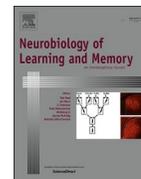




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Does memory reactivation during sleep support generalization at the cost of memory specifics?

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ABSTRACT

Sleep is important for memory, but does it favor consolidation of specific details or extraction of generalized information? Both may occur together when memories are reactivated during sleep, or a loss of certain memory details may facilitate generalization. To examine these issues, we tested memory in participants who viewed landscape paintings by six artists. Paintings were cropped to show only a section of the scene. During a learning phase, each painting section was presented with the artist's name and with a nonverbal sound that had been uniquely associated with that artist. In a test of memory for specifics, participants were shown arrays of six painting sections, all by the same artist. Participants attempted to select the one that was seen in the learning phase. Generalization was tested by asking participants to view new paintings and, for each one, decide which of the six artists created it. After this testing, participants had a 90-minute sleep opportunity with polysomnographic monitoring. When slow-wave sleep was detected, three of the sound cues associated with the artists were repeatedly presented without waking the participants. After sleep, participants were again tested for memory specifics and generalization. Memory reactivation during sleep due to the sound cues led to a relative decline in accuracy on the specifics test, which could indicate the transition to a loss of detail that facilitates generalization, particularly details such as the borders. Generalization performance showed very little change after sleep and was unaffected by the sound cues. Although results tentatively implicate sleep in memory transformation, further research is needed to examine memory change across longer time periods.

1. Introduction

Memory serves many functions in our daily lives. Two of those are recalling a specific event and generalizing across many instances to form a schema abstracted from prior knowledge. For example, a scuba diver may recall visiting the Great Barrier Reef and spotting a highly venomous stonefish resting on the reef's floor. This recollection is an example of a specific, highly detailed event memory. On the other hand, that same diver may see a similar fish while visiting the Solomon Islands, and based on shared characteristics like textured skin and spikey fins, hypothesize that it's a midget stonefish, smaller but equally venomous. This inference about the novel fish is an example of generalization. Memory researchers have long understood that these two types of

memory exist in parallel. However, an open question about these two types of memory, here called specific and generalized memory, is the degree to which they develop separately versus together in opposition with one another?

The complementary-learning-systems (CLS) approach tackles this question by ascribing the two types of memory to different brain circuits (McClelland & O'Reilly, 1995; O'Reilly & Norman, 2002; Schapiro, Turk-Browne, et al., 2017). In the CLS model, the hippocampus rapidly encodes unique, individual memories and distinguishes them from one another via pattern separation through sparse encoding (McClelland & O'Reilly, 1995; Schapiro, Turk-Browne, et al., 2017; Yassa & Stark, 2011). Then, over longer periods of time the cortex extracts shared features across many events to form a generalized memory. Generalized

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memory allows us to recognize relations between new experiences and past events to guide decision making in novel scenarios. This transformation of memory from specific to general has been studied using many paradigms, discussed further below, such as extracting hidden rules, creative problem solving, relational knowledge, and semantic category structure (Bejamini et al., 2014; Lerner & Gluck, 2019; Lutz et al., 2017; Schapiro, McDevitt, et al., 2017; Verleger et al., 2013). Several researchers have argued that the process of extracting regularities and forming generalized memories can occur throughout the day but is especially prevalent during sleep (Ellenbogen et al., 2006; Norman et al., 2005).

Memory consolidation processes that occur through sleep may be particularly important for transforming individual experiences into generalized memories. The process of stabilizing and integrating memories is referred to as memory consolidation. Memory consolidation is thought to rely on repeated reactivation of a prior memory, which is stabilized over time (Paller et al., 2020). Although it can be difficult to measure the neurophysiological interactions between the hippocampus and widespread neocortical regions engaged during memory consolidation, evidence is increasingly pointing to aspects of sleep as important for the consolidation process. Most relevant in the present context, sleep has been found to both protect specific memories and enhance generalization across memories to create schemas (Hanert et al., 2017; Marshall & Born, 2007; Bejamini et al., 2014; Inostroza & Born, 2013). In at least one case where researchers considered both specific and generalized memory over sleep and wake, a trade-off was observed between the two such that memory for specifics declined over sleep while generalization improved (Lau et al., 2011). However, there are interpretive issues in studies that compare periods of sleep to wake. Researchers often use delays of 10 h or more and rely on comparing overnight sleep to daytime wakefulness. This type of design leads to confounding differences in circadian factors such as attention and motivation (Murray et al., 2009; Valdez et al., 2005). Even if circadian factors are controlled, as in a nap study, interference from other learning typically is confounded between sleep and wake conditions, such that sleep benefits might arise merely from reduced interference in the sleep condition.

Rather than compare memory following periods of sleep versus wake, these interpretive shortcomings can be avoided by manipulating memory reactivation during sleep. Targeted memory reactivation (TMR) is an experimental tool that allows researchers to systematically manipulate memory reactivation and observe effects on consolidation (Oudiette & Paller, 2013). During learning, participants are exposed to an auditory or olfactory cue stimulus together with the information they are meant to learn, such as the locations of objects. During sleep, that cue is presented again in a manner designed to prevent rousing the participant to wakefulness. In many experiments, cues functioned to reactivate prior memories, such that on a later test after awakening participants produced better memory performance for cued compared to uncued information (see TMR meta-analysis by Hu et al., 2020).

Many of the earliest studies that established this TMR methodology focused on spatial memory (e.g., Rasch et al., 2007; Rudoy et al., 2009). A reasonable way to view these spatial TMR findings is that they represent improvement of detailed memories, because the higher accuracy found for cued compared to uncued objects required recall of specific locations in these spatial tests. Yet, spatial memory is only one of many types of memory that can be improved by cues presented during sleep. The recent literature shows that TMR can impact multiple subtypes of declarative memory (Hu et al., 2020), although the number of different memory paradigms that have been examined to date is still rather small. TMR has been used with several paradigms for assessing generalization memory, such as grammatical generalization, generalizing across emotional valence, and lexical competition (Batterink & Paller, 2017; Groch et al., 2016; Tamminen et al., 2017). These studies showed that TMR can be used to selectively improve generalization in these paradigms. However, there have been no studies using category

learning as a measure of generalization. It also remains unclear whether generalization improves in conjunction with the loss of detailed, specific memories. Our study thus addresses whether memory reactivation during sleep entails a trade-off between these two forms of memory. In the present study, we employ TMR as a tool for examining relationships between generalization and memory specificity during sleep consolidation.

Given our goal of understanding the possible relationship between a loss of memory details and the development of generalization, a paradigm is needed that can be used to measure both categorization and memory specificity. One such method involves naturalistic stimuli that can readily be categorized — paintings by different artists. In this case, generalization corresponds to the ability, developed after viewing many of an artist's paintings, to recognize that artist's style when confronted with a new painting. There are several advantages of examining memory for paintings. First, memory for specifics can be assessed in a straightforward way by asking participants whether they had seen a particular painting earlier in the experiment. Second, generalization memory can be assessed by showing new paintings and querying participants about which artist painted it, which conforms with a common sort of categorization knowledge. Third, we can construct these two tests so that they are similar in the level of performance produced and with the same baseline level (i.e., six-alternative forced-choice recognition, such that responding entirely randomly would yield a correct answer one out of six times on average). Fourth, we can be reasonably confident that the relevant learning took place during the experiment, given that participants are unlikely to have any knowledge of the works of art we selected. We thus adapted the procedures and paintings used in two prior studies of generalization learning (Kornell et al., 2010; Kornell & Bjork, 2008).

In the present study, we tested both types of memory using landscape paintings by six relatively unknown artists. Our aim was to evaluate whether memory reactivation during sleep altered specific or generalized memories. One test assessed the ability to recognize specific paintings and the other generalized knowledge of each artists' style with respect to new paintings. In a learning phase, participants viewed 36 paintings repeatedly and gradually became proficient at selecting the name of the corresponding artist when viewing each painting. We administered TMR during a nap that followed this learning, and we used electroencephalography (EEG) measures to ensure that cues were presented during slow-wave sleep (SWS). We hypothesized that generalization and memory specificity would be affected by memory reactivation during sleep in opposite directions, reflecting a trade-off between the two memory types (Witkowski et al., 2020).

2. Method

2.1. Participants

We enrolled 36 participants who were undergraduate students at Northwestern University or local community members. Data from seven participants were excluded: two failed to learn the sound-to-artist associations, one reported insomnia, one reported hearing sound cues during the nap, and three received no cues because they never reached SWS. Participants reported no history of neurological or sleep disorders. We requested that they wake up 2 h earlier than their usual wake time and abstain from caffeine on the day of the experiment. The Northwestern University Institutional Review Board approved the procedure and informed consent was obtained. The sample described here was comprised of 29 individuals (21 female, 1 non-binary, 7 male), they were right-handed except for one left-hander, and their mean age was 21.07 yrs.

2.2. Stimuli

The stimuli included 108 paintings by 6 different artists (18 paintings each). Four of these artists (Judy Hawkins, Philip Juras, Ron

Schlörff, George Wexler) were from the study by Kornell and Bjork (2008) and two (Richard McKinley & Jamie Grossman) were from the study by Noh, Bjork, and Preston (in preparation). The paintings depicted landscapes or skiescapes that were cropped to remove the artists' names. All but one participant claimed to be naive to the artists' names and all were naive to the paintings. For the learning and recognition portions, 72 paintings (12 by each artist) were divided vertically into 3 equal-sized sections, henceforth termed "slices."

In addition, we used six auditory stimuli, each 500 ms in duration (hoot, meow, thunder, applause, cricket, bell). Each sound was arbitrarily assigned to an artist, and the same sound-artist name pairings were used for all participants.

2.3. Procedure

Participants arrived at the lab between noon and 2 pm. They completed the Stanford Sleepiness Scale and then began the eight-phase study (Fig. 1a).

2.3.1. Sound-Name association training

Participants were instructed to learn the sound-name pairings for a later test. Participants heard each sound, and after a 500-ms delay, they saw the associated artist's name on the screen. The name remained for 500 ms, and then a "next" button appeared to signal participants that they could advance to the next pairing via a mouse click. The list of six sound-name pairings was presented three times, each time in a different random order.

2.3.2. Sound-Name association test

One sound was played through the speakers and participants had to select the corresponding artist name from a list of the six names. There was no time constraint on their selection. The participant was then shown the correct name. In this same way, forced-choice recognition of the entire list of six sound-name pairings was tested twice.

2.3.3. Learning

A series of painting slices appeared in a random order in the center of the screen above the six artist names (Fig. 1b). When each slice appeared, participants had 10 s to select the corresponding artist. After participants responded, they were shown the correct name, and the associated sound was played. Each block included six trials, each with one painting slice from each artist (and with the constraint that the other

two slices from the same painting were not shown in the learning phase). Each set of six painting slices was displayed five times per block, each time in a different random order. The learning phase included six blocks, each with unique painting slices, such that participants studied a total of 36 painting slices. Before the learning section began, participants were instructed that their memory would be tested for both the specific painting slice as well as their ability to generalize an artists' style.

2.3.4. Sound-name association Re-test

To verify that participants learned the sound-name associations, they were tested again. The procedure was the same as the Sound-Name Association Test, except the list of six pairings was tested once. Participants were required to correctly identify at least five of the sound-name associations in order to be included in the final analyses.

2.3.5. Pre-sleep memory tests

We then tested both generalization and memory specificity. The generalization test was always first (Fig. 1c). It included 18 whole paintings (3 by each artist) that were not previously seen either as slices or as a whole, nor were they ever shown again. One of these paintings was shown on each trial along with the six artist names (in a random order). Participants were instructed to select the artist they thought created the painting. They were allowed 10 s to respond and were not given feedback. Participants were not instructed to respond as quickly as possible on either of the tests.

In the memory specificity test (Fig. 1d), participants were tested on painting slices from the learning phase. On each trial, participants saw an array of six slices in two rows. Each row contained three slices, ordered from left to right such that participants could visualize the corresponding full paintings. The same artist created both paintings, which were similar, but one had never been seen before. Participants attempted to select the single slice that had appeared in the learning phase within 10 s; no feedback was given after their selection. There were 18 trials during the specificity test, 3 trials per artist, shown in a random order.

2.3.6. Sleep physiology

EEG, electro-oculogram, and electromyogram were recorded using a Neuroscan EEG system, with a sampling rate of 250 Hz and a bandpass of 0.1–100 Hz. Electrodes in a cap were located at 21 scalp locations from the 10–20 system (Cz, C3, C4, Fpz, Fp1, Fp2, Fz, F3, F4, F7, F8, Pz, P3, P4, T3, T4, T5, T6, Oz, O1, and O2). Additionally, electrodes were

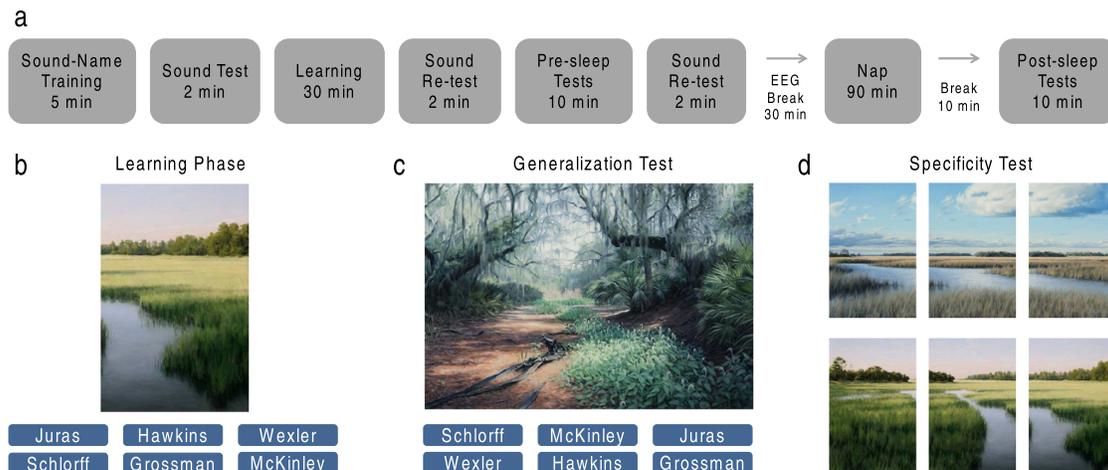


Fig. 1. Outline of the experimental organization. (a) Flowchart representing the phases of the experiment and approximate time of each phase. (b-d) Example trials from three phases of the procedure. (b) In the learning phase, participants viewed a painting slice and selected the artist's name. (c) In the generalization test, participants viewed a painting and selected the artist who painted it. (d) In the specificity test, participants saw six slices (from two paintings) and selected the slice they viewed during learning.

placed on the left and right mastoid, lateral to the right eye, below the left eye, and on the chin. Impedance was lowered for all electrodes (≤ 5 k Ω). EEG preprocessing was completed using the EEGLAB MATLAB package (Delorme & Makeig, 2004). Data were re-referenced to the averaged mastoids and excessively noisy scalp channels (7.2%) were interpolated using the spherical interpolation method in EEGLAB.

2.3.7. Nap

The futon chair used during most phases of the experiment was converted to a bed and covered with sheets, a pillow, and a blanket. White noise quietly played through speakers (around 35–40 dB), and participants were told they would have a 90-min nap opportunity. Sleep physiology was monitored online. When the experimenter estimated that the participant reached SWS for at least two 30-s epochs, half of the six sound cues were repeatedly presented in random order. The three cues were selected via an algorithm that sorted through all possible combinations of artists labeled as either cued or uncued. The algorithm then assigned the combination a value, denoting the difference in pre-sleep accuracy for both the generalization and specificity test. After iterating through all possible combinations, the algorithm produced the set of three cued artists that would have the smallest possible difference between cued and uncued for both tests. Each sound cue was 500 ms in duration with a 3500-ms interstimulus interval between the end of the previous cue and the start of the next. The sequence of sounds continued while the participant remained in SWS. If there was an arousal during SWS (as defined in the AASM scoring manual), cuing was paused and did not resume until at least two 30-s epochs of SWS occurred. After 90 min, participants were awakened if they weren't already awake. If the participant was still in SWS, the experimenter waited up to 15 min so that the participant could be woken from lighter sleep. After waking, participants were given a short break (approximately 10 min) to get water or use the restroom before beginning the post-sleep tests.

2.3.8. Post-sleep memory tests

The testing procedure was identical to that used with pre-sleep tests, but with different stimuli. Participants were first tested on 18 new paintings for generalization. In the memory specificity test, 18 painting slices from learning that weren't used in pre-sleep testing appeared together with new slices, always from the same artist. Additionally, participants completed the sound-name association test a final time.

2.3.9. Debriefing

Participants were asked whether they experienced any disturbances during the nap period. If they reported hearing a sound, they were asked to specify if it was one of the sound cues or another disruption. After completion of the final memory test, participants answered the Morningness-Eveningness Questionnaire. All participants were then paid for their participation.

2.4. Analyses

2.4.1. Behavior

We first conducted paired t-tests to verify that accuracy for cued and uncued artists were balanced before sleep. Next, we conducted two-way within-subjects ANOVAs with factors cuing (Cued, Uncued) and time (Pre-Sleep, Post-Sleep). These analyses were conducted separately for accuracy scores from generalization and memory specificity tests. All tests were two-tailed ($\alpha = 0.05$).

2.4.2. Sleep staging

Naps were scored offline using the sleep SMG package in MATLAB (<http://sleepsmg.sourceforge.net>). The 90-min nap was scored in 30-s epochs using scalp recordings from C3, Fz, Fp1, P4, and Oz, two eye channels (horizontal to the right eye, vertical to the left), and a chin-recorded EMG. To ensure accurate sleep scoring, an expert (D.G.) scored all sleep physiology data prepared without any indication of

when sounds were presented.

3. Results

3.1. Sleep

Polysomnographic scoring revealed time spent in each sleep stage, as shown in Table 1. Participants reported an average sleepiness rating of 3.21 ± 0.15 (SEM) on the Stanford Sleepiness Scale, where the scale ranges from 1 to 7 and smaller values indicate greater wakefulness. Participants also reported an average score of 42.82 ± 1.86 (range: 25–71) on the Morningness-Eveningness Questionnaire, indicating neither a preference for the morning nor evening. We found no significant correlations between time in each sleep stage and behavioral measures in the generalization and specificity tests.

3.2. Sound-name association accuracy

Participants were highly accurate at identifying the sound cues that matched each artist's name. Because there were 6 alternatives, chance-level recognition was 16.67%. On the three administrations of the sound-name association test, accuracy was $91.09\% \pm 5.30\%$, $96.55\% \pm 3.40\%$, and $96.55\% \pm 3.40\%$, respectively. By the last test, 26 out of the 29 participants recognized sound-artist associations with 100% accuracy and the other 3 selected the correct artist for five of the six sounds correctly.

3.3. Generalization performance

At pre-sleep memory testing, participants correctly identified the artists of novel paintings with $57.85\% \pm 2.87\%$ accuracy (range = 22.22–94.44%; chance = 16.67%). Pre- and post-sleep results are compared in Fig. 2a. Consistent with the goal of the stratification method for assigning artists to the two conditions, generalization accuracy did not differ between cued and uncued paintings prior to sleep, $t(28) = 0.72$, $p = 0.47$.

Next, we assessed the influence of TMR on the change in generalization accuracy from before to after sleep. There was no effect of TMR as reflected by the interaction of cuing and time (pre-post), $F(1, 27) = 0.01$, $p = 0.93$. Moreover, the mean change in generalization accuracy from pre-sleep to post-sleep, combined for cued and uncued conditions, averaged $1.72\% \pm 3.46\%$. This minor amount of forgetting was negligible, $F(1, 27) = 0.25$, $p = 0.62$.

3.4. Specificity performance

At pre-sleep testing, mean accuracy on the specificity test was $60.73\% \pm 2.37\%$ (range = 38.89% to 88.89%; chance = 16.67%). This level of accuracy exceeded 33%, which would be the accuracy expected if participants guessed after ruling out the three choices corresponding to the incorrect painting. Pre- and post-sleep results are compared in Fig. 2b. Consistent with the goal of the stratification method for assigning artists to the two conditions, specificity accuracy did not differ between cued and uncued paintings prior to sleep, $t(28) = 0.55$, $p = 0.59$.

We then assessed the influence of TMR on the change in specificity accuracy from before to after sleep. TMR differentially impacted performance as reflected by differences in cued and uncued conditions, $F(1, 27) = 5.77$, $p = 0.02$ (cuing \times time interaction). There was also an

Table 1
Time spent in each stage of sleep (min) across participants.

	Wake	N1	N2	SWS	REM
Mean	18.93	40.57	19.36	19.23	5.29
SEM	5.64	3.06	4.92	4.30	2.33

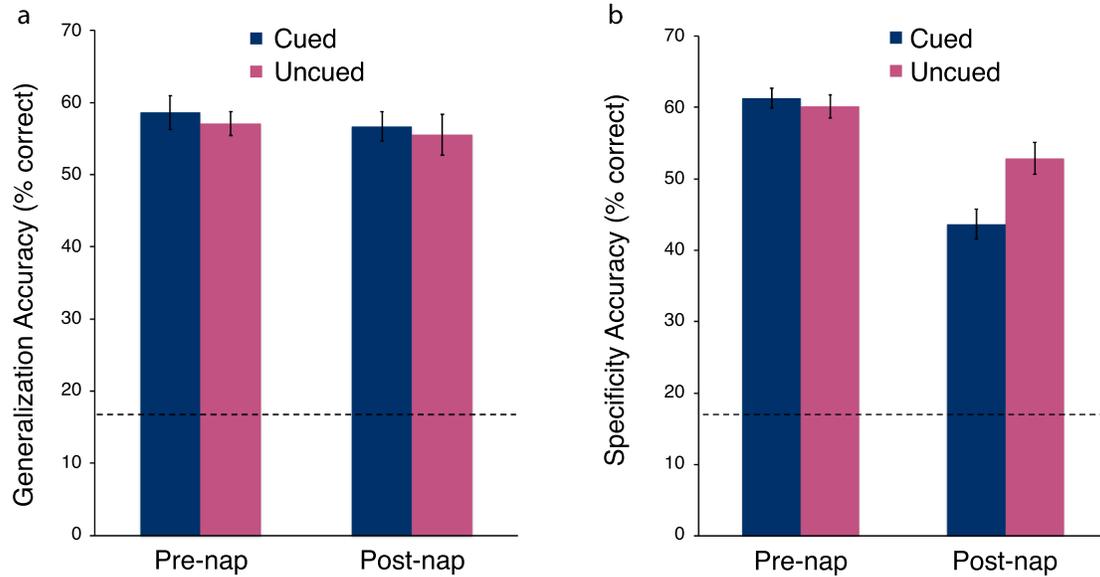


Fig. 2. Performance on the two memory measures. (a) Average percent correct on the generalization test for cued and uncued artists on pre-nap and post-nap tests. Dashed line represents chance performance (16.67%). Error bars show SEM. (b) Average percent correct on the memory specificity test for cued and uncued artists on pre-nap and post-nap tests. Dashed line represents chance performance (16.67%). Error bars show SEM.

overall decline in accuracy, $F(1, 27) = 32.55, p < 0.001$ (Cohen's $d = 0.25$), which measured $12.45\% \pm 2.18\%$ averaged across conditions. A larger decline was observed for cued paintings ($17.62\% \pm 2.84\%$) than for uncued paintings ($7.28\% \pm 3.28\%$; Cohen's $d = 0.08$).

We additionally considered a more lenient measure for memory specificity. Rather than asking if participants selected the correct slice, we examined whether participants selected a slice from the correct painting (regardless of whether that was the correct slice). At pre-sleep testing, mean accuracy on the lenient measure of the specificity test was $73.75\% \pm 2.13\%$ (range = 44.44% to 94.44%; chance = 50%). All but two participants exceeded the chance level of 50% accuracy, which would be the accuracy expected if participants guessed between the two paintings (regardless of slice). Although our stratification method did not assign artists to cued or uncued conditions based on this measure of performance, cued ($87.36\% \pm 2.06\%$) and uncued ($87.74\% \pm 2.03\%$) paintings were balanced at pre-sleep test [$t(28) = 0.13, p = 0.89$].

We then assessed the influence of TMR on the change in lenient accuracy from before to after sleep. TMR did not differentially impact performance as reflected by differences in cued and uncued conditions, $F(1, 27) = 0.11, p = 0.74$ (cuing \times time interaction). There was only an overall decline in lenient accuracy over time, $F(1, 27) = 15.95, p < 0.001$ for both cued ($78.93\% \pm 2.53\%$) and uncued ($80.84\% \pm 2.44\%$) conditions. The decline was $8.43\% \pm 3.20\%$ for cued whole paintings and $7.28\% \pm 3.27\%$ for uncued whole paintings.

3.5. Reaction times

Participants were not instructed to produce speeded responses, so there could have been idiosyncratic differences in speed across participants. However, we included an analysis to determine if TMR influenced speed of response. Overall, response times averaged $4.07\text{ s} \pm 0.19$ on the generalization test and $5.39\text{ s} \pm 0.22$ on the specificity test. Response speed did not differ between cued and uncued paintings prior to sleep in the generalization test [$t(28) = 0.55, p = 0.58$] or in the specificity test [$t(28) = 0.60, p = 0.55$]. Reaction times did not differ between TMR conditions across time (cuing \times time interaction) in the generalization test [$F(1, 27) = 0.62, p = 0.44$] or in the specificity test [$F(1, 27) = 1.69, p = 0.20$]. Finally, we tested whether reaction times across both

conditions (cued and uncued) changed from pre-sleep to post-sleep. In the generalization test, there was an increase in reaction time of $0.89\text{ s} \pm 0.17$ from pre-sleep to post-sleep, $t(28) = 2.85, p < 0.01$. There was no significant change in response speed in the specificity test, $t(28) = 0.78, p = 0.44$.

4. Discussion

In this study, we used targeted memory reactivation during sleep to test whether memory reactivation influenced two aspects of memory for paintings, generalization and memory specificity. Results showed that generalized knowledge of artists' styles a short time after learning was not affected by targeted memory reactivation, whereas detailed memory of individual paintings was selectively worsened. Our interpretation is that memory reactivation during sleep initiated a generalization process whereby some irrelevant details were lost (such as exact placement of features within the paintings or the exact way in which the landscape features were placed at the border of the painting), presumably in the service of ultimately extracting meaningful aspects of each painter's unique style. Loss of this detail made participants more likely to select one of the adjacent slices instead of the correct slice, which showed they remembered the painting at a general level but could not identify the exact section that they had previously viewed. Given this interpretation, this is the first study to link memory reactivation during sleep with a decline in memory specificity and thereby support the notion that sleep is operative for a beneficial process of memory transformation.

Our results may seem counter to previous TMR research, as the majority of findings show that cues produce only memory benefits (Hu et al., 2020). Here, on the specificity test administered after the nap, accuracy preferentially decreased for paintings by artists whose corresponding sound was presented during the nap. It is remarkable that participants performed worse on these specific paintings and did not even know that learning-associated sounds were presented while they slept.

A detrimental impact on memory could conceivably arise from various aspects of the TMR procedure. Some previous studies found that TMR was not helpful when cues occurred too closely together (Farthouat et al., 2017; Schreiner et al., 2015). In the present study, we attempted to

avoid potential interference of this sort by inserting a 3500-ms delay between consecutive cues. Another way in which TMR might disrupt memory is via sleep disruption. For example, TMR was found to negatively impact memory for cued items in an investigation of an at-home application of TMR (Göldi & Rasch, 2019). Memory accuracy decreased if participants reported that cues woke them or disrupted their sleep. Our participants did not complain of sleep disruption, although we did not obtain detailed self-reports. In a recent study of learning face-name associations, we used an electrophysiological method for assessing sleep disruption and found evidence linking sleep disruption with memory decline for cued information (Whitmore et al., 2021). In the present study, we conducted the same sort of analysis, focusing particularly on activity increases in the alpha band during the time after a cue. We found no evidence to link such electrophysiological signs of sleep disruption with memory effects on the specificity test.

Another possible explanation for TMR cues producing memory decline is that cuing a set of paintings with a single sound created interference. In other words, there could be a type of retrieval-induced forgetting, which typically occurs when rehearsal of some information leads to forgetting of other information that was originally learned at the same time (Perfect et al., 2004). For example, an artist sound may have preferentially reactivated one of the artist's paintings while simultaneously inhibiting the others, producing an overall memory decrement. Relatedly, we conducted another TMR study where each cue was associated with one, two, or six items in a spatial learning task (Schechtman et al., 2020). A similar memory benefit was found for these sets of cued items, regardless of set size. That is, six items cued by one sound showed the same spatial memory improvement as one item cued by one sound. The items of each set shared a categorical label (e.g., cats) and a semantically related cue (e.g., meow sound), apparently without interference among items in a set. Although a retrieval-induced forgetting mechanism may not account for the present results, we cannot rule out some interactions among memories that may have contributed to interference. In addition, the close temporal proximity of cues presented during sleep may have engendered some interference. Further studies are needed to explore such memory interactions, such as undertaken by Antony et al. (2018).

It may seem contradictory that TMR for some artists led to poorer recognition without a commensurate improvement in generalization. Our initial hypothesis that generalization would improve with TMR at the cost of lost specificity was only partially supported. Why wasn't a differential improvement in generalization for cued artists observed? Notably, previous TMR studies with spatial tasks generally show no absolute improvement above pre-sleep levels for cued items (Cairney et al., 2016; Creery et al., 2015; Rudoy et al., 2009; van Dongen et al., 2012). Rather, these studies typically show that cuing protects memories from forgetting. Because generalization performance didn't decrease after the nap for either cued or uncued artists, perhaps there was no opportunity for TMR to forestall forgetting. Changing the task by adding interference before test would increase difficulty and could have revealed an effect of TMR, as shown in prior research on sleep consolidation (Petzka et al., 2021). Future work should explore increasing the demands of the task, as well as comparing against a wake control group or other strategies to try to determine whether this form of generalization is sleep-dependent.

There have been other studies conducted using TMR to test generalization, although not with paradigms involving learning the artistic styles of different artists. Groch et al. (2016) studied a different form of generalization. They showed participants photos that could be interpreted either negatively or positively, and for each photo a spoken word was to be learned that disambiguated the situation depicted. Then, during overnight sleep, half of the words were presented. TMR improved the ability to recall the associated word when viewing the corresponding photo the next day, thus demonstrating a memory benefit. Generalization was assessed using new photos that each mapped onto one of the learned photos. The new photos were also ambiguous with regard to

valence. TMR biased ratings of these new photos in the direction corresponding to that of the word that had been associated with the learned photo (i.e., either positive or negative). The results thus suggest that memory reactivation during sleep-influenced generalization, perhaps through a spreading activation mechanism, although the results could also be explained by an indirect effect of retrieving the associated photo and then the associated word.

Abstraction of statistical regularities such as in a statistical learning task has sometimes been considered a form of generalization. One experiment conducted by Hennies and colleagues used an auditory statistical learning task to test whether memory reactivation led to an improvement in this form of abstraction (2017). Participants who received TMR during sleep performed worse than both the uncued sleep group and the wake group, perhaps supporting the conclusion that sleep negatively impacts generalization. However, meta-analyses on sleep studies that rely on extracting hidden statistical regularities show that results can vary widely based on the cognitive test used (Lerner & Gluck, 2019). We argue that identifying new paintings by a known artist does not represent the same kind of generalization as abstracting a rule such as in statistical learning. Indeed, with specific regard to Hennies' study, prior work shows the method of continuous cueing might have harmed the memory reactivation process. Specifically, Schreiner et al. (2015) demonstrated that immediate auditory stimulation after a cue abolishes the beneficial effect of TMR; this sort of disruption may have also been operative for Hennies et al. (2017).

Lexical competition, where a newly learned word competes with existing vocabulary, provides another experimental paradigm that touches on generalization. Slower reaction times are found to reflect greater competition between a newly learned word and its phonological neighbors, a sign of more lexical integration. Prior work has shown that lexical integration is impacted by sleep (Tamminen et al., 2010). In one experiment, researchers hypothesized that TMR would promote lexical integration of studied nonwords (Tamminen et al., 2017). Although they did not find a TMR effect on responses overall, they did find that TMR followed by a period of REM sleep improved integration. That is, participants high in REM sleep were preferentially slowed for cued compared to uncued words, presumably because the cued words were more integrated and therefore more confusable, producing slower judgments. The authors argued that activation of words cued during SWS were integrated during subsequent REM sleep. Together, these two studies hint that TMR may affect memory for multiple sorts of generalized knowledge.

In sum, the results obtained here expand knowledge of how memory reactivation during sleep may influence consolidation. Performance on the specificity test attests to the efficacy of the sounds presented during slow-wave sleep. Instead of producing no change in performance, sounds corresponding to specific artists were apparently effective in reactivating memories for individual paintings by those artists. Recognition memory, as assessed in a six-choice recognition test, declined for those specific paintings. Our explanation appeals to a natural tradeoff between memory specificity and generalization. In keeping with a few prior studies, we speculate that reactivation during sleep contributes to generalization, which in this paradigm entails dropping some of the details of a painting, such as where it has been cropped, in order to emphasize similarities among all the paintings by the same artist. Indeed, participants often made errors by selecting one of the other slides from the correct painting (perhaps reflecting a sort of boundary extension). Such a memory decline could promote generalization. Although the generalization test did not produce evidence to support this hypothesis, it may have been insufficiently sensitive to show an effect of memory reactivation. Future studies would benefit from a more sensitive test of generalization, perhaps with more artists to yield superior sensitivity to small changes. Alternatively, additional memory reactivation over many nights may produce larger effects. Indeed, generalization learning outside the lab often requires extended periods of time, not merely one short session. We conclude that memory

reactivation during sleep likely contributes to memory transformation as well as to preserving accuracy for select memories.

Credit authorship contribution statement

Sarah Witkowski: Conceptualization, Methodology, Investigation, Writing - original draft. **Sharon M. Noh:** Conceptualization, Writing - review & editing. **Victoria Lee:** Investigation. **Daniela Grimaldi:** Analysis, Validation. **Alison R. Preston:** Supervision, Writing - review & editing. **Ken A. Paller:** Conceptualization, Supervision, Writing - review & editing, Funding acquisition.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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