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# **Original Article**

# The relationship between REM sleep prior to analog trauma and intrusive memories

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#### Abstract

Intrusive memories are a common experience following trauma exposure but can develop into a symptom of posttraumatic stress disorder (PTSD). Recent research has observed a relationship between sleep disturbance and intrusive memory frequency following analog trauma exposure and disruptions in rapid eye movement (REM) sleep are found to contribute to emotional dysregulation and an amplified reaction to negative emotional stimuli. The current study examined the association between REM sleep prior to analog trauma and intrusive memories. To manipulate REM sleep, 27 healthy adults ( $M_{Agg} = 25.4$ , standard deviation = 2.89) were randomized to either a circadian misalignment (CM) condition or normal control (NC) condition for 4 nights. In CM, participants slept normally for 2 nights followed by a 4-hour phase advance on night 3 and an additional 4-hour phase advance on night 4. In NC, participants had 8-hour sleep opportunities each night. On day 5, participants watched a trauma film and kept an intrusive memory diary for the next 3 days. Greater REM sleep percentage (p = .004) and REM efficiency (p = .02) across 4 nights prior to analog trauma, independent of the group, were significantly associated with fewer intrusive memories in the 3 days after viewing the film. Findings suggest REM sleep may serve to protect individuals against experiencing intrusive memories. This is consistent with evidence suggesting REM sleep influences emotional memory regulation. Occupations (e.g. emergency services/military personnel) who experience circadian disruptions likely to decrease REM sleep (e.g. from shift work) may be at heightened risk of experiencing intrusive memories after trauma exposure, and thus at increased risk of developing PTSD.

Key words: sleep; REM sleep; intrusive memories; trauma; posttraumatic stress disorder

#### **Graphical Abstract**

#### Study protocol

#### Sleep manipulation (Day 1 to 5)

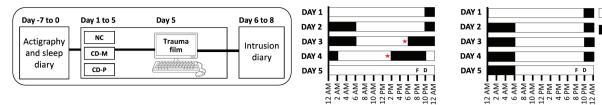
Wake

Sleep

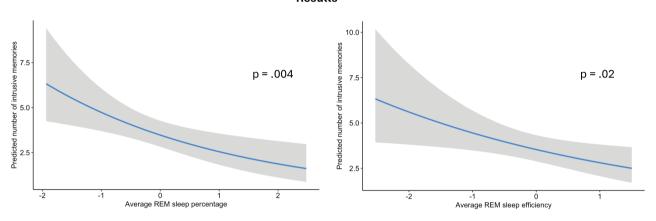
Drug/

Film

**D** Discharge



#### Results



### Statement of Significance

Sleep is known to influence the expression of posttraumatic stress disorder (PTSD) symptoms. Indeed, poor sleep either prior to or following trauma exposure increases the risk of developing PTSD. While prior studies have examined potential mechanisms explaining the role of sleep post-trauma, little is known about potential sleep mechanisms pre-trauma. Here, we show greater quantity and quality of rapid eye movement (REM) sleep across 4 days prior to analog trauma exposure predicts fewer intrusive memories in the 3 days following the exposure. Given intrusive memories are often an early symptom of PTSD, these findings suggest adequate REM sleep may serve as a protective factor when someone is exposed to trauma, perhaps especially in occupations marked by chronic sleep disturbances and frequent trauma exposure.

Most people worldwide will experience at least one traumatic event in their lifetime, with 8%-15% of them developing posttraumatic stress disorder (PTSD) following the trauma [1]. One early symptom of PTSD is re-experiencing traumatic event(s) through intrusive memories [2]. Intrusive memories are recurrent, distressing mental images or thoughts of a traumatic event that involuntarily intrude into conscious awareness [2, 3]. Higher re-experiencing symptoms (including intrusions) in the first few days following trauma predicts a later onset of PTSD [4, 5]. This association suggests intrusive memories and their mechanisms may contribute to the etiology and development of PTSD and are, therefore, a potential target for early intervention strategies. Key to identifying and implementing early interventions is the identification of modifiable mechanisms underlying the development of intrusive memories.

Sleep has been proposed as one such potential mechanism, due to its role in memory consolidation [6]. Following this, it was expected sleep deprivation immediately after trauma would weaken the initial consolidation of a traumatic event and reduce intrusive memories. In stark contrast to that hypothesis, a growing body of research, including three recent meta-analyses [7–9], demonstrates a period of sleep (not lack of sleep) following analog trauma exposure reduces the number of intrusive memories on

the following days. Two explanations have been advanced to explain sleep's role in reducing intrusive memories. First, sleeping following a traumatic event may decrease the emotional intensity of the memories, leading to fewer intrusive memories [10, 11]. Second, intrusive memories are theorized to result from incomplete consolidation of the trauma memory [12-15] and sleep, particularly rapid eye movement (REM) sleep, plays a role in processing emotional memories [11].

A recent review by Van Someren proposes specific mechanisms involved in disrupted REM sleep impede emotional memory processing [16]. During uninterrupted REM sleep, noradrenaline, responsible for arousal and stress responses, is not released, due to inactivity of the locus coeruleus (LC). The absence of noradrenaline signaling during REM sleep facilitates depotentiation and synaptic downscaling, particularly in the limbic regions, necessary for processing emotional memories [16]. However, disrupted REM sleep disinhibits the LC, resulting in ongoing noradrenergic signaling during REM sleep periods which, in turn, contributes to the dysregulation of emotional memories. Given (1) hypotheses from the PTSD field arguing impaired memory consolidation leads to intrusive memories [15] and (2) PTSD is associated with elevated nocturnal norepinephrine levels [17], this new hypothesis from Van Someren provides a theoretical framework to examine whether REM sleep quality and quantity are associated with heightened experiencing of intrusive memories.

The role of sleep in emotional memory may also be particularly salient in the context of PTSD and intrusive memories because sleep disruptions are ubiquitous in PTSD [18, 19]. For example, PTSD is associated with decreases in total time spent in REM sleep [20], reduced percentage of REM sleep [21], increased REM fragmentation [22], and increased REM density [23]. Furthermore, epidemiological and prospective studies have revealed REM sleep disruption is a consistent feature of poor psychiatric outcomes, including PTSD [24-26]. However, REM sleep is not the only sleep stage disrupted in PTSD. Indeed, two meta-analyses reported decreases in slow wave sleep (N3 sleep; SWS), in addition to REM sleep, in PTSD patients compared to healthy controls [23, 27]. Straus et al. reported one reason for inconsistent findings related to sleep stage abnormalities in PTSD may be due to the increased night-to-night variability of sleep in PTSD [28]. This, in turn, argues for studying sleep across multiple nights when looking at potential mechanistic links between sleep and PTSDrelated symptoms.

In summary, sleep, relative to a similar period of wake, following exposure to an analog trauma has been shown to reduce the number of intrusive memories experienced, and there is theoretical reason to believe this may be related to memory consolidation functions during REM sleep. However, sleep disruption prior to trauma exposure is also associated with the development of PTSD, but no studies to date have examined how sleep prior to analog trauma exposure may influence the development of intrusive memories. Therefore, this study aimed to examine the impact of REM sleep quality (REM efficiency) and quantity (REM percentage) prior to analog trauma exposure on subsequent intrusive memories in healthy young adults. Given the findings of decreased N3 in PTSD, we also conducted analyses to examine the impact of N3 on subsequent intrusive memories. Participants slept according to either a normal sleep schedule or one of twophase advance schedules designed to produce different levels of disruption to sleep, especially REM sleep. It was hypothesized that higher average REM sleep percentage and REM sleep efficiency across 4 nights would be associated with fewer intrusive memories reported over the 3 days following viewing an analog trauma film, while SWS would not be associated with intrusive memories.

# **Methods**

Data for this project were collected as part of a larger study at Monash University. Ethical approval was obtained from the Monash University Research Ethics Committee (MUHREC; project number: 9938), and funding was provided by the US Department of Defence.

## **Participants**

Participants were recruited from the general population via institutionally approved Internet advertisements and flyers posted in local suburbs. Ethical approval was obtained from Monash University Research Ethics Committee (MUHREC; project number: 9938). Data from 27 healthy participants (Female = 56%, age  $25.4 \pm 2.89$  years, age range: 18-39 years) were analyzed. Exclusion criteria were being a current or former smoker, current or planned pregnancy, current or prior drug user, consumed >400 mg of caffeine per day, consumed >14 standard drinks per week or more than 6 standard drinks per sitting in 1 week, or had a history of shift work in the past 4 months. In addition, a history of any Axis 1 diagnoses or a family history of mood disorders or psychotic disorders were exclusionary as sleep disruption may increase the risk of symptom exacerbation. These criteria were necessary for the larger study.

#### Procedure

#### General overview.

Participants maintained a regular sleep-wake schedule, monitored with actigraphy and a sleep diary for 7 days prior to their lab stay. During the 5-day in-lab stay, participants were randomly assigned to either a normal sleep condition or to a sleep disruption condition designed to manipulate REM sleep (see later). On day 5, the trauma film was administered. Participants then kept an intrusion diary for 3 days following their in-lab stay, where they recorded the frequency of intrusive memories elicited from the film (see Figure 1, top).

# At-home sleep monitoring (day -7 to 0).

Participants were required to maintain a regular sleep-wake schedule at home for 1 week prior to their lab stay to help ensure they were not sleep-deprived and their circadian system was stable upon arrival. Participants' sleep-wake schedules were based on their habitual sleep-wake schedule and agreed upon during a participant information and consent meeting prior to the at-home sleep monitoring phase.

## *In-lab sleep monitoring (day 1 to 5).*

During the lab stay, participants were randomly allocated to one of three sleep conditions: normal condition (NC), circadian disruption with melatonin (3 mg; CD-M), or circadian disruption with placebo (CD-P; Figure 1, bottom). Participants in the NC condition were provided with an 8-hour sleep opportunity each night in line with their regular sleep-wake schedule. Participants in both CD conditions were also provided with an 8-hour sleep opportunity in line with their regular sleep-wake schedule for the first 2 nights, then had their sleep schedules advanced by 4 hours on night 3, and an additional 4 hours (i.e. 8 hours in total) on night 4. Melatonin (3 mg) was administered to the CD-M condition on days 2 and 3 of the in-lab stay 4 hours prior to bedtime. A placebo was administered to the CD-P condition. Drug condition was double-blinded (research pharmacist held the blind).

The goal of the phase advance in the larger study was to manipulate REM sleep in a manner parallel to some operational settings involving night shifts. Phase-advancing participants' sleep schedules are known to result in less time in REM sleep, due to the circadian control of REM sleep timing [29], and melatonin administration during a phase-advance rescue REM sleep [30]. Thus, it was postulated the CD-P condition would show reduced REM sleep relative to NC, while the CD-M condition would show at least partially restored REM sleep. For the purposes of the current analyses, manipulation of REM sleep through the three conditions provided greater variability in our primary explanatory variable (REM sleep), relative to studying everyone under normal sleep conditions, prior to task administration. Greater variability, in turn, should afford more robust analyses.

In-lab sleep was monitored with polysomnography (PSG), including electroencephalography (EEG), electrooculography (EOG), and electromyography (EMG), and scored according to the standard criteria outlined by the American Academy of Sleep Medicine (AASM) [31]. Continuous EEG was obtained by using a Compumedics 4K PSG:EEG Amplifier and recorded with Compumedics Profusion 4. The EEG recording was gathered from

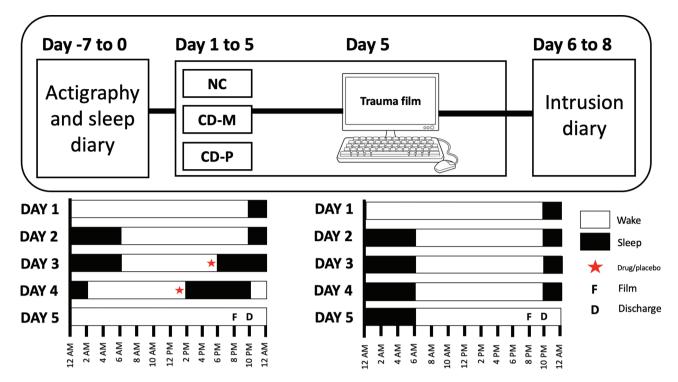


Figure 1. Overview of experimental procedures. Sleep-wake schedules are based on a participant whose habitual sleep-wake schedule is 10 pm to 6

13 scalp electrodes (Fz, FCz, F3, F4, Cz, C3, C4, Pz, P3, P4, O1, Oz, O2), which were applied using the standard 10/20 configuration and sampled at a rate of 512 Hz. Eye movements were monitored using two EOG electrodes positioned above and below the right and left eye, respectively. Participants were equipped with three electrodes on both sides of their jaw and chin to measure EMG

REM sleep percentage for each sleep period was obtained by calculating the amount of REM sleep in proportion to the total sleep time (TST). The average REM sleep percentage was calculated for each participant by averaging the REM sleep percentage across the 4 nights. REM sleep efficiency was obtained by dividing the amount of REM sleep in minutes by the total duration of all REM episodes [32, 33]. A given REM episode can, according to AASM scoring rules, include epochs of wake or other sleep stages interspersed among the REM sleep epochs. REM Efficiency is thus parallel to the concept of SE (which accounts for wake epochs interspersed among sleep epochs). The average REM sleep efficiency was then calculated for each participant by averaging the REM sleep efficiency across the four nights.

#### In-lab testing (day 5).

On day 5, participants watched the trauma film paradigm. The trauma film consisted of a 12-minute compilation of 11 distressing clips taken from television advertisements and archives from the public domain, designed to relate to real-life traumatic events that have been associated with PTSD development [34, 35]. The clips depicted scenes included, for example, car crashes, the aftermath of a genocide, and graphic surgeries. The trauma film paradigm has been commonly used as an experimental model of trauma in a laboratory setting [3]. Exposure to the film has been shown to elicit symptoms analogous to those experienced following trauma, although symptoms are often short-lived and typically subside within a week [36]. Participants were instructed

to give the film their full attention, to imagine themselves being present at the scene, and to not look away or close their eyes. The film was viewed on a computer screen with headphones on and the room lights turned off. Participants were monitored to ensure the film was watched in its entirety, by the researcher from outside the room.

Immediately pre- and post-film, participants were asked to rate their mood using the Visual Analog Mood Scale [35]. After viewing the film, participants were asked questions relating to their attention paid to the film, level of distress experienced, and personal relevance of the film. The film was administered approximately 14 hours after habitual wake time for both groups.

## Post-lab intrusion diary (day 6 to 8).

A pen-and-paper intrusion diary was kept over 3 days after viewing the trauma film to record intrusive memories. Participants were asked to record any intrusive memories experienced. A detailed description of the content of the intrusions was also required to verify it was elicited from a specific scene in the film. Participants were then asked to report the trigger eliciting the intrusion or indicate if there was no trigger, and to report the level of distress experienced at the time of intrusion, from 0 "not at all" to 10 "extremely." Verbal and written instructions were provided on how to complete the diary. Intrusive memories were defined as memories of the trauma film occurring spontaneously (i.e. not intentionally or consciously retrieved) [37]. The frequency of intrusive memories was calculated by summing all intrusive memories experienced over the 3-day period that were related to the content of the trauma film. Prior to analysis, two researchers blinded to group status examined the intrusion diaries independently and matched each intrusive memory to a specific clip in the film video to ensure accurate interpretation of the data. Any discrepancies were then discussed together, and a mutual agreement was made to either exclude or include the intrusive

memory for final analysis, with 11 of the 95 intrusive memories reported (11.6%) requiring discussion. Five of the 11 intrusive memories requiring discussion were excluded (44.5%; 5.2% of the total). Follow-up phone calls were made to participants who had incorrectly completed their diary, or in instances where the content of the diary required clarification (e.g. details of the intrusive memory were lacking).

# Data cleaning

Prior to analysis, the primary outcome (i.e. the frequency of intrusive memories) for one participant was identified as an extreme outlier (six times above the mean). Therefore, a 90% winsorization was performed as recommended by Howell [38]. and the number of intrusive memories was rounded to the nearest whole number. No univariate outliers were identified after conducting z-transformations of average REM sleep efficiency, average REM sleep percentage, average TST, and average non-rapid eye movement stage 3 (NREM3) percentage (z-score of ±2.58). No missing data were identified after inspecting the data. Table 1 outlines the descriptive statistics for the study variables

# Data analysis

All analyses were conducted using R version 4.0.2 (June 22, 2020) [39]. The alpha level was set at 0.05 for all analyses. To address both aims, a Poisson regression was conducted to investigate the relationship between average REM sleep percentage as well as average REM sleep efficiency and total intrusive memories in the 3 days after viewing the trauma film. A Poisson analysis was chosen based on the nature of the outcome variable (i.e.

Table 1. Descriptive Statistics for Main Study Variables

Main study variables	M (SD)	Range [minimum, maximum]
Average REM sleep percentage	23.1 (4.03)	18 [15.3, 33.1]
Average REM sleep efficiency	91.5 (4.21)	17 [80.9, 97.9]
Average NREM stage 3 percentage	36.23 (8.37)	31.17 [23.70, 54.87]
Average total sleep time (TST) (minutes)	425.24 (32.64)	111.75 [350.50, 462.25]
Intrusive memories	3.63 (2.72)	11 [0, 11]
Intrusive memory distress	3.44 (2.13)	6.5 [0, 6.5]

SD = standard deviation.

count data). The regression coefficients and confidence intervals (CIs) were exponentiated to obtain incident rate ratios for interpretation.

In exploratory analyses, we ran identical analyses examining the effect of average TST and average stage N3 on total intrusive memories in the 3 days after viewing the trauma film. Given the consistent finding that sleep, relative to wake, following the trauma film reduces the number of intrusive memories, we hypothesized that greater TST would predict fewer intrusive memories. The N3 analysis served as a sensitivity analysis to examine the specificity of the REM sleep effect.

#### Results

See Supplementary Table 1 which outlines descriptive statistics for participants. Table 2 outlines summary statistics for sleep study variables including TST, SE, and all sleep stage percentages in each sleep period.

A greater average REM sleep percentage across the 4 nights significantly predicted decreased intrusive memories reported over the 3 days. Specifically, for every standard deviation increase in average REM sleep percentage, the number of intrusive memories decreased by a ratio of 0.73 [95% CI = 0.60, 0.90], p = .004(see Figure 2). REM sleep percentage did not significantly affect distress levels of reported intrusions (p > .05).

As with REM sleep percentage, greater REM sleep efficiency across four nights significantly predicted fewer intrusive memories reported. Specifically, for every standard deviation increase in average REM sleep efficiency, the number of intrusive memories decreased by a ratio of 0.79 (95% CI = 0.66, 0.96), p = .02(see Figure 3). REM sleep efficiency did not significantly affect distress levels of reported intrusions (p > .05). Table 3 presents the regression coefficients for both analyses.

A greater average TST across the 4 nights significantly predicted decreased intrusive memories reported over the 3 days. Specifically, for every standard deviation increase in average TST, the number of intrusive memories decreased by a ratio of 0.82 (95% CI = 0.68, 0.99), p = .04 (see Figure 4).

The average stage N3 percentage across 4 nights was not significantly associated with intrusive memories reported (see Figure 5).

# Discussion

To our knowledge, the current study was the first to investigate the relationship between REM sleep quality and quantity prior to analog trauma and subsequent intrusive memories. The results support the hypothesis individuals with higher average REM sleep percentage and REM sleep efficiency prior to analog trauma report fewer intrusive memories in the 3 days following

Table 2. Sleep Study Variables for Each Sleep Period for All Participants

Study night	Total sleep time (TST) (minutes)	Sleep efficiency (SE) (%)	NREM1 (%)	NREM2 (%)	NREM3 (%)	REM (%)	REM sleep efficiency (%)
1	434.43 (30.56)	91.08 (5.27)	7.89 (3.83)	34.46 (8.30)	36.69 (9.19)	20.96 (4.50)	88.14 (8.38)
2	450.85 (11.68)	95.16 (1.85)	5.23 (2.66)	32.40 (9.25)	36.39 (9.12)	25.98 (4.76)	90.74 (5.85)
3	435.30 (36.44)	91.43 (7.35)	5.46 (3.02)	35.26 (11.03)	36.38 (10.07)	22.90 (5.31)	93.71 (6.39)
4	380.39 (90.93)	80.61 (18.64)	7.12 (3.82)	34.75 (10.07)	35.45 (10.18)	22.68 (6.72)	93.53 (6.60)
Average	425.24 (32.64)	89.57 (6.44)	6.42 (2.49)	34.21 (8.56)	36.23 (8.37)	23.13 (4.03)	91.53 (4.21)

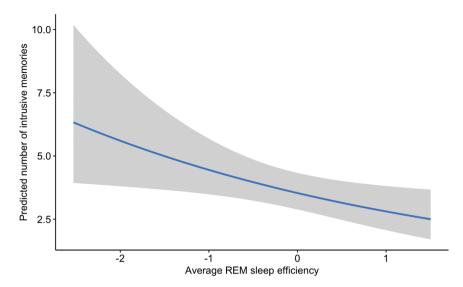


Figure 2. Association between average REM percentage and predicted number of intrusive memories. The X-axis is the average REM sleep percentage obtained by calculating the amount of REM sleep in proportion to the total sleep time, expressed as z-scores. The gray shading represents the 95% confidence interval.

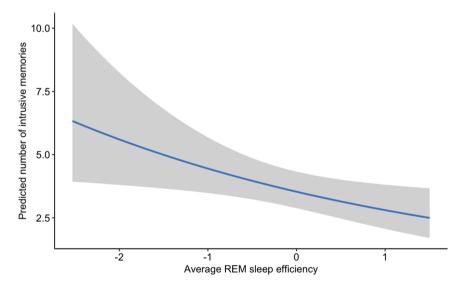


Figure 3. Association between average REM sleep efficiency and predicted number of intrusive memories. The X-axis is the average REM sleep efficiency calculated by averaging the REM sleep percentage across 4 nights, expressed as z-scores. The gray shading represents the 95% confidence interval.

Table 3. Regression Coefficients for the Poisson Regression Analysis Using Sleep Measures Averaged Across 4 Nights to Predict Intrusive Memories

Variable	Estimate		Z	Р	IRR	[95% CI]
		error	value	value		
Average REM sleep percentage	-0.31	0.11	-2.9	.004	0.73	[0.60, 0.90]
Average REM sleep efficiency	-0.23	0.10	-2.4	.02	0.79	[0.66, 0.96]
Average total sleep time	-0.20	0.09	-2.1	.04	0.82	[0.68, 0.99]
Average stage N3 percentage	-0.05	0.10	-0.52	.06	0.06	[0.77, 1.16]

IRR = incident rate ratio.

analog trauma. Specifically, for each additional 4% of average REM sleep, individuals reported 27% fewer intrusive memories, and for an additional 4% of REM sleep efficiency (representing greater consolidation of REM sleep), individuals reported 21% fewer intrusive memories. As expected, greater average TST in the 4 nights prior to viewing the film was also associated with fewer intrusive memories. Importantly, N3 sleep was not associated with intrusive memories, providing further evidence for the importance of REM sleep, specifically, in the development of intrusive memories.

Sleep disruptions are a consistent feature of PTSD [19, 23, 25, 26]. However, the role of specific sleep stages or sleep continuity measures in predicting the development of PTSD remains unclear [40] as does the specific pathway leading from sleep disruption to PTSD. Our findings suggest both the quality and quantity of REM sleep across 4 nights before analog trauma exposure predicts the frequency of

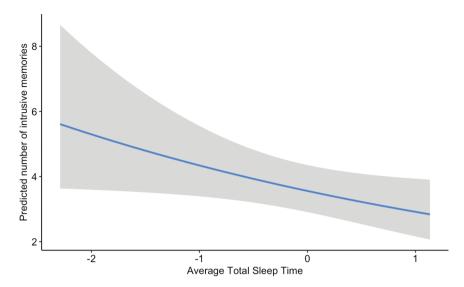


Figure 4. Association between average total sleep time and predicted number of intrusive memories. The X-axis is total sleep time calculated by averaging total sleep time across 4 nights, expressed as z-scores. The gray shading represents the 95% confidence interval.

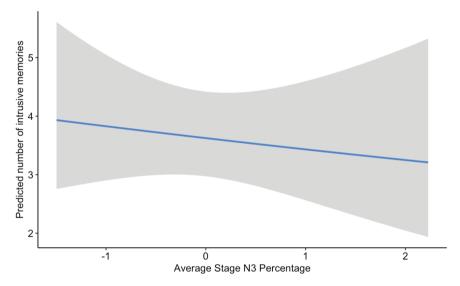


Figure 5. Association between average N3 percentage and predicted number of intrusive memories. The X-axis is the average N3 percentage calculated by averaging the N3 percentage across 4 nights, expressed as z-scores. The gray shading represents the 95% confidence interval.

intrusive memories, an early symptom of PTSD. Therefore, disrupted REM sleep prior to trauma exposure may serve as a vulnerability factor increasing the likelihood of experiencing more frequent intrusive memories in the aftermath of trauma exposure, which, in turn, may predict a subsequent PTSD diagnosis [4, 5].

Speculatively, disrupted or reduced REM sleep may contribute to intrusive memory formation mechanistically by affecting emotional processes. While the importance of REM sleep for emotional processes is not universally found, Van Someren's theory proposes disruptions in REM sleep result in ongoing noradrenergic activity which interferes with overnight emotional memory consolidation [16] and may exacerbate next-day emotional reactivity. The Dual Representation Theory, a prominent theory of intrusive memory development, proposes disruptions at encoding (e.g. due to severe stress) inhibit the connection between two memory systems formed during a traumatic event [26]. Compared to nontraumatic events, strong sensory representations and weak contextual representations of a traumatic experience result in the formation of intrusive memories. If reduced or disrupted REM sleep prior to analog trauma exacerbates emotional reactivity, according to the Dual Representation Theory, this may result in enhanced formation of sensory representations, leading to an increased number of intrusions. However, we did not measure the variables necessary to evaluate these processes, so further research is needed to examine these potential underlying mechanisms.

The research methods employed to modulate REM sleep were not only advantageous experimentally, but also in terms of realworld applications. Previous studies in the intrusive memory literature have examined that total sleep deprivation or daytime naps after analog traumas may influence intrusive memory development [41]. However, these methodologies do not accurately reflect sleep disruptions of individuals at risk of developing PTSD, such as military personnel and shift workers (i.e. frontline workers and emergency services personnel). Circadian disruptions are commonly observed in such individuals [42], and as REM sleep is

strongly influenced by the circadian system, these circadian disruptions typically result in REM sleep disruptions [43]. Our findings, then, suggest the circadian disruption secondary to shift work may enhance the risk of developing PTSD symptoms, specifically intrusive memories. The extent to which this would increase the risk of developing a full PTSD diagnosis is unclear. The pathway from trauma exposure to PTSD symptoms to PTSD diagnosis is complex, although circadian disruption at the time of trauma has been suggested as a specific risk factor for a recently described trauma-associated sleep disorder [44]. The current results present one additional piece of the puzzle by showing sleep, especially REM sleep, prior to analog trauma exposure influences the number of intrusive memories reported over a 3-day period. Future studies should replicate and expand on these findings by examining how they may interact with other known risk factors and potential mechanisms related to the development of PTSD.

The trauma film paradigm is a widely used analog model of trauma known to be effective in inducing intrusive memories [45, 46]. Intrusive memories can arise not only through direct experience of a traumatic event, but also through indirect methods such as viewing negative visual stimuli in a work-related setting [47]. Whilst this paradigm does allow for the experimental manipulation of factors occurring both before and after analog trauma [7], it must be acknowledged the trauma film is very different than, and does not create the same level of stress as, real-world trauma. In line with previous studies examining sleep and intrusive memory frequency [35, 48, 49], we did not find a significant association between REM sleep and distress associated with intrusive memories. This may, in part, be due to the low level of distress elicited by the trauma film and is a limitation of this paradigm. Whether the effects reported in the literature related to trauma film paradigms would be stronger or weaker in real-world traumas is an open question. Examining the relationship between REM sleep and intrusive memories in clinical or high-risk populations is warranted to expand the findings from this literature and increase external validity.

In addition to REM sleep, there are several other factors that could have influenced intrusive memory frequency in the current study. First, circadian disruption affects attentional processes [50]. It is possible participants experienced varying degrees of attentiveness whilst watching the films, which would influence intrusion frequency. However, to control for this, participants were monitored when watching the films and asked about their attentiveness afterward. No participants were excluded based on observed or reported inattentiveness. Second, as intrusive mental imagery occurs across different psychological disorders [51], a tendency to experience intrusive cognition generally (e.g. intrusive thoughts/images, worry) may have also influenced intrusive memories of the films. We attempted to minimize this risk by excluding participants with any history of psychological disorders. Explicitly accounting for certain psychological traits (especially anxiety) dimensionally and trait-level tendencies toward intrusive cognition in future studies may shed further light on mechanisms underpinning the influence of sleep on intrusive memory frequency. Third, intrusion frequency may also be affected by personally relevant events related to the specific films used. Participants were asked about the personal relevance of the film content and none were excluded based on relevance ratings. Finally, circadian disruption like that experienced here likely affected physiological responses beyond just sleep (e.g. stress responses). It is unclear how such responses may have influenced the development of intrusive memories, and future studies may wish to directly assess this question.

One further limitation of the current study is we did not examine the effect of each sleep condition on intrusive memory development, so we were unable to examine the group-level effect of circadian disruption or the efficacy of melatonin to reverse any adverse effects observed. However, our main aim revolved around REM sleep, rather than conditions per se, and the different conditions served to increase the variability of REM sleep within the sample. While our original goal was to additionally examine these group-level effects, COVID-related lockdowns prevented a sufficient sample size to conduct that analysis. Sample size also prevented us from including all sleep variables of interest (REM, N3, TST) in the same model. In the future, larger studies attempting to replicate these findings should include more sleep variables in a single model to better determine the unique contribution of each to reports of intrusive memories. Finally, it is unclear the extent to which our findings would translate to clinical populations.

In summary, the current study explored the associations between REM sleep prior to analog trauma and intrusive memory development in a group of healthy controls. Complimenting previous studies examining the role of sleep after trauma through consolidation processes, the current study demonstrated that reduced REM sleep percentage and REM sleep efficiency prior to analog trauma were associated with an increase in intrusive memory frequency [3, 5]. The findings highlight the importance of REM sleep in intrusive memory development. This finding has potential implications for populations at high risk of trauma, who commonly experience shifts in their circadian systems and who are frequently exposed to traumatic events (emergency service/ military personnel), although much further research is needed to fully explicate those implications. The current study sets the stage for future research to examine these associations in highrisk populations and clinical samples, particularly in individuals with PTSD.

# Supplementary material

Supplementary material is available at SLEEP online.

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### Disclosure Statement

Financial disclosure: none. Non-financial disclosure: none.

# Data Availability

The data underlying this article will be shared on reasonable request to the corresponding author.

# References

1. Kilpatrick DG, Resnick HS, Milanak ME, Miller MW, Keyes KM, Friedman MJ. National estimates of exposure to traumatic events and PTSD prevalence using DSM-IV and DSM-5 criteria. J Trauma Stress. 2013;26(5):537-547. doi:10.1002/jts.21848

- 2. Association AP. Diagnostic and Statistical Manual of Mental Disorders. Vol. 5. Washington, DC: Diagnostic and Statistical Manual of Mental Disorders; 2013.
- 3. James EL, Lau-Zhu A, Clark IA, Visser RM, Hagenaars MA, Holmes EA. The trauma film paradigm as an experimental psychopathology model of psychological trauma: intrusive memories and beyond. Clin Psychol Rev. 2016;47:106-142. doi:10.1016/j. cpr.2016.04.010
- 4. O'Donnell ML, Bryant RA, Creamer M, Carty J. Mental health following traumatic injury: toward a health system model of early psychological intervention. Clin Psychol Rev. 2008;28(3):387-406. doi:10.1016/j.cpr.2007.07.008
- 5. Galatzer-Levy IR, Karstoft KI, Statnikov A, Shalev AY. Quantitative forecasting of PTSD from early trauma responses: a Machine Learning application. J Psychiatr Res. 2014;59:68-76. doi:10.1016/j.jpsychires.2014.08.017
- 6. Rasch B, Born J. About sleep's role in memory. Physiol Rev. 2013;**93**(2):681–766. doi:10.1152/physrev.00032.2012
- 7. Larson O, Schapiro AC, Gehrman PR. Effect of sleep manipulations on intrusive memories after exposure to an experimental analogue trauma: a meta-analytic review. Sleep Med Rev. 2023;69. doi:10.1016/j.smrv.2023.101768
- 8. Davidson P, Marcusson-Clavertz D. The effect of sleep on intrusive memories in daily life: a systematic review and meta-analysis of trauma film experiments. Sleep. 2023;46(2). doi:10.1093/sleep/zsac280
- 9. Schäfer SK, Lüder CC, Porcheret K, et al. 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. Behav Res Ther. 2023;167. doi:10.1016/j.brat.2023.104359
- 10. Goldstein AN, Walker MP. The role of sleep in emotional brain function. Annu Rev Clin Psychol. 2014;10:679-708. doi:10.1146/ annurev-clinpsy-032813-153716
- 11. Walker MP, van der Helm E. Overnight therapy? The role of sleep in emotional brain processing. Psychol Bull. 2009;135(5):731-748. doi:10.1037/a0016570
- 12. Kleim B, Wysokowsky J, Schmid N, Seifritz E, Rasch B. Effects of sleep after experimental trauma on intrusive emotional memories. Sleep. 2016;39(12):2125-2132. doi:10.5665/sleep.6310
- 13. Zeng S, Lau EYY, Li SX, Hu X. Sleep differentially impacts involuntary intrusions and voluntary recognitions of lab-analogue traumatic memories. J Sleep Res. 2021;30(3). doi:10.1111/
- 14. Sopp MR, Brueckner AH, Schäfer SK, Lass-Hennemann J, Michael T. Differential effects of sleep on explicit and implicit memory for potential trauma reminders: findings from an analogue study. Eur J Psychotraumatol. 2019;10(1). doi:10.1080/20008 198.2019.1644128
- 15. Sopp MR, Friesen E, Schäfer SK, et al. Wakefulness impairs selective consolidation of relevant trauma-associated memories resulting in more frequent intrusions. Behav Res Ther. 2021;136. doi:10.1016/j.brat.2020.103776
- 16. Van Someren EJW. Brain mechanisms of insomnia: new perspectives on causes and consequences. Physiol Rev. 2021;101(3):995-1046. doi:10.1152/physrev.00046.2019
- 17. Mellman TA, Kumar A, Kulick-Bell R, Kumar M, Nolan B. Nocturnal/daytime urine noradrenergic measures and sleep in combat-related PTSD. Biol Psychiatry. 1995;38(3):174-179. doi:10.1016/0006-3223(94)00238-X
- 18. Ross RJ, Ball WA, Sullivan KA, Caroff SN. Sleep disturbance as the hallmark of posttraumatic stress disorder. Am J Psychiatry. 1989;**146**(6):697–707. doi:10.1176/ajp.146.6.697

- 19. Mellman TA, Kulick-Bell R, Ashlock LE, Nolan B. Sleep events among veterans with combat-related posttraumatic stress disorder. Am J Psychiatry. 1995;**152**(1):110–115. doi:10.1176/ajp.152.1.110
- 20. Germain A. Sleep disturbances as the hallmark of PTSD: where are we now? Am J Psychiatry. 2013;170(4):372-382. doi:10.1176/ appi.ajp.2012.12040432
- 21. Mellman TA, Bustamante V, Fins AI, Pigeon WR, Nolan B. REM sleep and the early development of posttraumatic stress disorder. Am J Psychiatry. 2002;**159**(10):1696–1701. doi:10.1176/appi. ajp.159.10.1696
- Breslau N, Roth T, Rosenthal L, Andreski P. Sleep disturbance and psychiatric disorders: a longitudinal epidemiological study of young adults. Biol Psychiatry. 1996;39(6):411-418. doi:10.1016/0006-3223(95)00188-3
- 23. Kobayashi I, Boarts JM, Delahanty DL. Polysomnographically measured sleep abnormalities in PTSD: a meta-analytic review. Psychophysiology. 2007;44(4):660-669. doi:10.1111/j.1469-8986. 2007.537.x
- 24. Mellman TA, Hipolito MM. Sleep disturbances in the aftermath of trauma and posttraumatic stress disorder. CNS Spectr. 2006;**11**(8):611-615. doi:10.1017/s1092852900013663
- 25. Bryant RA, Creamer M, O'Donnell M, Silove D, McFarlane AC. Sleep disturbance immediately prior to trauma predicts subsequent psychiatric disorder. Sleep. 2010;33(1):69-74. doi:10.1093/ sleep/33.1.69
- 26. Brewin CR, Holmes EA. Psychological theories of posttraumatic stress disorder. Clin Psychol Rev. 2003;23(3):339-376. doi:10.1016/ s0272-7358(03)00033-3
- 27. Zhang Y, Ren R, Sanford LD, et al. Sleep in posttraumatic stress disorder: a systematic review and meta-analysis of polysomnographic findings. Sleep Med Rev. 2019;48:101210. doi:10.1016/j. smrv.2019.08.004
- Straus LD, Drummond SP, Nappi CM, Jenkins MM, Norman SB. Sleep variability in military-related PTSD: a comparison to primary insomnia and healthy controls. J Trauma Stress. 2015;**28**(1):8–16. doi:10.1002/jts.21982
- 29. Gonnissen HK, Mazuy C, Rutters F, Martens EA, Adam TC, Westerterp-Plantenga MS. Sleep architecture when sleeping at an unusual circadian time and associations with insulin sensitivity. PLoS One. 2013;8(8). doi:10.1371/journal.pone.0072877
- 30. Kunz D, Mahlberg R, Müller C, Tilmann A, Bes F. Melatonin in patients with reduced REM sleep duration: two randomized controlled trials. J Clin Endocrinol Metab. 2004;89(1):128-134. doi:10.1210/jc.2002-021057
- 31. Berry RB, Brooks R, Gamaldo C, et al. AASM Scoring Manual Updates for 2017 (Version 2.4). J Clin Sleep Med. 2017;13(5):665-666. doi:10.5664/jcsm.6576
- 32. Marshall AJ, Acheson DT, Risbrough VB, Straus LD, Drummond SP. Fear conditioning, safety learning, and sleep in humans. J Neurosci. 2014;**34**(35):11754–11760. doi:10.1523/JNEUROSCI.0478-14.2014
- 33. Straus LD, Acheson DT, Risbrough VB, Drummond SPA. Sleep deprivation disrupts recall of conditioned fear extinction. Biol Psychiatry Cogn Neurosci Neuroimaging. 2017;2(2):123-129. doi:10.1016/j.bpsc.2016.05.004
- 34. Lazarus RS, Alfert E. Short-circuiting of threat by experimentally altering cognitive appraisal. J Abnorm Psychol. 1964;69:195-205. doi:10.1037/h0044635
- 35. Porcheret K, van Heugten-van der Kloet D, Goodwin GM, Foster RG, Wulff K, Holmes EA. Investigation of the impact of total sleep deprivation at home on the number of intrusive memories to an analogue trauma. Transl Psychiatry. 2019;9(1):104. doi:10.1038/s41398-019-0403-z

- 36. Holmes EA, Brewin CR, Hennessy RG. Trauma films, information processing, and intrusive memory development. J Exp Psychol Gen. 2004;133(1):3-22. doi:10.1037/0096-3445.133.1.3
- 37. Holmes EA, James EL, Coode-Bate T, Deeprose C. Can playing the computer game "Tetris" reduce the build-up of flashbacks for trauma? A proposal from cognitive science. PLoS One. 2009;4(1). doi:10.1371/journal.pone.0004153
- 38. Howell DC. Fundamental Statistics for the Behavioural Sciences. Vol. 41. Boston: Cengage Learning; 2017.
- R Core Team. R: A language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing; 2021. https://www.R-project.org/.
- 40. Koren D, Arnon I, Lavie P, Klein E. Sleep complaints as early predictors of posttraumatic stress disorder: a 1-year prospective study of injured survivors of motor vehicle accidents. Am J Psychiatry. 2002;**159**(5):855–857. doi:10.1176/appi.ajp.159.5.855
- 41. Porcheret K, Holmes EA, Goodwin GM, Foster RG, Wulff K. Psychological effect of an analogue traumatic event reduced by sleep deprivation. Sleep. 2015;38(7):1017-1025. doi:10.5665/
- 42. Rajaratnam SM, Howard ME, Grunstein RR. Sleep loss and circadian disruption in shift work: health burden and management. Med J Aust. 2013;199(8):S11-S15. doi:10.5694/mja13.10561
- 43. Rajaratnam SM, Polymeropoulos MH, Fisher DM, et al. Melatonin agonist tasimelteon (VEC-162) for transient insomnia after sleep-time shift: two randomised controlled multicentre trials. Lancet. 2009;373(9662):482-491. doi:10.1016/ S0140-6736(08)61812-7

- 44. Mysliwiec V, Brock MS, Creamer JL, O'Reilly BM, Germain A, Roth BJ. Trauma associated sleep disorder: a parasomnia induced by trauma. Sleep Med Rev. 2018;37:94-104. doi:10.1016/j. smrv.2017.01.004
- 45. Horowitz MJ. Intrusive and repetitive thoughts after experimental stress. a summary. Arch Gen Psychiatry. 1975;32(11):1457-1463. doi:10.1001/archpsyc.1975.01760290125015
- 46. Holmes EA, Bourne C. Inducing and modulating intrusive emotional memories: a review of the trauma film paradigm. Acta Psychol (Amst). 2008;127(3):553-566. doi:10.1016/j. actpsy.2007.11.002
- 47. Holman EA, Garfin DR, Silver RC. Media's role in broadcasting acute stress following the Boston Marathon bombings. Proc Natl Acad Sci U S A. 2014;**111**(1):93–98. doi:10.1073/pnas.1316265110
- 48. Woud ML, Cwik JC, Blackwell SE, et al. Does napping enhance the effects of cognitive bias modification-appraisal training? An experimental study. PLoS One. 2018;13(2). doi:10.1371/journal. pone.0192837
- 49. Gvozdanovic G, Schoch S, Stampfli P, Seifritz E, Rasch B. Neural correlates of sleep-induced benefits on traumatic memory processing. Hum Brain Mapp. 2023;44(9):3506-3518. doi:10.1002/ hbm.26294
- 50. Valdez P. Circadian rhythms in attention. Yale J Biol Med. 2019;92(1):81-92.
- 51. Brewin CR, Gregory JD, Lipton M, Burgess N. Intrusive images in psychological disorders: characteristics, neural mechanisms, and treatment implications. Psychol Rev. 2010;117(1):210-232. doi:10.1037/a0018113