHEET**

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| **Title** | UNderstanding CONSciousness Connectedness and Intraoperative Unresponsiveness Study-3: a randomised, double-blind, cross-over trialhealthy volunteers |
| **Short Title** | **UN-ConsCIOUS-3** |
| **Protocol Number** | X23-0174 |
| **Project Sponsor** | Sydney Local Health District |
| **Coordinating Principal Investigator/ Principal Investigator** | Professor Robert Sanders |
| **Location** | Royal Prince Alfred Hospital |

**1. Introduction**

You are invited to participate in this research study as you meet the eligibility criteria of being between the ages of 18-40 years old and in good health. The aim of this study is to examine changes to consciousness while being sedated. Anaesthetic doctors routinely use medicines to change levels of consciousness and this study will help to inform and guide anaesthetic practice and consciousness sciences.

The study is being conducted within this institution by Professor Robert Sanders, Academic Head of Department (Anaesthesia). The Principal Investigator and Associate Investigators of this trial have no conflict of interest to declare.

People usually volunteer to take part in research because they have a medical condition. Your role in this study is different. You are a healthy volunteer. The study will not confer any therapeutic benefit on you. As such, you need to carefully consider the risks associated with the research before you consent to take part. Even small risks should be considered by you, as you do not need to take part in this research for the treatment of a medical condition.

Your participation in this research is voluntary, and you have the right to not participate in this study. Your decision whether to participate or not will have no effect on future care you may receive at Royal Prince Alfred Hospital. If you decide to participate, you may change your mind at any time without penalty or loss of benefits that you had prior to the commencement of the study. During the study you will be informed of any new and significant findings or issues that may impact your decision to continue with the study.

This Participant Information Sheet (PIS) will tell you what is involved in the study and help you decide whether or not you wish to take part. Please read this information carefully. If there is anything you do not understand or if you feel you need more information about anything, please ask. Before you make a decision, please feel free to talk things over with a relative, a friend or your doctor.

**2. Study Procedures**

All medications, drugs and devices have to be approved for use by the Australian Federal Government and are used regularly during anaesthesia and standard medical care. This study will be conducted under the Therapeutic Goods Administration (TGA) Clinical Trials Notification (CTN) Scheme. The investigators will conduct this study once it has been assessed and approved by an authorised Human Research Ethics Committee (HREC).

If you agree to participate in this study, you will be asked to sign the Participant Consent Form at the end of this document.

Following the telephone screen/assessment, we will arrange a date and time for you to attend Royal Prince Alfred Hospital for the study visit. The study visit will take approximately 8-9 hours (including recovery time), please ensure you have no time restrictions or commitments for this day in the rare instance your recovery is delayed.

You will be asked to follow these instructions:

* Fast from midnight prior to your study visit (no food).
* Drink clear fluids only from midnight up to 2 hours prior to the visit.
* Do not take any recreational drugs, sedatives, sleeping medication or drink alcohol 24-hours before your visit.

This information will be provided to you in advance, and you will receive a reminder phone call on the day prior to your sedation visit.

Additionally, we will provide you with discharge and recovery instructions, you will need to confirm the following:

* You have an escort to pick you up and accompany you home.
* You should not drive any commercial or private vehicle (car, motorcycle, boat, truck etc.) or operate heavy machinery for 24-hours following your sedation visit.
* No taking medications that will affect your central nervous system for 24-hours following your visit.

**Study Visit:** On arrival an anaesthetic doctor will meet with you to discuss the study face-to-face, during this time you can ask questions and the doctor will get you to sign the consent form. The doctor will ask you for a brief medical history, current/past medication and drug use, and anaesthetic history. Additionally, an airway assessment and brief physical examination, including vital signs, will be done to ensure you are safe to enroll in the study and that there are no increased risks for your health and safety. The doctor will confirm that you continue to meet the eligibility criteria, have adhered to the fasting protocol and have an escort to pick you up and take you home. If you are female, you will be asked to take a pregnancy urine test on the day of the sedation to reduce risk to unborn babies. Once deemed safe to progress you will be prepared for the study activities.

**All sedation visits will occur in an operating theatre with full access to standard clinical monitoring, equipment, and rescue medications as well access to resuscitation teams.**

In the procedural area you will have an electroencephalogram (EEG) cap placed and a 20-gauge intravenous catheter will be placed for drug delivery by an experienced anaesthetic doctor. The EEG is a machine used to record electrical signals between brain cells, the cap used sits firmly on your head and has many small rubbery electrodes that will sit against your scalp. Supplemental oxygen will be provided at 0-10 L/minute via nasal cannula as required. You will also receive normal saline 0.9% or Hartmann’s solution during the sedation visit. Standard monitoring used during anaesthesia will be applied- including- ECG (electrocardiograph – measuring heart activity), non-invasive blood pressure, SaO2 (oxygen levels), and exhaled CO2 (carbon dioxide) will be monitored continuously. Before each experiment, the anaesthesia machine and drugs will undergo routine pre-anaesthetic scrutiny, and the availability of resuscitation drugs and equipment will be confirmed and documented.

An anaesthetist whose sole responsibility for your welfare will administer the sedative (dexmedetomidine) and will be responsible for monitoring physiological status and documenting vital signs on the standard anaesthesia record. Your level of consciousness will be assessed routinely, and you will not have a breathing tube for this study. The anaesthetic doctor will administer the sedation drug and some baseline EEG data will be collected. While you are sedated, members of the research team will perform the following activities- collect data (EEG recordings and notes by anaesthetist) and video record the study activities.

**Schedule of Activities:**

* Stage 1: Resting/Awake state (approximately 1 hour). Prior to the administration of sedatives, you will be asked to relax with your eyes open and closed for a set amount of time. Over this hour you will be asked to relax for up to 10 cycles of 5-7 minutes, during some of these time periods you may be played some tones from a speaker. During these activities EEG data recorded onto a computer attached to the and you will be asked some basic questions by the anaesthetic doctor after every time block.
* Stage 2: Sedation Start (approximately 1 hour). The anaesthetist will administer light sedation and some baseline EEG recordings will be collected with eyes open and closed. Over this hour you will be guided to fall asleep for up to 10 cycles of 5-7 minutes, during some of these time periods you may be played some tones from a speaker. The anaesthetic doctor will wake you up after every time block (approximately 10 times over 1 hour). You will be woken up by verbal commands and touch (mild touch or shaking), when awake you will be asked some questions about your thoughts and perceptions of being sedated.
* Randomisation: During the next two stages of the study you will be randomly allocated using a computer program to the active stimulation group or sham group (no stimulation). Stimulation is done using a transcranial alternating current stimulation (TACS) – a machine that sends low-intensity electrical currents to the brain through electrodes sitting against your scalp. Randomisation will be done at the beginning of each time block.
* Transcranial alternating current stimulation (TACS): this machine sends low-intensity currents to the brain through electrodes sitting against the scalp. Some lubricating gel may be applied to your head under the electrodes. There will be 5 electrodes placed around the back and central areas of your head.
* Stage 3: TACS/Sham Stimulation Activity 1. You will be sedated again by the anaesthetic doctor and for periods of 5-minutes will be stimulated using TACS or Sham (based on computer randomisation). After each 5-minute block, the research staff will wake you up and ask you about your experience of consciousness. This process will be repeated for approximately 3 hours or 30 wake ups (15 blocks of real stimulation and 15 blocks of no stimulation or sham).
* Stage 4: TACS/Sham Stimulation Activity 2. You will be randomly allocated to TACS or Sham again using the computer program. This stimulation will be applied for 15 minutes and then the sedation drug will be turned off. The research staff will measure time to spontaneous wake up, collect EEG data and ask you questions about your experience once you are awake.
* Recovery: Following the study activities, you will be recovered by a registered nurse or doctor and assessed to ensure that you meet discharge criteria, this can take 1-3 hours. You will be provided with written and verbal instructions on what to expect during your recovery and a letter for your GP.

As per hospital policy you will be required to have an escort collect you from the hospital and accompany you home. You will be instructed to not operative machinery, drive and consume other drugs (sedatives, sleeping with nervous system activity for 24 hours – this includes sedatives, sleeping pills or opioids. **These instructions and confirmation of escort will be confirmed prior to beginning study activities.**

**Sedation Appointment Follow-Up**

On the day following your sedation visit a member of the research team will call you and ask you about your recovery and ensure you have not experienced any adverse events (headache, nausea, dizziness etc.), this information will be recorded in your participant file. A week following the sedation visit you will be emailed or text an optional Research Participant Feedback Survey via a secure link.

**3. Risks**

All medical procedures - whether for diagnosis or treatment, routine or experimental – involve some risk of injury. In addition, there may be risks associated with this study that are presently unknown and unforeseeable. In spite of all precautions, you might develop medical complications from participating in this study.

**Intravenous Cannula**

Prior to the commencement of the study activities, an anaesthetic doctor will place an intravenous cannula in your arm or hand to be used for sedation medication and fluids. This may cause slight discomfort on insertion. Risks of having an IV cannula are minimal but include discomfort, infection or the risk of fluids going into surrounding tissue. Staff will monitor the site for infection during the visit and ensure it is clean and dressed properly prior to discharge.

**Transcranial alternating current stimulation (TACS)**

All known side effects do not last long. The currents used are weak but there is a small risk of minor discomfort, tingling, redness or itching at the site of the electrodes. Additional side effects associated with current stimulation techniques include headaches, visualization of lights/flashes of light and dizziness. The TACS machine will be tested and certified safe by the Department of Biomedical Engineering at Royal Prince Alfred Hospital and the Therapeutic Good Administration will be submitted a Clinical Trial Notification Scheme for the use of the device.

**Dexmedetomidine**

The risks of participating in this study are similar to that of having light sedation for a procedure. This includes possible side effects related to the sedation drug, Dexmedetomidine.

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| Possible Risk/Side Effect | When this may occur? | How often this may occur? |
| Intravenous Cannula Insertion:  -discomfort  -tissuing  -bleeding  -infection (rare) | On insertion/during sedation visit | Rare to moderate likelihood. An experienced anaesthetist will insert the cannula and ensure antiseptic techniques as per policy. The cannula will be removed following recovery and dressed by a registered nurse. If there are any issues with the cannula such as tissuing or discomfort, the anaesthetic doctor will treat this with standard interventions, which may involve re-siting the cannula or providing a hot compress. Instances of bleeding and infection are rare and the site will be inspected prior to discharge. |
| Risks associated with sedation:  -respiratory depression  -nausea and vomiting  -dry mouth  -prolonged sedation | During/after sedation visit | Rare to moderate likelihood of occurrence. Any risks associated with sedation will be managed by the anaesthetic doctor as per standard care. Airway support and additional oxygen may be provided. In rare occasions nasal tubes/breathing tubes may be used to protect and support respiration. Additional fluids or medication may be used to counteract these side effects if required. Prolonged sedation may require a longer recovery period. |
| Risks associated with sedation:  -hypotension (low blood pressure)  -bradycardia (slow heart rate) | During/after sedation visit | Rare to moderate likelihood. All sedative drugs can cause cardiovascular changes. If these occur the anaesthetic doctor will respond in line with standard care including fluid administration or medications. Recovery may be prolonged if these issues persist. |
| Allergy to Dexmedetomidine | During sedation visit | Rare, the anaesthetic doctor present will respond to a potential reaction to the medication by stopping the drug immediately. The doctor will take the same action as if this occurred during an operation and protect the airway, administer drugs and provide interventions to support cardiovascular status. |

**4. Benefits**

We intend that this research study furthers medical knowledge and may improve anaesthetic care treatment, it will not be of direct benefit to you.

**Compensation for injuries or complications**

If you suffer any injuries or complications as a result of this study, you should contact the study doctor as soon as possible, who will assist you in arranging appropriate medical treatment. If you are eligible for Medicare, you can receive any medical treatment required to treat the injury or complication, free of charge, as a public patient in any Australian public hospital. In addition, you may have a right to take legal action to obtain compensation for any injuries or complications resulting from the study. Compensation may be available if your injury or complication is sufficiently serious and is caused by unsafe drugs or equipment, or by the negligence of one of the parties involved in the study (for example, the researcher, the hospital, or the treating doctor). You do not give up any legal rights to compensation by participating in this study

**5. Costs**

Participation in this study will not cost you anything.

You will be reimbursed for time and expenses occurred for travel with a voucher at the value of $200 AUD following the sedation visit.

**6. Voluntary Participation**

Participation in this study is entirely voluntary. You do not have to take part in it. If you do take part, you can withdraw at any time without having to give a reason by contacting Kaitlin Kramer (02 9515 8789 or Kaitlin.Kramer@health.nsw.gov.au).

If you decide to withdraw from the study, we will not collect any more study-related information from you. If you want to withdraw, please let us know and tell us what you would like us to do with the information we have collected from you up till then. If you wish, your information will be removed from our study records. It will not be included in the study results, unless we have analysed and published the results.

**7. Confidentiality**

Upon enrolment in this study, you will be allocated a unique study ID, this will be used on all data collection forms and to identify you in the database. A separate master code sheet will be kept with identifying information, and only the Principal Investigator and research nurse will have access to this information.

All the information collected from you for the study will be treated confidentially and will be stored on a research database called REDCap (managed by the Sydey Local Health District IT department). Paper documents will be stored in a locked cupboard in the Department of Anaesthetics and only accessed by approved research staff.

The data will be analysed by the researchers at the Royal Prince Alfred Hospital. All data for use in journal publications and presentations will be de-identified (de-identified data means that you/your information will not be identifiable). The files will be retained for 15 years from the day the study is completed. Once the retention expires the files will be disposed of in confidential recycling.

A copy of the video recorded during the study visit will be stored on the secure departmental research drive, no identifying information will be visible in the recording or saved to the drive- only the unique study ID will be recorded. The research staff will use the visual recording to connect documented data points and then delete the video from the recording device. A copy will be stored on the secure departmental drive and only accessible by the principal investigator and research nurse.

**8. Storage of Data**

The SLHD software licence for REDCap (Research Electronic Data Capture) will be used for to manage the collection and storage of research data. REDCap is a secure, web-based, non-commercial, data management tool designed for research purposes. Data collected by REDCap is stored on servers in the SLHD data centre. Data is secured and regularly backed-up to protect privacy and confidentiality

**9. Future use of Data**

The data collected in this project may also be used in future research studies. The results of this study and de-identified data may be shared in the future with national and international collaborators, any stored samples/data that is used for related or future research, will first be reviewed and approved and approved by an appropriately constituted Ethics Committee. You can indicate your agreement to this on the Participant Consent Form.

**10. Further Information**

When you have read this information, an anaesthetic doctor who is part of the research team will discuss it with you further and answer any questions you may have. If you would like to know more at any stage, please feel free to contact the research CNC on 02 9515 8789.

This information sheet is for you to keep.

**11. Ethics Approval and Complaints**

This study has been approved by the Ethics Review Committee (RPAH Zone) of the Sydney Local Health District. Any person with concerns or complaints about the conduct of this study should contact the Executive Officer on 02 9515 6766 and quote protocol number X23-0174.