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Stimulating brain rhythms during sleep (SeRCLES study)

PARTICIPANT INFORMATION SHEET

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Central University Research Ethics Committee Approval Reference: R89942/RE001

We would like to invite you to take part in a research project. This sheet provides some information to help you decide whether to do so. Please take time to read this carefully and discuss it with friends, family or your GP if you wish. If there is anything that you do not understand, or if you would like more information, please ask us. Please take time to consider whether you wish to take part.

What is the purpose of the research?

We would like to find out whether we can boost specific brain rhythms during sleep to improve memory formation.

Sleep is thought to play an important role for cognitive function. In particular, slow brain rhythms during deep sleep and their interactions with other rhythms in the brain are found to contribute to how well we remember something the next day. Considering that these brain rhythm interactions during sleep become less precise with age and in many neurological conditions, it is important that we understand how we can enhance them to improve cognitive function and quality of life.

Transcranial current stimulation (TCS) is a safe and painless method to stimulate the brain, to alter these brain rhythms during sleep. TCS involves delivering a very weak electrical current to the brain. Previous studies have found that this stimulation can be applied during sleep without waking people up.

The purpose of this study is to find the best part of the brain to stimulate in order to improve different types of memories. This includes memories of pictures and locations, as well as memories of learned movements. It is hoped that the results of this study will enable us to design future studies in people with neurological conditions that affect learning and memory.

Why have I been invited to take part?

You have been invited to take part because you have responded to an advertisement, or because you have taken part in other studies and agreed to be contacted again.

We are recruiting healthy adults between the ages of 18 and 35 years who are living in the United Kingdom and are fluent in English.

Unfortunately, not everyone can take part in this study. A researcher will go through a screening from with you to ensure that it is safe for you to take part in this study. You will be **unable to take part** in this study:

- If you have any current or recent (within the past 12 months) psychiatric disorder diagnosed by a specialist, such as major depression, bipolar disorder or schizophrenia (please ask the researcher if you are unsure).

- If you have any history of or current neurological condition (e.g., epilepsy, stroke).
- If you have a job that involves alternating shift patterns (i.e., day shifts and night shifts).
- If you have a diagnosed but untreated sleep disorder (e.g. sleep apnea)
- If you are currently receiving certain medications such as antiepileptics, antipsychotics, psychostimulants (please ask the researcher if you are unsure).
- If you have any metallic or electronic implants in or near the head (such as an aneurysm clip or deep brain stimulator, etc.).
- If you have a pacemaker
- If you are, or think you might be, pregnant (we will not test for pregnancy).

Please speak to the researcher if you have any specific questions about the inclusion or exclusion criteria.

Do I have to take part?

No. It is up to you to decide whether to take part. You can withdraw from the study, without giving a reason, and without negative consequences, by letting the researcher know. Any data that have been collected from you may still be used in the study, unless you request otherwise. If you want to withdraw your data, please advise the researcher within 1 month from when you took part.

If you are a student, there would be no academic penalty if you do not want to take part, or if you decide to stop at any point.

What will happen to me if I take part in the research?

If you would like to take part after reading this information, please let the researcher know by email or phone (contact details at the end of this document). A researcher will contact you to go over the information sheet and explain the procedures. The researcher will go through a screening form with you to make sure that it is safe for you to take part. If you are suitable, and happy to continue, they will then arrange a date for the first session at which you will be asked to sign a consent form.

This research includes 3 visits to the sleep laboratory at the Oxford Centre for Human Brain Activity, Warneford Hospital. There will be at least one week between each visit. Each visit takes approximately 5 hours (see figure 1 for an overview of what each session will involve)

Below are the different elements of each study session, more details of each step can be found on the following pages:

1. Screening to ensure it is safe for you to take part.
2. In the first visit, completion of the Consent Form, demographic information, handedness, and sleep quality questionnaires.
3. Sleep recording and brain stimulation setup.
4. An alertness task, one picture location learning task, and one movement (motor) learning task.
5. A 90–120 minute nap opportunity with brain stimulation and recording of your brain activity.
6. A repeat of the alertness, picture location, and movement tasks.

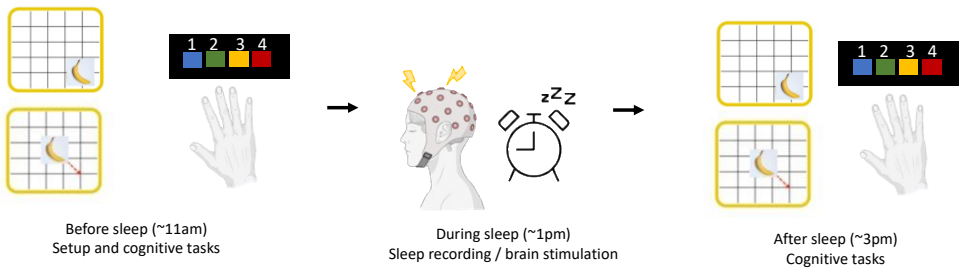


Figure 1: Schematic of each study visit. Before sleep, we ask that you complete some questionnaires and cognitive tasks. During sleep (90-120 minutes), we will record your brain activity and you will receive brain stimulation. After sleep, you will be tested again on the cognitive tasks.

Before the visit

We will ask you not to consume caffeine or alcohol for 12 hours before each study visit, and ask that you refrain from taking any recreational drugs for at least 24 hours before each study visit. We will ask you to wake up approximately 1 hour earlier than usual to increase the likelihood that you can fall asleep easily while in the sleep lab. Please bring comfortable clothing that you would like to sleep in.

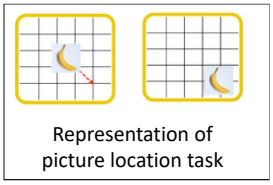
During the visit

When you arrive for the first session, a researcher will go through the details of the study again and you can ask any additional questions you may have. If you are still willing to take part, we will ask you to sign an informed consent form and a researcher will ask you to complete the screening questionnaire. You will then be asked to fill in a questionnaire about yourself (including age, sex assigned at birth, and ethnicity). We ask these questions so that we can determine how well the group of study participants represents the population. We will also ask you to complete a questionnaire to determine your hand preferences for different tasks (allowing us to quantify your handedness) and a questionnaire about your sleep quality. For sessions two and three, you will not need to complete all the questionnaires again, but we will ask you to check over your answers to the screening form and let us know if any of your answers have changed.

In all sessions, you will have the opportunity to get ready for sleep in our sleep lab (e.g. by changing into comfortable clothing). We will place electrodes/sensors on your scalp and face which will record your sleep and deliver the brain stimulation. Before we attach the electrodes, we will measure your head size, clear small patches of your skin (using alcohol swabs) and put conductive gel under each of the electrodes/sensors to make sure they have a good contact while you sleep (you will have the opportunity to wash your hair at the end of the session if you would like to). These sensors will capture your brain activity (EEG), your eye-movements and your muscle tone. This will allow us to know when during sleep is the right time to give the brain stimulation, and to measure how the brain stimulation alters your sleep. It should take no longer than 1 hour to set up the recording and stimulation equipment.

We will ask you to rate your sleepiness on a questionnaire and before completing three computer-based tasks. The first will be an alertness task measuring response time and accuracy, where you will need to press a button every time you see a specific cue on a computer screen in front of you. The following tasks will be two memory tasks, a picture location memory task and a motor (movement) memory task.

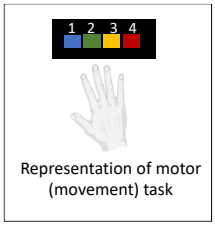
In the picture location task, you will be shown images of objects, scenes and faces on a computer screen in front of you and asked to try to memorise the location of each image on the screen. After viewing all the images, you will be shown each image and asked to use a computer mouse to drag the image to the location you think it was originally in. In the practice phase you will be given feedback on your accuracy. In the test phase (prior to and following sleep) you will be asked to drag each image to the location but will not receive feedback on your accuracy.



Representation of picture location task

In the motor memory task, we ask that you press a series of buttons in a repeated order when you see cues appear on the screen.

You will be shown the tasks and can ask any questions before you start. Combined these tasks should take less than 1 hour to complete.



Representation of motor (movement) task

You will then have the opportunity to nap for 90-120 minutes. During the nap we will stimulate your brain using a very weak electrical current. Two small rubber electrodes (e.g. a circle 2cm across or a rectangle up to 5 cm across by 7 cm long) are placed on your scalp either with some conducting gel or by placing them into sponges soaked in salty water (saline). These are then held in place with bands wrapped around the head or a fabric cap on your head. As we are aiming to compare the effects of different stimulation locations, in some sessions we will place one electrode on your forehead and the other on your neck near your ear. In other sessions we will place one electrode on the top of your head and the other on your neck. If you wear your hair tied up (e.g. in a pony tail) it might be necessary for you to put your hair down so that we can place the electrodes correctly on your scalp. A weak current is then passed through these electrodes. In some of

the sessions you will receive real (active) brain stimulation and in some of the sessions you will not receive stimulation. The order of these conditions is randomly allocated and neither you, nor the researcher, will know whether you receive active stimulation or not.

For most people brain stimulation (TCS) is a painless procedure, but some people can feel a slight tingling sensation under the electrodes, especially when the current is switched on. Some people also experience some short-lasting redness on their skin. We will stimulate when you are in the deeper stages of sleep, so we do not expect you to feel anything or to wake up during the stimulation. However, if you do wake up or find it uncomfortable, you are free to stop at any time. You will have access to a buzzer so you can reach the researchers at any time during the sleep period.

After the nap, we will ask you to complete the questionnaire about your sleepiness again as well as repeat the computer-based tasks (alertness, picture location and motor memory tests). This should take less than 1 hour to complete. If you changed into comfortable clothing for sleeping you are free to change back into your other clothes before or after these tasks, depending on your preference. We will also ask you about your experience of the stimulation and whether you felt any sensations on your scalp. Once the session is finished you will have the opportunity to wash your hair if you would like to (we will provide a towel, shampoo, hair dryer, and you can use the sink in the sleep lab or if you prefer have access to a shower). After the session we will provide you with a light lunch if you would like it (please let the researcher know prior to the session of any dietary requirements).

You can ask to pause or stope the research activities at any time by letting the researcher know.

Please note that because the stimulation takes place in the deepest stages of sleep, we will be unable to stimulate if you do not sleep deeply enough to reach these stages. If this should occur in the first session, we would ask that you do not return to the subsequent sessions to reduce data waste and avoid wasting your time and the time of the researchers and the sleep lab. However, you will be compensated for your time as well as receive the additional bonus payment (see expenses and payment section).

Are there any disadvantages or risks in taking part?

Some people might find it unusual to wear the electrodes/sensors while they sleep, however, for most people, this does not disrupt sleep. The reason we apply these electrodes at the start of the session is so that you have time to become more familiar with the sensation of wearing them before trying to nap. The electrodes will be cleaned and disinfected between participants (if multi-use electrodes). The skin surface under the electrodes will be cleaned using hypoallergenic swabs before application. If multi-use electrodes are used, a conductive gel will be used to aid recording (to make sure we get a good contact with your skin). This gel will be anti-allergenic, as will any cleaning solutions used for cleaning electrodes, or the area of the skin to be recorded from. You will be able to wash off any gel at the end of the session if required. The measurements used within this study are for research only and are not designed to identify any sleep/health problems, and the researchers conducting this study are not trained to identify any sleep/health-related problems from the recordings.

TCS uses a very low current and is not known to be harmful. There have been many studies throughout the world using this technique and no side effects have been seen, apart from the slight tingling feeling mentioned above, and occasional headaches. However, as with all techniques that directly stimulate the brain, TCS has the possibility to induce seizures (fits) in people who are more susceptible to them (although there are no known reports of this in healthy participants). We will ask you to fill in a screening questionnaire to make sure it is safe for you to participate. As a precaution, it may not be possible to give TCS to someone with a personal or close family (first-degree relative e.g. parent, sibling, child) history of epilepsy, certain neurological (brain) or psychiatric disorders. If you are unsure, please ask the researchers. If you are taking any medication, you should discuss this with the researcher beforehand.

How often an individual can safely participate in non-invasive brain stimulation research is unclear. Many studies use non-invasive brain stimulation to treat disorders (e.g. depression) and administer stimulation daily, as the therapeutic effects are thought to accumulate across periods of stimulation. Sessions separated

by 2 days or more do not show cumulative (carry over) effects, however. To minimise the possibility of cumulative effects of brain stimulation, we recommend that participants receive brain stimulation on a maximum of two consecutive days and no more than four sessions in one month. While no guideline has been provided for "cooling-off" between stimulation periods, some have suggested it to be between 48 hours and one week after stimulation. Therefore, we recommend that you should not take part in another study using brain stimulation for at least one week after completing this study.

It is our policy not to give TCS to someone who is pregnant. We do not routinely test for pregnancy. If you think there is a possibility that you are pregnant, you must not take part in this research.

Are there any benefits in taking part?

There are no immediate benefits for those people participating in the project.
It is hoped that this research will help us to develop this technique further, which could have the potential to benefit memory consolidation in various populations.

Expenses and payments

You will receive £40 per session for your time (plus reimbursement of reasonable travel expenses upon production of a receipt). You will also receive a bonus payment of £30 if you complete all three sessions (therefore up to £150 in total). This will be transferred from the University to your bank account, or alternatively we can send you a shopping (e.g. Amazon) voucher. If you do not complete all sessions of the study, you will receive payment for the number of sessions that you have attended.

Note. If the reason you are unable to complete all sessions is because the researcher informs you that you are withdrawn from the study (e.g. if you are unable to sleep sufficiently deeply in the first session, or if something in your medical history changes that means the researcher determines that you no longer pass safety screening) then you will still receive the bonus payment.

What information will be collected and why is the collection of this information relevant for achieving the research objectives?

We will keep identifiable data about you (name, email address, phone number) until the study data has been analysed. This excludes research documents with personal information, such as paper consent and screening forms, which will be stored safely in locked cabinets in a secure University of Oxford building for 5 years after publication or public release of the work of the research. Screening forms are accessible by authorised centre staff. If you are excluded or withdraw from the study following consent, your screening form will be kept unless you request all data already collected to be withdrawn.

Other research data will be stored (using a code rather than your name) for at least 5 years after publication or public release of the work.

Your personal details (name, address, bank account number, National Insurance number, nationality) need to be shared with the finance department of the University of Oxford in order for you to receive payment for your participation. The University finance department will keep these details for 7 years. If you do not want to provide this information for this purpose, then we can give you a shopping (e.g. Amazon) voucher instead.

The research team will have access to the research data. Responsible members of the University of Oxford may be given access to data for monitoring and/or audit of the research.

With your consent, we will keep your contact details on a secure database for up to 5 years, in order to let you know about future studies. We will keep a copy of your consent form with this database, as your consent is our legal basis for re-contacting you under UK data protection law. If you are contacted about a future study, you **do not** have to agree to participate. You can have your details removed from the database at any

time by contacting the researchers. If you do not consent for your contact details to be kept, they will be deleted as soon as no longer needed for this study.

Research data may be transferred to, and stored at, a destination outside the UK and the European Economic Area. Details that directly identify you will be removed and any data transfer will be done securely and with a similar level of data protection as required under UK law.

We may use data from this research in future studies and share this with other researchers (e.g. in online databases). This will only be in a form that does not identify you.

Will the research be published? Could I be identified from any publications or other research outputs?

The findings from the research may be written up as part of a grant application, academic publication or in a student thesis/dissertation. Findings may also be presented at conferences or public presentations, or put on our website. It will not be possible to identify you in these outputs.

If data is included in a student thesis, a copy of their thesis / dissertation will be deposited both in print and online in the Oxford University Research Archive where it will be publicly available to facilitate its use in future research.

Data Protection

The University of Oxford is the data controller with respect to your personal data and, as such, will determine how your personal data is used in the research.
The University will process your personal data for the purpose of the research outlined above. Research is a task that we perform in the public interest.
Further information about your rights with respect to your personal data is available from https://compliance.web.ox.ac.uk/individual-rights.

Who has reviewed this research?

This study has ethics approval from a subcommittee of the University of Oxford Central University Research Ethics Committee. (Ethics reference: R89942/RE001**)**.

Who is organising and funding the research?

This study is organised by Dr Melanie Fleming and Dr Anna Guttesen from the Nuffield Department of Clinical Neurosciences. The study is funded by the Wellcome Trust, Guarantors of Brain and the University of Oxford Medical & Life Sciences Translational Fund.

Who do I contact if I have a concern about the research or I wish to complain?

If you have a concern about any aspect of this research, please contact Dr Anna Guttesen, sleep-win@ndcn.ox.ac.uk or Dr Melanie Fleming, melanie.fleming@ndcn.ox.ac.uk , ph 01865611461, and we will do our best to answer your query. We will acknowledge your concern within 10 working days and give you an indication of how it will be dealt with. If you remain unhappy or wish to make a formal complaint, please contact the Chair of the Medical Sciences Interdivisional Research Ethics Committee (MS IDREC) at the University of Oxford who will seek to resolve the matter as soon as possible - Email: ethics@medsci.ox.ac.uk; Address: Research Services, University of Oxford, Boundary Brook House, Churchill Drive, Headington, Oxford OX3 7GB.

Further Information and Contact Details

If you would like to discuss the research with someone, or if you have any questions, please contact:

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