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A study investigating whether sleep can be measured accurately at home in people with early Alzheimer's disease

Submission date
01/03/2023

Recruitment status
No longer recruiting

Registration date
22/03/2023

Overall study status
Completed

Last Edited
08/04/2026

Condition category
Nervous System Diseases

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims:
New approaches to treatment of Alzheimer's disease (AD) are desperately needed. AD brain changes build up for 2-3 decades before diagnosis. Amyloid beta (abeta) plaques and another protein, tau, appear before clinical symptoms. There are no licensed treatments for AD that can delay progression. Through targeting therapy early in the course of disease before symptoms interfere with day-to-day life, we could slow progression of AD. Delaying progression to AD dementia by 3 years would reduce the number of cases in the UK by 394000 with save £12.7 billion per year.
Modifying sleep quality is an untapped opportunity with potential to delay progression of neurodegenerative diseases such as AD while promoting physiological processes that improve cognition, mental health and wellbeing. Poor sleep is associated with increased likelihood of future dementia, AD worsens sleep and poor sleep is linked to worse cognition. Deficits in sleep have been associated with the degree of abeta and tau burden prior to AD onset as well as memory impairment. Treating sleep might therefore help slow AD progression and improve symptoms of memory loss.
Before we can improve sleep in AD we need to:
-Understand how best to measure sleep in people with AD
-Test new blood tests for AD to see how accurate they are in early disease.
To do this, we are running two substudies. Substudy 1 tests whether new home sleep recording works in people with AD (rather than current gold-standard, but burdensome, testing in laboratories). Substudy 2 will test whether blood tests for AD are as accurate as standard invasive tests.
This feasibility, acceptability and diagnostic sensitivity data will be translated directly into clinical trials to delay progression of Alzheimer's and improve independence and quality of life in older people at risk of AD.

Who can participate?
Substudy 1: People with a diagnosis of Mild Cognitive Impairment or early Alzheimer's Disease over the age of 50. Participants must be able to fully understand the purpose of the study and give their consent to taking part.

Substudy 2: Patients who have recently attended the Southmead Hospital (Bristol) Cognitive Disorders Clinic and have been referred for a lumbar puncture for biomarker testing.

What does the study involve?
Substudy 1: Stage 1 involves a screening visit at Southmead Hospital (or over video consultation) to check that you are eligible to take part, and to complete baseline assessments. This involves a short memory test, questionnaires on sleep and your health, and a blood test to look at proteins related to neurodegeneration. Stage 2 involves taking part in sleep recordings at home. For 3 nights, you will be asked to wear an electroencephalography (EEG) cap on your head whilst you sleep to measure your brainwave activity. You will also be asked to wear a pulse oximeter for 2 nights to screen for a sleep disorder called obstructive sleep apnoea. A researcher will visit your home each evening to set up the equipment. To ensure a good connection for the sensors in the EEG cap, the researcher will apply a very small amount of gel where each sensor touches the skin. The whole process usually takes 30-45 minutes. The cap is designed to be comfortable to sleep in, and allow you to move normally. You will remove the cap yourself when you wake in the morning. A member of the research team will be contactable throughout the study, including overnight, in the unlikely event of experiencing any problems. Other activities include completing a short sleep diary each morning, a further memory test, and a brief questionnaire at the end to give us valuable feedback on the experience.

Substudy 2: If you agree to take part, you will have your lumbar puncture in the normal way. We always take blood tests at the same visit as lumbar puncture as we need to compare blood and spinal fluid results for some tests. At the time of your routine blood test, we will take another 2 tubes of blood – a maximum of 20ml (4 teaspoons full). As an optional addition to the study, we will also take an extra < 5 ml (1 teaspoon full) of cerebrospinal fluid for testing and storage as long as it does not prolong the procedure by more than 1 minute.

What are the possible benefits and risks of participating?
For both substudies: There are no direct benefits from participating in this study except perhaps the satisfaction in contributing to research that helps us to improve our understanding of dementia. We will not give feedback o the results as they are being collected purely for research purposes.
For Substudy 1: The risks are few and very low. The main risk is that either the EEG cap or the gel causes irritation or an allergic reaction on the skin. The chance of this happening is very small. If you choose to give a blood sample, this can leave a small bruise, although our staff aim to minimise this.
For Substudy 2: The risks are few and very low. Occasionally blood tests can make people feel faint or leave a bruise. We will stay with you for at least 10 minutes after blood testing to make sure you do not feel faint. You would have been having the blood test anyway, but it may last 30-60s longer due to our research. We will only take a Cerebrospinal Fluid (CSF) sample if flowing freely during the procedure. You produce 500ml of CSF per day and so will very quickly replace the sample that is taken. We do not expect that taking an extra 5ml of CSF will cause any side effects, but there is a tiny risk it could worsen headache afterwards and so this part of the study is optional.

Where is the study run from?
University of Bristol (UK)

When is the study starting and how long is it expected to run for?
January 2022 to October 2026

Who is funding the study?
The Teresa Rosenbaum Golden Charitable Trust (Rosetrees Trust) (UK)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Integrated Research Application System (IRAS)
316465

Central Portfolio Management System (CPMS)
54927

Protocol serial number
OoR2021\100003

Study information

Scientific Title
Feasibility of measuring sleep-dependent brain activity at home in people with prodromal and mild Alzheimer's disease to help delay symptoms (SleepAD)

Acronym
SleepAD

Study objectives
Substudy 1 primary hypothesis: Home high-density EEG are feasible and acceptable in people with Mild Cognitive Impairment and Alzheimer’s Disease
Substudy 2 primary hypothesis: Blood biomarkers are feasible and acceptable in people with Mild Cognitive Impairment and Alzheimer’s Disease

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 09/02/2023, West of Scotland 4 REC (West of Scotland Research Ethics Service, Ward 11, Dykebar Hospital, Grahamston Road, Paisley, PA2 7DE, UK; +44 (0)141 3140213; WoSREC4@ggc.scot.nhs.uk), ref: 23/WS/0007

Primary study design
Observational

Study design
Observational cross-sectional

Study type(s)
Other

Health condition(s) or problem(s) studied
Dementias and neurodegeneration, Alzheimer's disease

Interventions
SleepAD SUB-STUDY 1

Design: Single centre, prospective observational feasibility study.
Setting: Southmead Hospital cognitive disorders clinic and participants’ homes.

Screening consultations can be conducted in-person or remotely.

Each potential participant will be reviewed by an International Conference on Harmonisation Good Clinical Practice (ICH GCP) trained member of the study team. Participants will first be given a detailed explanation of the study, orally as well as another copy of the PIS if they wish. The research team will check understanding of the PIS and an opportunity to ask questions will be provided. If they agree to take part in the study each participant will sign an Informed Consent Form (ICF). Participants scheduled for remote consultation will have received a copy of the PIS and ICF via post and will be asked to return a signed copy to the research team.

Each prospective participant will subsequently be reviewed against inclusion/exclusion criteria before final eligibility is determined.

The participant will subsequently undergo medical screening before undergoing baseline assessments if eligible.

Any participant unsure or requiring more time to make a decision as regards to consent will be offered this opportunity and given as much time as they need, providing recruitment is ongoing.

Consent:
Anyone taking part will be informed of the study aims and protocol. It will be made clear to participants that if they wish to, they may withdraw their consent at any time without the need to provide an explanation and that this will not affect future medical care.

The investigator taking consent will be trained in taking consent and will act in accordance with GCP. Capacity to consent is assessed by the researcher as they discuss the information sheet with the patient. The researchers will ensure the volunteer has understood and retained information for long enough to allow risks and benefits to be considered and that a decision can be relayed clearly.

Once the volunteer has given consent, they will perform the Montreal Cognitive Assessment (MoCA). This is a widely used assessment for measuring cognitive ability within clinical and research settings. If a participant scores below 11/30 they will be withdrawn from this study as this is highly likely to be associated with a reduced capability to provide informed consent and adhere to study procedures.

Screening assessments: The following information will be gathered during the initial screening assessment:-
• Medical History and Current Diagnoses
Specifically to determine the presence of severe medical comorbidities likely to impact on sleep or the presence of a primary sleep disorder unrelated to a neurodegenerative cause
• Previous Investigation Results
Including neuroimaging data, CSF biomarker results and neuropsychometry data; information historically collected as part of routine clinical care.
• Medication History
• Physical Observations*
Blood pressure measurement only
* If undergoing face-to-face consultation

The following assessments will occur following informed consent during the initial consultation. These are validated questionnaires and post hoc analysis will allow us to probe whether any of these questionnaires can help stratify in which patients home EEG will be feasible for future trials.

Cognitive Assessments
• Montreal Cognitive Assessment (MoCA)

Sleep Assessments
• Pittsburgh Sleep Quality Index (PSQI)
• Epworth Sleepiness Scale (ESS)
• STOP-BANG (OSA Screening Questionnaire)
• Ultra-Short Munich Chronotype Questionnaire (μ-MCTQ)
• REM Sleep Behavioural Disorder Single Screening Question

Blood biomarkers - Venepuncture of 5-10 ml blood biomarkers taken for analysis of biomarkers (P-tau & NFL, GFAP and abeta42/40, and possibly others in future)
Other Assessments
• Restless Leg Syndrome Single Screening Questionnaire
• Generalised Anxiety Disorder – 7 Questionnaire (GAD-7)
• Geriatric Depression Scale Short Form (GDS-15)
• Apathy Evaluation Scale Self-Rated (AES-S)
• SleepAD sleep questionnaire

The study team will also record basic demographic information (e.g. age, sex, ethnic group, occupation, employment status).

Main Study Assessments

1. Venepuncture of 5-10 ml blood biomarkers taken for analysis of biomarkers (P-tau & NFL, GFAP and abeta42/40, and possibly others in future). The blood sample will either be arranged to be taken during a routine clinical appointment venepuncture at the Brain Centre (i.e. not an extra venepuncture), or during a separate appointment (which would require a new venepuncture).
2. Sleep recording - participants will undergo EEG recording at home for 3 nights and will also complete a Consensus Sleep Diary questionnaire each night. The sleep monitoring will be performed using high-density at-home EEG equipment which will be set up by the researcher in the participant's home. This will involve participants undergoing full polysomnography (PSG), where electrophysiological data from electrodes placed on the scalp, face and body will be recorded. The home setup is designed to closely replicate the setup used in sleep laboratories. Participants will wear a 32-channel sleep cap including scalp and auxiliary channel location using a wireless LiveAmp 32-channel active electrode system (BrainProductsUK). EEG recordings are acquired on an internal memory system and will subsequently be downloaded to a secure University of Bristol server. Although we do not currently have experience of sleep recordings in Alzheimer's disease, we have experience from recording sleep in patient populations of similar age, living with chronic pain. In our experience, these patients tolerate sleep recordings well. Numerous EEG studies in Alzheimer's disease are reported in the literature, as reviewed elsewhere.
3. Pulse oximetry – participants will be asked to undergo two nights of overnight pulse oximetry (concurrent with EEG recording) during the 3 night window of sleep recordings. A pulse oximeter is a device routinely used in NHS practice to collect pulse oximetry data, and will be used in line with NHS protocols to monitor pulse and oxygen saturation levels and screen for obstructive sleep apnoea (OSA). Overnight pulse oximetry is an accepted and widely used screening tool for moderate to severe OSA. Those with abnormal results will be offered referral to the Non-invasive Ventilation Clinic and their GP will be informed with the participant's consent.
4. Sleep dependent memory testing - a long-term memory word test delivered by the researcher on either the second or third evening of testing (order counterbalanced)

5. Acceptability - participants will be asked to complete a brief questionnaire within 1 week of their final testing session to feedback on their experience

SleepAD SUB-STUDY 2

Design: Single centre, prospective observational feasibility study.
Setting: Southmead Hospital cognitive disorders clinic and participants' homes.

Consent:
Anyone taking part will be informed of the study aims and protocol. It will be made clear to participants that if they wish to, they may withdraw their consent at any time without the need to provide an explanation and that this will not affect future medical care.

The investigator taking consent will be trained in taking consent and will act in accordance with GCP. Capacity to consent is assessed by the researcher as they discuss the information sheet with the patient. The researchers will ensure the volunteer has understood and retained information for long enough to allow risks and benefits to be considered and that a decision can be relayed clearly.

Baseline Assessments: The study team will also record basic demographic information (e.g. age, sex, ethnic group, occupation, employment status) and clinical diagnoses.

Main Study Assessments
Venepuncture of 5-10 ml blood biomarkers taken for analysis of biomarkers (P-tau & NFL, GFAP and abeta42/40, and possibly others in future). In all participants undergoing LP, this will be at the time when bloods are taken alongside LP in any case (i.e. there will be not an extra venepuncture, just more blood drawn). In very rare situations, for example, participants who have another form of biomarker testing (e.g. PET scanning), a new venepuncture will be needed. As an optional addition, an extra < 5 ml of CSF will be taken during the routine LP for analysis and storage, as long as this does not prolong the procedure by more than 1 minute.
All patients will have had a MoCA cognitive test as part of routine care within 3 months of CSF collection. In the very rare case that this has not happened as part of routine clinical care, we will also carry out a MoCA as close as possible in time to their lumbar puncture (taking into account they might be nervous on the day of the procedure, we may do this at a different hospital visit).

Intervention Type
Other

Primary outcome(s)
Baseline screening only:
Sub-study 1:
1.1. Amount of missing data for sleep nights with high density EEG.
1.2. Acceptability ratings for home EEG (Acceptability will be measured using a non-validated experience questionnaire, developed to evaluate acceptability at the end of the study)
1.3. Various sleep metrics, including time spent (in minutes) in different sleep stages as measured from EEG
1.4. Number of datasets for sleep nights with pulse oximetry

Sub-study 2:
2.1. Number of lost/degraded blood samples
2.2. Diagnostic accuracy of the separate index tests (Neurofilament light chain, NFL; phosho-tau, p-tau) for Alzheimer's Disease, at pre-published thresholds, compared to reference standard

(Cerebrospinal Fluid, CSF) via AUROC curves. We will also explore heterogeneity in diagnostic accuracy of AD index tests by pre-specified factors listed using cut offs for AD/no AD extrapolated from UCL clinical laboratories.
2.3. The relationship between biomarkers (p-tau and NFL; blood levels measured using validated Single Molecular Array assays of NFL and P-tau-181) and sleep metrics (including Total sleep time [mins], Sleep Latency [mins], Wake After Sleep Onset [mins], Awakening [frequency], Nap duration [mins], Nap [frequency], N1/N2/N3/REM duration [mins], Micro-arousal index, Sleep fragmentation index, Apnea-hypopnea index; measured using a high-density EEG sleep cap and pulse oximeter) in patients who have had both blood biomarkers and high-density EEG.

Key secondary outcome(s)
There are no secondary outcome measures

Completion date
30/10/2026

Eligibility

Key inclusion criteria
For Sub-Study 1:
1. Age > 50 years
2. All participants must express that they are willing to take part in this study and adhere to the study procedures
3. Full capacity to consent to involvement
4. Clinical diagnosis of MCI due to AD or mild AD according to standardised criteria

For Sub-Study 2:
1. All participants undergoing CSF testing clinically including CSF biomarkers of AD.
2. All participants must express that they are willing to take part in this study and adhere to the study procedures.
3. Full capacity to consent to involvement

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
50 Years

Upper age limit
120 Years

Sex
All

Total final enrolment
0

Key exclusion criteria
For Sub-Study 1
1. Severe medical or psychiatric co-morbidity, which, in the opinion of the investigator, may substantially impact on sleep.
2. Clinically significant sleep disorder as defined by ICD-10 or equivalent pre-dating and / or not related to AD pathology.
3. Diagnosis of dementia other than AD.
4. Montreal Cognitive Assessment (MoCA) < 11/30

For Sub-Study 2
1. Severe medical or psychiatric co-morbidity, which, in the opinion of the investigator, may substantially impact on the ability to tolerate withdrawal of an extra 10ml of blood.

Date of first enrolment
15/03/2023

Date of final enrolment
31/05/2026

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Southmead Hospital
North Bristol NHS Trust
Southmead Road
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Sponsor information

Organisation
University of Bristol

ROR
https://ror.org/0524sp257

Funder(s)

Funder type
Charity

Funder Name
Rosetrees Trust

Alternative Name(s)
Rosetrees, Teresa Rosenbaum Golden Charitable Trust

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
After the study has ended our data will be deposited in the University of Bristol Research Data Storage Facility and held for 20 years, and will then be securely disposed of. This is a secure set of disks and servers for the long-term storage of data. Anonymised data may be made available to approved reputable researchers only, and their research institution would need to complete a request form and sign a Data Access Agreement. In addition, anonymised data may be securely uploaded, and held in perpetuity, on the Dementia Platforms UK Data Portal, for approved reputable researchers to use in future ethically-approved research.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Participant information sheet	version 4.0	02/02/2023	21/03/2023	No	Yes
Participant information sheet	version 4.0	02/02/2023	21/03/2023	No	Yes
Protocol file	version 6.0	06/09/2024	30/09/2025	No	No