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**Title:** No Effect of Targeted Memory Reactivation during Slow-Wave Sleep on Emotional Recognition Memory

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**Abstract**

Recent work has suggested that the benefits of sleep for memory consolidation are enhanced for highly salient (vs. non-salient) memories. Using a technique known as targeted memory reactivation (TMR) it is possible to selectively strengthen newly learned memories by re-exposing the sleeping brain to auditory cues. The aim of the current study was to examine whether emotionally salient memories are also more responsive to TMR in slow-wave sleep (SWS) than neutral memories. In an initial training phase participants memorised emotionally negative and neutral pictures, which were each paired with a semantically related sound. Recognition for the pictures was assessed before and after a 90 minute nap opportunity, during which half the sounds were re-presented during SWS (as assessed via online polysomnographic sleep monitoring). We observed no effect of TMR on the recognition of emotionally negative or neutral memories. Our results highlight the importance of the memory paradigm used to assess TMR and suggest that the robust and durable nature of recognition memory may make it an insensitive measure of behavioural TMR benefits. To fully assess the impacts of TMR on emotional memory processing in sleep, future studies should adopt experimental paradigms that maximise the salience of emotional stimuli while also providing a sensitive index of memory accuracy.

**Introduction**

There is now a wealth of evidence that sleep facilitates memory consolidation: the process by which new and initially liable memory traces become strong and enduring representations (Rasch & Born, 2013; Walker, 2009). Recent work has suggested that sleep-dependent consolidation operates in a highly discerning manner, whereby salient memories (i.e. memories that noticeably stand-out) are strengthened ahead of non-salient memories (Wilhelm et al., 2011; Stickgold & Walker, 2013). As such, memories for intense emotional events appear to receive greater consolidation benefits from sleep than memories for emotionally neutral experiences (Hu et al., 2006; Wagner et al., 2001; Wagner et al., 2006). Offline consolidation process exclusive to sleep may therefore play an important role in the long-term persistence of emotional memory information.

There are divergent lines of evidence with respect to the specific components of sleep responsible. Behavioural evidence links rapid eye-movement (REM) sleep with emotional processing, although the neural mechanisms are unclear (Hutchison & Rathore, 2015). A larger body of research implicates non-raid eye-movement sleep (NREM) sleep in memory consolidation, with a specific role for slow-wave sleep (SWS) physiology. *Active Systems* accounts of sleep-dependent consolidation propose that newly formed memories are reactivated during SWS, as indexed by spontaneous patterns of neural activity in the brain regions employed at learning (Diekelmann & Born, 2010). Reactivation is believed to reflect systems-level communication between hippocampal networks and long-term memory stores within the neocortex. This cross-talk facilitates a shift in memory dependence from the hippocampus to the neocortex, leading to durable long-term memory representations. Recent adaptions of this model propose that highly salient memories are preferentially reactivated in SWS, and thereby better stabilised in long-term memory (Born & Wilhelm, 2012; Rasch & Born, 2013). Indeed, a selective benefit of SWS for the consolidation of emotionally negative memories has been observed in recent work (Cairney et al., 2015), suggesting that sleep-specific emotional memory reactivations in SWS may be integral to affective memory processing.

 Recently, a causal role of reactivation in memory consolidation has been demonstrated via a technique known as targeted memory reactivation (TMR). In a typical TMR experiment, individuals form associations between newly-learned memories and semantically-related sounds, a subset of which are then replayed in SWS to selectively cue memory reactivations (Oudiette & Paller, 2013). Memories are better remembered after cueing with TMR, indicating a mechanistic role of reactivation in sleep-dependent consolidation (Cairney et al., 2016; Fuentemilla et al., 2013; Oudiette et al., 2013; Rudoy, Voss et al., 2009).

If emotional memories are preferentially reactivated in SWS, then the impacts of TMR may be stronger for emotional relative to neutral memory information. In keeping with this view, Cairney et al. (2014) observed a selective benefit of TMR in SWS for emotionally negative (vs. neutral) memories. However, unlike previous work (Oudiette et al., 2013; Rudoy et al., 2009), the benefits of TMR were found in participant response times and not memory accuracy. How TMR influences emotional memory consolidation in sleep is therefore still very much unclear. The task employed by Cairney et al. (2014) included a strong spatial memory component, which may have dampened the emotional salience of the experimental stimuli at encoding. Placing greater emphasis on the explicit emotional properties of a novel memory trace may thus increase its responsiveness to TMR in sleep.

 In the current study, we investigated the impact of TMR in SWS on the consolidation of highly salient emotional memory representations. To achieve this, we combined our TMR protocol with a recognition paradigm that promotes the emotional features of newly-formed memories, and is compatible with previous studies of sleep and emotional memory (Hu et al., 2006; Sterpenich et al., 2007; Sterpenich et al., 2009). In an initial training phase, participants memorised emotionally negative and neutral pictures, which were each paired with a semantically related sound. Baseline memory performance was assessed using a Remember/Know procedure, which differentiates between respective recollection and familiarity in recognition memory (Tulving, 1985). In a subsequent nap, half of the sound cues associated with the negative and neutral pictures were continuously replayed in SWS and emotional memory was re-assessed upon awakening. Despite our focus on episodic memory content, we also sought to examine the impacts of TMR on spatial components of emotional memories. Accordingly, each image was presented in one of the four PC screen quadrants at encoding and recall for these locations was assessed at recognition testing. We hypothesised that memories cued via TMR in SWS would be better recognised, and show greater retention of the spatial memory component, compared to non-cued memories. These effects were further predicted to be stronger for emotionally negative (vs. neutral) memories.

**Methods**

***Participants***

Thirty-nine participants (27 female) aged 18-29 years (mean ± SD age; 22.01 ± 1.80 years) were recruited for this study. Participants were not using any psychologically active medications and agreed to abstain from alcohol and caffeine for 24 hours prior to the start of the study. Written informed consent was obtained from all participants in line with the Research Ethics committee of the Department of Psychology, University of York. In order to assess the role of TMR on recognition memory, we required participants to enter and remain within SWS long enough to successfully receive at least 50% of intended sound replays without wakening. In total, 19 participants did not meet this criterion and were excluded from the analysis. Of these, 5 participants received replay but did not reach the 50% criterion, 12 participants failed to enter and remain within SWS for memory replay and 2 participants did not sleep in the nap period. A further participant was excluded for failing to follow task instructions, resulting in a final sample size of 19.

***Stimuli***

One-hundred and twenty target pictures (60 negative and 60 neutral) were selected from the International Affective Picture System (IAPS, Lang, Bradley, & Cuthbert, 2005) and the internet. Each picture was paired with a semantically related sound (500 ms) taken from the International Affective Digitized Sounds battery (Bradley & Lang, 2007) or freesound.org to create 60 negative and 60 neutral picture-sound pairs. An example of a picture-sound pair is an image of an aggressive dog (negative image) paired with the sound of a dog barking. A further two-hundred and forty images (120 negative, 120 neutral) were selected from the IAPS and internet to be used as foils in the pre- and post-sleep recognition tests. Human content was counterbalanced between the negative and neutral images.

***Procedure***

The study began at 1 pm (± 30 minutes) and was carried out in the Sleep, Language and Memory Laboratory, Department of Psychology, University of York, UK. Two experimental sessions were separated by a ~90 minute nap opportunity. Participants were informed that they were taking part in the study of memory and sleep, but were unaware that TMR would be used in the nap phase. Before the first session began, electrodes were attached to the head and face to allow for sleep monitoring with polysomnography (PSG).

*Encoding*

Participants encoded 120 picture-sound pairs (60 negative and 60 neutral). For each randomised trial, a fixation cross appeared in the centre of the PC screen for 2 s before a picture was presented in one of the four screen quadrants (i.e. upper/lower left/right) for 1.5 s. Negative and neutral pictures were counterbalanced so that 15 of each set appeared in each of the four screen quadrants. The quadrant position of each picture was also counterbalanced across participants. Each picture was presented at the same time as a semantically-related sound, which participants heard via headphones. A blank screen appeared for 500 ms before participants were prompted to provide an emotional valence judgement for the image (9-point scale, 1 = negative, 5 = neutral, 9 = positive) using the keyboard. Participants were instructed to memorise each image and its screen location for a future test.

*Recognition (Pre-Sleep)*

Immediately after encoding, participants carried out a 240-trial recognition test consisting of the 120 trained target pictures and 120 foil pictures (60 negative and 60 neutral). For each randomised trial, a fixation cross appeared in the centre of the screen for 2 s before a picture was presented in the centre of the screen for 3.5 s. No sounds were presented during recognition testing. So that we could address both recollection and familiarity in recognition memory (Tulving, 1985), participants were required to make one of three responses to the picture: 1) ‘Remember’ (R) – conscious recollection of the picture from encoding, 2) ‘Know’ (K) – familiarity for the picture in the absence of conscious recollection, or 3) ‘New’ (N) – the image is new. When participants provided an R or K response, they were also prompted to recall the screen quadrant that the picture had appeared during encoding. All responses were made using the keyboard and participants were asked to respond as accurately and as quickly as possible. To ensure that the pictures had been adequately encoded, participants were required to have provided a correct R or K response to at least 50% of the target pictures in both categories (i.e. at least 30 negative pictures and 30 neutral pictures).

*Nap with TMR*

Participants were asked to get into bed and move into a supine position ready for sleep. For each participant, correctly recognised negative and neutral images in the pre-sleep test (images that received an R or K response) were randomly divided into two equal sets. The sounds associated with one set were used in the TMR condition (mean ± SD number of negative sounds used for TMR = 26.60 ± 3.72; neutral sounds = 24.20 ± 5.12), while the sounds associated with the other set were used in the no-TMR condition, thereby assuring that pre-sleep performance was equivalent for cued and non-cued memories (Cairney et al., 2016; Fuentemilla et al., 2013; Rudoy et al., 2009). Bedroom lights were switched off at 2.30 pm (± 30 minutes) and participants were left to sleep. Sound replay was initiated after participants had exhibited ~2 minutes of SWS (as determined via online PSG monitoring). The replayed sounds were presented in random order throughout the duration of SWS with a presentation rate of one sound per 5 s. The mean (± SD) number of full sound set replays was 3.81 (± 2.18). The sounds were immediately stopped if PSG recordings showed signs of micro-arousal or awakening, but were restarted if participants returned to SWS. The nap opportunity ended after ~90 min; participants were only awoken from sleep stages I or II and never from SWS or rapid eye movement sleep (REM). To attenuate sleep inertia, participants then took a ~20 minute break, during which the PSG electrodes were removed.

*Recognition (Post-Sleep)*

Participants repeated the recognition test. New foil images (i.e. different to those presented in the pre-sleep test) were used here (60 negative and 60 neutral).

*Sound Discrimination*

Participants were informed of the true purpose of the experiment and asked whether they had been aware of any sound replay during sleep. They then completed a sound discrimination task in which they were re-presented with each of the 120 study sounds and asked to indicate whether they had or had not been replayed in sleep (via keyboard press).

***Equipment***

*Experimental Tasks*

All tasks were implemented on a PC with E-Prime version 2.0 (Psychology Software Tools, Inc.). Sounds were heard through headphones (Beyerdynamic DT 234 PRO). Visual stimuli were presented ~ 0.5m from participants on a 27" flat screen monitor (resolution = 1920 x 1080 pixels) positioned at eye level

*Sound Replay (TMR)*

Sound replay in sleep was implemented with E-Prime version 2.0. Sounds were played via a speaker mounted ~1.5 m above the bed, which was connected to an amplifier in a separate control room. To habituate participants to auditory stimulation during sleep, and thus reduce the risk of arousals or awakenings during sound replay, low intensity brown noise was played into the bedroom for the entirety of the nap phase (overall sound intensity level of ~50 dB).

*PSG and Sleep Scoring*

An Embla N7000 PSG system with RemLogic version 3.4 software was used to monitor sleep during the nap phase. After the scalp was cleaned with NuPrep exfoliating agent (Weave and Company), gold-plated electrodes were attached using EC2 electrode cream (Grass Technologies) and medical tape. EEG scalp electrodes were attached in accordance with the international 10-20 system at six standardised locations: frontal (F3 and F4), central (C3 and C4), occipital (O1 and O2), and each was referenced to an electrode on the contralateral mastoid (A1 or A2). Left and right electrooculography electrodes were attached, as were electromyography electrodes at the mentalis and submentalis bilaterally, and a ground electrode was attached to the forehead. Each electrode had a connection impedance of < 5 kΩ and all signals were digitally sampled at 200 Hz.

For TMR, online sleep scoring was conducted on the referenced central electrodes (C3-A2 and C4-A1). To ensure that sound replay had been initiated in SWS, PSG recordings were subsequently scored in accordance with the criteria of the American Academy of Sleep Medicine (Iber, Ancoli-Israel, Chesson, & Quan, 2007) Sleep data was partitioned according to the percentage of total sleep time spent in stage I, stage II, SWS and REM. PSG data scored offline confirmed that sound replay had occurred for all participants during SWS.

**Results**

***Emotion Ratings***

Participants provided an emotional valence rating for each image during the encoding phase of the study (1-9 scale; 1 = negative, 5 = neutral, 9 = positive). The negative pictures were rated as significantly more negative than the neutral pictures (negative mean ± SD; 2.89 ± 0.54, neutral mean ± SD; 6.08 ± 0.61, *t* (18) = -15.34, *p* < .001).

***Recognition Memory***

*Overall Recognition Accuracy (d*ʹ*)*

Recognition trials were classified according to whether R, K or N judgements were correct or incorrect, and from these classifications we calculated the dʹ– a measure of recognition accuracy according to signal detection theory (MacMillan & Creelman, 1991). The loglinear approach was adopted to account for extreme values (Hautus, 1995) and trials in which participants failed to make a response were excluded from the analysis (0.59% of trials). A summary of the responses are presented in Table 1.

[Table 1 here]

*R Responses (d*ʹ*)*

A repeated measures analysis of variance (ANOVA) was performed to assess the impact of Session (pre-sleep, post-sleep) and Emotion (negative, neutral) on recognition memory (see Figure 1). This analysis revealed a significant main effect of Emotion (F(1, 18) = 12.86, *p* = .002, ηp2 = .42), with an advantage for the recognition of negative over neutral items. T-tests with the Bonferroni corrected alpha level of .025 indicate that this difference was significant only in the pre-sleep test (pre-sleep; t(19) = 4.26, *p* < .001, post-sleep; t(19) = 2.11, *p* = .048). There was no main effect of Session (F(1, 18) = 0.15, *p* = .699, ηp2 = .01) or Session × Emotion interaction (F(1, 18) = 0.52, *p* = .480, ηp2 = .03).

[Figure 1 here]

*K Responses (d*ʹ*)*

The same ANOVA was performed to assess the impact of Session (pre-sleep, post-sleep) and Emotion (negative, neutral) on the number of K judgements (see Figure 2). This analysis did not reveal any significant main effects, suggesting that emotional valence (F(1, 18) = 0.24) *p* = .629, ηp2 = .01) and testing session (F(1, 18) = 0.09, *p* = .766, ηp2 = .01) had no impact upon K responses. There was also no Session × Emotion interaction (F(1, 18) = 0.30, *p* =.590, ηp2 = .02).

[Figure 2 here]

***Recognition Memory and Targeted Memory Reactivation***

The following analyses focus upon post-sleep recognition memory, analysing only those items that had been recognised before sleep (i.e. items that correctly received an R or K response in the pre-sleep test, items that received an N response were discounted). This was to match the TMR and no-TMR conditions by ensuring all items had been encoded and recognised prior to sleep. Post-sleep recognition responses were classified according to whether participants gave an R K or N judgement and are presented in Table 2. We do not have TMR / no-TMR foils and therefore were unable to calculate scores of *d*ʹ to assess the impact of TMR on recognition memory. As false alarm rates were generally were very low (see Table 1) we have calculated the proportion or correctly provided R and K responses for the subsequent analyses.

[Table 2 here]

*R Responses*

To assess the impact of TMR on the proportion of correctly provided R responses, a 2 x 2 repeated measures ANOVA was performed with the factors Emotion (negative, neutral) and Replay (TMR, no-TMR). This analysis did not reveal a main effect of Replay, suggesting that cueing item memory during sleep using TMR did not alter the rates of R judgements (F(1, 18) = 0.73, *p* = .403, ηp2 = 0.04). There was no main effect of Emotion (F(1, 18) = 2.42, *p* =.137, ηp2 = 0.12) and no Session × Emotion interaction (F(1, 18) = 0.50, *p* = .489, ηp2 = 0.03).

*K Responses*

The impact of TMR on provided K judgements was analysed using the same repeated measures ANOVA with the factors Emotion (negative, neutral) and Replay (TMR, no-TMR). This analysis also revealed no main effect of Replay (F(1, 18) = 0.002, *p* = .967, ηp2 = 0.001) or Emotion (F(1, 18) = 1.70, *p* = .209, ηp2 = 0.09) and no Session × Emotion interaction (F(1, 18) = 0.02, *p* = .901, ηp2 = 0.001).

***Spatial Memory***

Participants were asked to provide a spatial memory judgement following an R or K response, accuracy is therefore calculated as the proportion of correctly recalled screen locations for all recognised items in the pre- and post-sleep tests (see Table 3).

[Table 3 here]

Data were analysed using a 2 x 2 repeated measures ANOVA with the factors Session (pre-sleep / post-sleep) and Emotion (negative / neutral). This analysis revealed no significant main effects; spatial memory was equivalent for negative and neutral items (F(1, 18) = 3.98, *p* = .061, ηp2 = 0.18) and did not differ between pre- and post-sleep tests (F(1, 18) = 1.30, *p* = .269, ηp2 = 0.07). There was also no Session × Emotion interaction (F(1, 18) = 1.00, *p* = .330, ηp2 = 0.05).

***Spatial Memory and Targeted Memory Reactivation***

To assess the impact of TMR on spatial memory accuracy, the analyses focused upon post-sleep memory. Only items that had been recognised in both the pre- and post-sleep sessions were included in comparisons between conditions of TMR and no-TMR (this was to ensure comparable levels of pre-sleep recognition, in line with the previous TMR analyses, and because participants were only able to provide location judgements for recognised items in the post-sleep test).

 Accuracy scores were analysed using a 2 x 2 repeated measure ANOVA with the factors Emotion (negative, neutral) and Replay (TMR, no-TMR). This analysis revealed no main effect of Replay (F(1, 18) = 2.48, *p* = .133, ηp2 = 0.12) or Emotion (F(1, 18) = 0.34, *p* = .566, ηp2 = 0.02) with no Session × Emotion interaction (F(1, 18) = 0.07, *p* = .794, ηp2 = 0.004).

***Sleep Data***

The sleep data are summarised in Table 4. To assess the relationship between specific sleep parameters and TMR, we calculated an index measure of the TMR benefit for negative and neutral recognition memory (separately for R and K responses, recognition TMR index = post-sleep recognition accuracy for TMR items – post-sleep recognition accuracy for non-TMR items, Table 2) and negative and neutral spatial memory (spatial TMR index = post-sleep spatial accuracy for TMR items – post-sleep spatial accuracy for non-TMR items, Table 3). We then correlated these behavioural measures with total sleep time (minutes) and the time spent in Stage I, Stage II, SWS and REM sleep. All correlations were non-significant (*p* ≥ .071, uncorrected for multiple comparisons, see Table 4).

 The recognition and spatial TMR index measures (described above) were not significantly correlated with the mean number of full sound-set replays that took place during sleep (all correlations *p* ≥ .332).

[Table 4 here]

***Sound Discrimination***

All participants professed to having no knowledge of sound replay taking place during sleep and were unable to discriminate between the sounds that were replayed and those that were not (t (18) = 0.62, *p* = .546).

**Discussion**

We investigated how TMR in SWS influences the consolidation of emotional memories using a recognition paradigm. On account of previous work indicating that sleep selectively strengthens emotionally salient memory information (Hu et al., 2006; Wagner et al., 2001; Wagner et al., 2006) we predicted that the benefits of TMR for negative memories would outweigh those for neutral memories. In contrast to this hypothesis, we observed no benefit of TMR for the recognition of either emotionally negative or neutral pictures. Furthermore, we observed no benefit of TMR for recall of the screen locations in which pictures were presented at encoding. These null effects, taken in the context of several clear demonstrations of TMR in other memory paradigms (Oudiette et al., 2013; Rudoy et al., 2009; Cairney et al., 2016), suggest that recognition memory may not provide a sensitive measure of TMR benefits, although further research is necessary to confirm this interpretation.

***TMR and Recognition Memory***

Recent adaptations of the *Active Systems* model of memory consolidation propose that highly salient memories are preferentially reactivated and thereby strengthened during SWS, which may explain why sleep preferentially supports emotionally negative over neutral memories (Born & Wilhelm, 2012; Rasch & Born, 2013; Hu et al., 2006; Wagner et al., 2001; Wagner et al., 2006). From this perspective, the memory benefits of TMR may also be enhanced for emotional relative to neutral memories. This was first investigated by Cairney et al. (2014), who observed a reduction in retrieval response times for negative (vs. neutral) memories following auditory cueing in SWS. However, Cairney et al. (2014) did not observe the benefits of TMR for memory accuracy that are typically reported in TMR paradigms (Fuentemilla et al., 2013; Oudiette et al., 2013; Rudoy et al., 2009; Schreiner et al., 2015). This was possibly due to the experimental paradigm, which may have directed processing away from the central emotional salience to the spatial components of their task, preventing a benefit in emotional memory accuracy emerging. To address this issue in the current study, we employed a recognition paradigm that enabled the salient aspects of emotional stimuli to feature at the forefront of encoded representations. This approach also ensured compatibility between our findings and previous studies of sleep and emotional memory that have employed similar tasks (Hu et al., 2006; Sterpenich et al., 2007; Sterpenich et al., 2009). Nevertheless, we observed no impact of TMR on recognition memory, irrespective of emotional valence.

Unlike recall tasks that require individuals to actively retrieve information from declarative memory, recognition tasks involve re-exposure to target stimuli and thereby produce highly robust and durable memory performance across time (Standing 1973). The robust nature of recognition memory may have therefore prevented a benefit of TMR from emerging in the current study. The *Outshining* hypothesis (Smith & Vela, 2001) proposes that target items presented during recognition testing ‘outshine’ the benefits of other cues typically associated with memory enhancement (e.g. environmental context cues). From this perspective, re-exposure to target stimuli during post-sleep recognition testing, which lead to near ceiling levels of recognition accuracy, may have prevented a more subtle benefit of TMR from emerging in our data. Recognition paradigms may thus be unsuitable for studies investigating impact of TMR on sleep-dependent consolidation, particularly for those that involve the encoding of highly emotional memory representations.

In the context of a null effect it is worth considering whether some aspect of the design might reduce the sensitivity of the experiment to observe a significant effect. However, we do not believe the null effects observed in this study can be explained by methodological factors related to our study design. In accordance with previous studies that report effects of TMR, we adopted a nap paradigm, with participants obtaining ~85 minutes of sleep (Rody et al., 2009; Oudiette et al., 2013; Cairney et al., 2016). During this sleep period, we played sound cues to participants throughout the duration of SWS, resulting in each cue being presented multiple times (~3.81 presentations). Previous research suggests that the number of sounds replays is not important for benefits of TMR to emerge (Cairney et al., 2016) and in line with this suggestion, we do not observe a correlation between the number of replays and the benefit of TMR in this study. Furthermore, TMR benefits have been observed following the presentation of each cue only once during the sleep period (Rudoy et al., 2009; Creery et al., 2015), we therefore believe our sleep and replay protocol was sufficient to produce TMR benefits.

To provide further support for our interpretation of the null effect a post-hoc statistical power analysis was conducted with the programme G\*Power (Faul, Erdfelder & Lang, 2007). Based on the seminal study on auditory TMR from Rudoy et al., (2009) who compared reactivated to non-reactivated spatial memories, our power analysis used a Cohen’s effect size value of dz = 0.76 and a between measures correlation value of 0.81. For the simplest within-subjects TMR comparison and a sample size of 19, we observe a power estimate of 0.88, suggesting our study had sufficient power to detect a TMR benefit, had we adopted a typical TMR recall paradigm (Rudoy et al., 2009; Cairney et al., 2016). The suggestion that recognition memory provides an insensitive behavioural measure of TMR is supported by broader findings within the sleep literature, which report inconsistent behavioural benefits of sleep following tests of recognition (Diekelmann et al., 2009). We suggest that future studies addressing the impact of TMR on memory processing should adopt experimental paradigms that maximise sensitivity in order to detect behavioural benefits of TMR.

***TMR and Spatial Memory***

To investigate how TMR influences secondary spatial components of emotional memories, we also assessed whether auditory cueing in sleep impacted on recall for the screen locations where pictures were presented at encoding. In contrast to previous studies showing a benefit of memory cueing in sleep for spatial representations (Cairney et al., 2016; Oudiette et al., 2013; Rudoy et al., 2009) we observed no difference in location accuracy between the TMR and no TMR conditions. It is important to note, however, that location recall accuracy was not included in the criteria for TMR stimuli selection prior to sleep. We were therefore unable to control pre-sleep performance for locations that were subsequently cued or not cued in SWS, which may have prevented a TMR-memory benefit from emerging in our data. Of note, because pre-sleep spatial memory accuracy was particularly poor in the current study, TMR may have inadvertently strengthened inaccurate spatial representations.

 A second important difference between this and previous TMR studies is the measurement of spatial memory obtained. We used a four-alternative-choice paradigm to assess spatial memory accuracy. This is in contrast to very fine-grained measurements obtained in previous research, for example, Rudoy et al., (2009) measure the distance of spatial error in number of screen pixels. In consideration of this and recent work highlighting the impacts of memory accuracy on TMR (Cairney et al., 2016; Creery et al., 2015), further work is necessary to understand how spatial elements of newly-formed emotional memories are influenced by TMR.

***Conclusion***

We investigated the impact of TMR on emotional memory consolidation in sleep using a recognition memory paradigm. We observed no impact of TMR on the recognition of emotionally negative or neutral pictures and no impact on memory for the spatial locations associated with each image. We suggest that re-exposure to the target stimuli during recognition testing may have ‘outshone’ the memory benefits associated with cueing in SWS, preventing an impact of TMR from emerging in our data. Accordingly, future studies of TMR and emotional memory consolidation should adopt experimental paradigms that maximise the salience of affective stimuli while achieving a high level of test sensitivity.

**Tables**

**Table 1.** Mean number of hits, false alarms, correct rejections and misses for negative and neutral items at pre- and post-sleep recognition tests. Data presented as mean (± standard error).

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | Hits |  | False Alarms | Correct Rejections | Misses |
|  | R | K |  | R | K |
| Pre-Sleep |  |  |  |  |  |  |  |
| Negative | 41.47(± 3.15) | 14.00(± 2.71) |  | 0.32(± 0.13) | 0.58(± 0.21) | 58.74(± 0.27) | 4.16(± 1.02) |
| Neutral | 34.68(± 3.35) | 16.68(± 2.95) |  | 0.47(± 0.21) | 0.79(± 0.26) | 58.58(± 0.43) | 8.00(± 1.38) |
| Post-Sleep |  |  |  |  |  |  |  |
| Negative | 38.79(± 4.01) | 16.20(± 3.87) |  | 0.21(± 0.10) | 0.42(± 0.14) | 59.21(± 0.20) | 4.79(± 0.89) |
| Neutral | 34.63(± 3.79) | 18.21(± 3.50) |  | 0.26(± 0.10) | 0.79(± 0.21) | 58.63(± 0.33) | 6.53(± 1.29) |

**Table 2.** The proportions of remember (R), know (K) and new (N) responses in the post-sleep recognition test for items that were either replayed (TMR) or not replayed (no-TMR) during sleep. The TMR benefit was calculated by subtracting recognition rates for non-TMR items from TMR items. Data presented as mean (± standard error).

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | TMR |  | No-TMR |  | TMR Benefit |
|  | R | K | N |  | R | K | N |  | R | K |
| Negative | 0.68(± 0.07) | 0.27(± 0.07) | 0.05(± 0.01) |  | 0.67(± 0.07) | 0.27(± 0.07) | 0.05(± 0.01) |  | 0.005(± 0.02) | 0.001(± 0.02) |
| Neutral | 0.64(± 0.07) | 0.31(± 0.07) | 0.05(± 0.01) |  | 0.60(± 0.06) | 0.31(± 0.06) | 0.07(± 0.02) |  | 0.03(± 0.03) | -0.003(± 0.03) |

**Table 3.** Overall spatial memory in the pre- and post-sleep tests was calculated as the proportion of all correctly recognised items (those that received an R or K response) that were correctly located. Only items that were correctly recognised in both the pre- and post-sleep sessions were included in comparisons between conditions of TMR and no-TMR. The TMR benefit was calculated by subtracting recognition rates for non-TMR items from TMR items. Data presented as mean (± standard error).

|  |  |  |  |
| --- | --- | --- | --- |
|  | Overall Spatial Memory Accuracy |  | Replay Condition |
|  | Pre-Sleep | Post-Sleep |  | TMR | No-TMR |  | TMR Benefit |
| Negative | 0.42(± 0.03) | 0.38(± 0.03) |  | 0.35(± 0.03) | 0.38(± 0.03) |  | -0.03(± 0.02) |
| Neutral | 0.37(± 0.03) | 0.37(± 0.02) |  | 0.34(± 0.02) | 0.36(± 0.03) |  | -0.02(± 0.02) |

**Table 4.** Sleep stage data. Total sleep time (TST) and time spent in each stage of sleep (minutes) is presented. SWS – Slow-Wave Sleep, REM – rapid eye movement sleep. Data presented as mean (± standard error) along with correlational analysis between Stage II, SWS and REM sleep and the reported TMR benefit for recognition and spatial memory.

|  |  |  |
| --- | --- | --- |
|  |  | TMR – Benefit |
|  |  | Recognition Memory | Spatial Memory |
|  |  | Negative | Neutral | Negative | Neutral |
|  |  | R | K | R | K |
| Sleep Stage | Time (min) | r | *p* | r | *p* | r | *p* | r | *p* | r | *p* | r | *p* |
| Stage I | 16.63(± 1.60) | .22 | .37 | -.26 | .27 | -.03 | .91 | -.01 | .98 | .01 | .98 | -.21 | .39 |
| Stage II | 32.26(± 3.48) | -.18 | .47 | .11 | .66 | .11 | .64 | .10 | .69 | -.06 | .81 | -.18 | .47 |
| SWS | 29.32(± 2.86) | .24 | .32 | -.07 | .78 | -.21 | .38 | .02 | .93 | .01 | .96 | .31 | .19 |
| REM | 7.26(± 2.07) | .06 | .80 | .08 | .75 | .22 | .37 | -.42 | .07 | .40 | .09 | .17 | .49 |
| TST | 85.47(± 3.27) | .17 | .48 | -.13 | .61 | .06 | .81 | -.15 | .55 | -.32 | .18 | .09 | .72 |

**Figures**

**Figure 1.** Recognition accuracy (dʹ) for ‘Remember’ judgements (R) of emotionally negative and neutral pictures in pre- and post-sleep recognition tests. Error bars represent standard error of the means. Significant differences between stimulus types are indicated by asterisks, \*\*\* *p* <.001.

\*\*\*

**Figure 2.** Recognition accuracy (dʹ) for ‘Know’ judgements (K) of emotionally negative and neutral pictures in the pre- and post-sleep recognition tests. Error bars represent standard error of the means.

**Author Contributions**

JA, SC and GG conceptualised the study design. JA conducted the study and performed the statistical analyses. JA, SC and GG wrote the manuscript.

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