School of Psychology
Faculty of Science

CIRUS, Centre for Sleep and Chronobiology
Woolcock Institute of Medical Research

ABN 15 211 513 464

Dr. Angela D'Rozario

NHMRC-ARC Dementia Research Fellow,
School of Psychology, Brain and Mind Centre
and Charles Perkins Centre,
The University of Sydney

Research Leader, Sleep Neurobiology Theme,
CIRUS, Centre for Sleep and Chronobiology
Woolcock Institute of Medical Research

Woolcock Institute of Medical Research
431 Glebe Point Road, Glebe
The University of Sydney
NSW 2050 AUSTRALIA
Telephone: +61 2 9114 0435
Facsimile: +61 2 9114 0014
Email: angela.drozario@sydney.edu.au
Web: http://www.sydney.edu.au/
www.woolcock.org.au

TITLE OF STUDY: Sleep, cognition and neurodegeneration: A neurobiological phenotyping investigation to identify predictors of cognitive decline

[Short Title of Study: Poor sleep and cognitive decline in at-risk dementia]

PARTICIPANT INFORMATION STATEMENT

(1) What is this study about?

You are invited to take part in a research study about the relationship between sleep, cognitive functions and neurodegeneration. As part of the study your sleep and wake brain activity will be recorded using **high-density electroencephalography (hdEEG).** You will also complete cognitive tasks before and after sleep. We will examine changes in sleep and wake brain activity patterns and how these may relate to cognitive functions including memory. We aim to identify predictors of cognitive decline and examine how poor sleep may affect cognitive changes over time.

Purpose and background

Sleep is important for learning and memory processes and disrupted sleep may underlie changes in cognitive functions that occur with older age including memory impairment. High-density EEG is a non-invasive technique that uses a cap worn on the head to record detailed brain activity during sleep and wakefulness from 256 electrode sites. The purpose of this study is to examine brain waves during sleep and to understand the impact of altered sleep neurophysiology on cognition.

You have been invited to participate in this study because you have reported some changes in your cognitive function and / or have been assessed for mild cognitive impairment (MCI) at the Healthy Brain Ageing (HBA) clinic at the Brain and Mind Centre. This Participant Information Statement tells you about the research study. Knowing what is involved will help you decide if you want to take part in the research. Please read this sheet carefully and ask questions about anything that you don't understand or want to know more about.

Participation in this research study is voluntary

By giving your consent to take part in this study you are telling us that you:

- ✓ Understand what you have read.
- ✓ Agree to take part in the research study as outlined below.
- ✓ Agree to the use of your personal information as described.

You will be given a copy of this Participant Information Statement to keep.

(2) Who is running the study?

The study is being carried out by researchers and doctors from the Woolcock Institute of Medical Research and the Brain and Mind Centre at the University of Sydney. The following researchers will be running the study:

Dr. Angela D'Rozario, NHMRC-ARC Dementia Research Fellow, School of Psychology, Brain and Mind Centre and Charles Perkins Centre, The University of Sydney and Research Leader, Sleep Neurobiology Theme, CIRUS, Sleep and Circadian Research Group, Woolcock Institute of Medical Research.

Professor Sharon Naismith, Leonard P Ullman Chair in Psychology, School of Psychology of the University of Sydney and the Brain & Mind Centre

Professor Ron Grunstein, Professor of Sleep Medicine and NHMRC Senior Principal Research Fellow, Senior Specialist Physician; Chief Investigator, NHMRC Centre for Translational Sleep and Circadian Neurobiology, (NeuroSleep CRE) and CIRUS, Sleep and Circadian Group, Woolcock Institute of Medical Research, University of Sydney and Royal Prince Alfred Hospital

Associate Professor Delwyn Bartlett, Head, Medical Psychology Research Theme, CIRUS, Sleep and Circadian Group, Woolcock Institute of Medical Research

Dr Keith Wong, Staff Specialist in Respiratory and Sleep Medicine, Royal Prince Alfred Hospital & CIRUS Centre for Sleep and Chronobiology, Woolcock Institute of Medical Research

Associate Professor Brendon Yee, Staff Specialist in Respiratory and Sleep Medicine, Royal Prince Alfred Hospital & CIRUS Centre for Sleep and Chronobiology, Woolcock Institute of Medical Research

Dr Dev Banerjee, Sleep Physician and Medical Director, Woolcock Institute of Medical Research

Dr Shantel Duffy, NHMRC-ARC Dementia Research Fellow, Sydney Medical School & CIRUS, Woolcock Institute of Medical Research

Ms Anna Mullins, PhD Scholar, Sydney Nursing School & CIRUS, Woolcock Institute of Medical Research

Dr Negar Memarian, NeuroSleep Postdoctoral Fellow, NeuroSleep CRE & Brain & Mind Centre

Ms Carla Haroutonian, PhD Scholar, School of Psychology of the University of Sydney and CIRUS, Woolcock Institute of Medical Research

This work is supported by a NHMRC-ARC Dementia Research Development Fellowship Grant (Application ID 1107716) and a Sydney Medical School Kick Start Grant awarded to Dr Angela D'Rozario.

(3) What will the study involve for me?

This study will be in two-parts: a baseline assessment and a 2 year follow-up assessment.

PART 1: BASELINE ASSESSMENT

After completing your neuropsychological and medical assessment at the HBA clinic, Brain and Mind Centre, Camperdown, as part of the Clinical Staging Study (Protocol Number: 02-2011/13515), you will be invited to attend the Woolcock Institute of Medical Research, Glebe to attend a 1.5-2 h screening

and consent visit during the daytime. Eligible participants will then be invited to attend the Woolcock Institute for a baseline visit which will include an overnight sleep study with high-density EEG. The screening and baseline visits at the Woolcock Institute will take place within a 1-2 week period. Either on the afternoon of your sleep study or the morning after your sleep study you will undertake your 1hr brain MRI scan as part of the Clinical Staging Study (Protocol Number: 02-2011/13515) if you have consented to do so. One of our research team members will escort you to or from the MRI scan at the Brain and Mind Centre, Camperdown.

1. ***Screening and Consent Visit***

The screening visit will take approximately 1.5-2 hours. During this visit we will confirm your eligibility to participate in the study through a screening checklist, medical assessment and some simple screening questionnaires. You will also trial the high-density EEG cap – this will be worn on your head and you will be asked to lay down on a bed in a private bedroom in the sleep laboratory for a nap. This is to check that you can comfortably wear the cap in preparation for your overnight visits. Written informed consent to participate in the study will then be obtained from you. Appointments for your next visits will also be scheduled.

Actigraphy/Sleep diary

You would have been given an actiwatch to measure your sleep/wake activity patterns at your HBA clinic appointment, Brain and Mind Centre. This is a watch-like device that you will wear on your wrist to estimate sleep and wake for 2-week prior to the Baseline High-density EEG Night. This will provide us an overall indication of your sleep/wake duration, the ambient light exposure and your general activity level. During this period you will be asked to complete a daily diary which will ask you questions about your sleep/wake time and other aspects of your daily activities and work schedule. If an actiwatch and sleep diary wasn't provided to you at your HBA clinic appointment we will post these to you.

2. ***Baseline Visit***
   a. ***High-density EEG assessment: Overnight sleep study and resting wake brain activity recordings***

You will be asked to attend an overnight sleep study at the Woolcock Institute. During this visit, researchers will fit a 256-channel hdEEG head net cap on your scalp to monitor brain activity overnight. There are 256 electrodes interconnected into a single net and applied simultaneously. Along with monitoring hdEEG overnight, standard PSG measurements will be recorded. These include a nasal airflow piece, a belt around the waist and chest, and an oximeter probe on the finger to monitor breathing and oxygen levels in the blood. Heart rate (ECG), leg movements, sleeping position and snoring are also recorded. It is part of a routine sleep study to include video and audio recordings while you sleep.

In the evening while wearing the head net, we will use a hand-held device to measure the position of the sensors as they sit on your scalp. This device is called a GeoScan Digitization Sensor. You will not need to do any tasks but simply sit in a chair while one of the study teams moves around you with the device. This test will take approximately 10 minutes.

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. The Karolinska Sleepiness Scale (KSS) is a simple 1-9 momentary sleepiness scale designed to assess your state of sleepiness at any given time. You will complete this scale prior to the KDT in the evening and the morning.

In the afternoon prior to your sleep study, you will have a brief consultation with one of our sleep physicians. A follow-up consultation will also be arranged 4-5 weeks following your sleep study.

b. Questionnaires, Neurobehavioural Assessment & Memory Tasks

Before we apply the hdEEG net, you will be asked to complete some questionnaires and neurobehavioral assessment (PVT) to measure cognitive functioning. Following hdEEG net application, approximately 1 to 2 hours before your normal bedtime you will perform memory tasks – this should take about 1 hour. The KDT, PVT and memory tasks will be repeated upon waking and should take 30 minutes. All tests and questionnaires during this visit are explained below:

Questionnaires:

- Epworth Sleepiness Scale (ESS) - asks about your sleepiness in the last two weeks.
- Insomnia Severity Index (ISI) – asks you to rate any insomnia-related sleep problemsHospital Anxiety and Depression Scale (HADS) – a questionnaire to assess your mood and depressive symptoms over the past week.
- Depression Anxiety and Stress Scale (DASS) – a second questionnaire to assess your mood, depressive and stress symptoms.
- Horne and Östberg Morningness-Eveningness Questionnaire - asks how you function in the morning and the evening.

You would have completed some other sleep and cognition questionnaires during your HBA clinic appointment including: Pittsburgh Sleep Quality Index (PSQI) – asks you to rate your sleep quality; Wechsler Test of Adult Reading (WTAR) – a test related to your IQ; and the Mini-Mental State Examination (MMSE) – a test of cognitive functioning. With your permission we will access this clinical research data as part of this research study.

Neurobehavioural Assessment Battery:

- *Psychomotor Vigilance Task (PVT):*
  The PVT is a 10-minute sustained reaction time test. You will be asked to press a button in response to numbers appearing across the stimulus window on a small box. This test tells us whether your reaction time is improving. You will be asked to do this test in the evening before sleep and upon waking.

Memory Tasks:

In the evening before your high-density EEG sleep study, you will be asked to complete some tests of memory (e.g. learning a list of words, and tapping your fingers in sequence) when you come into the sleep laboratory. These tests will take approximately an hour to complete.
Following a night of sleep, about 1 hour after you have been woken up, you will be assessed on these same tasks which will take about 30 minutes. We will measure your performance in the morning and compare it to the previous night.

- *Declarative Memory (40 mins):*
  The first task is to learn a set of 32 pairs of words, for example, desk – ice. That is, when presented with the first word, e.g. desk, you can recall the corresponding pair, e.g. ice.
- *Procedural Memory (12 mins):*
  The Motor Sequence Task (MST) requires you to type repeatedly a 5-element number on a keyboard with your non-dominant hand. The specific number sequence, which must be typed, is displayed in front of you on the computer screen at all times. Typing is done in 30 second trials separated by 30 second rest periods. Training (before sleep) involves 12 trials and retest (after sleep) involves 6 trials.
- *Spatial Navigation Memory (20-25 mins):*
  The virtual morris water maze (vMWM) task requires you to learn a route to find a target item in a 3D open arena. You will have 5 trials to learn this route, always starting from the same location. You will then have 2 test phases: The 1st test phase is to navigate to the location of the target item from the route that you have learnt and mark the spot with an "X". The 2nd test phase requires you to find the location of the target item, starting from an unfamiliar start location.

PART 2: FOLLOW UP ASSESSMENT

After approximately 2 years, we will invite you to return for a follow-up visit. This will be optional and require you to undergo similar assessments as outlined above. We may then invite you to return for

additional follow-up at 2-yearly intervals. At this time you will be given the option of consenting or not to ongoing follow-up assessments.

Access to Heathy Brain Ageing (HBA) clinical information: We also want to look at the clinical assessment you had at the HBA clinic as part of the Clinical Staging Study (Protocol Number: 02-2011/13515) and request your permission to access your HBA medical records to obtain clinical research data relevant to this study (e.g. diagnosis and clinical assessments, symptoms ratings, neuropsychology assessment, actigraphy and sleep diary, brain imaging scans) that were collected at baseline and follow up assessment as part of that study). We would like to examine these clinical data in relation to the sleep and cognitive assessments conducted in this research project. No personal contact information will be extracted from your HBA clinical records.

(4) How much of my time will the study take?

The study involves a 1.5-2 hour daytime screening visit followed by an overnight stay at the sleep laboratory (Baseline Night) and then an optional follow-up assessment 2 years later. Overnight stays involve a sleep study with high density EEG and cognitive testing. On these visits you will be asked to arrive at the sleep laboratory between 3-4pm and will be able to leave the following morning around 9am.

(5) Who can take part in the study?

- Individuals aged 50 to 90 years who report new changes in their cognition that are not due to a pre-existing medical or psychiatric condition (subjective memory complaints); or have received a confirmed diagnosis of amnestic or non-amnestic multi-domain mild cognitive impairment (MCI)

You will not be able to participate in this study if you:

- do not have English as a primary language;
- have other major neurological problems (e.g. stroke, epilepsy, head injury);
- have a severe mental health disorder (e.g. schizophrenia, bipolar disorder);
- have a current diagnosis of major depression
- have any other serious medical conditions, such as cancer;
- are regularly taking sleep-affecting medication including benzodiazepines, sedative hypnotics, antipsychotics, antidepressants;
- are a shift worker or have travelled overseas within the last 2 weeks;
- have a diagnosis of dementia

(6) Do I have to be in the study? Can I withdraw from the study once I've started?

Being in this study is completely voluntary and you do not have to take part. Your decision whether to participate will not affect your current or future relationship with the researchers or anyone at the Woolcock Institute of Medical Research, the Brain Mind Centre or the University of Sydney.
If you decide to take part in the study and then change your mind later, you are free to withdraw at any time. You can do this by contacting a member of the research staff.
If you decide to withdraw from the study, we will not collect any more information from you. Please let us know at the time when you withdraw what you would like us to do with the information we have collected about you up to that point. If you wish your information will be removed from our study records and will not be included in the results, up to the point that we have analysed and published them.

(7) Are there any risks or costs associated with being in the study?

Aside from the time taken to participate in the study, there are no expected costs associated with participating in this study. Participation in this study will not cost you anything. While you will not be paid to participate in the study, out of pocket expenses (e.g. travel costs) incurred as a result of participating in this study will be reimbursed. Arrival at the Woolcock before your sleep study is 3-4pm, breakfast is provided but please bring along your evening meal. You will also be offered a $100 department store voucher after the baseline assessment and a further $50 voucher after the long-term follow-up assessment.

The risks associated with participating in this study are considered minimal. However, the memory tasks may cause mild anxiety. The tasks are not designed to be overly difficult, however it is not expected that you will be able to remember all of the items on the tests. Any anxiety will usually lessen once testing begins, and you will be able to discuss any concerns with the researchers, who are trained to be able to assist you should these feelings arise. Measuring brain activity (EEG) and eye movements (EOG) involve no safety risks. The EEG monitoring device is electrically approved and conforms to hospital standards for electrical safety. The special paste used to attach the electrodes may cause some minor discomfort and/or skin irritation.

(8) Are there any benefits associated with being in the study?

While it may not be of direct benefit to you, we intend that this research study will further medical knowledge and may improve the clinical care of future patients with symptoms of cognitive impairment and neurodegenerative disease. It will also provide greater understanding about how disrupted sleep relates to brain function and cognitive impairment in some patients.

(9) What will happen to information about me that is collected during the study?

We will collect recordings of your sleep obtained when you come in for your sleep studies as well as high-density EEG recordings. Your performance on the neurobehavioural tests and memory tasks will also be collected.

By providing your consent, you are agreeing to us collecting personal information about you for the purposes of this research study. This includes medical history, questionnaire responses and sleep data recorded in your overnight studies. Your information will only be used for the purposes outlined in this Participant Information Statement, unless you consent otherwise.

Should your study results indicate you require follow up medical care or treatment, this will be communicated to you and your referring physician with your consent.

All information will be held in a secure location at the Woolcock Institute and kept strictly confidential, except as required by law. Your personal data will be de-identified. All electronic information will be stored on a secure computer network and only the study researchers will have access to this information.

The results will be published, but you will not be individually identifiable in these publications.

After completion of the study, the research data will be kept for 15 years, in accordance with the Woolcock Institute's policy. When files are disposed of, secure destruction methods will be employed ensuring contents cannot be recovered.

The data collected in this project will be available for use by other researchers, unless prevented by University policy, legislative requirements or ethical, contractual or confidentiality obligations.

(10) Can I tell other people about the study?

Yes, you are welcome to tell other people about the study.

(11) What if I would like further information about the study?

When you have read this information, one of the research team will be available to discuss it with you further and answer any questions you may have. If you would like to know more at any stage during

the study, please feel free to contact Dr. Angela D'Rozario, Chief Investigator, on +61 2 9114 0435 or by email at angela.drozario@sydney.edu.au. For day to day enquiries, please contact Carla Haroutonian, Study Coordinator, on 9114 0491 or email carla.haroutonian@sydney.edu.au.

(12) Will I be told the results of the study?

You have a right to receive feedback about the overall results of this study. You can tell us that you wish to receive feedback by ticking the relevant box on the Consent Form provided. You will receive this feedback after the study is finished.

(13) What if I have a complaint or any concerns about the study?

Research involving humans in Australia is reviewed by an independent group of people called a Human Research Ethics Committee (HREC). The ethical aspects of this study have been approved by the HREC of the University of Sydney *[Protocol No. 2016_1019].* As part of this process, we have agreed to carry out the study according to the *National Statement on Ethical Conduct in Human Research (2007).* This statement has been developed to protect people who agree to take part in research studies.

If you are concerned about the way this study is being conducted or you wish to make a complaint to someone independent from the study, please contact the university using the details outlined below. Please quote the study title and protocol number.

The Manager, Ethics Administration, University of Sydney:

- **Telephone:** +61 2 8627 8176
- **Email:** ro.humanethics@sydney.edu.au
- **Fax:** +61 2 8627 8177 (Facsimile)

This information sheet is for you to keep