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Cueing vocabulary in awake subjects during the day has no effect on memory

Formation of long-term memories requires a phase of consolidation of the memory trace after their encoding [23]. During consolidation, initially instable memory traces are gradually stabilized involving several cascades of electrochemical and protein-synthesis-dependent processes [8, 24, 46]. In addition, numerous recent studies now provide evidence that several aspects of memory consolidation are optimally performed during off-line periods like sleep (see [34] for an overview). While different causal mechanisms have been discussed to underlie the memory function of sleep [10, 44], the active system consolidation hypothesis proposes that during sleep, memory traces are gradually strengthened and integrated into cortical long-term memory based on repeated and spontaneous hippocampal reactivations of newly acquired memories during non-rapid eye movement (NREM) sleep [6, 13, 42]. Importantly, the active system consolidation assumes that these processes are sleep specific and do not occur during post-learning wakefulness.

Numerous animal studies now provide evidence that memories are indeed spontaneously reactivated during NREM sleep ([25] for a review): firing patterns and sequential activity of hippocampal place cell activity in rodents observed during wakefulness consistently re-emerge during subsequent NREM sleep [26, 29, 45], frequently associated with characteristic hippocampal sharp-wave ripple (SW-R) events. Such reactivations processes acting during sleep also arise in various other memory-related brain regions (e.g., prefrontal cortex, ventral striatum [17, 32, 33]), occur in different species from songbirds to humans [22, 30], and appear to be sensitive to relevant and rewarded memories [19, 20]. However in rodents, hippocampal memory reactivations as well as SW-Rs have also been observed during quiet wakefulness after memory encoding [2, 18]. Furthermore, hippocampal replay also occurs during active behavior (e. g., before and after a new run in maze, [5, 15]) and reactivation-association SW-R during postlearning rest are predictive for later memory performance [9]. These results suggest that replay activity during wakefulness might be involved in recapitulation and anticipation of behavior and possibly also in subsequent memory consolidation.

In humans the functional significance of memory reactivations during sleep has been repeatedly demonstrated by cueing approaches termed as targeted memory reactivations [28]. In a first study by Rasch et al. [35], participants learned spatial locations while smelling an odor. During subsequent slow wave sleep (SWS) the odor was given again to trigger the reactivation of the associated memory trace. Re-exposure to the memory-associated odor during post-encoding SWS activated the hippocampus and improved recall performance tested after sleep. The beneficial effect of cueing memories by odors during NREM sleep on consolidation was confirmed in two further studies [7, 36]. In addition, several recent studies extended this finding by successfully using auditory cues like sounds or melodies to reactivate and strengthen individual memories during sleep [1, 11, 37, 38]. For olfactory cues, the beneficial effect of cueing appeared to be specific to sleep, as cueing during postlearning wakefulness had either no or even detrimental effects on memory stability [7, 35].

For auditory cues, results are less clear: While cueing of melodies during postlearning wakefulness did not improve motor memories [38], re-exposure to sounds during NREM sleep tended to improve memory for sound–place associations [27, 37]. Given further reports of the relevance of spontaneous wake replay for memory processes in humans [4, 12, 31, 40], it is still unclear whether the benefits of auditory cueing on memory consolidation are sleep-specific or similarly occur after cueing during postlearning wakefulness.

In a recent study [39], we showed that re-exposure to Dutch words during NREM sleep improved memory for the previously learned German translation. Verbal cues were presented during 3 h of nighttime sleep. To examine the sleep specificity of the effect, we examined two wake control groups: In the active wake group, verbal cues were presented again during performance of a working memory task, while cueing occurred during quiet resting without any task performance in the passive wake group. The 3 h wake retention interval occurred at the same time as the sleep interval in

Table 1 Baseline performance

	Preretention performance
Active waking	62.21 ± 2.67
Passive waking	60.31 ± 1.93
Sleep[a]	63.06 ± 2.50
Active waking[a]	60.70 ± 2.71
Passive waking[a]	58.17 ± 1.79

Data are means ± s.e.m; Numbers indicate absolute values of correctly recalled words before the retention interval; [a] indicates experimental groups derived from a previous study [39]

the sleep group to exclude circadian influences. In contrast to the sleep group, verbal cueing of Dutch words neither during active nor passive wakefulness after learning improved later memory for the foreign vocabulary. However, as participants stayed awake during nighttime, the ineffectiveness of cueing during wakefulness might alternatively be explained by increased tiredness of the participants in this study. To exclude tiredness as a confounding factor, we tested the effect of postlearning cueing of foreign vocabulary during active and passive daytime wakefulness. We hypothesized that cueing during waking does not improve memory consolidation, even when participants are well rested.

Materials and methods

Subjects

A total of 32 healthy, right-handed subjects (26 women, mean age 22.95 ± 0.36 years), whose native language was German and without Dutch language skills participated in the study. Thus, 16 subjects participated in each of the two experimental groups (i. e., active waking and passive waking group). Age and gender distribution did not differ between the experimental groups (both $P > 0.75$).

None of the participants were taking any medication at the time of the experiment and none had a history of any neurological or psychiatric disorders. All subjects reported a normal sleep–wake cycle and none had been on a night shift for at least 8 weeks before the experiment. On experimental days, subjects were instructed to get up at 7.00 h and were not allowed to consume caffeine and alcohol or to nap during the daytime. The study was approved by the ethics committee of the Department of Psychology, University of Zurich, and all subjects gave written informed consent prior to participating. After completing the whole experiment, participants received 60 Swiss francs (CHF).

Comparison with former study

As results of the present study will be later on compared to results obtained in a recent study [39], we additionally investigated potential differences between all five experimental groups included in the upcoming analysis concerning age, gender distribution, and preretention memory performance. There were no significant differences with regard to age and preretention memory performance (age: $F_{(4,76)} = 1.02$, $P = 0.41$; preretention memory performance: $F_{(4,76)} = 0.71$, $P = 0.588$). Gender distribution differed significantly between conditions ($F_{(4,76)} = 3.52$, $P = 0.01$), indicating that in the present study the gender distribution was less well balanced (26 women, 5 men) than in the experimental groups derived from the former study (24 women, 25 men). However, since we could not find any effect of gender on memory performance neither in the present study (preretention performance: $F_{(1,30)} = 0.09$, $P = 0.75$; cueing benefit score: $F_{(1,30)} = 0.23$, $P = 0.62$) nor in the former study (preretention performance: $F_{(1,47)} = 1.53$, $P = 0.22$; cueing benefit score: $F_{(1,47)} = 0.31$, $P = 0.57$), this limitation should not severely affect the comparability of results between groups.

With regard to our behavioral findings, we directly compared the results of the current study with the effects of word re-exposure during the night obtained in our previous study [39] using planned contrasts. Initially, the cueing benefit score (i. e., correctly recalled and cued words minus correctly recalled and uncued words) of the sleep group was compared to all other wake groups. Subsequently the sleep group's cueing benefit score was compared to both daytime waking groups as well as both nighttime waking groups and finally both daytime groups were directly compared with both nighttime waking groups (Table 1).

Design and procedure

In both experimental groups, the beginning of the learning phase was distributed over the entire day (9 a.m.–3 p.m.). All participants started with the vocabulary learning task (Dutch–German word pairs, for a detailed description see section Vocabulary learning task). The learning task was followed by a 3 h retention interval. During the retention interval, a selection of the previously learned Dutch words was presented again during active or passive waking for a total duration of 90 min (see below for a detailed description of the reactivation phase). After the retention interval, recall of the vocabulary was tested in both experimental groups.

Vocabulary learning task

The vocabulary learning task consisted of 120 Dutch words and their German translation, randomly presented in three learning rounds (please refer to the supplementary information of [39] for a list of all vocabulary pairs). Dutch words were presented aurally (duration range 400–650 ms) via loudspeakers (70 dB sound pressure level). In the first learning round, each Dutch word was followed by a fixation cross (500 ms) and subsequently by a visual presentation of its German translation (2000 ms). The intertrial interval between consecutive word pairs was 2000–2200 ms. The subjects were instructed to memorize as many word pairs as possible.

In a second round, the Dutch words were presented again followed by a question mark (ranging up to 7 s in duration). The participants were instructed to vocalize the correct German word or to say, "next" (German translation: "weiter"). Afterwards, the correct German translation was shown again for 2000 ms, irrespective of the correctness of the given answer. In the third learning round, the cued recall procedure was repeated without any feedback of the correct German translation. Recall performance of the

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Abstract

Background. It is assumed that the beneficial effect of sleep on memory relies on spontaneous reactivation of memories during sleep. We recently showed that reactivation by re-exposure to previously learned foreign vocabulary cues during sleep benefits vocabulary learning. Cueing foreign vocabulary during active or passive wakefulness at night did not improve memory, suggesting that memory benefits of cueing are specific to sleep. However, the ineffectiveness of cueing during wakefulness might also be explained by increased tiredness of the participants in this former study.
Objectives. To exclude tiredness as a confounding factor, we tested the effect of vocabulary cueing during active and passive daytime wakefulness. It was hypothesized that cueing during waking does not improve memory consolidation, even when participants are well rested.
Methods. A total of 32 subjects learned 120 Dutch–German word pairs. During a 3 h retention interval, parts of the previously learned Dutch words were replayed. Subjects of the active waking group ($N = 16$) were distracted from hearing the Dutch words by an n-back task, while subjects of the passive waking group ($N = 16$) were not distracted. After the retention interval, memory for word pairs was tested by a cued recall.
Results. Replay of Dutch words during daytime wake did not improve later memory for the German translation in either of the waking groups. We observed no difference in recall performance between cued and uncued words, neither in the active waking nor in the passive waking group.
Conclusion. Cueing Dutch words during wakefulness does not exert beneficial effects on memory, even when subjects are well rested and under full control of their cognitive capacities. This result gives further evidence that the beneficial effects of cueing are solely specific to sleep.

Keywords

Sleep · Memory reactivation · Vocabulary · Memory training · Long-term memory

Die Reaktivierung von Vokabeln an wachen Personen am Tag hat keinen Einfluss auf die Gedächtnisleistung

Zusammenfassung

Hintergrund. Es wird angenommen, dass die förderliche Wirkung von Schlaf auf die Gedächtniskonsolidierung auf spontanen Reaktivierungen zuvor gelernter Inhalte beruht. Wir konnten bereits zeigen, dass das Wiederabspielen zuvor gelernter holländischer Vokabeln im Schlaf zu einer verbesserten Gedächtnisleistung führt. Da dasselbe Vorgehen in einer aktiven und einer passiven Wachgruppe während der Nacht zu keiner Gedächtnisverbesserung führte, wurde die gedächtnisförderliche Wirkung des Wiederabspielens als schlafspezifisch interpretiert. Die fehlende Wirkung im Wachzustand könnte aber auch auf die erhöhte Müdigkeit der Versuchspersonen zurückzuführen sein.
Ziel der Arbeit. Um Müdigkeit als konfundierenden Faktor ausschließen zu können, wurden in der vorliegenden Studie die Effekte des Wiederabspielens zuvor gelernter holländischer Vokabeln während des Tages erfasst. Die Hypothese war, dass das Wiederabspielen im Wachzustand nicht zu einer Verbesserung des Gedächtnisses führt, selbst wenn die Probanden ausgeruht sind.
Material und Methoden. 32 Versuchspersonen lernten 120 deutsch-holländische Wortpaare. Während einer 3-stündigen Konsolidierungsphase wurden ihnen ein Teil der zuvor gelernten holländischen Wörter wieder vorgespielt. Versuchspersonen der aktiven Wachgruppe ($N = 16$) führten während des Hörens der Wörter eine n-Back-Aufgabe durch, während Versuchspersonen der passiven Wachgruppe ($N = 16$) nicht abgelenkt wurden. Im Anschluss wurde die Gedächtnisleistung für alle holländisch-deutschen Wortpaare geprüft.
Ergebnisse. Das wiederholte Abspielen der holländischen Wörter verbesserte nicht die Gedächtnisleistung für die deutschen Übersetzungen, weder in der aktiven noch in der passiven Wachgruppe.
Diskussion. Auch wenn Probanden ausgeruht sind, führt das Abspielen von holländischen Vokabeln zu keiner gedächtnisförderlichen Wirkung. Dieses Ergebnis ist ein weiterer Beleg für die Schlafspezifität der gedächtnisförderlichen Wirkung von Reaktivierungen auf die Gedächtnisbildung.

Schlüsselwörter

Schlaf · Gezielte Gedächtnisreaktivierung · Vokabeln · Gedächtnistraining · Langzeitgedächtnis

third round (without feedback) was taken as preretention learning performance.

In the third round, participants recalled on average 62.41 ± 1.71 words (range 44–84 words) of the 120 words correctly, indicating an ideal medium task difficulty (recall performance 52 %) without any danger of ceiling or floor effects. We observed no difference in preretention memory performance between the two experimental groups (main effect of "group": $F_{(1,30)} = 0.57$; $P = 0.45$), no difference in preretention memory performance between later cued and uncued words (main effect "cueing": $F_{(1,30)} = 0.77$; $P = 0.38$) and no interaction between "group" and "cueing" ($F_{(1.30)} = 0.47$; $P = 0.49$; see Table 2 for descriptive statistics).

Reactivation of vocabulary

During the 3 h retention interval, Dutch words were presented aurally without the German translation. The presentation occurred via loudspeakers (50 dB sound pressure level). Of the 120 words learned before the retention interval, 60 words were cued and 60 were not cued during the subsequent retention

Table 2 Overview of memory performance

		Cued	Uncued	*t*	*P*
Active waking group					
Cued recall	Learning	30	32.62 ± 2.67	−0.98	0.34
	Retrieval	26.62 ± 0.76	27.56 ± 2.02	−0.54	0.59
	Change	−3.37 ± 0.71	−4.43 ± 1.06	0.85	0.41
	% Change	88.75 ± 2.54	86.61 ± 3.55	0.51	0.61
Recognition	Hits	49.50 ± 0.88	48.81 ± 1.58	0.64	0.53
	% Hits	82.50 ± 1.48	80.35 ± 2.64		
	d′	2.01 ± 0.15	2.02 ± 0.16	−0.12	0.89
Passive waking group					
Cued recall	Learning	30	30.31 ± 2.01	−0.15	0.86
	Retrieval	26.50 ± 0.92	26.68 ± 1.65	−0.12	0.90
	Change	−3.50 ± 0.92	−3.43 ± 1.00	−0.04	0.96
	% Change	88.33 ± 3.08	89.21 ± 2.73	−0.19	0.84
Recognition	Hits	48.31 ± 1.07	46.75 ± 1.49	1.02	0.32
	% Hits	80.52 ± 1.79	77.91 ± 2.49		
	d′	1.61 ± 0.11	1.53 ± 0.11	0.66	0.51

Data are means ± s.e.m; Numbers indicate absolute or relative values of correctly recalled or recognized words that where presented during the retention interval (cued words, 60 in total) or not (uncued words, 60 in total). For cued recall testing, number of correctly recalled words during the learning phase before and the retrieval phase after the retention interval are indicated. Change (% Change) refers to the absolute (relative) difference in performance between learning and retrieval phases. Hits (%Hits) refers to the absolute (relative) number of correctly recognized words as "old" (since %Hits = Hits * 100/60, statistics are redundant). The sensitivity measure d′ reflects recognition performance according to signal detection theory based on the proportion of Hits and False Alarms [21]

interval. The 60 cued words consisted of 30 words that participants remembered during the preretention learning phase (cued hits) and 30 words that participants did not remember before the retention interval (cued misses). The words were individually and randomly chosen for each participant using an automatic MATLAB algorithm. In addition, 30 new words were presented during the retention interval that had not been included in the preretention learning list, serving as control stimuli. Thus, in total 90 Dutch words were presented during the retention interval. Presentation occurred every 2800–3200 ms in a randomized order for a total of 90 min, resulting in 10–11 exposures to each word.

In the active waking group, cueing of Dutch words occurred during performance on a computerized n-back task. The 3 h wake retention interval was divided into 30 min periods. In the first, third, and fifth 30 min period, participants performed on the n-back task (including a total of 27 blocks for 67 s of 0-back, 1-back and 2-back blocks, in a randomized order, for more details see task description). Subjects were instructed to focus on the task and were given feedback on accuracy after each 30 min period. While subjects accomplished the n-back task, Dutch words were replayed. Between the three blocks of word reactivation, subjects completed questionnaires and played an online computer game (bubble shooter).

In the passive waking group, Dutch words were replayed during passive waking of the participants, allowing full attention on the replayed Dutch words. Participants were re-exposed to the Dutch words in the first, third and fifth 30 min period of the 3 h retention interval. They were instructed that they would hear some of the Dutch words again and should attentively listen to the words. In the remaining 30 min periods, the participants performed on the n-back task and filled out questionnaires, without any auditory stimulation.

Recall of vocabulary after the retention interval

During retrieval, the Dutch words were presented via loudspeaker in a randomized order. In addition to the 120 words which were learned before the retention learning, the 30 control words from the reactivation phase and 30 entirely new words were tested. Initially participants had to indicate whether the word was old (part of the learning material) or new. If the current word was recognized as old, subjects were asked to vocalize the German translation.

As an index of memory recall of German translations across the retention interval, we calculated the percentage of correctly recalled words at retrieval relative to correctly recalled words at learning, with the level of learning set to 100 %.

For recognition memory of Dutch words, we calculated the sensitivity index *d'* (i. e., hits/true positives – false positives/true negatives) according to signal detection theory. Proportions of 0 and 1 were replaced by $1/(2N)$ and $1-1/(2N)$, respectively, with N representing the number of trials in each proportion (i. e., $N = 60$, see [21]). The memory indices for cued recall and recognition were calculated separately for cued and uncued words (**Fig. 1**).

n-Back test

Subjects of both waking groups accomplished intermixed 0-, 1-, and 2-back versions of the n-back working memory task [14]. In this task different letters appear successively in the center of the screen. In the 0-back version subjects had to press a key whenever the letter *x* appeared on the screen. In the 1-back version subjects had to respond to a letter repetition (h-f-**f**-k), while the 2-back version requires subjects to respond to a letter repetition with one intervening letter (h-f-s-**f**; **Fig. 2**).

Results

Effects of verbal cueing during wake on cued recall performance

As expected, re-exposure to Dutch words after learning during daytime wakeful-

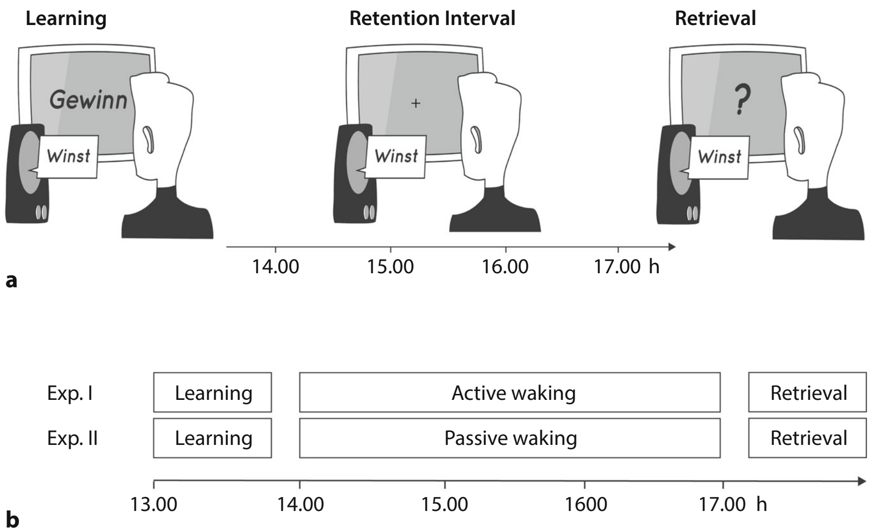

Fig. 1 ▲ Experimental procedure. **a**, **b** Participants studied 120 Dutch–German word pairs during the daytime. During the retention interval, 90 Dutch words (30 prior remembered, 30 prior not remembered, and 30 new words) were repeatedly presented. Cueing of vocabulary occurred during performance of a working memory task (active waking), or during rest (passive waking). After the retention interval, participants were tested on the German translation of the Dutch words using a cued recall procedure

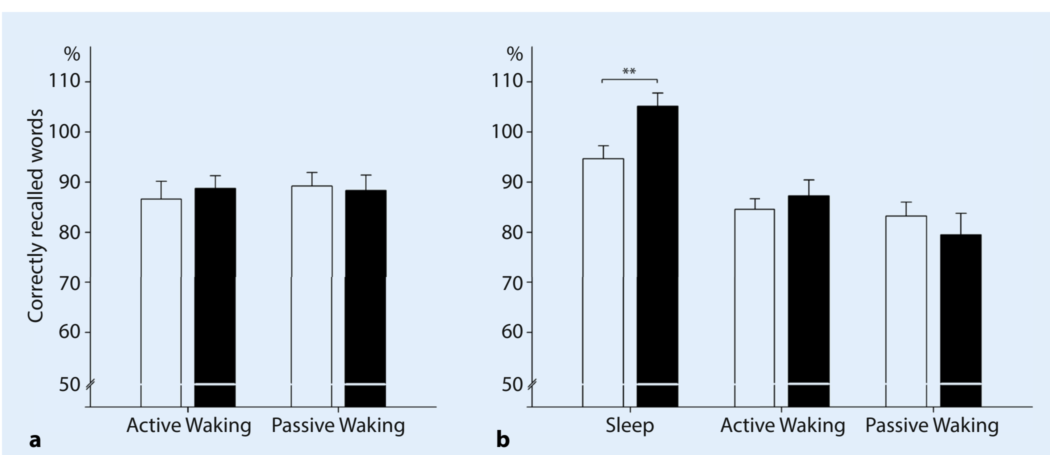

Fig. 2 ▲ Behavioral results. **a** No enhancing effects of cueing during daytime on later memory retrieval occurred in both waking groups. Memory for cued word pairs (*black bar*) did not differ from uncued pairs (*white bar*). **b** This figure was adopted from [39] illustrating the behavioral results of cueing during sleep and nighttime waking. In the sleep group, memory for cued word pairs (*black bar*) was significantly improved when compared with uncued pairs (*white bar*). No enhancing effects of cueing on later memory retrieval occurred in both waking control groups. Additionally planned contrasts revealed that the beneficial effects of cueing on memory during sleep differed significantly from both daytime waking groups as well as both nighttime waking groups. Retrieval performance is indicated as percentage of recalled German translations with performance before the retention interval set to 100 %. Values are mean ± SEM. $^{**}P \leq 0.01$

ness did not improve later memory for the German translation in either of the waking groups. Overall after cueing during daytime wakefulness, participants recalled 88.54 ± 1.96 % of the cued words and 87.91 ± 2.21 % of the uncued words (main effect of "cueing": $F_{(1,30)} = 0.041$; $P = 0.84$; please note that the retrieval performance is indicated as percentage of recalled German translations with performance before the retention interval set to 100 %). The effect was similarly lacking after re-exposure to Dutch words during active as well as passive waking (no interaction between "cueing" and "group"; $F_{(1,30)} = 0.23$; $P = 0.62$, ◘ **Table 2** for descriptive values). In order to elucidate potential influences of the time of day on the behavioral results, we correlated the onset time of the experiment with the preretention performance and the cueing benefit score. Both correlations remained nonsignificant (preretention performance: $r = -0.05$, $P = 0.77$; cueing benefit score: $r = -0.26$, $P = 0.14$), safely excluding potential timing influences.

In addition, we directly compared the results of the current study with the effects of word re-exposure during the night obtained in our previous study [39]. In order to assess the influence of different brain states (i. e., wake–sleep), we conducted planned contrast on a cueing benefit score (i. e., correctly recalled and cued words minus correctly recalled and uncued words). In a first step, the sleep group was compared to all other wake groups. The benefit score of the sleep group differed significantly from the overall wake group score ($t_{76} = 2.75$; $P = 0.01$), indicating a general sleep specificity concerning the beneficial effects of cueing. Furthermore, the sleep group's cueing benefit score was compared to both daytime waking groups as well as both nighttime waking groups in order to prove that the beneficial effects of cueing during sleep differ from waking effects irrespective of day- and nighttime, respectively. Again the benefit score of the sleep group differed significantly from the waking groups score, both for the daytime waking groups ($t_{76} = 2.17$; $P = 0.03$) and for the nighttime waking groups ($t_{76} = 2.68$; $P = 0.01$). Thus, regardless of whether cueing happened during daytime or nighttime waking, the beneficial effects were dependent on sleep. To further demonstrate that cueing during wakefulness has no beneficial effect on memory irrespective of day-/nighttime we directly compared both daytime groups with both nighttime waking groups. As expected the benefit score did not differ ($t_{76} = 0.17$; $P = 0.89$), further demonstrating that the lacking effect of cueing during wakefulness is not dependent on the time of day (**Table 2**).

Effects of verbal cueing during wake on recognition memory

As with the results concerning the cued recall, re-exposure to Dutch words did not have any effect on recognition memory in either waking group. There was no difference in recognition performance between cued and uncued words ($d' = 1.70 \pm 0.15$ vs. $d' = 1.68 \pm 0.14$; main effect of cueing: $F_{(1,30)} = 0.21$; $P = 0.64$). In addition, no interaction between "cueing" and "condition" ($F_{(1,30)} = 0.37$; $P = 0.54$; see **Table 2** for descriptive statistics and absolute values) was observed. Thus, recognition memory performance was also unaffected by the cueing procedure.

In addition, we explored whether the presentation of new words during the retention interval resulted in deteriorated recognition performance as compared to memory performance for the entirely new words, which were presented during recognition testing for the first time. As one might expect, presentation of new words during the retention interval worsened recognition memory (cued new words % Hits: 73.02 ± 2.62; entirely new words % Hits: 83.64 ± 2.81; $t = -5.21$, $P < 0.001$).

In our previous study [39], cueing did not affect recognition performance either for the sleep group or the two nighttime wake groups. In addition, when including the current two daytime wake groups, none of the calculated planned contrasts reached significance (all $P > 0.28$), indicating that effects of cueing on recognition performance were not altered by the circadian time of the retention interval.

Discussion

In this study, we show that cueing foreign vocabulary during a wake retention interval after learning has no beneficial effect on recall performance, when cueing takes place during rested wakefulness. Our current findings are in line with results of our recent study [39], indicating that cueing Dutch vocabulary during the retention interval improves recall of the newly learned German translations only when cueing occurs during postlearning sleep, but not during postlearning wakefulness. Importantly, in our former study participants had to stay awake during the night, which might have prevented positive effects of cuing due to the potential participants sleepiness. In this study, it was demonstrated that cueing memories during wakefulness during the day is still ineffective, even when participants are well rested and at the height of their cognitive capability.

Furthermore, the availability of attentional resources had no bearing on the obtained results since unattended (active wake group) as well as attended cues (passive wake group) failed to improve later recall performance. The missing effect of cueing during wakefulness is well in line with the active system consolidation hypothesis [34], which assumes that the enhancing effect of sleep on memory consolidation critically relies on spontaneous memory reactivations during sleep. The model posits that the state of NREM sleep offers ideal conditions for a strengthening of memories after their reactivation, due to the presence of slow oscillations, sleep spindles, a minimal cholinergic tone, and the exclusion of external interference (see also [3, 7]). In contrast, memory reactivations during wakefulness are ineffective in strengthening memories due to the absence of the above mentioned factors, or possibly even render already consolidated memories again into a labile state as proposed by the reconsolidation theory [34].

Evidence for the assumption that reactivations during sleep play a functional role for strengthening memories during sleep is provided by a constantly growing number of experiments demonstrating that increasing reactivation during sleep by cueing improves later memory recall after sleep [28]. However, the assumption of a sleep-specific role of reactivations for memory consolidation is less clear. Several studies in rodents have shown that replay of hippocampal place cells occurs similarly during quiet waking of the animal as well as before and after task performance during wakefulness [25]. In addition, a growing number of recent studies using functional magnetic resonance imaging (fMRI) [4, 31, 43] reported spontaneous reactivations of learning-related activity during waking rest, which are predictive for later memory performance. Thus, spontaneous memory reactivations exist during wakefulness, and they might even be involved in the process of memory consolidation during wakefulness.

In support for a functional role of reactivations during postlearning wakefulness, one afternoon nap study by Oudiette et al. [26] reported beneficial cueing effects during waking. In this experiment participants had to learn an object location task, where each object was presented in parallel with a characteristic sound. Furthermore, each object belonged to a high value or a low value category, indicating subsequent payoff. During a subsequent retention interval either of sleep or wakefulness, parts of the low value sounds were replayed again. Here cueing memories exerted a beneficial effect on subsequent memory performance, when cueing took place during wakefulness, while participants performed a working memory task. In contrast to this finding, most other studies (including our own) using targeted memory reactivation did not observe memory benefits after cueing during postlearning wakefulness. Thus, it might be possible that the reported cueing benefit during wakefulness reported by Oudiette et al. is linked to specific features of the task used in this study. For example, the expectancy of reward might have increased the beneficial effects of targeted memory reactivation, as reward-associated memories are preferentially reactivated [19, 20, 33]. Future studies will be needed to determine whether reward expectancy is critical for cueing benefits on memory consolidation during post-learning wakefulness.

Conclusion

Our results add evidence to the notion that the benefits of memory reactivations for memory strength and later recall are sleep specific and do not occur during nighttime or daytime wakefulness. Furthermore, recent studies also indicate that targeted reactivations during REM sleep are similarly ineffective [3, 41], suggesting that reactivations strengthen memories exclusively during NREM sleep. Thus, even though memory reactivations might occur during passive and active wakefulness as well as NREM and REM sleep, the consequence for memory strength seems to differ between these brain states. The reasons and underlying mechanisms why only reactivations during NREM sleep strengthen memories are still not completely understood. The absence of external interfering input as well as the occurrence of slow waves and sleep spindles are probably necessary conditions for a strengthening effect of reactivations on memories. In addition, the low cholinergic tone characteristic for NREM slight might be a prerequisite for disinhibiting hippocampal–neocortical feedback loops [16], allowing successful integration and strengthening of reactivated memories into cortical knowledge networks. However, further studies will have to identify the underlying neural mechanisms and critical factors of the beneficial role of reactivation during NREM sleep on long-term memory formation.

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Compliance with ethical guidelines

Conflict of interest. T. Schreiner and B. Rasch state that there are no conflicts of interest.

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975 (in its most recently amended version). Informed consent was obtained from all patients included in the study.

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Die DGIM in der Zeit des Nationalsozialismus

„Die Deutsche Gesellschaft für Innere Medizin ist beschämt, weil sie 70 Jahre hat verstreichen lassen, bis ihr Handeln in der Zeit des Nationalsozialismus wissenschaftlich untersucht und öffentlich gemacht wurde", verlas Prof. M. Hallek zur Eröffnung der Ausstellung zur Geschichte der DGIM in der NS-Zeit. Die Fachgesellschaft bekennt sich zu ihrer Verantwortung und arbeitet ihre Vergangenheit auf. Erste Ergebnisse präsentierte sie auf dem 121. Internistenkongress in Mannheim. Aufgrund des großen Interesses stellt sie diese nun als Wanderausstellung zur Verfügung.

„Es war uns als Vorstand der DGIM ein Anliegen, in einer Erklärung die Sicht der Fachgesellschaft auf die Ergebnisse der Nachforschungen in der Historie der DGIM darzulegen", betont Prof. U.R. Fölsch, Generalsekretär der DGIM aus Kiel. In dem Dokument drückt die Fachgesellschaft ihre Missbilligung der Anpassung einzelner Mitglieder an das Unrechtsregime aus. Sie verurteilt darin die Vertreibung von Kolleginnen und Kollegen jüdischer Herkunft ebenso wie die Misshandlung und Tötung von Menschen in Konzentrationslagern, Lazaretten und Kliniken.

Einige an NS-Unrecht Beteiligte sind in der Nachkriegszeit zu Ehrenmitgliedern der DGIM ernannt worden. „Diese Ernennungen sind keinesfalls zu billigen", betont Prof. Fölsch. Dennoch sieht die Fachgesellschaft laut Erklärung von der rückwirkenden Aberkennung jener Ehrenmitgliedschaften ab, um deutlich zu machen, dass im historischen Bewusstsein bleiben soll, welche Verfehlungen Mitglieder der DGIM im Nationalsozialismus begangen haben.

Quelle: Deutsche Gesellschaft für Innere Medizin (DGIM) e.V., www.dgim.de