Research study: Light to improve sleep, circadian rhythms, cognition and day time alertness

INFORMATION FOR PARTICIPANTS

You are invited to take part in a research study about sleep, day time alertness, cognition and body clock. We are going to study sleep, body clock, day time alertness and cognition of participants that are older than 50 years with sleep disturbances. We will investigate if a simple intervention such as exposure to light will improve sleep, body clock, day time alertness, mood and mental activities.

Background

The daily light and dark cycle is the strongest external time cue for humans to maintain circadian rhythmicity (keeping the body clock in time). Some individuals need brighter light for extended periods daily resetting their circadian rhythms and for maintaining daytime alertness. Interestingly, different light wavelengths (colour composition of the light) exert distinctive effects with bluish light increasing alertness and amber-red light promoting sleep.

Chronic dysregulation of circadian rhythms is usually accompanied by sleep disturbances which have major impacts on quality of life causing daytime fatigue, poor concentration, impaired mental activities, social isolation and worsening of health problems, such as cardiovascular disease, depression, neurodegenerative diseases, obesity and premature death. Sleep disruption is mainly treated using pharmacological therapies but with limited effectiveness and negative side-effects. We propose to investigate whether Light Therapy (LT) of variable wavelengths can act as an alternative therapy to improve sleep quality, daytime alertness, circadian rhythmicity and cognitive function.

The study is being conducted by the following researchers:
A/Prof Christopher Gordon, A/Prof Craig Phillips, Dr Angela D'Rozario, Dr Maria Comas, Professor Ron Grunstein, Professor Sharon Naismith, Dr Camilla Hoyos, A/Prof Wendy Davis, Dr Wenye Hu, Dr Sean Cain, and Dr Svetlana Postnova.

Study Coordinator:
Paula Ordonez at (02) 9114 0495 or paula.ordonezartunduaga@sydney.edu.au
Teha Pun at (02) 9114 0498 or tpun9449@uni.sydney.edu.au

Please contact the study coordinator for day to day enquiries.

Why have I been invited to participate in this study?

This study may be suitable for you because you are over the age of 50 years and are currently experiencing sleep disturbance, a condition which may benefit from this study as well as provide information to improve therapies in the future.

Is participation in this study voluntary?

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. Whatever your decision, please be assured that it will not affect your medical treatment or your relationship with the staff who are caring for you.

What does this study involve?

Part 1

Part 1 is a field-based study in your home and other living environments over 1 week and is open for any people aged 50 or older. You will be asked to wear two devices:

- An actiwatch – a watch-like device, which records wrist movements to determine sleep wake patterns (a sleep diary is to be completed in parallel).
- A light sensor pin – a small, unobtrusive pin device, worn on your clothing designed to measure light exposure.

You will also be invited to repeat this part of the study after 12 months.

Part 2

1. **Screening Visit 1: Consultation with a physician and medical screening**

At this visit you will also see a physician to conduct a routine medical and sleep assessment in order to rule out any conditions which may affect your eligibility for this study. Following the sleep physician, you will be provided with a small wrist-worn device (Nonin WristOx 3150^{TM}) which will be used to test for at-home obstructive sleep apnoea (OSA) screening. You will simply attach the device to your wrist like a wristwatch and placing the probe over your finger. This will be worn overnight and sent back for analysis to the Woolcock Institute of Medical Research. We will also measure your height and weight

If eligible, 1 week prior to your lab visit you will receive an actiwatch and a light-sensor pin to be worn for 7 days as you did during Part 1. You will also be asked to keep a sleep diary.

2. **Laboratory Visit 1: Stay at the Woolcock Institute of Medical Research for 3 days and 3 nights.**

During this visit you will stay in a suite at the Woolcock Institute and will be exposed to one of two light conditions during the daytime with all natural sunlight blocked out. On each day participants will be required to complete a battery of questionnaires and computer-based exercises regarding mood, alertness, cognitive abilities and sleepiness. We will also conduct multiple sleep studies during each day, and you will remain attached to the sleep study leads during the night for monitoring. In addition, on the third day your temperature will be measured every two hours during wake time and we will ask you to provide hourly saliva samples starting from 5 hours before habitual bedtime until bedtime.

Furthermore, if you wish to provide an optional mucosa sample for research (a separate PIS and consent form will be provided to you) you will be asked to provide a mouth swab on day 1.

3. **Laboratory Visit 2: Stay at the Woolcock institute of Medical Research for 3 days and 3 nights.**

After 2 weeks, we will ask you to come back to the Woolcock Institute to repeat most of the procedures but under the light you were not exposed to the first time (either light simulating daylight or control light) during day time. All tests and procedures will be the same as in visit 2 but you will not need to provide a mouth swab and questionnaires will not be needed to be filled out again.

What do these tests involve?

Baseline Assessment of Sleep and Daytime Functioning

- Actigraphy

You will be provided with an actiwatch which is a small watch-like device that measures wrist movements to determine sleep and wakefulness. Recording wrist movements over a period of a maximum of 1 week will help us assess your sleeping and physical activity. You will also fill out a sleep diary every day that you are wearing the actiwatch that will help us study your sleep patterns. You will receive written and verbal instructions on how to use the actiwatch.

- Light Profiling

You will also be asked to monitor your light exposure at home and work. You will receive a light-sensor pin device, which can be attached to your clothing. You will be asked to wear this device at all times during the day (taken off during showers, or swimming; making sure not to cover it with items of clothing) and at night, placed on the bed side table face up. You will receive written and verbal instructions on how to use the pin.

Questionnaires

- Sociodemographic questionnaire: ethnicity selection lifestyle questionnaire, and level of education selection
- Medical History and Medications: Medical history and concomitant medication information will be collected by the study coordinator and sleep physician.
- The Epworth Sleepiness Scale (ESS): rating of general sleepiness in the last two weeks (8 questions).
- Karolinska Sleepiness Scale (KSS): assessment of your sleepiness over the last 5 minutes (1 question).
- Insomnia Severity Index (ISI): rating of insomnia-related sleep problems (5 questions).
- Pittsburgh Sleep Quality Index (PSQI): assessment rating sleep quality over the past month (10 questions).
- Horne & Ostberg Morningness-Eveningness Questionnaire: assessment of what time of the day participants are most productive (13 questions)
- The Multivariate Apnoea Prediction Index (MAPI) Questionnaire: assessment for the presence and frequency of apnoea symptoms over the last month (3 questions)
- The Short Form (36) Health Survey: a patient-reported survey of patient health (11 questions).
- Hospital Anxiety and Depression Scale (HADS): a questionnaire which assesses mood and depressive symptoms over the past week (14 questions).
- Mini-Mental State Exam (MMSE): a 30-point questionnaire that is used to measure cognitive impairment (11 components). (Part 2 only)

All subsequent tests apply to participants in Part 2 only

- **Neurobehavioral Performance Assessments and Memory Tasks**

- Wechsler Test of Adult Reading (WTAR): a neuropsychological assessment tool that estimates an individual's level of intellectual functioning before the onset of injury or illness. Requires verbal pronunciation of a specific set of words and is not timed.

- Psychomotor Vigilance Task (PVT): a tool which is used to assess sustained attention via a simple reaction time task. You will be asked to press a button as quickly as possible in response to numbers appearing across the stimulus window on a small box for 10 minutes.
- N-Back: a visuospatial test that assesses working memory, encompassing short term memory storage and information processing. During this test, you will watch letters appear in different locations on the screen and you will try to match those in the same location. The N-Back takes 4 minutes to finish.
- The Stroop Task: This computerised test requires you to respond to a series of words that are displayed in colours (e.g. the word 'red' is displayed in blue) and identify the colour of the word or the definition of the word. Each attempt takes 45 seconds.
- Letter Cancellation Task: This 10-minute test evaluates concentration, attention and visuospatial scanning ability or neglect. You are shown an array of letters and are required to select a specific type of letters from those shown.
- Declarative Memory (Word Pair) Task: a computerised memory test where subjects are required to learn a set of word pairs and recall them at different stages following the learning stage.
- Procedural Memory (Finger Tapping) Task: assessment of the participants ability to memories procedures. This Motor Sequence Task (MST) requires you to repeatedly type a 5-element number on a standard computer keyboard with your non-dominant hand. The specific number sequence, which must be typed, is always displayed in front of you on the computer screen.
- Symbol Digit Modality Test: a cognitive function tests that asks participants to pair specific numbers with given geometric figures. It is a timed 5-minute test.
- The Buschke Selective Reminding Test: this is a verbal learning and memory test that involves a list-learning procedure over multiple trials. Not timed.

- **Collection of an oral mucosa sample (optional)**

If the participant agrees to this component of the study, you will be asked to collect an oral mucosal sample using a painless swab technique. You will use a mouth swab (a small brush-like device) to rub the inside of your cheek for 60-90 seconds. These mucosa samples will be used to study a body clock gene (Per3) that may predict response to light treatment.

- **Collection of multiple saliva samples**

A trained clinical trial coordinator will collect saliva samples from the participants into salivettes (special tubes) at multiple times prior to bed time. These saliva samples will be used to determine levels of melatonin, which is a physiological phase marker of the sleep body clock.

- **Sleep Study (Polysomnography)**

During the laboratory study participants may undergo a routine sleep study, called polysomnography (PSG). The PSG involves trained technicians affixing a number of leads on your head to record your brain activity (EEG) and sensors on your body. As part of your study, full video capture will be recorded and collected.

- **High-density EEG assessment**

On the last night of each 3-day visit, we will ask you to undergo two hdEEG assessments (one in the evening and one in the morning), while you are performing some cognitive tasks. As part of your study, full video capture will be recorded and collected.

Hd-EEG consists of researchers fitting a hdEEG sensor net cap on your scalp to monitor brain activity. There are 256 electrodes interconnected into a single net and applied simultaneously.

- **Karolinka Drowsiness Test (KDT)**

Brief resting awake high-density EEG recordings of brain activity as part of a Karolinska Drowsiness Test (KDT) will be performed prior to lights out and upon awakening in the morning. During the KDT you will be seated and quietly resting in a chair. You will be asked to look at a dot on the wall for approximately 2 minutes with your eyes open, followed by your eyes closed, and then with your eyes open again as instructed by the researcher. The test lasts 7.5 minutes in total.

- **Body temperature measurements**

On the last day of each 3-day visit, body temperature (oral and aural (ear) temperatures) will also be measured.

How much time will the study take?

The total time that you will be enrolled in this study from start until completion will be 6 weeks, divided in two visits of 3 days each with 2 weeks in between visits. You will also spend about 1 hour at the Woolcock Institute to receive a copy of this participant information sheet and have the study fully explained, to sign the consent form if you wish to take part in the study. You will also need to see a physician and undergo at-home screening.

How many other participants are there in the study?

It is anticipated that up to 80 participants will be enrolled into this study.

What are my responsibilities as a participant in this study?

If you decide to participate in this research study, you will be expected to follow the guidelines contained in this Information for Participants, and those provided by the study Medical Practitioner and staff. You will also be expected to:

- Keep all clinic appointments.
- Contact the study coordinator if you decide to discontinue your participation in the study.
- You must also tell your study Medical Practitioner about any other medications that you are already taking, e.g. over-the-counter medicines, herbal preparations, vitamins. It is important that you talk with the study Medical Practitioner before starting or stopping any prescription medications during this study.

Are there any side-effects and/or risks associated with this study?

No, there are no side effects or risks associated with this study.

Compensation for injuries or complications

If you suffer any injuries or complications as a result of this study, you should contact the study Medical Practitioner 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 Medical Practitioner). You do not give up any legal rights to compensation by participating in this study.

In the event of loss or injury, the parties involved in this study agree to be bound by the Medicines Australia Guidelines for Compensation for Injury Resulting from Participation in

an Industry-Sponsored Clinical Trial. A copy of these guidelines is available from the Executive Officer of the Ethics Review Committee.

Benefits

While we intend that this research study furthers medical knowledge and may improve treatment of several disorders in the future, it may not be of direct benefit to you.

Therefore, you need to carefully consider whether you want to take part on the study 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. You need to balance this risk against your wish to be a part of the research project, before you consent to take part.

Study costs & compensation

Participation in this study will not cost you anything; you will not be reimbursed for any costs for your time and travel during this study. If you have any questions, please discuss this matter with the study team.

Reimbursement

Participants who complete the entire protocol (Part 1 and Part 2) will be reimbursed for their time.

Could my study participation be terminated?

Your participation in the study may be stopped for any of the following reasons:

- If you do not follow the study Medical Practitioner's instructions.
- The study Medical Practitioner decides it is in the best interest of your health and welfare to discontinue.
- There are not enough participants in the study, or the study has reached the required number of participants.

Do I have to be in or finish the study?

Your participation in this study is voluntary. If you decide to take part, you will be given this information to keep and be asked to sign the Consent Form. You may choose not to take part in this study or, once in the study, you may decide to discontinue participation at any time. You must inform your study Medical Practitioner if you decide to do this. He/she

will explain the best way for you to discontinue your participation in this research study. Your decision not to take part in the study or to stop participating in the study will not affect your current or future medical care, or any benefits to which you may otherwise be entitled. Any study data that are collected before you discontinue from the study will be used in the analysis of the study results.

What Will Happen to Information About Me?

All data will be captured or entered electronically on a web-based database platform. This will be done at the Woolcock Institute of Medical Research or securely through a password protected, cloud-based platform on a secure server.). Any original study forms will be entered and kept on file at the Woolcock Institute of Medical Research. Access to your data will only be granted to designated and qualified research personal and your data will be maintained for 15 years after the completion of the trial. All biological material will be destroyed after 5 years of collection.

Data uploaded from the light-pin device will be stored in a secure Google cloud drive. It is only accessible by those that have been granted access to it. Only researchers on this study will be given access to the drive, and technical staff who may need to perform updates/maintenance work on the software where possible. These staff will not have access to other participant data.

For security, a complete back-up of the Woolcock Institute of Medical Research data collection server is available at another physical location. Data back-ups are performed on a daily basis.

Confidentiality and Disclosures of Information

All information obtained during this study, including hospital records, personal data and research data will be kept confidential. Any information taken from these records will be coded with a study number and your initials. By signing the Consent Form, you consent to these conditions and understand that any data published in scientific journals will not identify you.

Further Information

When you have read this information, Paula Ordonez/Teha Pun 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 Paula on (02) 9114 0495 or at paula.ordonezartunduaga@sydney.edu.au or Teha on (02) 9114 0498 or at tpun9449@uni.sydney.edu.au.

Ethics Approval and Complaints

The conduct of this study at the Woolcock Institute of Medical Research has been authorised by the 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 X17-0379.

Any person with concerns or complaints about the conduct of this study at the Woolcock Institute of Medical Research may also contact the Research Governance Officer, Ms Joanne Elliot, on 02 9114 0412 and quote protocol number X17-0379.

This information sheet is for you to keep.

PARTICIPANT CONSENT FORM

Light to improve sleep, circadian rhythms, cognition and day time alertness

I, ... [PRINT NAME], agree to take part in this research study.

In giving my consent I state that:

- I consent to Participating in Part 1 – field-based study YES NO
- I consent to participating in Part 1 and 2 – field based study **and** in-lab study YES NO
- I understand the purpose of the study, what I will be asked to do, and any risks/benefits involved.
- I have read the Participant Information Statement and have been able to discuss my involvement in the study with the researchers if I wished to do so.
- The researchers have answered any questions that I had about the study and I am happy with the answers.
- I understand that being in this study is completely voluntary and I do not have to take part. My decision whether to be in the study will not affect my relationship with the researchers or anyone else at the Woolcock Institute of Medical Research or the University of Sydney now or in the future.
- I understand that I can withdraw from the study at any time.
- I understand that personal information about me that is collected over the course of this project will be stored securely and will only be used for purposes that I have agreed to.
- I understand my referring physician may provide a relevant medical history to researchers, including any sleep complaints.
- I understand that if my study results indicate follow up medical care or treatment is required, this will be communicated to me and my referring physician with my consent.
- I understand my data generated from my stay at the Woolcock Institute will be shared with the researchers of this study.
- I understand that information about me will only be told to others with my permission, except as required by law.
- I understand that the results of this study may be published, and that publications will not contain my name or any identifiable information about me.
- You have been fully advised that as part of your sleep study and/or daytime test, full video capture will be recorded and collected. This footage will be used for best analysis of your sleep study and/or daytime test. The footage remains securely part of your sleep study and/or daytime test and copies are not retained on separate data files. CCTV is also in operation throughout the facility in bedrooms, common areas, waiting rooms, corridors, and staff monitoring rooms for patient and staff safety. Bathrooms are NOT monitored.

In addition, I agree to provide a buccal (cheek) swab for genetic study YES☐ NO☐

I would like to receive feedback about the overall results of this study YES☐ NO☐

If you answered **YES I would like to receive feedback** please indicate your preferred form of feedback and address:

☐ Postal: _____

☐ Email:_____

.....	.....
Signature and date	**PRINT name**
.....	.....
Signature and date of individual obtaining consent	**PRINT name**