To Sleep or Not to Sleep, That Is the Question: A Systematic Review and Meta-Analysis on the Effect of Post-Trauma Sleep on Intrusive Memories of Analog Trauma

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Abstract

Distressing intrusive memories of a traumatic event are the hallmark symptom of posttraumatic stress disorder. Thus, it is crucial to identify early interventions that prevent the occurrence of intrusive memories. Both, sleep and sleep deprivation have been discussed as interventions, yet previous studies yielded contradicting effects. Our systematic review aims at evaluating existing evidence by means of traditional and individual participant data (IPD) meta-analyses to overcome power issues of sleep research. Until May 16th 2022, six databases were searched for experimental analog studies examining the effect of post-trauma sleep versus wakefulness on intrusive memories. Nine studies were included in our traditional meta-analysis (8 in the IPD meta-analysis). Our analysis provided evidence for a small effect favoring sleep over wakefulness, M(log-ROM) = 0.25, $p < .001$, suggesting that sleep is associated with a lower number of intrusions but unrelated to the likelihood of the occurrence of intrusions. We found no evidence for an effect of sleep on intrusion distress. Heterogeneity was low and certainty of evidence for our primary analysis was moderate. Our findings suggest that post-trauma sleep has the potential to be protective by reducing intrusion frequency. More research is needed to determine the impact following real-world trauma and the potential clinical significance.

Keywords: posttraumatic stress disorder, sleep, distressing intrusions, trauma, meta-analysis, systematic review

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The majority of the world's population will experience at least one potentially traumatic event during their lifetime (e.g., physical or sexual assault, natural disasters, war, or other catastrophic events; Kessler et al., 2017). Following trauma, up to 59% of survivors experience stress-related symptoms (Kliem & Kröger, 2013). In most survivors, these symptoms remit naturally over time. A significant subgroup (15% to 30%) experiences ongoing and chronic stress-related symptoms, manifesting in the form of posttraumatic stress disorder (PTSD; Kessler et al., 1995). PTSD is characterized by spontaneous, involuntary (intrusive) memories of the traumatic event, which are highly distressing, vivid, and feature a sense of "nowness" (i.e., events seem to be happening in the present). By continuously intruding into the everyday life of trauma survivors, intrusive memories lead to a sense of continuous threat and are hypothesized to trigger hyperarousal (e.g., irritability, anxiety, sleep disturbances) and avoidance of potential trauma reminders (i.e., self-isolation; Ehlers & Clark, 2000). This hypothesis is supported by longitudinal research showing that early intrusion characteristics (i.e., frequency, distress, "nowness", and lack of context; Kleim et al., 2013; Michael et al., 2005) predict persistent PTSD symptoms.

PTSD patients experience on average 17 intrusive memories over one week (Pfaltz et al., 2013). This high symptom frequency results in severe decrements of role performance (Alonso et al., 2010), comorbid physical (e.g., cardio-respiratory diseases) and mental disorders (e.g., depression), and impairments of quality of life (Alonso et al., 2004; Olatunji et al., 2007). Critically, many patients (48% to 82%) experience a chronic course of PTSD, retaining their diagnosis for several decades (Perkonigg et al., 2005; Zlotnick et al., 2004). Research efforts are thus focused on developing effective prevention strategies, which can be deployed in proximity to the traumatic event.

Abbreviations

AG: actigraphy; BDI: Beck's Depression Inventory; GRADE: Grading of Recommendations, Assessment, Development and Evaluations; ID: intrusion distress; IF: intrusion frequency; IPD: individual participant data; ITT: Intrusion Triggering Task; NREM: non-rapid eye movement; PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses; PSG: polysomnography; PTSD: posttraumatic stress disorder; REM: rapid eye movement; SWA: slow wave activity; SWS: slow wave sleep

To divert the path from early intrusive memories to persistent PTSD, intervention strategies target at their underlying memory processes (Iyadurai et al., 2018; Iyadurai et al., 2019). According to the cognitive model of PTSD (Ehlers & Clark, 2000), intrusive memories arise from the impact of traumatic stress on memory formation. That is, traumatic stress is proposed to enhance data-driven processing (i.e., bottom-up processing that relies heavily on perceptual and sensory information) which, in turn, strengthens associative learning and reduces the elaboration of explicit trauma memories as well as the integration of the trauma into the autobiographical memory system. As a result, trauma reminders trigger implicit - but not explicit - memory recall, facilitating the emergence of spontaneous, involuntary trauma memories. Moreover - due to the deficient explicit recall - trauma survivors lack awareness that their current sensory impressions derive from a past event (i.e., autonoetic awareness). In a similar vein, Brewin et al. (2010) propose that traumatic stress reduces the formation of contextual representations of the traumatic event, which impairs voluntary, explicit memory retrieval. Conversely, they suggest that stress enhances the formation of sensory representations, which drive intrusive trauma memories. Intrusion development is assumed to be further facilitated by weak contextual representations, which fail to exert top-down control over strong sensory representations (Bisby & Burgess, 2017).

Based on these models, prevention strategies have been focused on reducing implicit (sensory) trauma memories and strengthening explicit (contextual) trauma memories in the post-encoding phase by targeting either consolidation or reconsolidation processes (Deeprose et al., 2012; Hørlyck et al., 2019; Krans et al., 2009). One line of research has specifically focused on a prolonged stage of consolidation, referred to as 'systems consolidation' (Kleim et al., 2016). During systems consolidation, new memory representations are redistributed from short-term storage in the hippocampus to neocortical long-term stores (Diekelmann & Born, 2010). This process is assumed to occur during sleep. Accordingly, research shows that sleep - as opposed to wakefulness - enhances the retention of previously acquired emotional memories (Sopp et al., 2018). These effects are evident across different memory domains but are most pronounced for episodic memories, facilitating explicit, contextually rich memory recall (Atienza & Cantero, 2008; Drosopoulos et al.,

2005). However, specific studies also found the opposite pattern, indicating that a lack of sleep reduces implicit fear memories without affecting explicit memory recall (Kuriyama et al., 2010).

On a neurophysiological level, memory redistribution is assumed to occur during slow wave sleep (SWS), mediated by the propagation of slow oscillations and sleep spindles (Diekelmann & Born, 2010). However - in the context of emotional memory consolidation - empirical findings also suggest an involvement of rapid eye movement (REM) sleep (Hutchison & Rathore, 2015; Schäfer et al., 2020). Consonantly, REM theta activity (4–7 Hz) - the oscillatory signature of REM sleep - has been shown to correlate with post-sleep emotional memory performance (Nishida et al., 2008; Sopp et al., 2017). Beyond sleep's impact on memory retention, studies have also indicated that consolidation processes occurring during sleep may affect the emotional tone of memories. On the one hand, these processes have been suggested to reduce the affective tone of emotional memories (van der Helm & Walker, 2009). On the other hand, empirical findings have found sleep to preserve or even intensify the affective charge associated with emotional stimuli (Jones & Spencer, 2019; Pace-Schott et al., 2011).

Based on these findings, researchers have considered sleep after trauma as a potential target for reducing intrusive trauma memories. However, in light of the heterogeneity of empirical findings, the underlying assumptions and suggested interventions differ dramatically. One line of research (Kuriyama et al., 2010; Porcheret et al., 2015) hypothesizes that sleep-related consolidation mechanisms strengthen implicit memory processes, thereby facilitating intrusion development after trauma. Consequently, sleep deprivation during the night after trauma is proposed as a prevention strategy. Another line of research (e.g., Kleim et al., 2016; Sopp et al., 2019; Zeng et al., 2021) suggests that - by selectively strengthening explicit rather than implicit trauma memories - sleep may reduce the likelihood of intrusion development. These effects are assumed to emerge because facilitating explicit, contextually rich recall should - in turn - inhibit stimulus-driven reactivation of sensory representations (Bisby & Burgess, 2017). Moreover, explicit contextually rich recall supports autonoetic awareness, which may prevent the "nowness" quality of any arising intrusions (Ehlers,

2010). Based on these assumptions, interventions promoting restful post-trauma sleep are proposed to reduce intrusions, and thereby the development of persistent PTSD symptoms.

To summarize, the present state of scientific knowledge regarding the effects of sleep on intrusions has yielded highly conflicting results, and thereby produced opposing theoretical perspectives to explain such effects. In order to shed further light on this issue, the current systematic review aims to provide a synthesis of available evidence from experimental analog studies comparing the effects of post-trauma sleep and wakefulness. To this end, we performed an in-depth qualitative analysis of study findings focusing on potential underlying memory processes and the association of intrusive memories with sleep physiology, which forms the base for our quantitative synthesis. For this quantitative summary, researchers of the field have provided primary datasets of their studies, which were analyzed on study level (traditional meta-analysis based on aggregated data) and on a participant level (individual participant data [IPD] meta-analysis). These complementary approaches give us the unique opportunity to investigate how effects add up quantitatively, and whether moderator variables related to study designs and sampling account for potential discrepant findings. Moreover, as a result of the collaborative effort, we were able to achieve extraordinarily high statistical power relative to primary studies, which are limited in sample size due to high resources required for conducting sleep research.

Methods

This systematic review was prepared in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Page et al., 2021) and recommendations for reporting IPD meta-analysis (Stewart et al., 2015). As the project evolved from a multi-lab collaborative effort into a systematic review, it was registered retrospectively on the Open Science Framework (registration doi: 10.17605/OSF.IO/4DH2V, link to OSF project: https://osf.io/j2av3/), where we also provide materials and aggregated data relevant to this review. Changes from registration to final review were only minor and are presented in Supplementary Material SM1.

Literature Search

Relevant search terms were identified by the research team to cover the most frequently used terms in the literature on post-trauma sleep and intrusive memories of analog trauma. Using these terms, a literature search based on title, abstract, and keywords was performed in six databases: EBSCOhost (PsycINFO and PsycARTICLES), PTSDpubs, PubMed, Scopus, and Web of Science (see Supplementary Material SM2 for search strings). Moreover, reference lists of included studies and a related qualitative review were checked for eligible studies (Azza et al., 2020). Additionally, authors of studies included in the IPD analyses were asked if they were aware of other (un)published experimental studies meeting our inclusion criteria. A date-of-publication criterion was not defined. The most recent literature search was run on May 16th 2022.

Selection Criteria

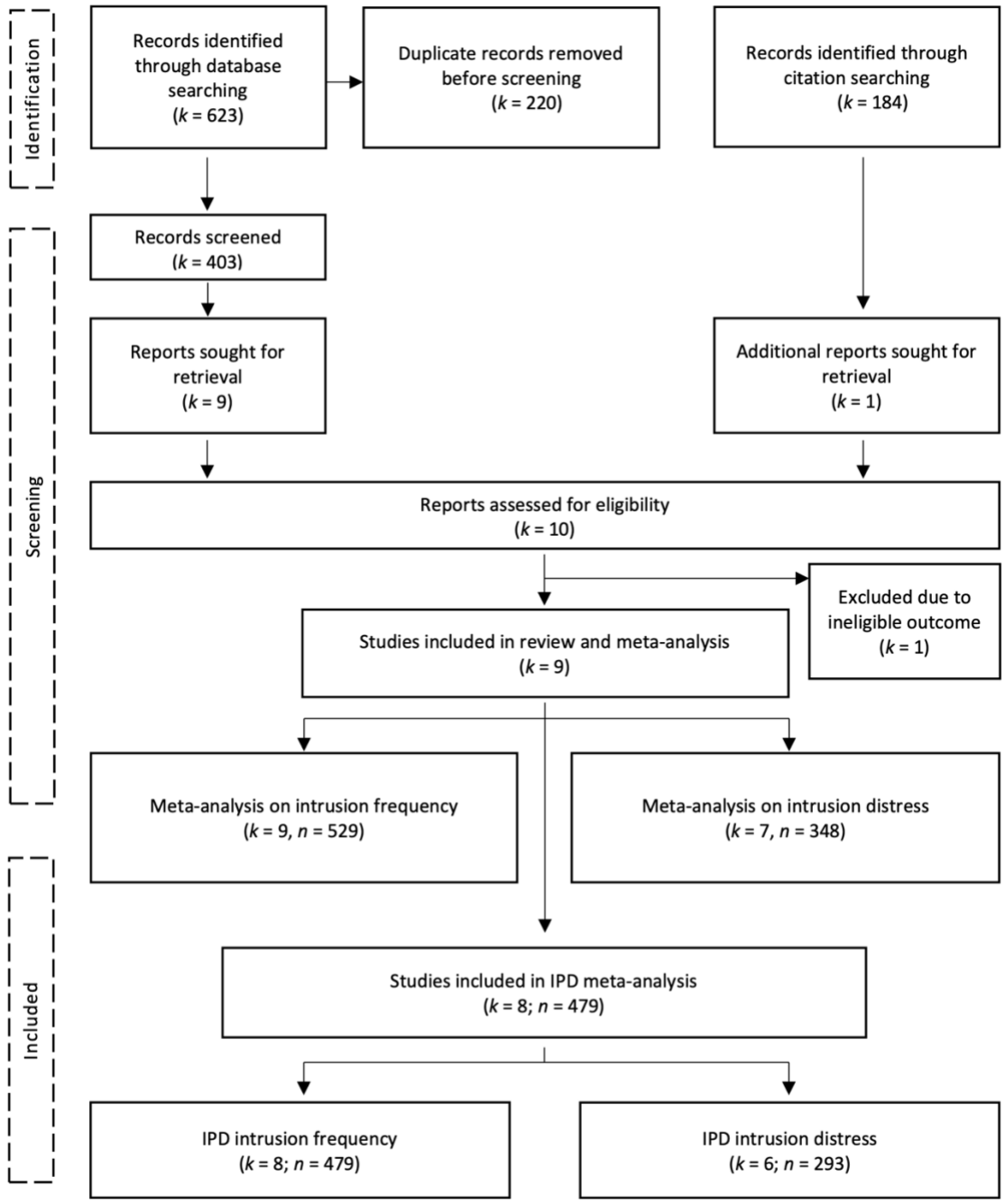
Studies meeting the following criteria were included: 1) The experimental study reported on a sample that encoded aversive visual stimuli (e.g., trauma film, aversive pictures). 2) One group of participants subsequently underwent a post-trauma (or post-aversive stimuli) sleep opportunity, while another group stayed awake during the daytime or was exposed to (partial) sleep deprivation during the nighttime (e.g., REM sleep deprivation). 3) Following sleep or wakefulness, the frequency of intrusive memories was assessed using an intrusion diary or a laboratory intrusion assessment (e.g., intrusion triggering task). 4) Participants were mentally healthy adults. Samples were excluded if 1) they exclusively investigated the effect of sleep in the context of specific memory tasks (e.g., think-no-think paradigm), or 2) the necessary data for effect size calculation were not available by May 16th 2022 (for the meta-analysis on aggregated data) or December 31st 2021 (for IPD meta-analysis).

Study Selection

The study selection procedure is illustrated in the PRISMA flowchart (see Figure 1). Authors CL, EF, and SKS screened titles and abstracts in duplicate for inclusion eligibility. The interrater

agreement achieved for inclusion/exclusion decisions was excellent, *kappa* = 1.0 (initially, it was planned to resolve potential disagreement via discussion or consultation of a third reviewer, RS or SKS). After abstract screening, the full texts of 10 records were independently assessed by authors CL and EF, resulting in nine eligible studies. All studies obtained sufficient information to be included in the meta-analysis based on aggregated data. Subsequently, corresponding authors of all identified studies were contacted and asked to provide raw data from their study to perform the IPD meta-analysis. Of the nine identified studies, raw data were obtained for eight studies. Data of one study (Kleim et al., 2016) could not be obtained. So, the study was only included in our meta-analysis on aggregated data but not in the analysis based on IPD.

Figure 1. PRISMA Flowchart of the Study Selection Process



Note. Lastly updated on May 16th 2022. IPD= individual participant data, *k* = number of studies, *n* = number of participants

Data Extraction

Meta-Analysis on Aggregated Data

Using a standardized Excel form, data for each study was extracted by two independent coders (CL, EF). The interrater agreement for extracted data was excellent, *kappa* = 1.0 for sample sizes,

means, and *SDs*. Data on intrusion distress were coded as a secondary outcome. For intrusion distress, we adopted the definition used in the original studies (e.g., Porcheret et al., 2015; participants were asked to rate the level of distress experienced with the intrusion from 0 = "not at all" to 10 = "extremely"). The only exception was the study by Werner et al. (2021), for which aversiveness ratings served as an index of intrusion distress. Other coded variables were related to study characteristics (e.g., type of wake group) or sample characteristics (e.g., participants' mean age, percentage of female participants).

Individual Participant Data Meta-Analysis

Two independent review team members (CL, student research assistant) extracted IPD based on generic standardized Excel forms and integrated single study datasets into one individual participant dataset. All disagreements between coders were resolved through discussion or consultation of a third reviewer (RS or SKS), and in unclear cases, study authors were contacted to provide additional information. All data were checked for integrity (e.g., reasonable data for primary and secondary outcomes).

Data Synthesis

Combining meta-analysis on aggregated data and IPD, our analyses compared results from data reported in individual studies (i.e., meta-analysis on aggregated data) and those obtained from multilevel analyses (i.e., meta-analysis on IPD). The former allowed for the inclusion of all eligible studies, while the latter allowed for modeling participant-level moderators (e.g., participants' age, gender; Mathew & Nordström, 2010). All analyses were performed in *RStudio* version 2022.02.3 (RStudio Team, 2020). Analytic code and aggregated data are available at the Open Science Framework (OSF project: https://osf.io/j2av3/). Due to data privacy reasons, data for the IPD analyses will be made available upon reasonable request by the study authors.

Manipulation Check for Negative Mood

First, we used IPD to check whether the exposure to analog trauma resulted in a significant increase in negative mood. This analysis was performed using the *R* package *lme4* (Bates, 2010) and employed a multilevel model with time and group as fixed effects and a random intercept and slope for study. We expected negative mood to increase from pre-to-post exposure to the traumatic material, without any difference between experimental groups (i.e., sleep vs. wake group).

Meta-Analysis on Aggregated Data

Meta-analyses on aggregated data were performed using the *R* package *metafor* (Viechtbauer, 2010).

Database. To mirror findings from a meta-analysis solely based on published findings, these analyses mostly used data reported in published articles (e.g., means reported in a table of the respective publication). Means and *SDs* were only calculated from IPD in case no other information was available.

Effect Size Calculation. For effect size calculation, experimental groups per study were chosen to be as similar as possible across studies. In case there was more than one condition relevant to our research question, they were either combined or we selected the one that is most comparable to other studies. As most of the studies did not comprise more than two conditions, we decided not to use multilevel meta-analyses (Van den Noortgate et al., 2015). The meta-analyses used log-transformed *ratio of means* (log-ROMs) and corresponding sampling variances as effect size measures (Friedrich et al., 2011), with positive log-ROMs indicating that intrusion frequency or distress were lower in the sleep as compared to the wake group. For illustrative purpose, we transformed log-ROMs to ROMs that express the percentage increase in the mean value of intrusion frequency and distress of the wake group relative to the sleep group. We decided to use log-ROMs instead of *standardized mean differences* (SMDs) as our IPD analyses revealed that raw data for intrusion frequency and intrusion distress followed non-normal distributions (see *Individual Participant Data Meta-Analysis*) and recent simulation studies found nonnormality from primary

studies to bias SMD estimates (Sun & Cheung, 2020). We used 95% confidence intervals (CIs) as indicator of significance and report 95% prediction intervals (PIs) as the interval within which the effect size of a new study randomly selected from the same population would fall (InHout et al., 2016; Nagashima et al., 2019).

Main Analyses. All analyses used maximum likelihood estimations, weighted studies based on an inverse-variance approach, and relied on random-effects models that allow for true between-study variance and for inferences to the wider population (Field & Gillett, 2010). Residual heterogeneity of study effects was indicated by means of τ^2 (estimating the variance of the "true" population effect size; Borenstein et al., 2021), Cochran's *Q* statistic (i.e., weighted sum of squared differences between the observed effects and the weighted mean effect size, which can be tested for statistical significance, whereby a significant *Q* statistics indicates substantial heterogeneity), and I^2, which expresses heterogeneity as percentage (0%–100%; Higgins et al., 2003). I^2 reflects the proportion of variance that reflects true variance in effect sizes rather than sampling error (Borenstein et al., 2017), with values of 50% and above indicating substantial between-study heterogeneity (Deeks et al., 2022).

Outliers and Influential Cases. Outliers and influential cases were identified based on studentized deleted residuals (SDRs), Cook's distances (CD), and covariance ratios (COVRATIO). SDRs below and above ± 1.96, CD values > 0.45, and COVRATIOs < 1 were considered as outlier or influential case (Cook & Weisberg, 1982; Viechtbauer & Cheung, 2010).

Moderator Analyses. The impact of moderators on effect sizes estimates was investigated by meta-regression for continuous variables (e.g., % females), with significance being assessed using *QM* statistics.

Meta-Analysis on Individual Participants Data

Effect Size Calculation. Analyses followed a one-step approach, that is, analyses were performed on a merged dataset containing all IPD with participants being clustered in studies (Mathew & Nordström, 2010). IPD meta-analysis was performed using the *R* packages

GLMMapdative (Rizopoulos, 2019), *glmmTMB (Brooks et al., 2017),* and *DHARMa* (Hartig, 2020). We conducted separate multilevel analyses to examine the effect of sleep versus wakefulness on intrusion frequency (Model 1, primary outcome) and intrusion distress (Model 2, secondary outcome). Intrusion frequency and intrusion distress were used as dependent variables and group as independent variable. For intrusion frequency, we used the absolute number of reported intrusions. For intrusion distress, we divided the severity of reported distress levels by the number of intrusions, whose result was further divided by the range of distress assessment (i.e., intrusion distress = [total score of reported distress / frequency of intrusions] / range of distress assessment). This resulted in scores ranging from 0 to 1, with 1 indicating maximum distress for each intrusion on the respective scale. Participants who did not experience any intrusion were removed from this analysis.

Model Selection and Diagnostics. All models were examined to fit our data based on residual distributions (i.e., under- and overdispersion, zero-inflation, normal distribution [Kolmogorov-Smirnov]; Borhan et al., 2020; Perumean-Chaney et al., 2013). For intrusion frequency as count variable, our analyses started with a Poisson model, which was checked for overdispersion. Due to overdispersal residuals, we decided to use zero-inflated negative binominal models, which model the occurrence and absence of intrusions separately. Specifically, the zero part of the model provides information on the occurrence of any (vs. no) intrusions, and the count part of the model estimates the severity of intrusions. In contrast to (negative binominal) hurdle models, zero-inflated negative binominal models assume that zeros may result from two processes: One specific to the occurrence of zeros (as assumed in hurdle models) and as the lower end of the severity distribution (Feng, 2021; Gurmu & Trivedi, 1996). As it is not yet clear what model suits (analog) PTSD symptoms best (Jaffe et al., 2017; Rehder & Bowen, 2019), we based our model choice on model fit (Akaike information criterion [AIC], Bayesian information criterion [BIC]), and residual diagnostics. For intrusion distress as a continuous variable, we started with a Gaussian distribution and checked residual distributional assumptions. Due to significant zero inflation, intrusion distress was modeled using a hurdle model for semi-continuous data, which was found to be superior to similar zero-inflated gamma distribution

models. Moreover, all models allowed for random intercepts per study. The inclusion of random slopes per study was evaluated based on the change in model fit using a likelihood ratio test (LRT).

Outliers. Outliers were examined as part of the residual diagnostics.

Moderator Analyses. We examined the effects of participant-level variables on the intrusion frequency, intrusion distress and their interaction with the experimental group (moderator effect). The moderators include age, gender, depressive symptoms at baseline, and increases in negative mood due to aversive stimuli. Cluster mean centering was applied for all individual participant level moderators.

Risk of Bias Assessment

Publication Bias

Results of meta-analyses may overestimate the true population effect due to publication bias (DeVito & Goldacre, 2019). To reduce its potential impact, our search also included grey literature (i.e., dissertations, preprints) and study authors were asked for available unpublished data. Although the number of studies was small (k = 9), publication bias was assessed on an exploratory basis for the meta-analysis on aggregated data using visual inspection of funnel plots and rank correlation tests (Kendall's τ) to examine their symmetry (Egger et al., 1997). A significant rank correlation test provides evidence for the presence of a publication bias. In addition, we used contour-enhanced funnel plots to examine if “missing” studies would fall into the area of non-significant findings (Peters et al., 2008).

Internal Risk of Bias

Meta-analytical findings can be biased by insufficient study quality such as flaws in study design, analysis, or reporting (Higgins et al., 2011). Since standard internal-bias assessment checklists were not applicable, we used an adapted version of a quality checklist developed for a meta-analysis on the impact of sleep on emotional memory (Schäfer et al., 2020). The 11-item checklist is based on state-of-the-art criteria in sleep research (e.g., study design, control of wake/sleep deprivation

conditions). Study quality as indicator of internal risk of bias was rated independently by two raters (CL, student research assistant). Ratings could range between 0 and 1, with higher scores indicating better quality (i.e., lower risk of bias). Meta-regression was used to statistically examine the impact of internal risk of bias on the effect size estimation.

Certainty of Evidence

The certainty of evidence for intrusion frequency and intrusion distress was assessed in duplicate using GRADE (Grading of Recommendations, Assessment, Development and Evaluations; Schünemann et al., 2022). We used the internal risk of bias assessment described above for the GRADE domain "risk of bias". To assess imprecision, we calculated optimal information sizes based on standard recommendations (Garcia-Alamino et al., 2017). According to GRADE, certainty can either be very low, low, moderate, or high.

Sensitivity Analyses

To examine the robustness of our findings, we performed sensitivity analyses investigating the impact of analytic decisions. We decided to use log-ROMs as effect size measure of our meta-analysis on aggregated data as nonnormality from primary studies was found to bias SMD estimates (Sun & Cheung, 2020). However, as comprehensive simulation studies on log-ROMs are missing, we re-ran our meta-analyses on aggregated data using SMDs (instead of log-ROMs) as check for robustness. Moreover, as statistical approaches varied between primary studies (i.e., Poisson regressions; Porcheret et al., 2015; *t*-tests; Sopp et al., 2021), we examined if our results from the IPD meta-analysis largely depended on specific modeling decisions. For this purpose, we recalculated our analyses based on comparable distributions (i.e., intrusion frequency: negative binominal hurdle model instead of zero-inflated negative binominal model; intrusion distress: zero-inflated gamma model instead of lognormal hurdle model for semi-continuous data).

Results

Qualitative Summary of Potential Underlying Memory Processes and Associations with Sleep Physiology

Effect of Sleep Versus Wakefulness on Intrusion Frequency and Intrusion Distress

Sleep Versus Total Sleep Deprivation During Nighttime. Three studies investigated the effect of total sleep deprivation versus sleep during the first night after analog trauma on subsequent intrusive memories. In the first study on this subject, Porcheret et al. (2015) exposed participants to a traumatic film after which they either returned home to sleep or underwent a full night of sleep deprivation in the laboratory (see Table 1 for study characteristics). Intrusive memories were assessed using a 7-day intrusion diary. Results demonstrated significantly higher intrusion frequencies in the sleep group than in the sleep deprivation group. These effects were evident on the first two days after exposure to the trauma film, thus including the period of acute sleep deprivation. In addition, distress ratings as assessed by the Impact of Event Scale-Revised (Weiss, 2007) were significantly higher in the sleep than in the sleep deprivation group. In a follow-up study to their first experiment, Porcheret et al. (2019) reinvestigated the effects of sleep as opposed to sleep deprivation on analog intrusions. Their design was largely identical to their 2015 study with the exception that sleep deprivation was conducted at home rather than at the lab. Analyses revealed different effects, depending on the inclusion of the high rate of participants who slept to some extent in the sleep deprivation group. Without excluding these participants, results did not reveal any consistent differences between groups. After their exclusion, analysis revealed significantly lower intrusion frequencies in the sleep group than in the sleep deprivation group. No differences emerged for intrusion distress. Finally, using a similar design, Zeng et al. (2021) reinvestigated the impact of sleep versus full night sleep deprivation at the lab on intrusive memories of a traumatic film. Results showed fewer intrusions in the sleep than in the sleep deprivation group but provided no evidence for a difference in distress ratings.

--- Table 1 is provided at the end of the preprint ---

Sleep Versus Wakefulness During Daytime. Two studies investigated the effects of sleep as opposed to wakefulness during *daytime* (or both day- and nighttime). In the study of Kleim et al. (2016), participants were exposed to a traumatic film and either had a full night of sleep at home afterwards or were deprived of sleep. Half of the wake group was exposed to the trauma film in the evening and was subsequently sleep deprived during the night, whereas the other half was exposed to the trauma film in the morning and subsequently remained awake during the day. Wakefulness during the daytime versus nighttime did not have any effects on outcome measures, allowing the authors to collapse these subgroups for their analyses. Analyses of diary data, which were collected during seven subsequent days, revealed significantly lower intrusion frequencies in the sleep than in the wake group. Interestingly, these effects were most pronounced on days 3–7 indicating a delayed benefit of sleep. Groups were also found to differ in intrusion distress with the sleep group reporting significantly lower ratings than the wake group. In another study, Sopp et al. (2021) investigated the impact of sleep as opposed to wakefulness on analog intrusions during the daytime. After being exposed to traumatic picture stories, participants either had a full night of sleep, with half of the participants sleeping at the lab and the other half sleeping at home, or a 12-hour period of wakefulness during daytime. Groups did not differ on intrusion frequency in a laboratory intrusion triggering task.

Sleep Versus Partial Sleep Deprivation. Two studies investigated the effect of sleep as opposed to partial sleep deprivation on analog intrusions. In the study by Sopp et al. (2019), participants viewed traumatic picture stories prior to a full night sleep or a limited sleep opportunity with sleep deprivation during the second night half, with both interventions being conducted at the lab. Partial sleep deprivation aimed to systematically reduce the amount of REM sleep (Ekstrand et al., 1977). Intrusions were assessed in the morning using a laboratory intrusion triggering task. Results demonstrated lower intrusion frequency in the sleep than in the partial sleep deprivation group. Werner et al. (2021) similarly manipulated sleep duration to compare participants that underwent a nap with REM sleep, a nap with REM awakening, and a nap without REM sleep at the lab after having been exposed to traumatic pictures. Participants completed an intrusion diary for

three consecutive days. Analyses revealed significantly reduced intrusions (number and duration) in the REM sleep group and REM awakening group as compared to the no REM sleep group on day 3. Groups were also found to differ in distress of picture memories (i.e., aversiveness), with the REM sleep group and the REM awakening group showing lower distress.

Nap Sleep Versus Wakefulness. Finally, two studies investigated the effects of *nap sleep* as opposed to wakefulness during the daytime. In the study by Woud et al. (2018), participants first viewed a traumatic film and were then subjected to a cognitive bias modification training. Subsequently, they were either given a nap opportunity of 90 min or remained awake during this time, with both groups staying at the laboratory. Collapsing effects across training groups provided evidence for an effect of nap sleep on intrusive memories assessed during seven consecutive days, with participants of the nap group reporting fewer intrusions than their wake counterparts. In another study, Wilhelm et al. (2021) investigated the effect of a 90-min nap opportunity in the lab as opposed to a 90-min wake period during the daytime on intrusive memories of a traumatic film. Intrusion frequency and distress assessed using a 7-day intrusion diary did not differ between groups. In a secondary analysis, the authors found that participants who reached REM sleep reported lower intrusion distress than those with no REM sleep or no sleep at all. There was no evidence for an effect of sleep on intrusion frequency.

Effect of Sleep Versus Wakefulness on Explicit and Implicit Trauma Memory

Our summary the effects of sleep on trauma memory follows the differentiation of explicit and implicit trauma memory proposed by Kuriyama et al. (2010).

Effects of Sleep on Explicit Trauma Memory. Two studies investigated the impact of sleep as opposed to sleep deprivation during the nighttime on explicit trauma memory using a *visual* recognition memory test. Porcheret et al. (2019) examined visual recognition memory at day 2 after a night of sleep in both groups using 11 images from the trauma film and 11 new images. Participants were asked to indicate for each image whether the image had been shown in the trauma film or not. Analyses indicated that participants of the sleep group recognized significantly more images from the

trauma film than participants from the sleep deprivation group, with no evidence for a difference in correctly rejected new images. Zeng et al. (2021) conducted an immediate (day 1; morning-after sleep / sleep deprivation) and delayed (day 8) visual recognition memory test using 60 screenshots from the trauma film as old stimuli, with half of them containing aversive scenes and the other half depicting neutral scenes. Sixty new screenshots (30 negative, 30 neutral) were selected from similar, but unwatched films. Analyses revealed that participants of the sleep group had better recognition memory than participants of the sleep deprivation group on day 1. These differences emerged because the sleep group showed a higher rate of correct rejections to new neutral pictures. No evidence for between-group differences emerged on day 8.

Two studies investigated the impact of sleep as opposed to wakefulness during the day- or nighttime on explicit trauma memory using a *visual* recognition memory test that differentiated between divergent retrieval processes. That is, studies differentiated between recollection- and familiarity-based retrieval, which is important since only recollection is linked to episodic contextually rich memories (Yonelinas, 2002). Sopp et al. (2019) assessed explicit memory of traumatic picture stories by presenting 30 objects that had been embedded into the picture stories and 30 new objects. After awakening or sleep deprivation in the second night half, participants were asked to indicate for each object whether it had been presented in the picture stories or not. For each object that they identified as 'old', they were additionally asked to indicate whether their recognition judgement was based on remembering details of its previous presentation ("Remember") or on a feeling of "knowing" ("Know"). Analyses revealed that participants of the sleep group showed higher recollection-based recognition memory than participants of the partial sleep deprivation group. No evidence for a difference emerged for familiarity-based recognition memory. In a follow-up study, Sopp et al. (2021) investigated explicit memory for relevant and irrelevant objects that were presented in traumatic picture stories. Participants were exposed to picture stories that contained 48 relevant and 48 irrelevant objects, which were supplemented with 96 new items during a recognition test at baseline (after viewing the picture stories) and after sleep or wakefulness during daytime. Again, recollection and familiarity-based recognition were

differentiated during the test phase. Results revealed higher recognition memory for relevant objects in the sleep as compared to the wake group. There was no evidence of a difference for irrelevant objects.

Two studies investigated the impact of (nap) sleep as opposed to wakefulness during the day- or nighttime on explicit trauma memory using a *verbal* recognition memory test. Woud et al. (2018) used seven questions about aspects of the film to assess explicit memory of the trauma film seven days post-sleep intervention. Each question was followed by two answers and participants had to choose one. Analyses did not reveal any significant differences between the nap and wake group. Porcheret et al. (2019) asked participants to perform a verbal explicit memory task, which required them to rate if 32 written statements relating to the trauma film were true or false. The test took place on day 2 after a night of sleep in both groups. No differences were evident between the sleep and sleep deprivation group.

Effects of Sleep on Implicit Trauma Memory. One study investigated the impact of sleep as opposed to partial sleep deprivation on implicit trauma memory, assessed in terms of *processing fluency*. Prior to conducting the explicit memory test described above, Sopp et al. (2019) presented half of the objects from the traumatic picture stories and 20 distractor objects in a blurred picture identification task. Participants were asked to label the blurred objects as soon as they recognized them. No evidence for a between-group difference emerged.

Four studies investigated the impact of (nap) sleep as opposed to wakefulness on implicit trauma memory, assessed in terms of *fear ratings*. Porcheret et al. (2019) measured fearfulness on a visual analog scale for images from the trauma film and for neutral pictures of similar content that were not used in the recognition task. Participants gave their ratings immediately before the trauma film, after the trauma film, and on day 2 after a night of sleep in both groups. No evidence for reliable differences emerged between groups. During the recognition memory test in the study by Zeng et al. (2021), participants were additionally asked to provide a fear rating for each old and new image. Analyses revealed a decline in fear ratings over time in the wake group, but not in the sleep group. However, no evidence for group differences was found neither at immediate nor at delayed test and

the decline of fear ratings over time in the wake group was driven by heightened fear ratings in the sleep deprivation group in the immediate test. In the study of Werner et al. (2021), 20 aversive and 20 neutral pictures were rated prior to sleep (i.e., no REM sleep, REM awakening, REM sleep), immediately after (+ 15 min), and after a longer delay (+ 1 hour). Aversiveness was rated on a visual analog scale. There was no evidence for reliable between-group differences. Finally, Wilhelm et al. (2021) used 11 pictures from the trauma film to assess emotional responses 8 days after exposure to the traumatic material. Before and after viewing aversive pictures, subjective mood and arousal were measured by two visual analog scales as well as current affective state using a questionnaire. Analyses revealed that mood generally decreased across presentation and that this effect was less pronounced in the nap group as compared to the wake group. There was no evidence for other between-group differences.

The Relationship Between Sleep Physiology and Intrusions

Four studies assessed polysomnography and reported correlation analyses between sleep physiology and intrusions. Of these studies, one study provided support for a role of slow wave sleep (SWS) in modulating intrusive memories. Sopp et al. (2021) examined Non-REM sleep duration, SWS duration, slow wave activity as well as sleep spindles, and found that only SWS duration (% and min) was significantly and negatively correlated with intrusion frequency. Another study found support for an involvement of REM sleep. Werner et al. (2021) examined REM sleep duration and found evidence for a consistent pattern of negative correlations between REM sleep duration (% and min) and delayed (day 3) intrusion frequency, duration, and aversiveness. Finally, two studies provided evidence for the involvement of both Non-REM and REM sleep. Kleim et al. (2016) examined all sleep stages, sleep spindles, and rapid eye movements during REM sleep. They found evidence for negative correlations between stage 2 sleep and parietal fast sleep spindles (13–15 Hz) and intrusion frequency. By contrast, they found that stage 1 sleep, more time spent awake after sleep onset, and rapid eye movements were positively correlated with intrusion frequency. Wilhelm et al. (2021) examined REM sleep duration, REM sleep theta activity, slow wave activity, and spindle activity. They

found that REM sleep and slow wave activity were negatively correlated with intrusion distress. REM theta activity was negatively correlated with intrusion frequency. However, the latter correlation did not survive correction for multiple comparisons.

Quantitative Summary

Characteristics of Included Studies and Participants

The final meta-analysis on aggregated data comprised nine studies (N = 529, n_{sleep} = 278, n_{wake} = 251) for intrusion frequency and seven for intrusion distress (N = 348, n_{sleep} = 179, n_{wake} = 169; see Table 1). The meta-analysis on IPD comprised eight studies (N = 479, n_{sleep} = 247, n_{wake} = 232) for intrusion frequency and six studies for intrusion distress (N = 293, n_{sleep} = 150, n_{wake} = 143). Five studies used student/university samples, while four samples were recruited from the general population. The weighted mean age was 22.71 years (SD = 2.73) for the meta-analysis on aggregated data (22.53 years, SD = 3.34, for the IPD meta-analysis), and 80.60% were female (78.03% for the IPD meta-analysis). All studies were published between 2015 and 2021. For intrusion frequency, three samples underwent a nap manipulation and six (5 for IPD meta-analysis) underwent nocturnal sleep. Four studies used partial sleep deprivation designs and five studies (4 for IPD meta-analysis) used wake group designs. For intrusion distress, three studies used nap designs and four studies nocturnal sleep (3 for IPD meta-analysis). Two studies employed partial sleep deprivation designs and five used wake groups (4 for the IPD meta-analysis).

Manipulation Check for Negative Mood

Our meta-analysis on IPD allowed us to examine whether the exposure to aversive stimuli resulted in an increase in negative mood. Across all studies, negative mood increased by 23.6% from pre-to-post exposure. A linear mixed model with random intercept and slope per study revealed a significant increase in negative mood, b = 0.11, 95% CI [0.06, 0.15], p = .002, that was independent from group (sleep vs. wake group), b = 0.00, 95% CI [-0.02, 0.03], p = .724.

Meta-Analysis on Aggregated Data

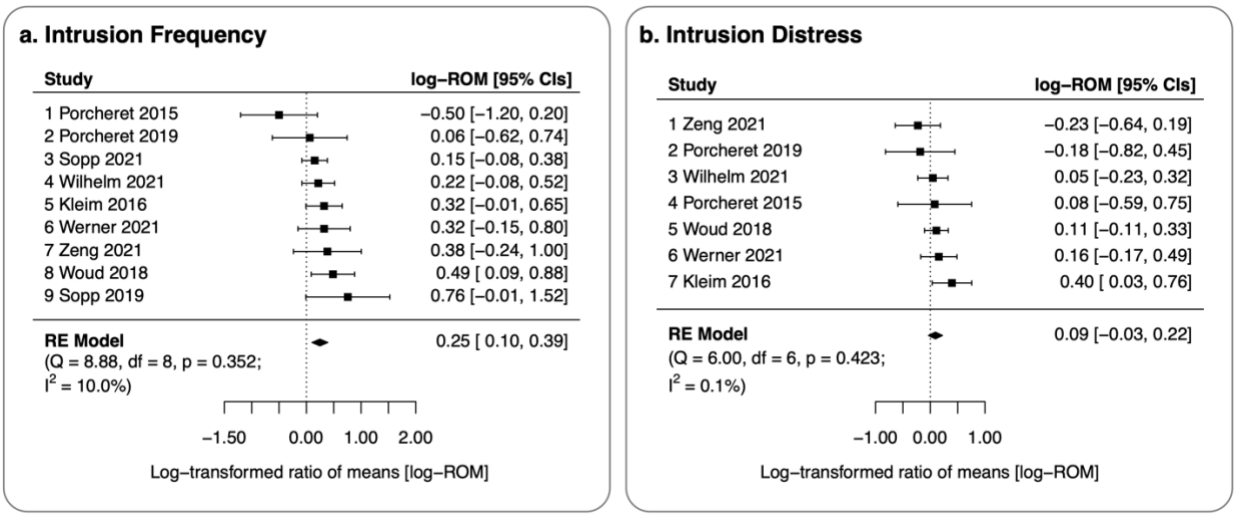
Main Analyses

Intrusion Frequency. The forest plot presented in Figure 2a displays the effect sizes and CIs of all samples. Effect sizes ranged from -0.50, 95% CI [-1.20, 0.20] to 0.76, 95% CI [-0.01, 1.52]. Most effect sizes (8 out of 9; 89%) were numerically positive, that is, participants who underwent post-trauma sleep as compared to wakefulness experienced fewer intrusions. Table 2 presents the results of the main meta-analysis using a random-effects model. The analysis provided evidence for an effect of sleep on intrusion frequency, *M*(log-ROM) = 0.25, 95% CI [0.10, 0.39], *p* = .001. Participants in the sleep groups experienced 28% fewer intrusions than those in the wake groups. With a likelihood of 95%, the effect size of a study from the same population would fall into the interval between log-ROM = 0.03 and log-ROM = 0.49. There was no evidence of heterogeneity of effect sizes as indicated by $\tau^2 = 0$, a non-significant *Q* statistic, *Q*(8) = 8.88, *p* = .352, and a I^2 of 9.95%. This absence of heterogeneity supports the generalizability of the findings beyond the included studies to the wider population. Certainty of evidence for the primary outcome was moderate due to the increased risk of bias resulting from the inclusion of nonrandomized studies (see Supplemental Material SM3).

Intrusion Distress. The forest plot presented in Figure 2b shows the effect sizes and CIs of all samples included in the analysis on intrusion distress. Effect sizes ranged from -0.23, 95% CI [-0.64, 0.19], to 0.40, 95% CI [0.03, 0.76]. Five out of seven effect sizes (71%) were numerically positive, that is, participants who were in the post-trauma sleep group reported lower levels of distress as those in the wake group. The meta-analysis provided no evidence for an effect of sleep compared to wakefulness on intrusion distress, *M*(log-ROM) = 0.09, 95% CI [-0.03, 0.22], *p* = .146. There was no significant heterogeneity between effect sizes as shown by τ^2 value of 0, a non-significant *Q* statistic, *Q*(6) = 6.00, *p* = .423, and a I^2 of 0.05%. With a likelihood of 95%, the effect size of a study from the same population would fall into the interval between log-*ROM* = -0.03 and log-*ROM* = 0.22. Certainty of evidence for intrusion distress was very low due to the inclusion of nonrandomized studies and imprecision.

--- Table 2 is provided at the end of the preprint ---

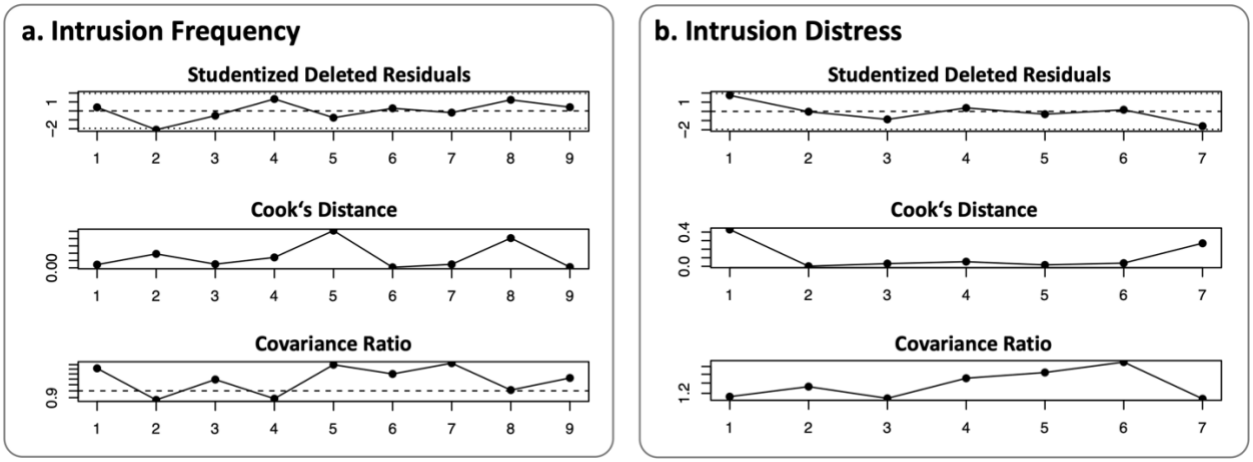
Figure 2. Forest Plots of Meta-Analyses on Intrusion Frequency and Intrusion Distress



Note. Forest plots of the meta-analysis on aggregated data on (a.) intrusion frequency and (b.) intrusion distress. CI = confidence interval; *M(*log-ROM*)* = log-transformed ratio of means; RE Model = random effects model

Outlier and Influence Analyses. Figure 3a and 3b display outlier and influence analyses based on SDRs, Cook's distances (CD), and covariance ratios (COVRATIO). For both outcomes, none of the studies was identified as outlier or influential case.

Figure 3. Outlier and Influence Diagnostics for the Meta-Analyses on Intrusion Frequency and Intrusion Distress

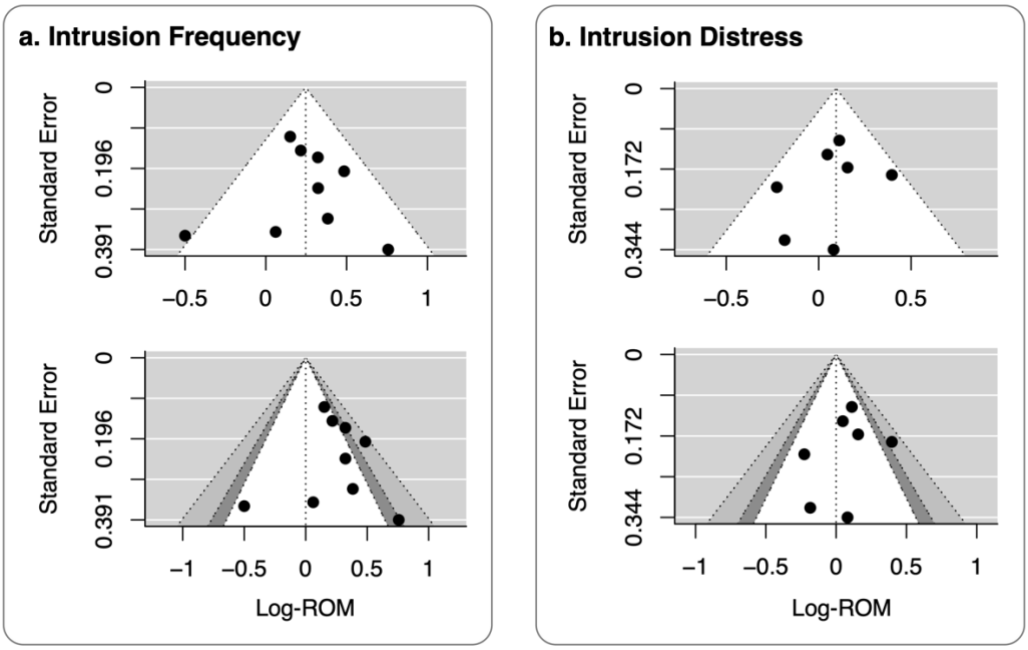


Note. Influence diagnostics of the meta-analysis on aggregated data on (a.) intrusion frequency and (b.) intrusion distress. Study numbers per outcome correspond to those presented in Figure 2.

Moderator Analyses. Given the homogeneous results for both outcomes, it is debatable if moderator analyses should be performed. However, most recommendations suggest performing a-priori planned analyses even in absence of heterogeneity to explore residual between-study variance (Geyskens et al., 2009). For intrusion frequency, there was no moderating effect of the samples' mean age, $QM(1) = 0.23$, $p = .633$, or gender, $QM(1) = 0.07$, $p = .785$. Also, neither the number of follow-up assessments, $QM(1) = 0.24$, $p = .622$, nor the average duration of post-trauma sleep, $QM(1) = 0.81$, $p = .369$, significantly predicted effect sizes. For intrusion distress, there was neither a moderating effect of mean age, $QM(1) = 1.43$, $p = .232$, gender, $QM(1) = 1.69$, $p = .194$, number of follow up-assessments, $QM(1) = 0.07$, $p = .788$, nor average post-trauma sleep duration, $QM(1) = 0.04$, $p = .838$.

Publication Bias. Visual inspections and non-significant rank correlation tests indicated symmetry of the funnel plots for intrusion frequency, Kendell's $\tau = 0.11$, $p = .761$ (see Figure 4a), and intrusion distress, Kendell's $\tau = -0.14$, $p = .773$ (see Figure 4b). Also, the contour-enhanced funnel plot did not indicate that non-significant findings were more likely to be missing (i.e., studies that would be balanced would fall into both the significant and non-significant area).

Figure 4. Funnel Plots for the Meta-Analyses on Intrusion Frequency and Intrusion Distress



Note. Funnel plots and contour-enhanced funnel plots of all studies included in the analysis on intrusion frequency (a.) and intrusion distress (b.). For the contour-enhanced funnel plots, the white area indicates findings being insignificant at $p \geq .10$, the darker grey areas indicate *p*-values between $.05 < p \leq .10$ (marginally significant findings), while the lighter grey areas mirror *p*-values between $.01 < p \leq .05$. All studies following beyond these boundaries would be significant at $p \leq .001$. log-ROM = log-transformed ratio of means.

Internal Risk of Bias. For our analyses on intrusion frequency, study quality ratings as indicators of risk of bias ranged between 0.50 and 1.00, with median study quality rating at 0.77. For intrusion distress, the range of quality ratings of the included studies was between 0.50 and 0.92, and median study quality was at 0.77. For both outcomes, effect sizes were not significantly related to study quality [intrusion frequency: $QM(1) = 0.03$, $p = .870$; intrusion distress: $QM(1) = 1.70$, $p = .193$].

Sensitivity Analyses. In order to examine if our findings were dependent on our decision to choose log-ROMs instead of SMDs as effect size measure, we re-ran our analyses on intrusion frequency and intrusion distress by using SMDs as the effect size measure. For intrusion frequency, this analysis provided evidence for an effect of sleep on intrusion frequency, $M(SMD) = 0.30$, 95% CI [0.13, 0.48], $p < .001$, suggestion fewer intrusions after post-trauma sleep compared to wakefulness, which was numerically - but not significantly - larger than the effect found using log-ROMs (see Table

2). For intrusion distress, consistent with the analysis using log-ROMs, there was no evidence for an effect of post-trauma sleep, *M*(SMD) = 0.15, 95% CI [-0.06, 0.36], *p* = .168.

Meta-Analysis on Individual Participant Data

Main Analyses

Intrusion Frequency. As models based on zero-inflated Poisson distributions showed significant overdispersion, *p* < .001, and models based on negative binominal distributions indicated significant zero-inflation, *p* = .016, we employed a zero-inflated binominal model. Including group as fixed effect in both parts of the model significantly improved model fit when compared to a model that only included a random intercept for study in both parts of the model, *LRT*(2) = 8.69, *p* = .013, while including a random slope did not result in a better model fit, *LRT*(7) = 1.65, *p* = .977. Residual diagnostics of the final model indicated a good fit (Kolmogorov-Smirnov test: *p* = .747) and identified no outliers (*p* = .062). The zero part of the model showed no between-group difference, *b* = 0.53, 95% CI [-0.40, 1.46], *p* = .266, that is, the likelihood of experiencing any intrusion versus no intrusion did not differ between sleep and wake groups (see Table 3). In the count part of the model, there was evidence for a between-group difference, *b* = -0.19, 95% CI [-0.35, -0.03], *p* = .020, indicating that the number of intrusions was higher in the wake groups as compared to the sleep groups. A sensitivity analyses based on a hurdle model did not change our results substantially.

Intrusion Distress. As a model based on a Gaussian distribution indicated significant zero inflation, *p* < .001, we employed a lognormal hurdle model for semi-continuous data. When we compared a model including group as fixed effect in both parts of the model with a random intercept only model, there was no significant increase in model fit, *LRT*(2) = 0.51, *p* = .775. The same applied to the inclusion of a random slope, which also did not improve model fit compared to the random intercept only model, *LRT*(9) = 6.78, *p* = .660. Although the inclusion of group did not improve model fit, we present a model including a fixed effect for group in both model parts for comparison with the meta-analysis on aggregated data (see Table 3, Model 1). Residual diagnostics of this model demonstrated good fit (Kolmogorov-Smirnov test: *p* = .122) and identified no outliers (*p* = .509). The

zero part of the model showed that the likelihood of experiencing any versus no intrusion distress was not significantly different between sleep and wake groups, b = -0.15, 95% CI [-1.15, 0.86], p = .773, and the continuous part of the model demonstrated that the severity of intrusion distress did not differ between groups, b = -0.06, 95 % CI [-0.22, 0.11], p = .522 (see Table 3, Model 1). When we employed a zero-inflated gamma distribution for sensitivity analyses, our results remained unchanged, pointing to the robustness of our findings against specific modeling decisions.

--- Table 3 is provided at the end of the preprint ---

Moderator Analyses

Intrusion Frequency. We examined moderator effects of age, gender, depressive symptoms, and increases of negative mood from pre-to-post exposure. Age and gender showed no moderator effects in the zero part of the model, ps ≥ .339 (see Table 3, Model 2), while age significantly moderated the effect of group (sleep vs. wake group) in the count part, b = -0.05, 95% CI [-0.10, 0.00], p = .038, indicating that the protective effect of sleep was more pronounced with increasing participant age. Depressive symptom levels had no moderator effect, neither in the zero part, b = -1.32, 95% CI [-4.52, 1.88], p = .417, nor in the count part of the model, b = -0.02, 95% CI [-0.08, 0.05], p = .600 (see Table 4). Larger increases of negative mood from pre-to-post exposure were associated with more severe intrusions in the count part of the model, b = 0.61, 95% CI [0.22, 1.01], p = .002, but did not moderate the impact of post-trauma sleep on intrusion frequency, b = -0.02, 95% CI [-0.81, 0.77], p = .963. In the zero part of the model, increases of negative mood did not show a significant main or moderator effect, p ≥ .817.

Intrusion Distress. For intrusion distress, there was no moderator effect of age and gender, neither in the count nor the zero part of the model, p ≥ .193, except for a three-way interaction between group, age, and gender in the zero part, b = -1.05, 95% CI [-1.98, -0.12], p = .026 (see Table 3, Model 2). However, neither for females nor males of all ages, there was evidence for an effect of group (sleep vs. wake group) on the occurrence of any (vs. no) intrusion distress. Depressive symptoms had no significant moderator effect in the zero part of the model but showed a significant

interaction with group (sleep vs. wake group) in the continuous part of the model, b = 0.06, 95% CI [0.00, 0.11], p = .048, with numerically larger effect size estimates for group (sleep vs. wake group) when levels of depressive symptoms were lower (see Table 4). However, even when limiting our sample to those with below median depressive symptom levels for illustrative purpose, the effect of group remained non-significant. Moreover, increases in negative mood from pre-to-post exposure had no moderator effect in both model parts, $p \geq .676$, but a significant main effect on intrusion distress in the count-part, b = 0.82, 95% CI [0.45, 1.18], $p < .001$, with stronger increases being associated with higher levels of intrusion distress.

--- *Table 4 is provided at the end of the preprint* ---

Discussion

This review aimed to provide a qualitative and quantitative summary of the current state of research on the effect of sleep versus wakefulness after exposure to experimental analog trauma on subsequent intrusive memories. Specifically, we aimed at answering the question of whether research supports a beneficial or detrimental effect of post-trauma sleep on subsequent intrusive memories. Moreover, our review aimed to explore whether potential moderators may account for discrepant effects found across individual studies. To this end, we performed an in-depth qualitative summary and effect size estimates of individual studies were aggregated quantitatively using a traditional meta-analytical approach. Additionally, to overcome concerns of insufficient statistical power due to resource intensiveness of sleep research, we analyzed individual participant data (IPD) in a multilevel framework to examine participant-level moderators and disentangle processes involved in the occurrence of any (vs. no) intrusion and frequency of intrusions.

Our qualitative summary showed that of nine studies investigating the impact of post-trauma sleep versus wakefulness on intrusive memories, five found evidence for a positive impact of sleep on analog intrusions (Kleim et al., 2016; Sopp et al., 2019; Werner et al., 2021; Woud et al.; 2018, Zeng et al., 2021). One study found evidence for a positive impact of sleep deprivation on analog intrusions (Porcheret et al., 2015), and three studies provided inconclusive results (Porcheret et al.,

2015; Sopp et al., 2021; Wilhelm et al., 2021). We also examined the effect of post-trauma sleep on explicit and implicit trauma memory: Of five studies investigating the impact of sleep versus sleep deprivation on explicit trauma memory, three found evidence for sleep significantly enhancing explicit trauma memory as compared to sleep deprivation (Sopp et al., 2021; Sopp et al., 2019; Zeng et al., 2021). One study provided mixed evidence, indicating that sleep enhanced visual memory but not verbal memory (Porcheret et al., 2019). Correspondingly, one study found no evidence for an impact of sleep on explicit trauma memory using a verbal memory test (Woud et al., 2018). Of five studies investigating the impact of sleep versus sleep deprivation on implicit trauma memory, four did not find any evidence for group differences (Porcheret et al., 2019; Sopp et al., 2019; Zeng et al., 2021; Werner et al., 2021). One study found that sleep compared to wakefulness reduced implicit memory as evident in mood responses (Wilhelm et al., 2021). Finally, four studies investigated associations between Non-REM and REM sleep physiology and analog intrusions. Two studies found evidence for an involvement of both Non-REM and REM sleep (Kleim et al., 2016; Wilhelm et al., 2021). Only single studies found evidence for an involvement of REM sleep (Werner et al., 2021) and SWS (e.g., Sopp et al., 2021).

Across both analytical approaches chosen for our quantitative summary, we found evidence in favor of a beneficial rather than a detrimental effect of post-trauma sleep on subsequent intrusion frequency. That is, participants experienced fewer intrusions if they had slept after exposure to analog trauma than if they remained awake or were partially sleep deprived. Due to the lack of heterogeneity, these effects can be generalized beyond the current samples to the wider population of healthy young adults experiencing analog trauma. IPD analyses further suggest that sleep does not affect the occurrence of intrusive memories per se, that is, sleeping did not affect the likelihood of experiencing none or any intrusions. However, in the subgroup of individuals who experienced any intrusions after exposure to analog trauma, post-trauma sleep compared to wakefulness was associated with fewer intrusions.

Overall beneficial effects of post-trauma sleep on intrusion frequency may emerge because post-trauma sleeping reduces the frequency of intrusions in participants that are prone to develop

intrusions in response to analog trauma. If confirmed by further research, these findings suggest that prevention strategies that aim to improve sleep should be developed and tested on individuals at-risk for intrusion development and later onset of PTSD. Such individuals could be identified based on pre-trauma (e.g., trait rumination, prior psychopathology; Schultebraucks et al., 2021) and/or peri-trauma (e.g., peritraumatic distress, dissociation; Massazza, Joffe, & Brewin, 2021; Massazza, Joffe, Hyland, & Brewin, 2021) risk factors. However, such an approach would require a strong (empirical) consensus on primary risk factors that should be targeted, which does not exist at present (Bonanno, 2021; Kalisch et al., 2017).

Moreover, it must be noted that our analyses revealed small-to-medium effect sizes reflecting a small difference of average intrusion frequency between sleep and wake groups. Given the high individual and societal burden associated with PTSD (Davis et al., 2022; Olatunji et al., 2007; Pacella et al., 2013), even small-to-medium effect sizes of prevention measures could make a great difference as they may prevent a substantial number of PTSD cases when delivered to a larger population of traumatized individuals. However, studies translating other interventions found to be effective in experimental psychopathology to clinical populations provided evidence for potential decreases of effect sizes and point to the importance of distinguishing lab-based research from randomized controlled trials with clinical samples (Wiers et al., 2018). Moreover, a recent meta-analysis on the effectiveness of consolidation/reconsolidation interventions for the prevention and treatment of PTSD provided evidence for smaller effect sizes for PTSD prevention (Astill Wright et al., 2021). Hence, further research in clinical populations needs to establish whether the magnitude of effects is sufficient to justify a clinical implementation of sleep-enhancing interventions. These studies may also examine whether sleep mainly targeting the process of memory consolidation might be used as a mechanism-focused adjunct of other interventions (Kleim et al., 2014; see Blackwell et al., 2020, for a similar idea on cognitive bias modification).

While our analyses support a beneficial effect of sleep on intrusion frequency, we did not find evidence for sleep-related effects on intrusion distress. On the one hand, this lack of evidence may have emerged since these analyses relied on a smaller subsample of studies and participants. On the

other hand, our results could indicate that the sleep-related processes that modulate intrusion frequency do not affect distress levels. In fact, there have been different accounts as to how sleep may reduce intrusions (Azza et al., 2020; Germain et al., 2008), with one assuming that sleep supports memory consolidation, thereby strengthening explicit trauma memory and inhibiting the occurrence of intrusions (based on e.g., Diekelmann & Born, 2010). The other account proposed a role of sleep in reprocessing and weakening of the affective component of traumatic memories, resulting in reduced intrusion distress (based on van der Helm & Walker, 2009). The current results seem to support the first hypothesis while providing no support for the second. However, since our analyses did not focus on underlying processes, caution is warranted in drawing strong conclusions. Some additional insights can be gathered from our qualitative synthesis. That is, four of five studies (i.e., Porcheret et al., 2019; Sopp et al., 2019; Sopp et al., 2021; Zeng et al., 2021) investigating the effect of sleep on explicit trauma memory found an enhancing effect of sleep. Implicit trauma memory - mostly assessed by pre- to post-sleep changes in mood/affective ratings during presentation of traumatic stimuli - was only found to be reduced after sleep in one of five studies (i.e., Wilhelm et al., 2021). These findings support the notion that sleep influences intrusions by modulating explicit trauma memory, rather than supporting the reprocessing of the affective component of traumatic memories. The neurophysiological underpinning of this process requires further investigation. Our qualitative synthesis showed mixed evidence for an involvement of Non-REM and REM sleep. However, this evidence is based on correlational findings, which - so far - have not been replicated across studies. For the current review, we were not able to perform meta-analyses on sleep characteristics and their association with intrusion frequency or intrusion distress due to substantial between-study heterogeneity of sleep assessments (home vs. lab-based) and reported associations. However, building on findings of the current review, future studies may explicitly focus on memory processes and their neurophysiological correlates, and thus make them a potential target for future meta-analyses.

Although our analyses provided evidence for sleep having a beneficial impact on intrusion frequency, one of the included studies has revealed opposing findings (Porcheret et al., 2015). We

aimed to find the source of these discrepancies by exploring differences between studies that could account for opposing effects (see e.g., Schenker et al., 2021). Traditional meta-analytical moderator analyses on study characteristics did not reveal any significant findings, which was not surprising as the main analyses pointed to homogeneous effect size estimates. Participant-level moderator analyses only revealed one robust finding, which was that the beneficial effects of sleep tended to increase with increasing participant age. However, it must be noted that the age range across studies was restricted (*Range* = 18–35 years), which limits the interpretation and generalization of this finding. Thereby, our results statistically point to the fact that differences in observed effect sizes may be explained by sampling error and divergent findings can be viewed as upper and lower end of a single effect size distribution. At the same time, the number of included studies was low, which limits the power of heterogeneity tests (von Hippel, 2015), and may have resulted in overlooked true between-study differences. Moreover, it is important to note that our moderator analyses in both meta-analyses only included variables that were available for a relevant number of included studies, limiting the scope of these analyses and thus our ability to clarify the emergence of opposing effects of sleep. Further research investigating multiple potentially relevant moderators, ideally in sufficiently powered studies and more heterogeneous samples (e.g., with respect to gender), is thus needed to characterize potential boundary conditions of the detrimental or beneficial impact of sleep on intrusive memories.

Beyond the limitations noted above, several others need to be considered. First, as this review started as a multi-lab project and only involved into a systematic review over time, therefore, it was not prospectively preregistered. There were no major changes with respect to research questions and modelling decisions in the course of our project, however, we cannot exclude that the retrospective registration biased our findings. Second, our analyses aggregated data across studies with very different designs (e.g., [partial] sleep deprivation, nap sleep) and assessment methods (e.g., laboratory intrusion triggering task, intrusion diary). However, the lack of significant heterogeneity supports the notion that - despite procedural differences - effect sizes were eligible for meta-analyses. Another limitation concerns the fact that the number of studies included in our

analyses (*k* = 9) is low compared to other meta-analyses in the trauma field (e.g., Clark et al., 2015; Schäfer et al., 2019). However, the limited number of studies gave us the unique opportunity to gather almost all primary datasets (*k* = 8) and conduct IPD meta-analysis. These analyses strongly improved interpretation by showing that sleep is not a significant predictor of any (vs. no) intrusions but of the number of intrusions. As such, the current study constitutes an example of how collaboration can advance the field beyond the contributions of individual studies. This is especially important in the field of sleep research that is often limited by small sample sizes. Multi-lab collaborative efforts and meta-analytical data analyses may help to answer questions that cannot be addressed by individual studies, while increasing the replicability of findings, which is essential to translate findings from experimental to clinical research. Finally, it is important to emphasize that all included studies investigated analog symptoms in healthy participants. Although this approach is commonly used in PTSD research (Iyadurai et al., 2019), it prevents us from drawing strong inferences on how effects may unfold after real-world trauma exposure. Relatedly, research indicates that disturbed sleep may have a different impact on emotional processing in those with mental disorders than in healthy individuals, thus putting into question whether findings from healthy samples can be generalized to clinical populations (Van Someren, 2021). Bridging the gap between experimental research in the lab and clinical research in the field thus constitutes an important next step (Blackwell & Woud, 2022), for which the present review may provide a base.

Future research should focus on investigating the effects of sleep on intrusions in the immediate aftermath of real-world trauma (see e.g., Porcheret et al., 2020) and how different sleep-related interventions may be used to reduce intrusions. In order to design such interventions, basic research needs to improve our understanding of the processes that affect intrusion development and their relation to specific sleep stages and characteristics. Generally speaking, interventions could comprise psychoeducational elements (e.g., information on how to promote restful sleep behaviourally; Prytys et al., 2010) as well as therapeutic techniques to improve sleep quality and depth (e.g., sleep-directed hypnosis; Cordi et al., 2020). Due to the high level of standardization, such

interventions could be disseminated in a self-guided web-based format, which would allow targeting traumatized individuals in the immediate aftermath of trauma.

Conclusion

The present systematic review was the first to summarize evidence on the effect of sleep versus wakefulness on intrusive memories after experimental analog trauma. By means of traditional meta-analysis, we found evidence for a small-to-medium-sized effect of sleep as compared to wakefulness on intrusive memory, with sleep being associated with a lower number of intrusions but unrelated to intrusion distress. Our meta-analyses on IPD supported these findings and provided additional insights such that sleep was related to lower intrusion frequency but did not affect the likelihood of experiencing any versus no intrusive memory. Despite divergent findings of individual studies employing different study designs, our meta-analyses yielded homogeneous results pointing to a small-to-medium beneficial effect of sleep after analog trauma. Future studies should critically examine the clinical significance of this effect as well as its association with memory processes and their neurophysiological underpinning.

Appendix. Supplementary Information

A1 Supplementary Material (SM1, SM2, SM3)

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Authors Contributions

SKS: conceptualization, methodology, formal analysis, data curation, writing (original draft), visualization; CL: formal analysis, data curation, writing (review & editing), project administration; KP: data curation, resources, writing (review & editing); XH: data curation, resources, writing (review & editing); JM: data curation, resources, writing (review & editing); TM: conceptualization, resources, writing (review & editing), supervision; EH: data curation, resources, writing (review & editing);GW: data curation, resources, writing (review & editing); MLW: data curation, resources, writing (review & editing); IW: data curation, resources, writing (review & editing); SZ: data curation, resources, writing (review & editing); EF: data curation, writing (review & editing), project administration, SHM: data curation, writing (review & editing); JLH: conceptualization, writing (review & editing); KL: methodology, resources, writing (review & editing); AK: methodology, writing (review & editing); BW: conceptualization, methodology, formal analysis, writing (review & editing); RS: conceptualization, methodology, resources, supervision, writing (original draft)

Declaration of Competing Interest

The authors declare to have no conflict of interest.

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Tables

Table 1. Study and Sample Characteristics of Studies Included in Meta-Analysis on Aggregated Data

Study	n_{sleep}	n_{wake}	Age *M*(*SD*)	% female	Aversive stimuli	Outcome Assessment	Follow-up (in days)	Sleep duration (in min.)	Sleep design	Sleep recording	Sleep context	Sleep deprivation	Risk of bias[5]
Kleim 2016	32	33	23.80 (3.09)	100	Trauma film	IF: diary ID: diary	7	420.00	Nocturnal sleep	PSG	home	daytime waking & nighttime sleep deprivation	high
Porcheret 2015	21	18	21.53 (1.95)	70.73	Trauma film	IF: diary ID: diary	6	NA	Nocturnal sleep	AG	home	nighttime sleep deprivation	low
Porcheret 2019	24	26	24.18 (3.73)	54.00	Trauma film	IF: diary ID: diary	6	433.20	Nocturnal sleep	AG, PSG	home	nighttime sleep deprivation	low
Sopp 2019[1]	21	20	22.44 (2.50)	65.85	Traumatic picture stories	IF: ITT	1	217.86	Nocturnal sleep	PSG	lab	nighttime sleep deprivation	low
Sopp 2021	38	37	22.51 (2.98)	82.66	Traumatic picture stories	IF: ITT	1	447.70	Nocturnal sleep	PSG	lab	daytime waking	high
Werner 2021[2]	28	21	22.32 (3.16)	100	Aversive pictures	IF: diary ID: diary	3	26.58	Nap	PSG	lab	daytime waking	low
Wilhelm 2021	33	23	23.50 (0.70)	100	Trauma film	IF: diary ID: diary	7	64.42	Nap	PSG	lab	daytime waking	low
Woud 2018[3]	51	43	23.09 (3.65)	76.60	Trauma film	IF: diary ID: diary	7	41.42	Nap	PSG	lab	daytime waking	high
Zeng 2021[4]	30	30	20.50 (2.02)	68.33	Trauma film	IF: diary ID: diary	7	403.62	Nocturnal sleep	AG	home	nighttime sleep deprivation	high

Note. AG = Actigraphy; IF = intrusion frequency; ID = intrusion distress; ITT = Intrusion Triggering Task (based on Streb et al., 2017; Wegerer et al., 2013); *n* = number of participants; NA = not available; PSG = polysomnography.

[1] Due to the partial nighttime sleep deprivation design employed by Sopp et al. (2019), second night half sleep duration is reported as sleep duration.

[2] The study of Werner et al. (2021) comprised more than one group that underwent post-trauma sleep or sleep deprivation. For the purpose of our meta-analysis, we chose the groups most similar to other studies (i.e., REM sleep deprivation and REM sleep) to reduce between-study heterogeneity. For our moderator analysis on sleep duration, we subtracted the sleep duration of the REM sleep deprivation group from the sleep duration of the REM sleep group (i.e, 80.38 min – 53.80 min = 26.58 min).

[3] The study by Woud et al. (2018) reported data on participants that received either positive or negative cognitive bias modification training. As this intervention was not of interest for our meta-analysis, both sleep and wake groups were combined.

[4] The study by Zeng et al. (2021) reported data on more than one intrusion measure. In this case, we chose the diary assessment as most similar to the majority of included studies.

[5] Risk of bias ratings reflect inverse measures of study quality, that is, 1 – study quality. Studies with quality ratings > 0.77 were assumed to have low risk of bias, studies with quality ratings < 0.77 were rated as high risk of bias.

Table 2. Results of the Meta-Analysis on Aggregated Data

Analysis				**95% CI**		**95% PI**							
	N/n	***k***	***M*(ES)**	**lower**	**upper**	**lower**	**upper**	***p***	***Q***	**df**	***p(Q)***	***I²***	**Certainty**
Main analyses (log-ROM)													
Intrusion frequency	529	9	0.25	0.10	0.39	0.05	0.45	< .001	8.88	8	.352	9.95	⊕⊕⊕◯ **Moderate**
			M(ROM) = 1.28	1.11	1.48	1.05	1.56						
Intrusion distress	348	7	0.09	-0.03	0.22	-0.03	0.22	.145	6.00	6	.423	0.05	⊕◯◯◯ **Very low**
			M(ROM) = 1.10	0.97	1.25	0.97	1.25						
Sensitivity analyses (SMD)													
Intrusion frequency	529	9	0.31	0.13	0.48	0.12	0.49	< .001	8.08	8	.426	0.94	⊕⊕⊕◯ **Moderate**
Intrusion distress	348	7	0.15	-0.06	0.36	-0.06	0.36	.168	5.86	6	.439	0.00	⊕◯◯◯ **Very low**

Note. ES = effect size; *N*/*n*= number of participants; *k* = number of studies; *M(*log-ROM/SMD) = log-transformed ratio of means/standardized mean difference; *M*(ROM) = ratio of means; *p* = significance value of *M(*log-ROM/SMD); 95% CI = 95% confidence interval; PI = 95% prediction interval; *Q* = *Q* statistic; df = degrees of freedom of Q statistic; *p(Q)* = significance value of *Q* statistic; I^2 = percentage of heterogeneity reflecting true effect size variance. The certainty column shows the overall GRADE rating (see Supplementary Material SM3 for details).

Table 3. Results of Multilevel Models for Intrusion Frequency and Intrusion Distress

	Model 1			Model 2		
	b	*95% CI*	*p*	*b*	*95% CI*	*p*
a. Intrusion frequency						
Count part						
(Intercept)	1.49	1.09, 1.88	< .001	1.48	1.10, 1.87	< .001
Group	-0.19	-0.35, -0.03	.020	-0.19	-0.35, -0.03	.017
Age				0.01	-0.01, 0.03	.354
Gender				0.21	-0.02, 0.44	.070
Group x Age				-0.05	-0.10, 0.00	.038
Group x Gender				0.28	-0.18, 0.74	.237
Age x Gender				0.05	-0.02, 0.12	.139
Group x Age x Gender				0.01	-0.13, 0.15	.878
Zero part						
(Intercept)	-2.40	-3.29, -1.50	< .001	-2.46	-3.37, -1.55	< .001
Group	0.53	-0.40, 1.46	.266	0.41	-0.56, 1.40	.413
Age				-0.05	-0.21, 0.11	.547
Gender				-0.24	-1.47, 0.99	.703
Group x Age				-0.07	-0.39, 0.25	.671
Group x Gender				-0.40	-3.00, 2.21	.766
Age x Gender				-0.17	-0.52, 0.18	.345
Group x Age x Gender				-0.33	-1.02, 0.36	.346
k_{Study}		8			8	
$n_{Participants}$		478			476	
b. Intrusion distress						
Continuous part						
(Intercept)	-1.55	-1.85, -1.26	< .001	-1.56	-1.84, -1.27	< .001
Group	-0.06	-0.22, 0.11	.522	-0.05	-0.22, 0.11	.525
Age				-0.01	-0.04, 0.01	.353
Gender				0.04	-0.21, 0.28	.764
Group x Age				0.02	-0.03, 0.07	.396
Group x Gender				0.33	-0.17, 0.83	.193
Age x Gender				-0.04	-0.12, 0.04	.311
Group x Age x Gender				0.09	-0.07, 0.25	.280
Zero part (hurdle)						
Intercept	-2.83	-3.61, -2.06	< .001	-3.14	-4.16, -2.12	< .001
Group	-0.15	-1.15, 0.86	.773	-0.53	-1.88, 0.83	.447
Age				-0.09	-0.32, 0.15	.467
Gender				-1.22	-2.54, 0.10	.070
Group x Age				-0.30	-0.79, 0.19	.228
Group x Gender				-1.62	-4.31, 1.08	.239
Age x Gender				-0.40	-0.85, 0.05	.085
Group x Age x Gender				-1.05	-1.98, -0.12	.026
k_{Study}		6			6	
$n_{Participants}$		293			292	

Note. *k* = number of effect sizes; *n* = number of participants.

Table 4. Details of Moderator Analyses

	Depressive symptoms				Increase of negative mood		
	b	95% CI	*p*		*b*	*z*	*p*
a. Intrusion frequency							
Count part				**Count part**			
(Intercept)	1.55	0.83, 2.28	< .001	(Intercept)	1.49	1.11, 1.87	< .001
Group	-0.25	-0.47, -0.02	.030	Group	-0.19	-0.35, -0.04	.015
Depressive symptoms	-0.01	-0.04, 0.02	.421	Increase in negative mood	0.61	0.22, 1.01	.002
Group x Depressive symptoms	-0.02	-0.08, 0.05	.600	Group x Increase in negative mood	-0.02	-0.81, 0.77	.963
Zero part				**Zero part**			
(Intercept)	-5.14	-12.19, 1.91	.153	(Intercept)	-2.38	-3.29, -1.47	< .001
Group	-0.02	-5.58, 5.53	.994	Group	0.51	-0.41, 1.43	.273
Depressive symptoms	-0.32	-1.47, 0.84	.589	Increase in negative mood	0.31	-2.34, 2.97	.817
Group x Depressive symptoms	-1.32	-4.52, 1.88	.417	Group x Increase in negative mood	0.22	-4.86, 5.31	.932
k_{Study}		4				8	
$n_{Participants}$		271				478	
b. Intrusion distress							
Continuous part				**Continuous part**			
(Intercept)	-1.53	-1.95, -1.12	< .001	(Intercept)	-1.55	-1.85, -1.26	< .001
Group	0.00	-0.19, 0.19	.989	Group	-0.06	-0.22, 0.10	.473
Depressive symptoms	0.00	-0.03, 0.03	.916	Increase in negative mood	0.82	0.45, 1.18	< .001
Group x Depressive symptoms	0.06	0.00, 0.11	.048	Group x Increase in negative mood	-0.15	-0.90, 0.59	.676
Zero part (hurdle)				**Zero part (hurdle)**			
(Intercept)	-3.32	-4.46, -2.19	< .001	(Intercept)	-2.84	-3.62, -2.06	< .001
Group	1.25	-0.25, 2.75	.102	Group	-0.16	-1.18, 0.85	.766
Depressive symptoms	0.04	-0.17, 0.25	.733	Increase in negative mood	-0.69	-3.52, 2.15	.656
Group x Depressive symptoms	-0.09	-0.52, 0.35	.693	Group x Increase in negative mood	-0.96	-6.72, 4.80	.890
k_{Study}		4				6	
$n_{Participants}$		220				293	

Note. *k* = number of effect sizes; *n* = number of participants.