

# Clinical and neurophysiological effects of imagery rehearsal therapy and targeted memory reactivation in post-traumatic stress disorder

Océane Lüthi

University of Geneva

Vincent Rochas

Fondation Campus Biotech

Audrey Theux

University of Geneva

Alice Clerget

University of Geneva

Laurence Bayer

University of Geneva

Lampros Perogamvros

[lampros.perogamvros@unige.ch](mailto:lampros.perogamvros@unige.ch)

University of Geneva

---

## Research Article

**Keywords:** trauma, sleep, neurophysiology, hyperarousal, dreams, electroencephalography

**Posted Date:** October 14th, 2026

**DOI:** <https://doi.org/10.21203/rs.3.rs-11359503/v1>

**License:**   This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

**Additional Declarations:** The authors declare no competing interests.

---

# Abstract

Post-traumatic stress disorder is frequently associated with post-traumatic nightmares, which may be related to cortical hyperarousal. Imagery Rehearsal Therapy is the first-line treatment for nightmares. Targeted Memory Reactivation, which reactivates specific memories during sleep to enhance memory consolidation, has been shown to enhance the effects of Imagery Rehearsal Therapy in idiopathic nightmares. This study investigated the efficacy of Imagery Rehearsal Therapy for traumatic nightmares and broader post-traumatic stress disorder symptoms, and whether these effects could be enhanced by Targeted Memory Reactivation. Thirty-six adults diagnosed with post-traumatic stress disorder received either Imagery Rehearsal Therapy alone ( $n = 17$ ) or Imagery Rehearsal Therapy combined with Targeted Memory Reactivation ( $n = 19$ ). Participants completed three weekly Imagery Rehearsal Therapy sessions and underwent polysomnographic recordings before and after the intervention. In the combined treatment group, a sensory cue associated with the positive therapy scenario was presented during sessions and reactivated nightly during rapid eye movement sleep at home using a sleep headband. Imagery Rehearsal Therapy significantly improved post-traumatic stress disorder symptoms and associated outcomes, including insomnia severity, nightmare frequency/distress, and depressive symptoms. No additional benefit of Targeted Memory Reactivation was observed. Compared to healthy individuals, trauma-exposed patients showed baseline polysomnographic alterations suggestive of cortical hyperarousal, including increased frontocentral beta activity during non-rapid eye movement sleep and reduced frontal delta activity during rapid eye movement sleep. Following treatment, beta activity decreased, while Targeted Memory Reactivation was associated with additional posterior sleep-related neural changes during rapid eye movement sleep, in regions previously implicated in dream experience.

## Introduction

Adverse life events are potentially traumatic events such as exposure to death, life-threatening situations, actual or threatened serious injury, or sexual violence. Exposure to such potentially traumatic events may lead to post-traumatic stress disorder (PTSD) in approximately one third of individuals (Tortella-Feliu et al. 2019), with a lifetime prevalence ranging from 3.4% to 26.9% in the general population (Schein et al., 2021). The DSM-5 of the American Psychiatric Association (APA, 2013) lists 5 criteria to diagnose PTSD (exposure to trauma, intrusion symptoms, avoidance, negative beliefs and emotions, arousal). PTSD affects individuals across the lifespan, with far-reaching consequences for multiple domains of life, such as mental and physical health consequences (Olf et al., 2025).

Sleep difficulties, such as intrusive nightmares or insomnia, are reported in up to 70% of all patients with PTSD (Leskin et al., 2002; Spoormaker & Montgomery, 2008) and are correlated with PTSD symptoms severity (Krakow, Germain, et al., 2001; Germain et al., 2004; Calhoun et al., 2007; Werner et al., 2016; Tahmasian et al., 2017). More specifically, chronic recurrent nightmares are one of the integral symptoms of PTSD (APA, 2013). These are intense dreams with strong negative emotions occurring during both NREM and rapid-eye movement (REM) sleep (Phelps et al. 2018). Posttraumatic nightmares

are recurrent replicative or non-replicative dreams related with the traumatic event, and they occur in about 70% of the PTSD patients (Lemyre et al., 2019).

Among objective sleep measures, REM sleep disruption is the most reported alteration in PTSD (Calhoun et al., 2007; Habukawa et al., 2007; Mellman et al., 2002; Pillar et al., 2000). Previous literature suggests the presence of fragmented and reduced REM sleep in the period shortly after trauma exposure, and relatively preserved or increased REM sleep in chronic PTSD (Mellman et al. 2014). At the EEG level, Wang et al. (2020) reported reduced delta power during NREM sleep and increased beta/gamma power across both NREM and REM sleep, suggesting heightened physiological arousal in PTSD compared to healthy individuals. Similar spectral modulations have been described during both NREM and REM sleep in patients with nightmares as a combination of reduced sleep-protective activity and increased hyperarousal suggesting an imbalance between sleep regulatory and wake-promoting systems (Blaskovich et al. 2020, Sayk et al. 2024). Overall, previous studies support the idea of cortical hyperarousal during sleep in both patients with PTSD and those with nightmares, characterized by low delta frequencies and/or high beta/gamma frequencies. This oscillation pattern should be verified and assessed according to the patient condition and its response to therapies.

According to current guidelines, first-line treatments of PTSD comprise trauma-focused psychotherapies, while pharmacotherapy is considered as a second-line treatment (APA, 2025). Psychotherapeutic techniques aim to reduce PTSD severity by directly addressing memories, thoughts and feelings related to the traumatic event (i.e., exposure therapy, cognitive processing therapy, trauma-focused cognitive behavioural therapy, eye movement desensitization and reprocessing) (Watkins et al. 2018). However, despite the effectiveness of psychotherapeutic treatment in the management of PTSD symptoms, many patients remain only partially responsive (Cusack et al. 2016, Watkins et al. 2018). One possible explanation is that avoidance, a core feature of PTSD, may reduce engagement with trauma-focused components of cognitive behavioural therapy (CBT), such as exposure-based techniques, thereby limiting treatment efficacy (Steenkamp et al. 2015). Moreover, sleep-related symptoms in PTSD appear to be among the most treatment-resistant symptoms, as classical CBT does not seem to alleviate sleep disturbances such as nightmares and insomnia (Lydiard & Hamner 2009). Yet addressing these symptoms is especially important, as they exacerbate daytime posttraumatic symptoms (Belleville et al., 2009; Spoormaker & Montgomery, 2008). Disturbed sleep thus constitutes a modifiable risk factor, and targeted sleep treatments may themselves enhance recovery from PTSD (Germain, 2013) and facilitate broader treatment outcomes (Belleville et al., 2011; So et al., 2025).

Several studies have demonstrated an efficiency of Imagery Rehearsal Therapy (IRT), first-line treatment for nightmares (Aurora et al. 2010), in reducing not only nightmare frequency, but most other PTSD symptoms too (i.e., flashbacks, dissociation, intrusive thoughts and hyperarousal) (Krakow et al., 2000; Krakow, Hollifield, et al., 2001; Davis & Wright, 2007a; Davis et al., 2011a; Casement & Swanson, 2012; Hansen et al., 2013; Kunze et al., 2017), suggesting that it is an effective treatment for PTSD. IRT is a cognitive technique in which patients rewrite a distressing nightmare with a less distressing ending and rehearse the new scenario during the day, while awake, for 5–10 minutes per day (Krakow and Zadra

2010). A significant remission of nightmare frequency and PTSD severity has been observed after regular use of the technique for at least two to three weeks (Krakow & Zadra, 2010; Davis et al., 2011b; Kunze et al., 2017).

In a recent study (Schwartz et al. 2022), we have used a relatively new method to enhance IRT treatment in patients with non-traumatic nightmares (i.e., with absence of trauma). Targeted memory reactivation (TMR) is a technique used to modify memory consolidation through the administration of cues during sleep (Oudiette et al., 2013). In a classic TMR protocol, a sensory (e.g., olfactory, auditory) cue is associated with a learning procedure during the day and administered during sleep. In that way, the replay of the associated memory and its corresponding neural representation in memory networks are artificially promoted, a procedure which will usually strengthen memory consolidation. Previous studies have shown that TMR in REM sleep reduces emotional arousal and modulates affective tone (Hutchison et al., 2021; Rihm & Rasch, 2015). In Schwartz et al. 2022, 36 adult participants with idiopathic nightmares performed an initial IRT session and, while they mentally rehearsed the new scenario of their recurrent nightmare, half of the patients were exposed to a sound (TMR group), while no such pairing took place for the other half (control group). As the patients in the TMR group had significantly less negative dreams than the control group after both two weeks and 3 months of IRT (Schwartz et al. 2022; Perogamvros et al., 2025), this finding suggests that TMR applied during REM sleep represents a potential new treatment for reducing not only nightmare frequency, but global PTSD symptomatology too.

In a similar design, the current study first tested whether IRT reduces PTSD severity as a primary outcome (post-treatment and 3-month follow-up). Secondary outcome measures investigated nightmare frequency and distress over time. It then examined whether adding TMR during REM sleep, a sleep stage that has been traditionally associated with the consolidation of emotional memories, enhances these clinical effects compared with IRT alone. Depression and sleep quality were also compared between these two groups of patients. Finally, secondary polysomnography EEG analyses assessed whether PTSD was associated with alterations in sleep EEG activity and cortical hyperarousal (i.e., decreased delta and/or increased beta power) during sleep compared with healthy controls, and whether IRT and TMR modulated sleep EEG activity across sleep stages.

## Methods

### Population

A total of 105 participants were screened, 60 underwent the first evaluation, 46 were enrolled, 36 completed the protocol including the follow-up (17 in the IRT group (10 females) and 19 in the TMR group (13 females)). Participants were required to be between 18 and 60 years old, to experience at least one nightmare a week for at least 6 months, and to meet criteria for post-traumatic stress disorder (PTSD) as assessed by the Clinician Administered PTSD Scale for DSM-5 (CAPS-5). Exclusion criteria included current treatment or interventions targeting their traumatic experiences, a diagnosis of severe

or unstable mental disorders according to Diagnostic and Statistical Manual of Mental Disorders (DSM-5) of the American Psychiatric Association (APA, 2013), the presence of unstable medical disorders or neurological disorder, patients undergoing significant substance use/withdrawal, pregnancy, or excessive smoking. To obtain a generalizable and ecologically valid sample, we included patients regardless of the presence or absence of psychiatric comorbidities or medication use. However, when present, medications were required to remain stable throughout the study protocol. Participants had to follow the protocol in French or in English. Participants signed a consent form at the beginning of the study and received a financial compensation after completion. Ethical approval for this study was given by the ethical committee of the canton of Geneva (Commission Cantonale d’Ethique de la Recherche sur l’être humain). Participants were recruited through posters in the Université de Genève and the Hôpitaux Universitaires de Genève (HUG), and through referrals from mental health professionals in Geneva between March 2023 and June 2025.

## Power analysis

Power calculations were conducted using the G\*Power software (Faul et al., 2007) with a power of 0.80 and an alpha level of 0.05. Based on the pre- to post- treatment CAPS-5 score changes between active and control groups reported by Krakow et al. (2001), an effect size of  $d = 0.98$  was assumed. This yielded a required sample size of at least 14 participants per group to detect a significant effect for IRT efficacy. In addition, based on two studies (Schwartz et al., 2022; Sterpenich et al., 2014) examining repeated TMR over several days and reporting large effect sizes ( $d > 1$ ), a total sample size of 34 participants was estimated to provide sufficient power to test the TMR hypothesis.

## Study design

Participants were first contacted and screened for eligibility using online questionnaires. Eligible participants attended an initial evaluation session (T1), during which they completed baseline questionnaires (including CAPS-5) and received access to the dream diary and an actigraph. During the following week, participants underwent a baseline polysomnography at the Centre de Médecine du Sommeil of the Hôpitaux Universitaires de Genève. Two weeks after the initial evaluation, participants attended three weekly individual IRT sessions and performed IRT at home. At the end of the first session, they received a sleep headband (Dreem, see following sections) and were instructed to wear it every night until the second evaluation, for a total of three weeks. Following the intervention, participants completed a second evaluation (T2), including the same questionnaires and a second polysomnography. A follow-up assessment (T3) including the same questionnaires was conducted three months later.

Our protocol included two intervention groups. The first group completed the full IRT protocol without TMR and served as the control group (IRT group). The second group received both IRT and TMR (TMR group). During therapy, participants associated the rehearsal of the imagery with a group-specific sound: the IRT group used a guiro sound (S1), whereas the TMR group used a piano sound (S2). Participants

were blind to the nature of the auditory stimulation delivered by the headband during sleep, which was the piano sound (S2) for both groups.

Boxes represent in-lab sessions with the participant and a clinician (screening, initial evaluation, IRT sessions, second evaluation, and follow-up), arranged chronologically from left to right. IRT = Imagery Rehearsal Therapy, T1: time-point 1, T2: time-point 2, T3: time-point 3. Light-coloured boxes at the bottom indicate the intervention and materials used at home throughout the study (dream diary, actigraph, and Dreem Headband).

## Questionnaires

PTSD symptoms were assessed using the Clinician-Administered PTSD Scale for DSM-5 (CAPS-5) (Weathers et al., 2013a) and the PTSD Checklist for DSM-5 (PCL-5) (Weathers et al., 2013b). Exposure to a qualifying traumatic event (Criterion A) was assessed using the Life Events Checklist for DSM-5 (LEC-5) (Weathers et al., 2013c). The CAPS-5 then assesses the severity of the DSM-5 PTSD symptom criteria, organized into four clusters: intrusion/re-experiencing (Criterion B), avoidance (Criterion C), negative alterations in cognitions and mood (Criterion D), and marked alterations in arousal and reactivity (Criterion E), along with dissociative symptoms as a specifier. The CAPS-5 served as the primary clinical outcome measure and was administered at the three time points of the protocol (T1, T2 and T3). A reduction of  $\geq 12$  points was considered clinically significant (Marx et al., 2022).

Nightmare-related distress and frequency were assessed using the Nightmare Distress Questionnaire (NDQ) (Belicki, 1992) and the Nightmare Frequency Questionnaire (NFQ) (Krakow et al., 2000) respectively. Sleep quality and insomnia severity were assessed using the Pittsburgh Sleep Quality Index (PSQI) (Buysse et al., 1989) and the Insomnia Severity Index (ISI) (Bastien, 2001; Stern et al., 2025), while depressive symptoms were assessed using the Beck Depression Inventory-II (BDI-II) (Beck, 1961; Beck et al., 1996). Risk for obstructive sleep apnea was screened using the STOP-Bang questionnaire (Nagappa et al., 2015).

Questionnaires were administered in French or English. All data were anonymized and stored in REDCap.

## Dream and sleep diary

Participants daily completed an online dream and sleep diary from baseline until the post-intervention assessment. The diary assessed the previous night's sleep, the taken medication and the presence, quality, and content of dreams. Dream content analysis will be reported in a separate publication focused on dream phenomenology.

## Sleep headband

The sleep headband Dreem 2 (Beacon Biosignals) is a wearable wireless device that monitored and analysed sleep using physiological signals (5 channel EEG with dry electrodes: 2 frontal, 1 ground and 2 occipitals, breathing frequency, movement, and heart rate) and an onboard decoding algorithm (Arnal et al., 2020). The device automatically sent sounds via its bone-conduction transducers during consolidated REM stages using the same algorithm as in Schwartz et al. 2022. Participants adjusted stimulation volume to a minimally audible level before sleep. Auditory cues were presented every 10 seconds during stable REM sleep and were automatically interrupted following arousals, movements, blinks, alpha activity, or transitions to another sleep stage. No participant reported awakenings due to the sound. Sleep and stimulation data were collected through a mobile application for logging.

## Polysomnography

Polysomnographic recordings were acquired at the Center for Sleep Medicine, University Hospitals of Geneva, using a DeltaMed Brainbox amplifier system and Coherence software (Deltamed, Natus Medical Incorporated, Middleton, WI, USA). EEG was recorded (512 Hz sampling rate) using a standard 32-channel montage referenced to FCz, together with bilateral electrooculography, chin electromyography, electrocardiography, respiratory monitoring, and leg movement recordings. Sleep staging was performed independently by 2 trained scorers according to the American Academy of Sleep Medicine criteria (Troester et al., 2023). After scoring, the different sleep stage proportions, total sleep time and sleep efficiency were extracted.

Not all participants completed a second polysomnography. One participant was excluded because of an irregular work schedule involving night shifts. Another participant underwent two baseline recordings due to technical issues during the first night; these data were not retained for longitudinal analyses. Participants diagnosed with obstructive sleep apnea ( $ODI > 15/h$  in the overnight pulse oximetry,  $n = 2$ ) or periodic limb movements ( $PLMi > 15/h$  in the polysomnography,  $n = 3$ ) were not invited for the second polysomnography but remained eligible for the clinical intervention and follow-up assessments.

EEG preprocessing was performed in MNE-Python ([doi.org/10.5281/zenodo.592483](https://doi.org/10.5281/zenodo.592483); [doi:10.3389/fnins.2013.00267](https://doi.org/10.3389/fnins.2013.00267)). Data were downsampled to 256 Hz and band-pass filtered (1–60 Hz, zero-phase FIR, Hamming window), with a 50 Hz notch filter. Bad channels and epochs were identified and marked. ICA was computed on REM sleep and applied to all data to remove ocular, muscular, and cardiac artifacts. Bad channels were interpolated, and data were re-referenced to the average reference.

Clean data were segmented into 5-s epochs, excluding previously marked bad segments and epochs with residual artifacts ( $< 1 \mu V$  or  $> 150 \mu V$ ). Epochs were balanced across sleep stages by random subsampling to the individual minimal number of epochs. Power spectral density (PSD) was computed using the multitaper method (DPSS tapers), after removal of DC offsets. PSD was estimated from 1–30 Hz with 0.4 Hz resolution. Values were normalized to broadband power across all sleep stages and averaged across cluster of electrodes for regions of the scalp (i.e. Frontal, Central, Parietal, Occipital, Temporal), frequencies bands (delta (1–4 Hz) and beta (15–30 Hz)), and sleep stages.

An independent sample of healthy participants underwent one baseline polysomnographic recording under the same conditions and was analysed using the same procedures for comparison with the patients' baseline data. This sample was matched to the patient subgroup included in the spectral analyses for age and sex (mean age: 29.18 vs. 31.07 years; female proportion: 53% vs. 41% for controls and patients, respectively).

## **IRT and TMR**

IRT was delivered individually over three weekly sessions focused exclusively on nightmares. In contrast to the standard IRT protocol (Krakow & Zadra, 2010), no psychoeducation component was included to minimize potential confounding effects and isolate the impact of scenarios rescripting and rehearsing. In each of the 3 sessions, participants selected a target nightmare and developed an alternative, non-distressing scenario, which they subsequently rehearsed mentally. At home, they were asked to practice the scenario daily for 5 minutes, ideally before bedtime with the headphones emitting the sound S1 or S2 (according to the group).

During imagery rehearsal, participants listened to a group-specific 1-sec auditory cue through headphones every 10 seconds. Participants in the IRT group were exposed to a guiro sound (S1), whereas participants in the TMR group were exposed to a piano sound (S2, a neutral piano chord C69). Following the first session, all participants received a Dreem headband and wore it nightly until the post-treatment evaluation.

During stable REM sleep, the Dreem headband delivered the piano sound (S2) via bone conduction. Consequently, only participants in the TMR group experienced the same auditory cue during both imagery rehearsal and REM sleep, allowing reactivation of the newly learned scenario during sleep.

## **Statistics**

The CAPS-5 score was used as the primary outcome variable at post-intervention and 3-month follow-up. Secondary outcome variables included the delta and beta power values across sleep stages, as well as the scores PCL-5, PSQI, ISI, NFI, NDQ, BDI-II at post-intervention and 3-month follow-up.

## **Analyses of questionnaires**

Descriptive statistics were computed in SPSS (IBM SPSS Statistics, v29.0.2.20). Baseline group differences on NFI, NDQ, CAPS-5 and age were assessed using independent t-tests. Differences in proportions between groups were tested using chi-square tests.

Outcomes were analyzed using multilevel regression models. Dependent variables were questionnaire scores, with Time (pre, post, follow-up), Group (TMR, IRT), and Medication Load (which was calculated as in Doell et al. 2020), included as fixed effects. Medication load is an index based on the sum of different dosages of medication, allowing for their inclusion as a covariate (Doell et al. 2020). A random

intercept for subjects was included to account for within-subject correlations. The model was estimated using Restricted Maximum Likelihood (REML), chosen to handle missing data due to attrition.

Fixed effects were evaluated using Type II ANOVA with F-tests, beginning with the Time  $\times$  Group interaction, followed by main effects. Significant effects were followed by pairwise t-tests. Multiple comparisons were controlled using the Holm–Sidak method. Degrees of freedom were approximated using Satterthwaite’s method. Analyses were conducted in R (v4.4.2) within RStudio (v2024.09.1 + 394). Statistical significance was set at  $\alpha = .05$ .

Effect sizes (Cohen’s d) were computed as the difference between estimated marginal means across time points divided by the baseline (T1) standard deviation, separately per group. Effect sizes were interpreted as small ( $\geq 0.20$ ), moderate ( $\geq 0.50$ ), and large ( $\geq 0.80$ ) (Cohen, 1988).

## Hypnogram analyses

Baseline group differences between PTSD patients and healthy controls were assessed using independent t-tests for TST, N1%, N2%, N3%, REM%, and sleep efficiency. Polysomnographic outcomes were analyzed using multilevel regression models analogous to questionnaire analyses.

## Spectral analyses

Group comparisons between PTSD patients at T1 and healthy controls were performed using an Ordinary Least Squares (OLS) analysis with Group (patients vs controls) and Medication as factors for each sleep stage, delta and beta frequency bands, and across scalp regions. This analysis included 29 PTSD patients (TMR:  $n = 17$ ; IRT:  $n = 12$ ) and 17 matched healthy controls.

To assess IRT effects in all patients ( $n = 29$ ), PSD measures were compared using paired t-tests between time points (PSG1 vs PSG2) for each sleep stage, delta and beta frequency bands, and across scalp regions.

To assess TMR versus IRT effects, difference scores (i.e. index of change at T2 compared with baseline at T1 as  $T2 - T1$ ) were computed for PSD measures and compared between groups. Differences scores were analyzed using an Ordinary Least Squares (OLS) with Group (TMR vs IRT) and Medication as factors for each sleep stage, delta and beta frequency bands, and across scalp regions.

Tests with a p-value below 0.05 were considered as significant results. Partial Cohen’s  $f^2$  effect sizes were computed for the OLS, and a Cohen’s  $f^2$  effect was computed for the t-tests results as  $(t^2/df)/(1(t^2/df))$  and reported in results section.

These *a priori* analyses were based on previous literature and were not corrected for multiple comparisons.

## Results

# Descriptive statistics

In total, 19 participants in the TMR group and 17 participants in the IRT group completed the protocol across the three time points. The two groups were comparable at T1 on all baseline variables (Table 1).

Table 1  
Baseline demographic and clinical characteristics

| Age (years)           | TMR group (n = 19)  | IRT group (n = 17)   | df        | t            | p value     |
|-----------------------|---------------------|----------------------|-----------|--------------|-------------|
|                       | <b>32,53 ± 9,77</b> | <b>33,88 ± 11,16</b> | <b>34</b> | <b>-0,39</b> | <b>0,35</b> |
| Female sex (%)        | 13 (68,4%)          | 10 (58,8%)           | 34        | 0,58         | 0,28        |
| CAPS-5 <sub>pre</sub> | 45,74 ± 12,42       | 42,29 ± 12,40        | 34        | 0,76         | 0,23        |
| NDQ <sub>pre</sub>    | 35,00 ± 6,00        | 32,94 ± 5,14         | 34        | 1,1          | 0,14        |
| NFQ <sub>pre</sub>    | 5,76 ± 4,83         | 4,32 ± 1,87          | 34        | 1,15         | 0,13        |
| PCL-5 <sub>pre</sub>  | 47,6 ± 13,42        | 50,56 ± 12,49        | 34        | -0,68        | 0,25        |
| BDI-II <sub>pre</sub> | 26,95 ± 15,40       | 26,29 ± 10,89        | 34        | 0,15         | 0,44        |
| ISI <sub>pre</sub>    | 17,89 ± 6,00        | 18,29 ± 3,92         | 34        | -0,24        | 0,41        |
| PSQI <sub>pre</sub>   | 11,58 ± 3,88        | 10,35 ± 3,43         | 34        | 1            | 0,16        |

Means, standard deviations, and comparison between the IRT and TMR group, for age, female sex, and outcome variables at pre-intervention. Values are reported as mean ± SD. For each variable, the degrees of freedom, Student's t value ( $\chi^2$  for female sex) and p value are reported. Pre, pre-intervention; CAPS-5, Clinician-Administered PTSD Scale for DSM-5; NDQ, Nightmare Distress Questionnaire; NFQ, Nightmare Frequency Questionnaire; PCL-5, PTSD Checklist for DSM-5; BDI-II, Beck Depression Inventory; ISI, Insomnia Severity Index; PSQI, Pittsburgh Sleep Quality Index.

41.67% of participants had a complex PTSD (PTSD-C). According to the Life Events Checklist for DSM-5, all participants had experienced at least two adverse life events, with a mean of 6,63 events ± 2,80 overall (Table 2).

Table 2

Percentage of participants who experienced adverse life events in the PTSD sample according to the Life Events Checklist, all patients confounded.

| Type of trauma                                                  | % of participants exposed to each trauma type |
|-----------------------------------------------------------------|-----------------------------------------------|
| Natural disaster                                                | 11,11                                         |
| Fire or explosion                                               | 22,22                                         |
| Transportation accident                                         | 47,22                                         |
| Serious accident at work, home, or during recreational activity | 30,56                                         |
| Exposure to toxic substance                                     | 11,11                                         |
| Physical assault                                                | 72,22                                         |
| Assault with a weapon                                           | 33,33                                         |
| Sexual assault                                                  | 47,22                                         |
| Other unwanted or uncomfortable sexual experiences              | 47,22                                         |
| Combat or exposure to a war-zone                                | 27,78                                         |
| Captivity                                                       | 22,22                                         |
| Life-threatening illness or injury                              | 52,78                                         |
| Severe human suffering                                          | 72,22                                         |
| Sudden violent death (for example, homicide, suicide)           | 41,67                                         |
| Sudden accidental death                                         | 41,67                                         |
| Serious injury, harm, or death you caused to someone else       | 0,00                                          |
| Any other very stressful event or experience                    | 30,56                                         |
| Other                                                           | 52,78                                         |

This is an ecologically realistic sample of PTSD patients, as these patients have usually other psychiatric comorbidities and are often under medication. The recorded psychiatric comorbidities indicated that, across the entire sample, 36.1% of patients had a diagnosis of attention-deficit/hyperactivity disorder, 30.6% of depression, 16.7% of borderline personality disorder, 11.1% of an anxiety disorder, 5.6% of autism spectrum disorder, 2.8% of mixed personality disorder, 2.8% of a substance use disorder, and 2.8% of an eating disorder. 64% of PTSD patients took stable doses of psychotropic medication (antidepressants, antipsychotics, psychostimulants, anxiolytics, mood stabilizers), while 30% of patients took sleeping pills (antipsychotics, Z-drugs, benzodiazepines, sedative antidepressants, melatonin, antihistamines, DORAs). Due to multiple comorbidities, and for medical ethical reasons, the

aforementioned medications were not interrupted and were kept stable during the protocol. Therefore, medication was added as a covariate in our between-group comparisons. Healthy participants had no medications.

## CAPS-5 trajectory

There was a significant effect of time ( $p < .001$ ,  $F(2, 65.69) = 22.44$ ) for the CAPS-5 score (Fig. 2). A pairwise t-test indicated that the time effect was significant at both T2 vs T1 ( $p < .001$ ,  $t(65.1) = 4.84$ ,  $d = -0.78$ ), and T3 vs T1 ( $p < .001$ ,  $t(66.0) = 6.40$ ,  $d = -1.06$ ). There was a significant effect of medication load ( $p < 0.05$ ,  $F(1, 32.63) = 7.23$ ). There was no effect of group ( $p = .78$ ,  $F(1, 32.94) = 0.08$ ) or time\*group interaction ( $p = .37$ ,  $F(2, 65.70) = 0.99$ ), providing no evidence for an additive clinical effect of TMR over IRT. There was no statistically significant difference ( $\chi^2(1) = 0.001$ ,  $p = .97$ ) in responder rates between groups, although numerically more patients responded ( $\geq 12$  points decrease) in the TMR group at T2 than IRT group (47.4% vs 41.2%).

T1 = first evaluation, T2 = second evaluation, T3 = follow-up.

## CAPS-5 clusters

All four CAPS-5 subclusters showed a significant main effect of time (B:  $F_{(2,68)} = 26.20$ ; C:  $F_{(2,68)} = 8.06$ ; D:  $F_{(2,68)} = 9.96$ ; E:  $F_{(2,68)} = 17.67$ ; all  $p < .001$ ), with significant reductions both from T1 to T2 (B:  $d = -0.85$ ; C:  $d = -0.50$ ; D:  $d = -0.50$ ; E:  $d = -0.64$ ; all  $p \leq .03$ ) and from T1 to T3 (B:  $d = -1.26$ ; C:  $d = -0.89$ ; D:  $d = -0.78$ ; E:  $d = -1.08$ ; all  $p < .001$ ), the larger effects appearing at the 3-month follow-up. No subcluster showed an effect of group (all  $p \geq .46$ ) or a time  $\times$  group interaction (all  $p \geq .40$ ). Medication load was a significant covariate for re-experiencing (B:  $F_{(1,33)} = 7.93$ ,  $p < .01$ ) and avoidance (C:  $F_{(1,33)} = 4.57$ ,  $p = .04$ ), but not for negative alterations in mood and cognition (D) or hyperarousal (E).

## Other questionnaires

All six secondary measures showed a significant main effect of time (NDQ:  $F_{(2,65.56)} = 20.01$ ; NFQ:  $F_{(2,65.26)} = 15.83$ ; PCL-5:  $F_{(2,63.54)} = 22.38$ ; BDI-II:  $F_{(2,64.82)} = 14.98$ ; PSQI:  $F_{(2,64.55)} = 10.21$ ; ISI:  $F_{(2,60.40)} = 20.88$ ; all  $p < .001$ ), with significant reductions from T1 to T2 ( $d$  between  $-0.55$  and  $-1.18$ , all  $p < .001$ ) and from T1 to T3 ( $d$  between  $-0.67$  and  $-1.58$ , all  $p < .001$ ), the only exception being the PSQI, for which the T1–T2 contrast was not significant ( $d = -0.24$ ,  $p = .11$ ) although the T1–T3 reduction was ( $d = -0.68$ ,  $p < .001$ ). No measure showed an effect of group (all  $p \geq .52$ ) or a time  $\times$  group interaction (all  $p \geq .15$ ). Medication load was a significant covariate for the PCL-5 ( $p = .03$ ), BDI-II ( $p = .03$ ), and PSQI ( $p < .01$ ), but not for the NDQ, NFQ, or ISI (all  $p \geq .18$ ).

## Hypnograms

At baseline (PSG1), patients showed significantly lower TST ( $-12.7\%$ ,  $t(45) = -2.34$ ,  $p = .02$ ) than healthy controls (see Table 3 for details).

In PTSD participants, TST significantly increased from PSG1 to PSG2 (+ 11.7%,  $F_{(1,25)} = 8.36$ ,  $p = .008$ ; whereas sleep efficiency did not ( $F_{(1,25)} = 2.31$ ,  $p = .14$ ), with no group or time  $\times$  group effects. N1 proportion also showed a significant time effect (29.1%,  $F_{(1,25)} = 4.66$ ,  $p < .05$ ), with no significant group or interaction effect. N2, N3 and REM proportions showed no significant effects of time, group, or interaction (all  $p > .10$ ) (see Table 3 for details).

Table 3

Sleep architecture in PTSD patients at baseline (PSG1) and post-intervention (PSG2), and in healthy controls. Values are mean (SD). Statistical comparisons are independent-samples t-tests contrasting PSG1 (patients, baseline,  $N = 29$ ) with healthy controls ( $N = 17$ ).

| Outcome   | Healthy controls | PSG1 (patients, baseline) | PSG2 (patients, post) |
|-----------|------------------|---------------------------|-----------------------|
| N1 (%)    | 6.89 (3.25)      | 9.45 (7.02)               | 6.70 (3.32)           |
| N2 (%)    | 45.25 (6.84)     | 48.64 (10.89)             | 48.86 (9.14)          |
| N3 (%)    | 25.19 (8.08)     | 21.90 (7.72)              | 23.21 (7.71)          |
| REM (%)   | 22.51 (5.39)     | 19.53 (8.50)              | 20.79 (7.74)          |
| TST (min) | 428.18 (47.95)   | 373.30 (104.72)           | 417.20 (82.98)        |
| SE (%)    | 87.50 (9.75)     | 80.82 (15.80)             | 85.43 (12.71)         |

## Spectral signatures

### Baseline comparisons (PTSD patients vs healthy controls)

At baseline, patients with PTSD showed significantly higher central delta power ( $f^2 = 0.115$ ;  $p = .036$ ) and fronto-central beta power ( $f^2 = 0.2$ ;  $p < .01$ ) in N2 sleep, compared to controls (see Table S1-3 in supplementary materials for details and Fig. 3). REM sleep results revealed less PSD in delta band in frontal regions ( $f^2 = -0.104$ ;  $p = .046$ ), compared to controls (Fig. 3). The medication factor showed significant effects in all sleep stages, in delta and beta (Figure S1 in supplementary materials). Specifically, higher medication load was associated with increased temporal delta power ( $f^2 = 0.17-0.287$ ) and decreased temporo-occipital beta power ( $f^2 = -0.236$  to  $-0.488$ ). These effects were more pronounced in REM, and more spread with additional occipital delta and parietal beta in N2 and N3.

## IRT effect

Within-subject comparisons in all patients together (merged groups), between PSG1 (T1) and PSG2 (T2) revealed significant time effect in N2 and N3 sleep stages (Fig. 4). Specifically, PSD in the beta band was significantly greater during N2 sleep at PSG1 relative to PSG 2, in both the central and frontal regions ( $f^2 = 0.2$ ;  $p < .03$ ). Similarly, beta band PSD in the occipital region was greater during N3 sleep at PSG1 than at PSG2 ( $f^2 = 0.16$ ;  $p = .043$ ). No other between-session differences were significant.

# TMR effect

Between-group comparisons of TMR and IRT participants were conducted on normalized data operationalised as the difference between PSG2 and PSG1 (positive values means more PSD at PSG2 compared to PSG1) and revealed group differences in REM sleep stage (Fig. 5). Relative to the IRT group, the TMR group exhibited significantly reduced parietal beta ( $f^2 = -0.212$ ;  $p = .034$ ) and increased central delta ( $f^2 = 0.199$ ;  $p = .039$ ) between the two polysomnographies. Additionally, the medication factor showed effect in REM as well, with proportionally higher beta in the parietal region ( $f^2 = 0.488$ ;  $p = .002$ ) (Figure S2 in supplementary materials).

## Discussion

The present study investigated the efficacy of IRT for global PTSD symptomatology, as well as the potential enhancing effect of TMR on IRT effect. Overall, the results support the short- and long-term efficacy of IRT on subjective and clinician-rated PTSD outcomes and reduction of cortical hyperarousal. Furthermore, TMR may modulate dream-related neurophysiological processes despite the absence of additional subjective therapeutic benefit.

PTSD symptomatology, as assessed with the Clinician Administered PTSD Scale for DSM-5 (CAPS-5) showed moderate-to-large effect sizes between T1 and T2 and between T1 and T3. These results are consistent with previous reports of the literature and support the hypothesized short- and long-term efficacy of IRT on PTSD symptoms (Casement & Swanson, 2012; Cook et al., 2010; Forbes et al., 2003; Germain & Nielsen, 2003; Hansen et al., 2013; Krakow, Germain, et al., 2001; Nappi et al., 2010). Beyond replicating previous evidence, the present findings suggest that the benefits of IRT may extend beyond nightmare reduction alone and impacts broader symptoms (all 4 PTSD clusters), as well as the long-term maintenance of positive changes. Although the exact mechanism is not known, the beneficial “halo” effect of IRT on overall PTSD symptoms (and not only nightmares) may be related to its mechanism of action, which appears to involve extinction learning (Schwartz et al. 2022).

A major strength of IRT, compared to more classical treatments for PTSD (e.g., CBT or EMDR), is that directly targets post-traumatic nightmares. Patients often feel anxious about working directly with their trauma and may therefore prefer focusing on nightmares, which represent a less directly trauma-focused therapeutic target. Moreover, analyses revealed significant effect of time for all questionnaires, with effect sizes ranging from small-to-moderate improvement for mood (BDI), and large for nightmare- and sleep-specific measures (NDQ, NFQ, PSQI and ISI). These findings support and extend prior evidence suggesting that IRT exerts broader therapeutic effect beyond nightmare frequency and distress reduction, encompassing improvements in core PTSD symptoms (Germain & Nielsen, 2003), as well as in depressive mood and improvement in sleep quality (Casement & Swanson, 2012; Krakow, Hollifield, et al., 2001), though effect sizes varied across domains. These improvements were also observed three months after IRT, consistent with previous reports of long-term effects of IRT (Casement & Swanson, 2012) which is of considerable clinical relevance.

In the current PTSD treatment guidelines (American Psychological Association, 2025), the specialist panel suggests there is insufficient evidence to recommend either for or against Imagery Rehearsal Therapy (IRT) for PTSD treatment. Taken together with the present findings, including the decrease of EEG arousal with IRT, discussed later, and with prior randomized controlled trials (Krakow et al., 2000; Krakow, Hollifield, et al., 2001; Davis & Wright, 2007b; Davis et al., 2011b; Hansen et al., 2013; Casement & Swanson, 2012; Kunze et al., 2017), our results suggest that IRT may have broader therapeutic effects beyond nightmare reduction and could be considered as a potential stand-alone treatment for full PTSD, although further large-scale comparative studies are warranted to confirm this indication.

Between-group analyses revealed no significant TMR-specific effect on CAPS-5 scores, thus providing no support for the hypothesis regarding the potentiation of clinical outcomes by TMR at short- and long-term. Enhancing therapy efficacy for PTSD with TMR was also suggested by Van Der Heijden et al. (2022). In that study, they examined whether one night with auditory TMR delivered during slow-wave sleep could potentiate the efficacy of a PTSD treatment (one session with eye movement desensitization and reprocessing (EMDR)). Although they found a reduction in PTSD avoidance symptoms in the TMR group, which correlated with the number of auditory cues administered during sleep, no additive decrease in CAPS-5 score attributable to TMR was found. In our study, findings also do not reveal a supplementary decrease in CAPS-5 scores due to auditory TMR during REM sleep over 3 weeks. Several reasons may account for the absence of an additive clinical effect of TMR. First, one possible explanation is a ceiling effect, whereby IRT alone produced such substantial improvements in PTSD symptoms, including nightmares, that there was limited room for TMR to provide additional benefit. Second, post-traumatic nightmares occur during both NREM and REM sleep (Phelps et al., 2018). Thus, conducting TMR during REM sleep (or exclusively during NREM sleep in Van Der Heijden et al. (2022)) may have been insufficient to capture the scope of trauma-related dream activity, whereas a combined NREM and REM sleep TMR may more adequately address the complexity of post-traumatic nightmares. Moreover, the CAPS-5 may be relatively insensitive to the dream-specific pathway engaged by TMR, which was nonetheless detectable at the neurophysiological level.

In comparison with the study by Schwartz et al. (2022) which also targeted REM sleep through auditory stimulation during sleep, our findings did not reveal a similar enhancement effect of TMR on IRT outcomes. This discrepancy may be attributable to differences in nightmare etiology, as the previous study found a significant enhancing effect of TMR on IRT's efficacy in reducing idiopathic nightmares. These subtypes of nightmares may differ in their underlying mechanisms, since post-traumatic nightmares are specifically related to trauma memory and conditioned fear responses. The rescripted positive imagery reactivated by TMR may therefore compete less effectively with the overlearned trauma memory in PTSD than with the more malleable content of idiopathic nightmares, rendering post-traumatic nightmares more resistant to reactivation-based augmentation. The distinction between idiopathic and post-traumatic nightmares, and whether they respond differently to sleep-based memory reactivation, has received little direct study and warrants dedicated comparative investigation. It is worth considering whether the 3-week TMR protocol was long enough to produce clinically detectable improvements in this population. Given the complexity and chronicity of trauma-related sleep

disturbances, a longer intervention window may be required before TMR can exert meaningful effects on nightmare severity.

In addition to the effects of IRT and TMR on PTSD symptomatology, neurobiological correlates were identified through spectral analyses on EEG activity during sleep. First, PTSD patients exhibited reduced delta power during REM sleep at baseline polysomnography (PSG1) in a frontal cluster and increased beta power during N2 sleep in fronto-central regions. The additional co-increase of delta power during N2 sleep in the central region may appear paradoxical, but it showed a smaller size effect and could be the manifestation of a general pattern of oscillation increase, involving inter-frequency coupling or sleep regulatory rebound. Together, these findings suggest a state of sleep-related cortical hyperarousal. While similar EEG alterations have been reported in patients with insomnia (Zhao et al. 2021) and anxiety disorders (Wang et al. 2025), these conditions substantially overlap with and may constitute core features of PTSD. Accordingly, the observed EEG modifications may reflect a transdiagnostic hyperarousal dimension that is strongly expressed within PTSD.

Hyperarousal is a core symptom of PTSD and reflects a failure to downregulate arousal during both wake and sleep, which may manifest as altered oscillatory activity across sleep stages and may underlie the symptoms captured by the CAPS-5 hyperarousal cluster (Cluster E). The reduction in delta power and increase of beta/gamma power during sleep of PTSD patients (with or without comorbidities) was also found in Wang et al. (2020), De Boer et al. (2020) and Woodward et al. (2000), especially in frontal or central regions. Similar findings were also shown in patients with nightmares (Blaskovich et al., 2020; Sayk et al. 2024) who reported decreased delta power and increased fast-frequency power (beta and gamma) during NREM and/or REM sleep in a nightmare group compared to controls (mostly in frontal and temporal regions), interpreting those results as markers of cortical hyperarousal. However, in the Sayk study only 1 out of 30 nightmare sufferers was diagnosed with PTSD. Interestingly, we found EEG markers of increased hyperarousal in N2 and REM sleep, the two stages where nightmares have been previously described in PTSD patients (Phelps et al. 2018). Whether these markers represent a specific nightmare or PTSD signature needs to be elucidated in the future, by comparing PTSD patients with and without traumatic nightmares and those with idiopathic nightmares.

A within-subject comparison between baseline (PSG1) and post treatment (PSG2) for all patients found a decrease of beta power (15–30 Hz) in NREM sleep in central, frontal and occipital regions, suggesting a positive effect of IRT in reducing hyperarousal. To the best of our knowledge this is the first study supporting a reduction of cortical arousal in PTSD patients with IRT. Similarly, Sayk et al. (2024) also reported reduced low gamma activity (31–35 Hz) during REM sleep of nightmare sufferers following IRT as compared to prior intervention, suggesting that cortical hyperarousal may be malleable through successful therapy. Our results concerned NREM sleep, supporting the idea that, unlike idiopathic nightmares, which occur almost exclusively during REM sleep, PTSD patients may also experience nightmares during NREM sleep (Phelps et al. 2018) and that IRT may have a neurophysiological effect on these sleep stages in traumatized patients.

Moreover, specifically during REM sleep, when TMR was administered, the TMR group exhibited lower beta power and higher delta power in PSG2 compared to PSG1 relative to the IRT group. Decreased beta power and increased delta power in posterior centro-parietal regions have previously been associated with reduced dreaming (Siclari et al., 2017; Rochas et al., 2026). In line with the findings of Schwartz et al. (2022), these results suggest that TMR during REM sleep combined with IRT for nightmares may exert specific effects on dreaming-related neural activity (rather than on overall PTSD symptomatology) and may potentiate the neurophysiological effects of IRT, even in the absence of greater subjective symptom improvement. To the best of our knowledge, this is the first study to demonstrate that TMR delivered during REM sleep can modulate the neural correlates of dreaming.

Interestingly, the results of PSD changes due to medication load showed a very stable hypoarousal pattern in the posterior regions when looking at the comparison with the healthy unmedicated control group, being opposite to the anterior regions involved in the effect of the group factor. The posterior increase of delta and decrease of beta might be due to pharmacological mechanisms (especially of antipsychotic medications (De Pieri et al., 2023)) and/or with reduced symptoms linked to insomnia or anxiety.

## Limitations and future perspectives

Several limitations should be acknowledged. The absence of a control group (without IRT) limits causal inference regarding treatment effects, while the small sample size prevented examination of potential moderators such as age, gender, trauma type, and psychiatric comorbidities. Despite these limitations, the study has several strengths, including its multimodal assessment, three-month follow-up, and ecologically valid home-based TMR protocol.

Future studies should replicate these findings in larger controlled samples, investigate the neurophysiological mechanisms underlying treatment response, and examine individual factors that may influence outcomes. Further research should also clarify the distinct contributions of NREM and REM sleep to PTSD and nightmares and explore other dream-focused interventions.

## Conclusions

These findings support previous evidence that IRT is an effective and durable treatment for trauma-related nightmares and associated PTSD symptoms. For the first time, IRT was also associated with neurophysiological changes consistent with reduced hyperarousal in these patients. Contrary to our hypothesis, TMR did not yield additional benefits on questionnaire-based outcomes. This may reflect the greater resistance of traumatic memories to TMR-based modulation. Nevertheless, compared with the IRT group, the TMR group showed reduced activity in regions implicated in dreaming. These findings suggest that TMR applied in the context of IRT during REM sleep may influence dream-related processes and could be further investigated in future dream engineering studies.

# Declarations

## Data availability statement:

The data that support the findings of this study are available from the corresponding author upon reasonable request.

## Conflict of interest disclosure:

Authors disclose no conflict of interest.

## Ethics approval statement :

Ethical approval for this study was given by the ethical committee of the canton of Geneva (Commission Cantonale d’Ethique de la Recherche sur l’être humain).

## Patient consent statement :

All participants signed a consent form at the beginning of the study.

## Acknowledgments

The authors would like to thank Lamyae Benzakour, Nader Perroud, Eva Rufenacht and the team of the Center for Sleep Medicine at the University Hospitals of Geneva. They would also like to acknowledge the contributions of the Clinical Research Center, the Louis-Jeantet Foundation, the University Hospital, and the Faculty of Medicine in Geneva.

# References

1. American Psychological Association (2025) *APA Clinical Practice Guideline for the Treatment of Posttraumatic Stress Disorder (PTSD) in Adults*. <https://www.apa.org/about/policy/guideline-ptsd-in-adults.pdf>
2. Arnal PJ, Thorey V, Debellemanniere E, Ballard ME, Bou Hernandez A, Guillot A, Jourde H, Harris M, Guillard M, Van Beers P, Chennaoui M, Sauvet F (2020) The Dreem Headband compared to polysomnography for electroencephalographic signal acquisition and sleep staging. *Sleep* 43(11):zsaa097. <https://doi.org/10.1093/sleep/zsaa097>
3. Aurora RN, Zak RS, Auerbach SH, Casey KR, Chowdhuri S, Karippot A, Maganti RK, Ramar K, Kristo DA, Bista SR, Lamm CI, Morgenthaler TI (2010) Best Practice Guide for the Treatment of Nightmare Disorder in Adults. *J Clin Sleep Med* 06(04):389–401. <https://doi.org/10.5664/jcsm.27883>
4. Bastien C (2001) Validation of the Insomnia Severity Index as an outcome measure for insomnia research. *Sleep Med* 2(4):297–307. [https://doi.org/10.1016/S1389-9457\(00\)00065-4](https://doi.org/10.1016/S1389-9457(00)00065-4)
5. Beck AT (1961) An Inventory for Measuring Depression. *Arch Gen Psychiatry* 4(6):561. <https://doi.org/10.1001/archpsyc.1961.01710120031004>

6. Beck AT, Steer RA, Ball R, Ranieri WF (1996) Comparison of Beck Depression Inventories-IA and-II in Psychiatric Outpatients. *J Pers Assess* 67(3):588–597.  
[https://doi.org/10.1207/s15327752jpa6703\\_13](https://doi.org/10.1207/s15327752jpa6703_13)
7. Belicki K (1992) *Nightmare Frequency Versus Nightmare Distress: Relations to Psychopathology and Cognitive Style*
8. Belleville G, Guay S, Marchand A (2009) Impact of Sleep Disturbances on PTSD Symptoms and Perceived Health. *J Nerv Mental Disease* 197(2):126–132.  
<https://doi.org/10.1097/NMD.0b013e3181961d8e>
9. Belleville G, Guay S, Marchand A (2011) Persistence of sleep disturbances following cognitive-behavior therapy for posttraumatic stress disorder. *J Psychosom Res* 70(4):318–327.  
<https://doi.org/10.1016/j.jpsychores.2010.09.022>
10. Blaskovich B, Reichardt R, Gombos F, Spoormaker VI, Simor P (2020) Cortical hyperarousal in NREM sleep normalizes from pre- to post- REM periods in individuals with frequent nightmares. *Sleep* 43(1):zsz201. <https://doi.org/10.1093/sleep/zsz201>
11. Borghese F, Henckaerts P, Guy F, Perez Mayo C, Delplanque S, Schwartz S, Perogamvros L (2022) Targeted Memory Reactivation During REM Sleep in Patients With Social Anxiety Disorder. *Front Psychiatry* 13:904704. <https://doi.org/10.3389/fpsy.2022.904704>
12. Buysse DJ, Reynolds CF, Monk TH, Berman SR, Kupfer DJ (1989) The Pittsburgh sleep quality index: A new instrument for psychiatric practice and research. *Psychiatry Res* 28(2):193–213.  
[https://doi.org/10.1016/0165-1781\(89\)90047-4](https://doi.org/10.1016/0165-1781(89)90047-4)
13. Calhoun PS, Wiley M, Dennis MF, Means MK, Edinger JD, Beckham JC (2007) Objective evidence of sleep disturbance in women with posttraumatic stress disorder. *J Trauma Stress* 20(6):1009–1018.  
<https://doi.org/10.1002/jts.20255>
14. Casement MD, Swanson LM (2012) A meta-analysis of imagery rehearsal for post-trauma nightmares: Effects on nightmare frequency, sleep quality, and posttraumatic stress. *Clin Psychol Rev* 32(6):566–574. <https://doi.org/10.1016/j.cpr.2012.06.002>
15. Cohen J (1998) *Statistical Power Analysis for the Behavioural Sciences*. Lawrence Erlbaum Associates, Hillsdale
16. Cook JM, Harb GC, Gehrman PR, Cary MS, Gamble GM, Forbes D, Ross RJ (2010) Imagery rehearsal for posttraumatic nightmares: A randomized controlled trial. *J Trauma Stress* 23(5):553–563.  
<https://doi.org/10.1002/jts.20569>
17. Cusack K, Jonas DE, Forneris CA, Wines C, Sonis J, Middleton JC, Feltner C, Brownley KA, Olmsted KR, Greenblatt A, Weil A, Gaynes BN (2016) Psychological treatments for adults with posttraumatic stress disorder: A systematic review and meta-analysis. *Clin Psychol Rev* 43:128–141.  
<https://doi.org/10.1016/j.cpr.2015.10.003>
18. Davis JL, Rhudy JL, Pruiksma KE, Byrd P, Williams AE, McCabe KM, Bartley EJ (2011) Physiological Predictors of Response to Exposure, Relaxation, and Rescripting Therapy for Chronic Nightmares in a Randomized Clinical Trial. *J Clin Sleep Med* 7(6):622–631. <https://doi.org/10.5664/jcsm.1466>

19. Davis JL, Wright DC (2007) Randomized clinical trial for treatment of chronic nightmares in trauma-exposed adults. *J Trauma Stress* 20(2):123–133. <https://doi.org/10.1002/jts.20199>
20. De Boer M, Nijdam MJ, Jongedijk RA, Bangel KA, Olff M, Hofman WF, Talamini LM (2020) The spectral fingerprint of sleep problems in post-traumatic stress disorder. *Sleep* 43(4):zsz269. <https://doi.org/10.1093/sleep/zsz269>
21. De Pieri M, Rochas V, Sabe M, Michel C, Kaiser S (2023) Pharmac-EEG of antipsychotic treatment response: a systematic review. *Schizophrenia (Heidelb)* 9(1):85. <https://doi.org/10.1038/s41537-023-00419-z>
22. Doell KC, Olié E, Courtet P, Corradi-Dell’Acqua C, Perroud N, Schwartz S (2020) Atypical processing of social anticipation and feedback in borderline personality disorder. *NeuroImage: Clin* 25:102126. <https://doi.org/10.1016/j.nicl.2019.102126>
23. Faul F, Erdfelder E, Lang A-G, Buchner A (2007) G\*Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behav Res Methods* 39(2):175–191. <https://doi.org/10.3758/bf03193146>
24. Forbes D, Phelps AJ, McHugh AF, Debenham P, Hopwood M, Creamer M (2003) Imagery rehearsal in the treatment of posttraumatic nightmares in Australian veterans with chronic combat-related PTSD: 12-month follow-up data. *J Trauma Stress* 16(5):509–513. <https://doi.org/10.1023/A:1025718830026>
25. Germain A (2013) *Sleep Disturbances as the Hallmark of PTSD: Where Are We Now?* <https://doi.org/10.1176/appi.ajp.2012.12040432>
26. Germain A, Buysse DJ, Shear MK, Fayyad R, Austin C (2004) Clinical correlates of poor sleep quality in posttraumatic stress disorder. *J Trauma Stress* 17(6):477–484. <https://doi.org/10.1007/s10960-004-5796-6>
27. Germain A, Nielsen T (2003) Impact of Imagery Rehearsal Treatment on Distressing Dreams, Psychological Distress, and Sleep Parameters in Nightmare Patients. *Behav sleep Med* 1(3):140–154. [https://doi.org/10.1207/S15402010BSM0103\\_2](https://doi.org/10.1207/S15402010BSM0103_2)
28. Habukawa M, Uchimura N, Maeda M, Kotorii N, Maeda H (2007) Sleep Findings in Young Adult Patients with Posttraumatic Stress Disorder. *Biol Psychiatry* 62(10):1179–1182. <https://doi.org/10.1016/j.biopsych.2007.01.007>
29. Hansen K, Höfling V, Kröner-Borowik T, Stangier U, Steil R (2013) Efficacy of psychological interventions aiming to reduce chronic nightmares: A meta-analysis. *Clin Psychol Rev* 33(1):146–155. <https://doi.org/10.1016/j.cpr.2012.10.012>
30. Hutchison IC, Pezzoli S, Tsimpanouli M-E, Abdellahi MEA, Pobric G, Hulleman J, Lewis PA (2021) Targeted memory reactivation in REM but not SWS selectively reduces arousal responses. *Commun Biology* 4(1):404. <https://doi.org/10.1038/s42003-021-01854-3>
31. IBM Corp (2022) *IBM SPSS Statistics for Mac* (Version 29.0.2.20) [Computer software]. IBM Corp, Armonk, NY

32. Knyazev GG (2012) EEG delta oscillations as a correlate of basic homeostatic and motivational processes. *Neurosci Biobehavioral Reviews* 36(1):677–695.  
<https://doi.org/10.1016/j.neubiorev.2011.10.002>
33. Krakow B, Germain A, Warner TD, Schrader R, Koss M, Hollifield M, Tandberg D, Melendrez D, Johnston L (2001) The relationship of sleep quality and posttraumatic stress to potential sleep disorders in sexual assault survivors with nightmares, insomnia, and PTSD. *J Trauma Stress* 14(4):647–665. <https://doi.org/10.1023/A:1013029819358>
34. Krakow B, Hollifield M, Johnston L, Koss M, Schrader R, Warner TD, Tandberg D, Lauriello J, McBride L, Cutchen L, Cheng D, Emmons S, Germain A, Melendrez D, Sandoval D, Prince H (2001) Imagery Rehearsal Therapy for Chronic Nightmares in Sexual Assault Survivors With Posttraumatic Stress Disorder: A Randomized Controlled Trial. *JAMA* 286(5):537. <https://doi.org/10.1001/jama.286.5.537>
35. Krakow B, Hollifield M, Schrader R, Koss M, Tandberg D, Lauriello J, McBride L, Warner TD, Cheng D, Edmond T, Kellner R (2000) A controlled study of imagery rehearsal for chronic nightmares in sexual assault survivors with PTSD: A preliminary report. *J Trauma Stress* 13(4):589–609.  
<https://doi.org/10.1023/A:1007854015481>
36. Krakow B, Hollifield M, Schrader R, Koss M, Tandberg D, Lauriello J, McBride L, Warner TD, Cheng D, Edmond T, Kellner R (2000) *Nightmare Frequency Questionnaire (NFQ)* [Database record]. APA PsycTests
37. Krakow B, Zadra A (2010) Imagery Rehearsal Therapy: Principles and Practice. *Sleep Med Clin* 5(2):289–298. <https://doi.org/10.1016/j.jsmc.2010.01.004>
38. Kunze AE, Arntz A, Morina N, Kindt M, Lancee J (2017) Efficacy of imagery rescripting and imaginal exposure for nightmares: A randomized wait-list controlled trial. *Behav Res Ther* 97:14–25.  
<https://doi.org/10.1016/j.brat.2017.06.005>
39. Lemyre A, Bastien C, Vallières A (2019) Nightmares in Mental Disorders: A Review. *Dreaming* 29(2):144–166
40. Leskin GA, Woodward SH, Young HE, Sheikh JI (2002) Effects of comorbid diagnoses on sleep disturbance in PTSD. *J Psychiatr Res* 36(6):449–452. [https://doi.org/10.1016/S0022-3956\(02\)00025-0](https://doi.org/10.1016/S0022-3956(02)00025-0)
41. Lydiard RB, Hamner MH (2009) Clinical Importance of Sleep Disturbance as a Treatment Target in PTSD. *Focus* 7(2):176–183. <https://doi.org/10.1176/foc.7.2.foc176>
42. Marx BP, Lee DJ, Norman SB, Bovin MJ, Sloan DM, Weathers FW, Keane TM, Schnurr PP (2022) Reliable and clinically significant change in the clinician-administered PTSD Scale for DSM-5 and PTSD Checklist for DSM-5 among male veterans. *Psychol Assess* 34(2):197–203.  
<https://doi.org/10.1037/pas0001098>
43. Mellman TA, Bustamante V, Fins AI, Pigeon WR, Nolan B (2002) REM Sleep and the Early Development of Posttraumatic Stress Disorder. *Am J Psychiatry* 159(10):1696–1701.  
<https://doi.org/10.1176/appi.ajp.159.10.1696>

44. Mellman TA, Kobayashi I, Lavela J, Wilson B, Hall Brown TS (2014) A Relationship between REM Sleep Measures and the Duration of Posttraumatic Stress Disorder in a Young Adult Urban Minority Population. *Sleep* 37(8):1321–1326. <https://doi.org/10.5665/sleep.3922>
45. Nagappa M, Liao P, Wong J, Auckley D, Ramachandran SK, Memtsoudis S, Mokhlesi B, Chung F (2015) Validation of the STOP-Bang Questionnaire as a Screening Tool for Obstructive Sleep Apnea among Different Populations: A Systematic Review and Meta-Analysis. *PLoS ONE* 10(12):e0143697. <https://doi.org/10.1371/journal.pone.0143697>
46. Nappi CM, Drummond SPA, Thorp SR, McQuaid JR (2010) Effectiveness of Imagery Rehearsal Therapy for the Treatment of Combat-Related Nightmares in Veterans. *Behav Ther* 41(2):237–244. <https://doi.org/10.1016/j.beth.2009.03.003>
47. Olff M, Hein I, Amstadter AB, Armour C, Skogbrott Birkeland M, Bui E, Cloitre M, Ehlers A, Ford JD, Greene T, Hansen M, Harnett NG, Kaminer D, Lewis C, Minelli A, Niles B, Nugent NR, Roberts N, Price M, Vujanovic AA (2025) The impact of trauma and how to intervene: A narrative review of psychotraumatology over the past 15 years. *Eur J Psychotraumatology* 16(1):2458406. <https://doi.org/10.1080/20008066.2025.2458406>
48. Oudiette D, Antony JW, Creery JD, Paller KA (2013) The Role of Memory Reactivation during Wakefulness and Sleep in Determining Which Memories Endure. *J Neurosci* 33(15):6672–6678. <https://doi.org/10.1523/JNEUROSCI.5497-12.2013>
49. Perogamvros L, Rochas V, Beau J-B, Sterpenich V, Bayer L (2025) The cathartic dream: Using a large language model to study a new type of functional dream in healthy and clinical populations. *J Sleep Res* 34(6):e70001. <https://doi.org/10.1111/jsr.70001>
50. Phelps AJ, Kanaan RAA, Worsnop C, Redston S, Ralph N, Forbes D (2018) An Ambulatory Polysomnography Study of the Post-traumatic Nightmares of Post-traumatic Stress Disorder. *Sleep* 41(1). <https://doi.org/10.1093/sleep/zsx188>
51. Pillar G, Malhotra A, Lavie P (2000) Post-traumatic stress disorder and sleep—What a nightmare! *Sleep Med Rev* 4(2):183–200. <https://doi.org/10.1053/smr.1999.0095>
52. Posit team, Posit, Software (2025) RStudio: Integrated Development Environment for R. PBC, Boston, MA. <http://www.posit.co/>
53. R Core Team (2024) R: A Language and Environment for Statistical Computing. R Foundation for Statistical Computing, Vienna, Austria. <https://www.R-project.org/>
54. Rihm JS, Rasch B (2015) Replay of conditioned stimuli during late REM and stage N2 sleep influences affective tone rather than emotional memory strength. *Neurobiol Learn Mem* 122:142–151. <https://doi.org/10.1016/j.nlm.2015.04.008>
55. Rochas V, Mammeri K, Bayer L, Tononi G, Perogamvros L (2026) *Content-specific and temporally evolving neural correlates of dream experiences* (Qbwnf\_v3). *PsyArXiv*. [https://osf.io/preprints/psyarxiv/qbwnf\\_v3/](https://osf.io/preprints/psyarxiv/qbwnf_v3/)
56. Sayk C, Saftien S, Koch N, Ngo H-VV, Junghanns K, Wilhelm I (2024) Cortical hyperarousal in individuals with frequent nightmares. *J Sleep Res* 33(2):e14003. <https://doi.org/10.1111/jsr.14003>

57. Schein J, Houle C, Urganus A, Cloutier M, Patterson-Lomba O, Wang Y, King S, Levinson W, Guerin A, Lefebvre P, Davis LL (2021) Prevalence of post-traumatic stress disorder in the United States: a systematic literature review. *Curr Med Res Opin* 37(12):2151–2161.  
<https://doi.org/10.1080/03007995.2021.1978417>
58. Schwartz S, Clerget A, Perogamvros L (2022) Enhancing imagery rehearsal therapy for nightmares with targeted memory reactivation. *Curr Biol* 32(22):4808–4816e4.  
<https://doi.org/10.1016/j.cub.2022.09.032>
59. Siclari F, Baird B, Perogamvros L, Bernardi G, LaRocque JJ, Riedner B, Boly M, Postle BR, Tononi G (2017) The neural correlates of dreaming. *Nat Neurosci* 20(6):872–878.  
<https://doi.org/10.1038/nn.4545>
60. So CJ, Bolstad CJ, Miller KE (2025) Status of Imagery Rehearsal Therapy and Other Interventions for Nightmare Treatment in PTSD. *Curr Psychiatry Rep* 27(11):671–678.  
<https://doi.org/10.1007/s11920-025-01639-z>
61. Spoormaker VI, Montgomery P (2008) Disturbed sleep in post-traumatic stress disorder: Secondary symptom or core feature? *Sleep Med Rev* 12(3):169–184.  
<https://doi.org/10.1016/j.smrv.2007.08.008>
62. Steenkamp MM, Litz BT, Hoge CW, Marmar CR (2015) Psychotherapy for Military-Related PTSD: A Review of Randomized Clinical Trials. *JAMA* 314(5):489. <https://doi.org/10.1001/jama.2015.8370>
63. Stern E, Chamontin M, Maruani J, Mouchabac S, Micoulaud Franchi J-A, Mauries S, Geoffroy PA (2025) Validation of the French version of the Insomnia Severity Index in a population with psychiatric disorders and sleep complaints. *L'Encéphale*, S0013700625001022.  
<https://doi.org/10.1016/j.encep.2025.04.003>
64. Sterpenich V, Schmidt C, Albouy G, Matarazzo L, Vanhaudenhuyse A, Boveroux P, Degueldre C, Leclercq Y, Baeteau E, Collette F, Luxen A, Phillips C, Maquet P (2014) Memory Reactivation during Rapid Eye Movement Sleep Promotes Its Generalization and Integration in Cortical Stores. *Sleep* 37(6):1061–1075. <https://doi.org/10.5665/sleep.3762>
65. Tahmasian M, Jamalabadi H, Abedini M, Ghadami MR, Sepehry AA, Knight DC, Khazaie H (2017) Differentiation chronic post traumatic stress disorder patients from healthy subjects using objective and subjective sleep-related parameters. *Neurosci Lett* 650:174–179.  
<https://doi.org/10.1016/j.neulet.2017.04.042>
66. Tortella-Feliu M, Fullana MA, Pérez-Vigil A, Torres X, Chamorro J, Littarelli SA, Solanes A, Ramella-Cravarro V, Vilar A, González-Parra JA, Andero R, Reichenberg A, Mataix-Cols D, Vieta E, Fusar-Poli P, Ioannidis JPA, Stein MB, Radua J (2019) Risk factors for posttraumatic stress disorder: An umbrella review of systematic reviews and meta-analyses. *Neurosci Biobehavioral Reviews* 107:154–165 & Fernández De La Cruz,. <https://doi.org/10.1016/j.neubiorev.2019.09.013>
67. Troester MM, Quan SF, Medicine AA of S., Berry RB (2023) *The AASM Manual for the Scoring of Sleep and Associated Events, Version 3*. American Academy Of Sleep Medicine.  
<https://books.google.ch/books?id=uKSczwEACAAJ>

68. Van Der Heijden AC, Van Den Heuvel OA, Van Der Werf YD, Talamini LM, Van Marle HJF (2022) Sleep as a window to target traumatic memories. *Neurosci Biobehavioral Reviews* 140:104765. <https://doi.org/10.1016/j.neubiorev.2022.104765>

69. Wang C, Ramakrishnan S, Laxminarayan S, Dovzhenok A, Cashmere JD, Germain A, Reifman J (2020) An attempt to identify reproducible high-density EEG markers of PTSD during sleep. *Sleep* 43(1):zsz207. <https://doi.org/10.1093/sleep/zsz207>

70. Watkins LE, Sprang KR, Rothbaum BO (2018) Treating PTSD: A Review of Evidence-Based Psychotherapy Interventions. *Front Behav Neurosci* 12:258. <https://doi.org/10.3389/fnbeh.2018.00258>

71. Weathers FW, Blake DD, Schnurr PP, Kaloupek DG, Marx BP, Keane TM (2013) *The Clinician-Administered PTSD Scale for DSM-5 (CAPS-5)*. [Assessment] Available from

72. Weathers FW, Blake DD, Schnurr PP, Kaloupek DG, Marx BP, Keane TM (2013) *The Life Events Checklist for DSM-5 (LEC-5)*. Instrument available from the National Center for PTSD at [www.ptsd.va.gov](http://www.ptsd.va.gov)

73. Weathers FW, Litz BT, Keane TM, Palmieri PA, Marx BP, Schnurr PP (2013) The PTSD Checklist for DSM-5 (PCL-5). Scale available from the National Center for PTSD at.

74. Werner KB, Griffin MG, Galovski TE (2016) Objective and subjective measurement of sleep disturbance in female trauma survivors with posttraumatic stress disorder. *Psychiatry Res* 240:234–240. <https://doi.org/10.1016/j.psychres.2016.04.039>

75. Woodward SH, Murburg MM, Bliwise DL (2000) PTSD-related hyperarousal assessed during sleep. *Physiol Behav* 70(1–2):197–203. [https://doi.org/10.1016/S0031-9384\(00\)00271-7](https://doi.org/10.1016/S0031-9384(00)00271-7)

Figures

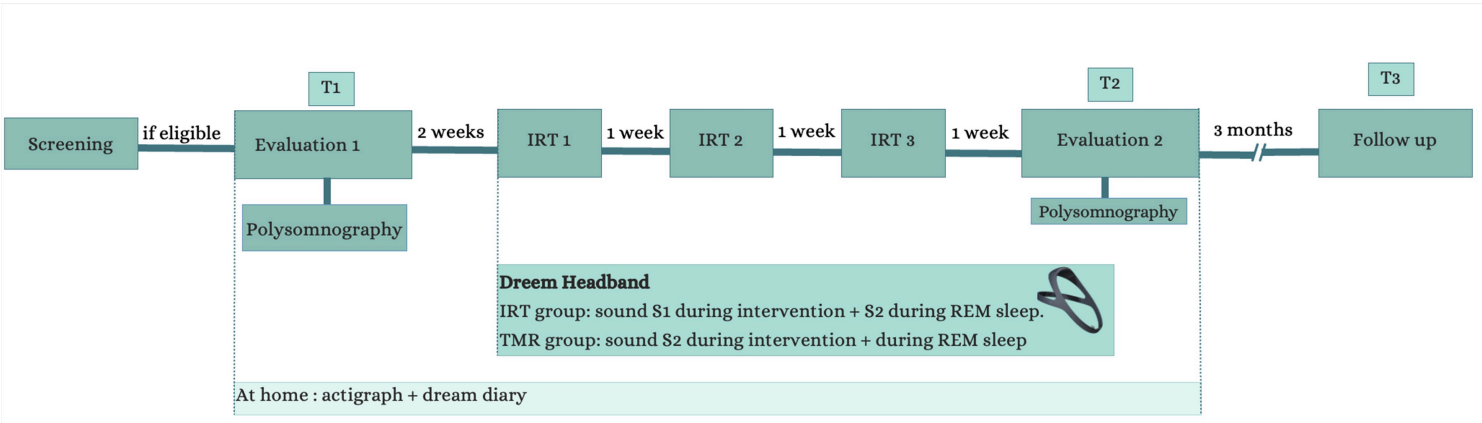


Figure 1

Overview of the study protocol

Boxes represent in-lab sessions with the participant and a clinician (screening, initial evaluation, IRT sessions, second evaluation, and follow-up), arranged chronologically from left to right. IRT = Imagery

Rehearsal Therapy, T1: time-point 1, T2: time-point 2, T3: time-point 3. Light-coloured boxes at the bottom indicate the intervention and materials used at home throughout the study (dream diary, actigraph, and Dreem Headband).

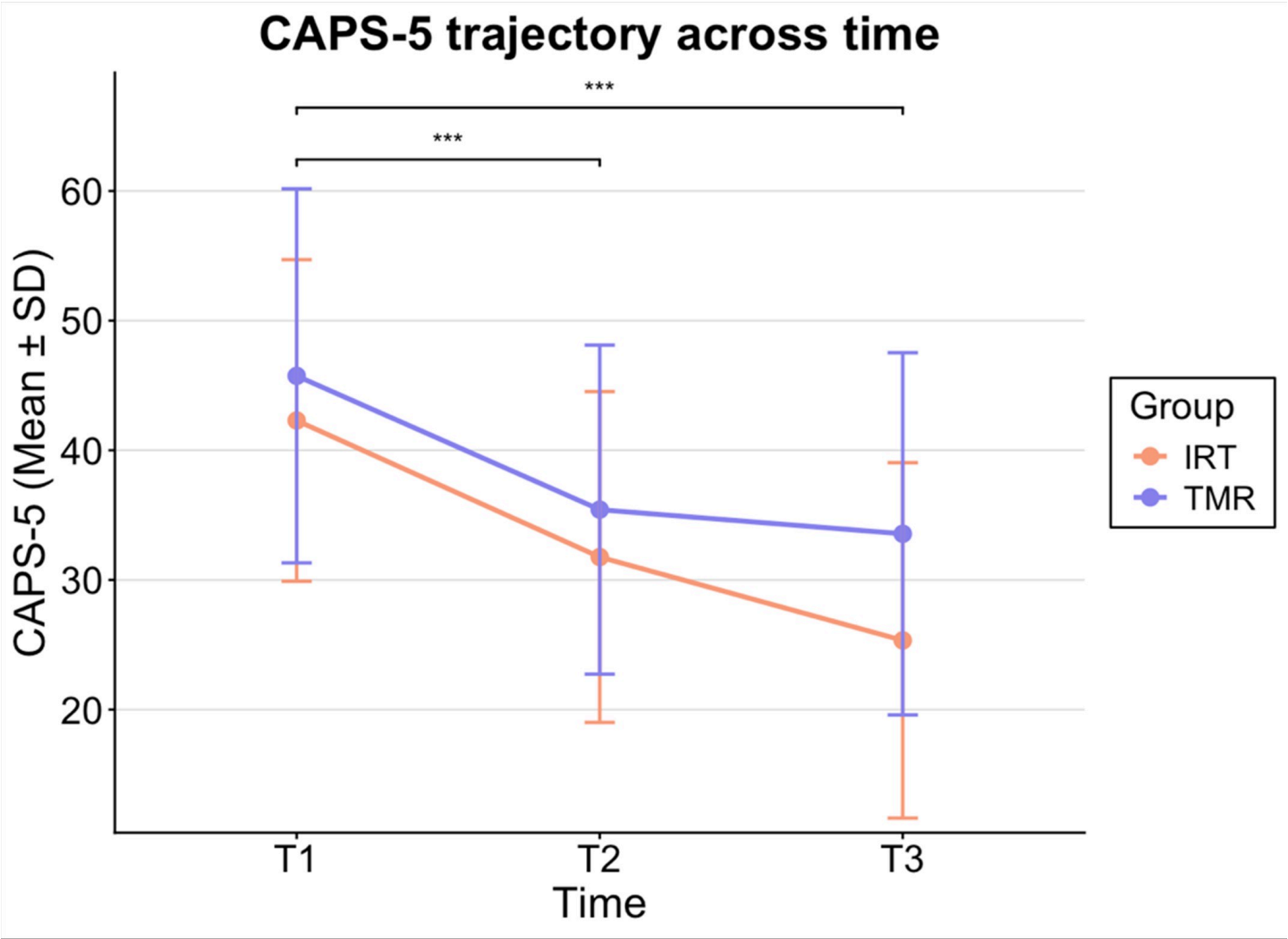


Figure 2

**CAPS-5 scores across the three time points**

T1 = first evaluation, T2 = second evaluation, T3 = follow-up.

## OLS All patients vs Healthy controls

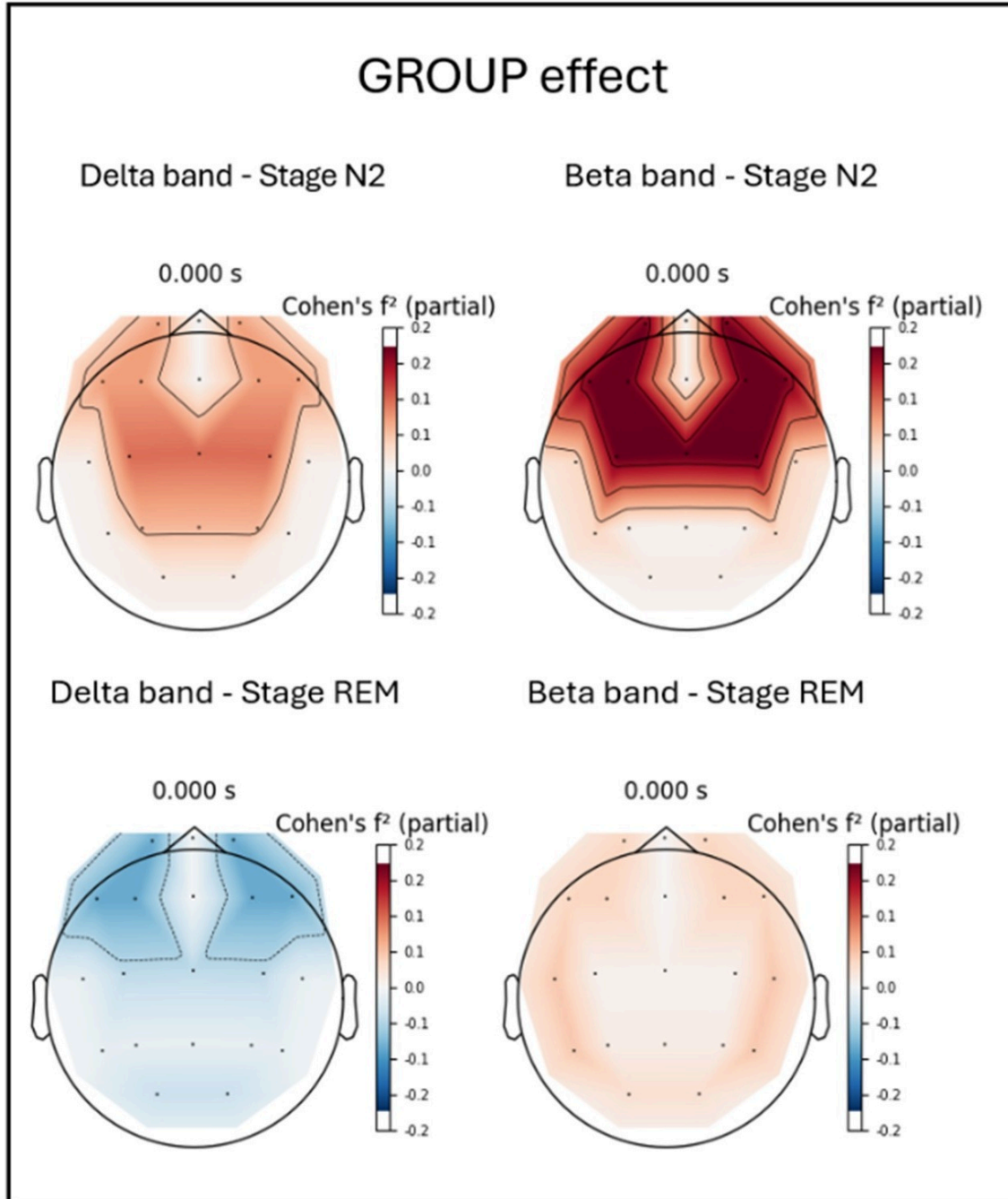


**Figure 3**

Topographical representation of effect sizes for the baseline comparisons of PSD between all patients (N=29) and healthy controls (N=17). Effect sizes are represented for sleep stages including significant effects. Effects of the Group factor are displayed by cluster of electrodes, with anterior up and posterior down, with warm/cold colours for PTSD patients vs healthy controls.

## T-tests PSG1 vs PSG2

### TIME effect

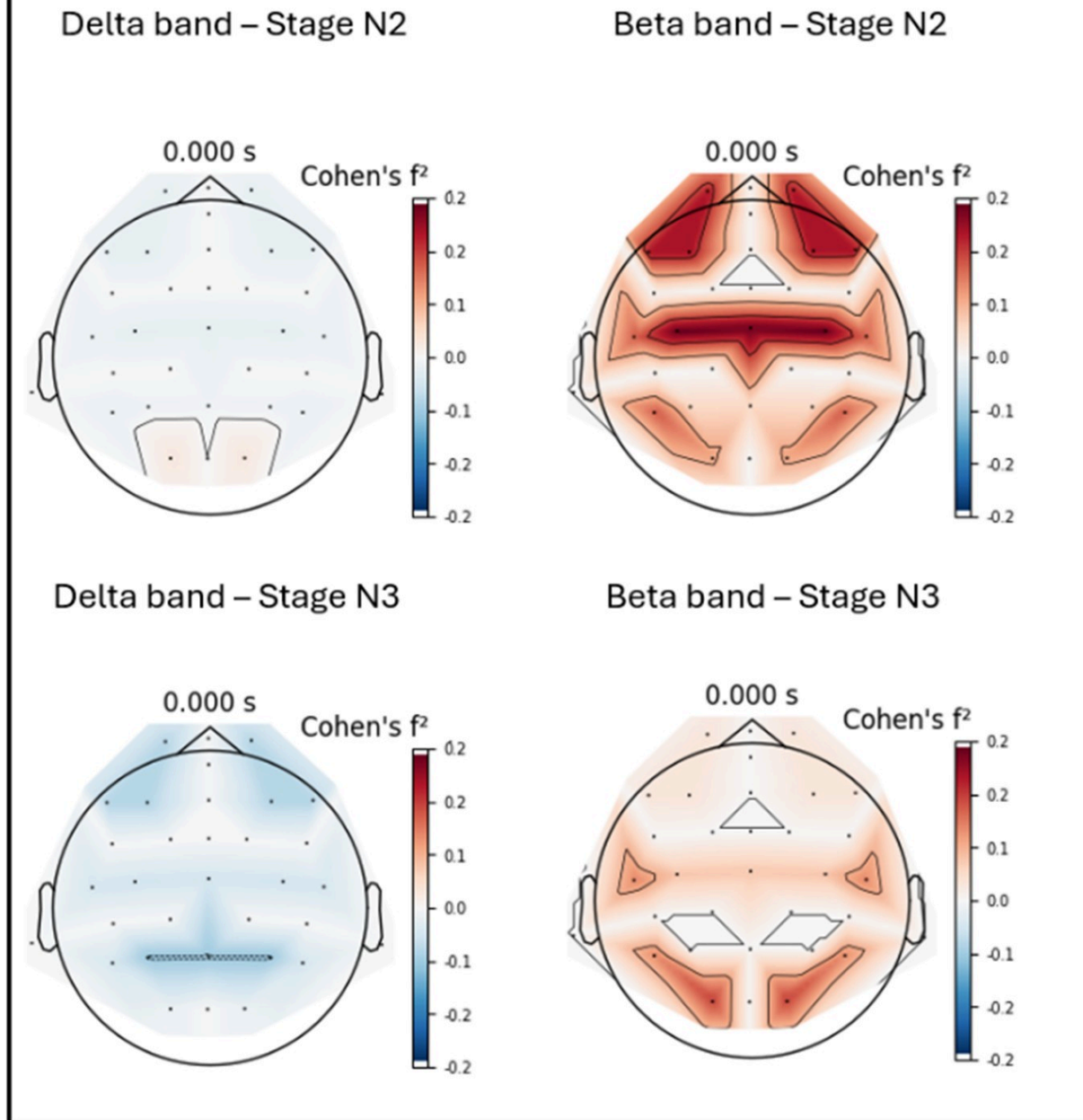


**Figure 4**

Topographical representation of effect sizes for comparisons of PSD over time in all patients. Effect sizes are represented for sleep stages including significant effects. Effects are displayed by cluster of electrodes, with anterior up and posterior down.

# OLS TMR vs IRT

## GROUP effect

Delta band – Stage REM

Beta band – Stage REM

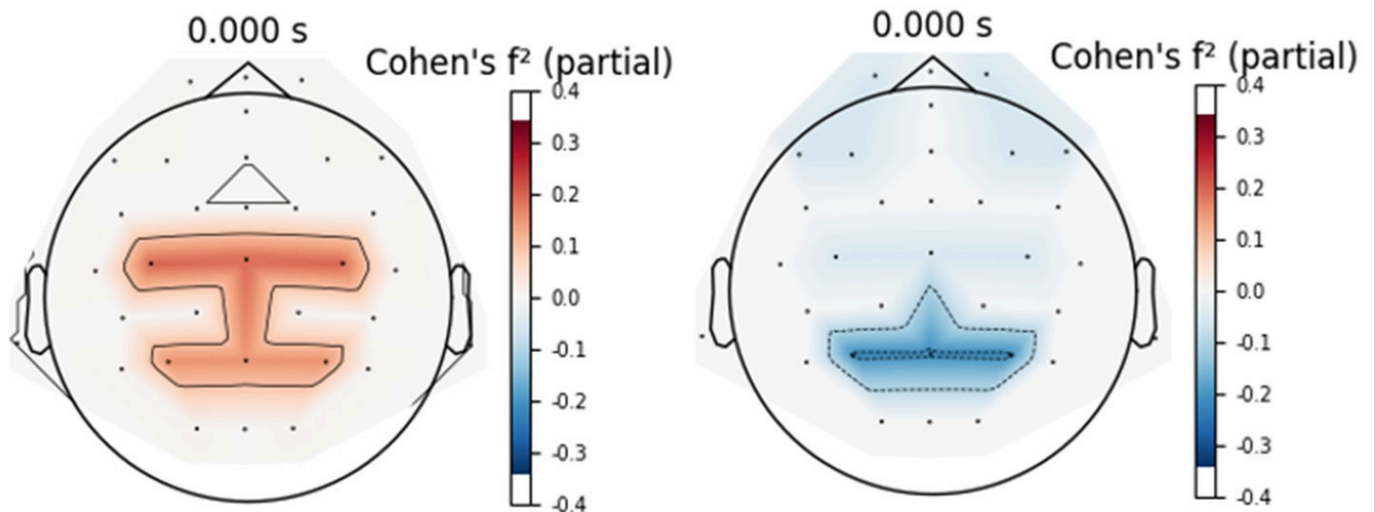


Figure 5

Topographical representation of effect sizes for comparisons of PSD differences over time (PSG2-PSG1) between TMR (N=17) and IRT groups (N=12). Effect sizes are represented for sleep stages including significant effects. Effects of the group are displayed by cluster of electrodes, with anterior up and posterior down, and with warm/cold colours for TMR patients vs IRT patients.