# Sleep as a window to target traumatic memories

Published: 25-10-2017
Last updated: 12-04-2024

The two primary objectives of this study are: 1. To increase therapeutic effectiveness of an EMDR treatment session in PTSD patients by reactivating the updated traumatic memory during post-treatment sleep using TMR; and 2. To provide a neural base...

| | |
|---|---|
| **Ethical review** | Approved WMO |
| **Status** | Recruitment stopped |
| **Health condition type** | Anxiety disorders and symptoms |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON55394

**Source**
ToetsingOnline

**Brief title**
Sleep and traumatic memories

### Condition

- Anxiety disorders and symptoms

**Synonym**
Post-traumatic stress disorder, PTSD

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** Vrije Universiteit Medisch Centrum
**Source(s) of monetary or material Support:** ZonMw

## Intervention

**Keyword:** Functional MRI, Post-traumatic stress disorder, Sleep, Targeted memory reactivation

## Outcome measures

### Primary outcome

The following primary study parameters will be assessed pre- and post TMR:

1. Subjective (e.g. ratings of distress, vividness and emotionality) and physiological (heart rate and salivary cortisol) indexes of fear and arousal related to the targeted, traumatic memory as probed during a script-driven recall and imagery procedure (symptom provocation task);

2. Overall PTSD symptom level;

3. Number of intrusions (and related level of distress) of the targeted traumatic memory;

4. Brain activation and functional connectivity patterns as measured with fMRI during a script-driven imagery task.

### Secondary outcome

The following secundary study parameters will be obtained during 1 week (or several days) before and during intervention to test their association with the TMR effect:

- Divers sleepparameters such as subjective and objective sleep quality, percentage of time spent in (non-)REM sleep, number and density of sleep spindles and spectral power in the theta, delta and sigma range of the respective sleep phases.

The following secundary study parameters will be obtained 1 day before intervention and compared between PTSD patients and trauma controls:

- Brain activation patterns and functional connectivity patterns as measured with fMRI during the script-driven imagery task.

The following secundary study parameters will be obtained during intervention and compared between PTSD patients (in the No reactivation group) and trauma controls:

- Divers sleepparameters as mentioned above.

# Study description

**Background summary**

Post-traumatic stress disorder (PTSD) is a severe mental disorder associated with significant personal and societal burden. Traumatic memories are at the core of its pathophysiology, resulting in key-symptoms such as nightmares and flashbacks. Currently, first-choice treatment, consisting of exposure-based psychotherapy, such as eye movement desensitization and reprocessing (EMDR), proves ineffective in half of PTSD-patients. Hence, there is an urgent need to improve treatment. Sleep is crucial in the treatment of traumatic memories. During exposure-based treatment, traumatic memories get reactivated and subsequently re-encoded with lower fear. This treatment effect is then solidified during memory consolidation while asleep when the 'neutralized' memories get integrated in long-term storage, stabilizing them and further reducing their affective charge. Recent advances in basic memory research show that memory consolidation can be significantly enhanced by presenting reminder cues (sounds/scents that were linked to the memory at encoding) during subsequent sleep (targeted memory reactivation (TMR)). Here, we apply these memory reactivation strategies during sleep for the first time in (PTSD) patients to increase therapeutic effectiveness. Using a controlled design, we predict that re-administering auditory cues, that are already part of a specific PTSD treatment during post-treatment sleep, will increase therapeutic outcome. This is measured as reduced subjective and physiological fear in relation to the targeted memory, as well as reduced overall PTSD symptom level. To visualize the underlying transfer of the memory trace to higher-order memory

networks, we will obtain functional MRI during scripted recall of the traumatic event pre/post study.

## Study objective

The two primary objectives of this study are: 1. To increase therapeutic effectiveness of an EMDR treatment session in PTSD patients by reactivating the updated traumatic memory during post-treatment sleep using TMR; and 2. To provide a neural base for this augmented treatment effect by showing a (enhanced) system-level reorganization of the targeted memory trace using fMRI. In addition, three secondary objectives will be investigated: 1. To test whether diverse sleep parameters (measured both pre-treatment and during the experimental night) are associated to the effect of TMR; 2. To test the effect of TMR itself on sleep macro- and microstructure; and 3. To identify abnormal brain function in PTSD by comparing structural and functional MRI measures (e.g. resting state fMRI and script-driven imagery) between patients and trauma controls. The groups will additionally be compared on all obtained sleep measures to identify sleep deficits distinctive for PTSD.

## Study design

All primary and secondary objectives (except secondary objective 3) will be studied using a randomized, controlled, between-subjects design, comparing 1. Reactivation with the EMDR sound during sleep, 2. No reactivation (treatment as usual) during sleep, and 3. Presentation of a new sound during sleep unrelated to the EMDR session (to rule out general effects of sound presentation during sleep).

## Intervention

Patients will be treated with a single session of EMDR by a certified therapist. EMDR is a first-choice treatment for PTSD, which has been shown to be safe and effective. After successful EMDR treatment, patients will undergo TMR during post-treatment sleep. TMR is a recently described experimental procedure which aims at strengthening memory consolidation processes during sleep by re-administering context cues, such as auditory or olfactory stimuli, that are linked to the targeted memory at awake encoding.

## Study burden and risks

Total participation time will be approximately 22 hours over a 2,5-week time period, consisting of 5,5 hours of clinical interviews, questionnaires and baseline measurements, 45 minutes EMDR therapy session, approximately 1 hour MRI scanning (2 x 30 minutes), daily diary reports of ca. 10 minutes and a night of sleep at the sleep laboratory. Participation time for trauma controls is 17 hours). The risk associated with participation can be considered minimal

and the burden moderate. No adverse effects of TMR have been reported. Participation in the EMDR session and script-driven imagery procedure can cause distress due to the exposure element in the procedures.

## Contacts

**Public**
Vrije Universiteit Medisch Centrum

de Boelenlaan 1108
Amsterdam 1081HZ
NL
**Scientific**
Vrije Universiteit Medisch Centrum

de Boelenlaan 1108
Amsterdam 1081HZ
NL

## Trial sites

### Listed location countries

Netherlands

## Eligibility criteria

**Age**
Adults (18-64 years)
Elderly (65 years and older)

### Inclusion criteria

PTSD patients
* PTSD diagnosis according to DSM-5 criteria as assessed with the CAPS-5
* PTSD as primary diagnosis
* 18-65 years of age
* Capability to provide informed consentTrauma controls
* Having experienced a type A-trauma according to DSM-5 criteria as assessed with the LEC-5 (as part of the CAPS-5).

* No PTSD diagnosis according to DSM-5 criteria as assessed with the CAPS-5
* 18-65 years of age

## Exclusion criteria

PTSD patients
* Current bipolar disorder, psychotic disorder, alcohol or substance dependence as assessed with the M.I.N.I. International Neuropsychiatric Interview. Note comorbid depressive or anxiety disorders will be allowed if PTSD is the primary diagnosis.
* Current personality disorder as assessed with the SCID-5-P (preceded by a screener)
* Active suicidal ideation
* Major head trauma or neurological disease, current or in history
* MRI contraindications such as metal implants, claustrophobia, pregnancy
* Self-reported inability or unease to cease smoking for 24 hours prior to testing (for salivary cortisol sampling)
* Endocrinological disorders or regular use of corticosteroids (for salivary cortisol sampling)
* Use psychotropic medication up to 6 weeks pre-study (or in case of benzodiazepines or other sleep medication 1 week)
* Use of recreational drugs over the entire study period (Day -7 to Day 11).
* Use of alcohol during Day -7, Day 1, Night 1, Day 2, Night 2, Day 3 and Day 11.
* Irregular sleep/wake rhythm (e.g., regular nightshifts or cross timeline travel)
* A sleep window outside 10 pm and 10 am

Trauma controls
* Any current psychiatric disorder as assessed with the M.I.N.I. International Neuropsychiatric Interview or known to the patient her/himself.
* Lifetime PTSD diagnosis
* Impossibility to isolate a circumscribed traumatic memory that can be used for the audioscript and for target selection in EMDR.
* Reactivation of the traumatic memory that is used for the audioscript and for target selection in EMDR, leads to severe dissociative complaints/signs*
* Not speaking/understanding Dutch sufficiently
* Active suicidal ideation
* Major head trauma with co-occurring loss of consciousness in the recent past
* (Neurological) disorder of the central nervous system, current or in history
* MRI contraindications such as metal implants, claustrophobia, pregnancy
* Use of psychotropic medication (other than benzodiazepines or other sleep medication), except when on a stable dose for at least 6 weeks (after start or alteration of dosage). Use of benzodiazepines or other sleep medication in the period of 1 week prior to study until end of study (Day 10).

* Use of recreational drugs over the entire study period (Day -7 to Day 10).
* Use of alcohol during Day -7, Day 1, Night 1, Day 2, Night 2, Day 3 and Day 10.
* Irregular sleep/wake rhythm (e.g., regular nightshifts or cross timeline travel)
* A sleep window outside 10 pm and 10 am
* Sleep walking or REM sleep behaviour disorder

# Study design

## Design

| | |
|---|---|
| Study type: | Interventional |
| Intervention model: | Other |
| Allocation: | Randomized controlled trial |
| Masking: | Open (masking not used) |
| Control: | Active |
| Primary purpose: | Basic science |

## Recruitment

NL

| | |
|---|---|
| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 18-02-2019 |
| Enrollment: | 92 |
| Type: | Actual |

# Ethics review

| | |
|---|---|
| Approved WMO Date: | 25-10-2017 |
| Application type: | First submission |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 03-01-2018 |
| Application type: | Amendment |

| | |
|---|---|
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 20-03-2018 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 12-07-2018 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 29-01-2019 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 14-03-2019 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 04-06-2019 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 12-09-2019 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 06-03-2020 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 29-01-2021 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |

# 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 | NL62909.029.17 |
| Other | Nummer NTR volgt nog |