# The role of dreams in memory consolidation and reactivations during sleep

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Primary Objective: This study aims to investigate the role of dreams in memory consolidation during sleep. These are our 2 primary objectives and the associated hypothesis:1) To replicate the result of our previous study in large sample size: Only…

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| **Ethical review** | Approved WMO |
| **Status** | Completed |
| **Health condition type** | Other condition |
| **Study type** | Observational non invasive |

## Summary

### ID

NL-OMON54358

**Source**
ToetsingOnline

**Brief title**
Dream Memory

### Condition

- Other condition

**Synonym**
Memory, Retention

**Health condition**

neuro-psychological

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** Donders Institute for Brain, Cognition, and Behavior, Radboud University Nijmegen
**Source(s) of monetary or material Support:** Swiss National Science Foundation;Cogito Foundation;Dream Research Foundation

## Intervention

**Keyword:** Consolidation, Dream, Memory, Sleep

## Outcome measures

### Primary outcome

The main endpoints are the performance in the picture-word association task, as well as emotional valence and arousal rating of the pictures of the picture-word association task. EEG will also be used for sleep staging.

### Secondary outcome

Secondary aims of the proposed research include EEG correlates of dreaming and dream reports and potential analysis of the sleep EEG (e.g. spindle/slow wave analyses).

* Other study parameters (if applicable)

Other exploratory analysis are possible using the EEG, stool samples and questionnaire data.

# Study description

### Background summary

Memory is essential to humans throughout their lifespan enabling us to survive in environments with both changing and static components. A broad range of literature has shown that sleep is important for memory functions (for a review see Rasch & Born, 2013). While encoding and retrieval of memories occur during wake, sleep has been proposed to be the optimal state for memory consolidation

(Kirov et al., 2009). Memory consolidation encompasses both the strengthening of memory (often measured as performance on a memory task) and the emotional processing of memory (Walker & van Der Helm, 2009). Evidence is emerging that the two sleep stages, rapid eye movement sleep (REM) and Non-REM sleep (NREM, further divided into 3 stages), might each be important for one of these functions. A broad range of studies has shown the effect of sleep on memory strength for different types of memory (e.g. Plihal & Born, 1997, 1999) and different age groups (e.g. Aly & Moscovitch, 2010; Seehagen et al., 2015). Many studies have shown an association of NREM sleep with overnight changes in memory strength (e.g. Holz et al., 2012; Tucker et al., 2006). The active system consolidation hypothesis (Diekelmann & Born, 2010) proposes that sleep plays an active role in memory consolidation by spontaneous and repeated neural reactivations(i.e. activations of the same neurons in the same sequence) particularly in the hippocampus, which have been measured in both rodents and humans (Hirase et al., 2001; Pavlides & Winson, 1989; Peigneux et al., 2004). The hypothesis assumes that during sleep, memories are redistributed from the hippocampus to the neocortex. This redistribution is posited to be orchestrated by slow waves and spindle-ripple events (Staresina et al., 2015); both features of NREM sleep. Studies in humans have shown that these reactivations can also be induced by presenting cues (e.g. sounds) associated with a specific memory during sleep, so-called targeted memory reactivations (TMR, Rasch et al., 2007). In rats, it has been shown that these cues lead to reactivation events of the specific associated memory (Bendor & Wilson, 2012). The function of REM sleep in memory consolidation is less clear. One proposed function could be the removal of the associated affective tone of emotional memories (Walker & van Der Helm, 2009). Repeated reactivations during REM sleep could lead to depotentiation of emotional valence (i.e. positive or negative) of a memory. On the other hand, sleep with more REM has been linked to increased valence ratings on emotional images in the next morning (Lara*Carrasco et al., 2009). Potentially, REM sleep increases emotionality short-term but decreases long-term valence of emotional memories. One aspect of sleep has often been overlooked in these studies: dreaming. This is partially because dream research relies on the participants* reports of their dreams. This means that we cannot disentangle a lack of dreams from a lack of remembering dreams and we cannot study dreams unless they are remembered and reported. While research has investigated when we dream (McNamara et al., 2010; Siclari et al., 2017), what we dream about (Griffith et al., 1958; Schredl et al., 2004), the question of potential functions of dreaming is still unsolved. Studies have shown, that dreams often reflect recent waking-life experiences (Schredl, 2003), and learning a game before sleep leads to incorporation of the game into dreams (Stickgold et al., 2000).

Therefore, dreams could potentially reflect memory consolidation processes. If that is true, then dreaming of a task should lead to better recall of said task. However, it would make sense that the dual functions of the different sleep stages for different aspects of memory consolidation also apply to dreams from the respective stages. Humans report dreams when awoken from both NREM and REM sleep, however, dream reports from REM are more frequent, longer, more

emotional and more vivid. This reflects the different neural environments present during the different sleep stages. A recent article that reviewed 12 published studies on dreaming and memory consolidation has shown discordant results (Plailly et al., 2019). Only five of the studies showed (at least partial) associations between dreaming of a task and task performance. The review included experiments using different types of memory, which rely on different brain structures and therefore might be influenced by sleep and dreams in different ways. Additionally, many of the studies included in the review are underpowered (sample sizes less than 20, tasks with less than 10% incorporation rate) and only our previous study (Schoch et al., 2019) differentiated between NREM and REM dreams. Based on the findings of sleep and memory research, we hypothesize, that only NREM dreams are associated with memory strength, which is what we found in our previous study, which, however, only included a small sample size (Schoch et al., 2019). In fact, when dividing the studies in the review by sleep stage the dream reports are collected from, a similar pattern appears: when only REM dreams are used positive findings are rare (1/5 studies), but both studies with only NREM dreams show an association (2/2). Therefore, it seems plausible that dreams reflect the specific consolidation processes happening during each sleep stage. Additionally, supporting this hypothesis is the finding from a study that shows that the incorporation of stressful events into REM dreams is associated with better mental health outcomes (Cartwright et al., 2006). TMR presents interesting possibilities to not only study associations between dream content and memory performance but also directly manipulate dream content using external cues. Applying TMR and next to researching spontaneous incorporation will give a much more detailed and mechanistic understanding of how dreams relate to declarative memory processes in the night. Furthermore we are exploring how measurements of autonomic activation (heart rate and stomach contractions) relate to sleep, dreaming and memory consolidation processes during sleep.

**Study objective**

Primary Objective: This study aims to investigate the role of dreams in memory consolidation during sleep. These are our 2 primary objectives and the associated hypothesis:

1) To replicate the result of our previous study in large sample size: Only incorporations in NREM dreams are related to memory strength and to elicit the role of REM dreams in memory consolidation. Our first research hypothesis is the following:
H1) NREM and REM dreams reflect different aspects of memory consolidation pro-cesses during sleep.
A) Incorporations of the picture categories of the memory task into NREM dreams, but not REM dreams, are associated with improved performance on the memory task the next morning and 4-days later.
B) Incorporating the picture categories of the memory task during REM dreams is associated with lower emotional and arousal ratings the next morning and at a

4-day follow-up.
2) To use TMR to verify that dreams reflect memory reactivations during sleep. The memory task we have used in my previous experiment and plan to re-use has been designed for use with targeted memory reactivations (Lehmann et al., 2016). We will use this to cue specific images during sleep and then verify with subsequent dream reports if they were incorporated into dreams. My second research hypothesis is the following:
H2) TMR leads to subsequent incorporation of the associated image categories into dreams during NREM and REM sleep stages.

Secondary Objective(s):
We have three more objectives we want to investigate with the dataset we plan to collect:

4) To research the body-brain axis during sleep and dreaming. This will be done using three methods: 1) ECG: We will investigate the associations between heart rate variability as well as heartbeat evoked potentials and dreaming as well as dream experience. 2) EGG: We will ex-amine the amplitude and regularity of gastric rhythms in relation to sleep and dreaming, as well as the coupling of the gastric rhythm with the EEG. 3) Gut microbiota: We will examine the relationship between gut microbiota composition and sleep parameters collected using the Fitbit over 4 weeks.

5) To generate a large dataset of dream reports and corresponding neural activity. This will be used to apply machine learning to decode dream content and emotion. We will use the EEG data leading up to the dream reports (2 min interval) and use a convolutional neural network as well as Phase Space Reconstruction and Complex Networks to see if it can predict from the neural activity if the dream was neutral, positive or negative and what the dream content was (based on the 6 topics used).

6) To establish the reliability of dream reports of dreams collected in multiple conditions. Because the current project will utilize different methods for the study of dreaming, it is a unique opportunity to reflect on the trustworthiness of dream reports allowing us to further optimize the conditions and methods for their collection. For example, targeted memory reactivation and decoding provide an additional source of evidence that in combination with dream reports might allow our team to triangulate underlying aspects of dream experience. We will also address specific questions related to this project,

for example whether a potential mismatch between decoding results and descriptions in dream reports is due to technical failures or systematic weaknesses in dream reports.

**Study design**

Healthy adult volunteers will be recruited by advertisement. All subjects will visit the EEG lab of the Donders Centre for Cognitive Neuroimaging (DCCN) for one intake session, one adaptation night, and to two experimental sessions, additionally, there will be two recalls the participants can fill out online at home. Before and after each experimental session, participants will be asked to write down their dream reports for 7 days prior and after (online questionnaire, approximately 2-3 minutes per day) and measure their sleep using a Fitbit and a sleep diary.

Recruitment: Participants will initiate the first contact following the study advertisement (see E1). Study advertisement will be posted on SONA as well as distributed on social media (fa-cebook, twitter and Instagram) and via mailing lists and hung up as flyers. Additionally, a short recruitment video to be posted on social media. After this, interested participants will receive detailed information about the experiment and example informed consent forms will be sent via email (see E2 and E3). In a short telephone call, the study details and inclusion criteria will be discussed. They will be explicitly asked whether they fulfill the inclusion criteria. This proce-dure is added to prevent possible dropouts based on our exclusion criteria. If the inclusion criteria are fulfilled, and they have considered the participation and wish to participate, an in-take session is scheduled. Because we only recruit participants with high English language proficiency, all recruitment letters and information will only be provided in English.

Intake session: In a one-hour intake session, a brief recap of the study procedure will be given. Participants will also be informed that they will be excluded from participation in case they (i) do not fit one of the inclusion criteria, (ii) fit any exclusion criteria, or (iii) when no data of sufficient quality can be acquired due to any unforeseen reasons. This explicit declaration is followed by the opportunity for the participant to ask any remaining questions. Once all questions are answered, the participants will sign the informed consent agreement (5 minutes). Then they will fill out all questionnaires and tasks used to screen eligibility for the study (BNT, PSQI, BDI, BAI, MCTQ, MRI, Dream Recall Frequency). The questionnaires will be presented digitally using Castor EDC and are then checked for exclusion criteria. If a par-ticipant meets one of the exclusion criteria, they will be excluded from participation (and paid 6 ¤), and a replacement participant will be recruited. If all criteria are fulfilled, the participants will do a structural T1 and T2 Magnetic Resonance Imaging (MRI) scan on a Prisma or PrismaFit (3T) (20 minutes). Then the three nights in the sleep laboratory (adaptation and both experi-mental nights) are scheduled. The participants will

start collecting sleep data using a sleep tracker (Fitbit Inspire 2) and a sleep diary, as well as a dream diary for one week before the first experimental session. Both are presented digitally and can be filled out on a computer or phone. The sleep and dream tracking procedure is explained in detail, and participants can ask questions (10 minutes). Participants will get a reminder on their phones to fill out their questionnaires each morning.

Adaptation night: The adaptation night is scheduled as closely as possible to the first exper-imental night (the night before the first experimental night, maximally seven nights before). Participants will be invited to the Donders EEG laboratory at 21:30. They will be asked to re-frain from any alcohol/drug intake during the study day, caffeine intake after lunch (maximum of 2 coffees in the morning according to their usual intake) and get up at or before 08:00 (checked with participant report and sleep tracker). The participants will get a short descrip-tion to read of the adaptation night. Then after the participants are bed-ready, we will apply the EEG cap and EOG, EMG, ECG, and EGG (if opted in) electrodes. During this time, the partic-ipants will fill out the following questionnaires: a check on alcohol/drug/caffeine intake (2 minutes) the *Schlaffragebogen A* (sleep questionnaire A, lab translated from German, SQQ 10 minutes) about the previous night and the *Mehrdimensionaler Befindlichkeitsfragebogen* (multidimensional mood questionnaire, lab translated from German, MDBF, 3 minutes), a lab-developed dream memory questionnaire (30 minutes on project OSF), and the daydreaming frequency scale (DDFS, 5 minutes). They will complete a color-naming Stroop task across one practice and five experimental blocks (24 congruent, 12 incongruent trials, 10 minutes). Additionally, they will complete the trail-making test (TMT, 5 minutes).
At 23:00, participants will go to bed and be able to sleep until 07:00. An investigator will always be present, and participants are instructed to knock on the wall if they need anything (e.g., go to the toilet). If participants cannot fall asleep (either after 1.5 hours or when participants re-quest it), we will first remove the EGG. If they still cannot sleep (after 3 h or when they re-quest it), we will remove all electrodes and discontinue the study (they will have the option to sleep in the laboratory or go home). At 07:00, the sleep opportunity will end. They will fill out a questionnaire about their sleep quality (SQQ) and recall their dreams. Then the EEG and oth-er electrodes will be removed, and participants can shower and get dressed. Afterward, we will confirm that they want to continue the study and are eligible based on the sleep quality. At around 7:40, the adaptation night will be done.

Experimental Sessions
The two experimental sessions will be counterbalanced between the participants with random assignment and additional counterbalancing of the memory task categories (random number generator (sample in R) will be used for each participant). Participants are blinded to the con-dition. The two experimental conditions are scheduled at least 14 days apart. Participants are instructed to abstain from alcohol and drugs on experimental days and to get up before 08:00.

No caffeine intake is allowed after lunch, with a maximum of two coffees in the morning. Alco-hol and caffeine intake is checked with a questionnaire. Furthermore, sleep tracker data will be checked to confirm that no sleep nights have been skipped in the previous week. A stool sample is collected by the participant with a kit (OM-NIgene•GUT | OM-200) on the day of the experimental session (not analyzed within this study, opt-in by participants). The experimental sessions will start at 19:30. The participants will get a written instruction explaining the experimental session. Afterward, they will get ready for bed. Then the EEG will be applied.

Session A: Awakenings
During the EEG application, the participants will be able to ask any questions about the awak-ening protocol (the same questions as used at home). For the remaining time during EEG application, the participant will fill out the following questionnaires: the alcohol/coffee check (2 minutes), the Mannheim Dream Questionnaire (MADRE, 10 minutes), the Brief-COPE ques-tionnaire (10 minutes), the MDBF (3 minutes), the need for closure scale (NFCS, 15 minutes), and the Freiburg Mindfulness Inventory (FMI, 5 minutes). Afterward, the participants will un-dergo the learning blocks of the memory task. Between the learning blocks and the recall, there will be a short 10 minutes break during which the participants will fill out the MDBF again and the SQQ for the previous night. Recall happens in 2 blocks which take approximately 30 minutes. At 23:00, participants will go to bed. When the participant is lying in bed, we will do a resting-state EEG measurement (1.5 min eyes open, 1.5 min eyes closed, 1.5 min eyes o

**Study burden and risks**

Considering the extensive exclusion criteria, the screening procedure, constant monitoring of the subjects we do not expect (S)AE (serious adverse effects) side effects. EEG, EGG and MRI measurements themselves do not pose any risk, if appropriate precautions are made. However, for the MRI the noise and the relative confined space of the MRI scanner may cause discomfort to some subjects. However, the scan will only be very short (< 20 mins).

In case of an incidental finding concerning a deviation in the MRI scan, step 1, the researcher will immediately contact the MRI lab manager:
a. If it concerns a healthy subject the MRI lab manager will send the images out for assessment by a radiologist. At this stage the participant is not informed, but the incidental finding will be documented (proceed to step 2).
b. If it concerns a patient and/or minor the researcher is required to consult the responsible study MD.
* The responsible MD is trained to judge the images adequately proceed step 3.
* The responsible MD is not trained to judge the images proceed step 1a.
Step 2, if, according to a written report of the radiologist,
a. No clinically relevant finding is obtained, the participant will not be informed, but the docu- mentation updated.

b. A clinical relevant finding is obtained; the home physician will receive a letter. Also the par- ticipant will receive a letter, which, however, does not reveal any diagnosis but which asks the participant to contact his/ her home physician.
c. The incidental finding will be centrally documented at the DCCN.
Step 3, if the responsible MD considers the abnormality as clinically relevant the home physi- cian or the treating specialist will be personally contacted by the responsible MD. (for details see K6b).
Because of the repeated awakenings, participants will be asked to not drive after the study because of the awakenings. We also recommend not to use the bicycle, but ideally to take the public transport or be picked up by someone. If this is not possible for the participants, we will offer to arrange a taxi to go home.
The consent discussion starts sufficiently in advance of the initiation of study-related procedures to allow potential subjects time to reflect on the potential benefits and risks and possible discomforts. Participants are informed about our standard studies per email before they agree to sign up and they are able to see a consent form and take time to reflect if they want to participate in the study. Participants are informed that the risk associated with participation in this study in total can be regarded as minimal. The results of this study will provide us with better insight into dreams specifically in relation to memory consolidation but additionally also about the associated neural activity and dream reports.

## Contacts

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## Trial sites

### Listed location countries

Netherlands

## Eligibility criteria

**Age**
Adults (18-64 years)

### Inclusion criteria

• Age between 18 and 35 years
• Willingness and ability to sign informed consent
• Physically and mentally healthy
• High dream recall frequency (at least several times a week)
• High English language proficiency (at least 10 items of the BNT)
• Ability to sleep in the sleep laboratory

### Exclusion criteria

• History of or current sleep disorder (PSQI score > 7, skipping sleep in 6 days before adaptation night)
• Current physical or mental illness (BDI * 20 or BAI > 15)
• Medication that influences the sleep/wake cycle and/or memory consolidation
• Daily drug use
• Extreme coffee drinkers (more than 4 cups/day)
• Skin diseases at intended electrode sites (EMG, EEG)
• Chronotype incompatible with study time window (Regular bedtime after 1 am or later)
• Inability to sleep during the adaptation night (sleep efficiency < 70%)
• Intake of coffee or alcohol on study day
• Contraindications for MRI
• Pregnancy or nursing

## Study design

### Design

**Study type:** Observational non invasive

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|---|---|
| Masking: | Open (masking not used) |
| Control: | Uncontrolled |
| Primary purpose: | Other |

### Recruitment

NL

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|---|---|
| Recruitment status: | Completed |
| Start date (anticipated): | 23-02-2023 |
| Enrollment: | 92 |
| Type: | Actual |

## Ethics review

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|---|---|
| Approved WMO Date: | 08-03-2021 |
| Application type: | First submission |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |
| Approved WMO Date: | 15-02-2022 |
| Application type: | Amendment |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |
| Approved WMO Date: | 20-04-2023 |
| Application type: | Amendment |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |

## Study registrations

### Followed up by the following (possibly more current) registration

No registrations found.

### Other (possibly less up-to-date) registrations in this register

No registrations found.

## In other registers

| Register | ID |
| --- | --- |
| CCMO | NL75927.091.20 |