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Consolidating skill learning through sleep

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Skill learning depends on retaining memories of skill-use experiences over time. These memories need to be robust against interference and therefore depend on consolidation. Further, skills must generalize beyond the learning experiences to be useful in novel but related situations. We review the role of sleep in the consolidation of skill learning, along with research findings that sleep: (1) reduces the effects of interference on skill learning, (2) protects against future interference with skill learning, (3) aids in the abstraction and generalization of skill learning. We discuss theories of sleep consolidation in terms of putative neural mechanisms and describe the key paradigms and questions in sleep research.

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Introduction

We sleep (if lucky) for a substantial portion of our lives, but the role of sleep in mind and biology is still not well understood [1]. Although there has been a longstanding interest in the role of sleep in learning, ranging from studies of frozen cockroaches [2] to soccer skills [3] to studies of dreaming (cf. [4]), there are many unanswered questions, such as how sleep aids learning and memory. One of the primary theories of learning and memory is that the learning of one thing makes it harder to learn something different but similar afterwards, and learning something new can interfere with the prior learning — called proactive and retroactive interference (see [5]). Although both proactive and retroactive interference can be classified as either informational (via the overlap of content: A maps to B and A also maps to C) or processing oriented (via mental exertion or memory formation) [5], for the purposes of the present discussion such a distinction is less relevant than the recognition that (1) prior learning and subsequent experiences can have adverse effects on learning a task and (2) that sleep plays a role in mitigating such interference [6]. However, it has been demonstrated that conscious framing — i.e., the way the participant understands the task or expectations about the task — can affect both interference effects in motor sequence learning and sleep consolidation [7]. Understanding the mechanisms of interference may ultimately be linked to a clearer understanding of sleep consolidation.

An early view of the function of sleep is that it aids memory passively, simply because sleeping reduces opportunities for interference from subsequent experience via the lack of consciously directed activity [8]. Research rejected this simple view of sleep (e.g., [9]) and replaced it with an alternative view that sleep actively consolidates memories [10]. However, there are new theories proposing different possible mechanisms operating during sleep to protect or consolidate memory [11]. One broad neural network view holds that sleep operates to consolidate immediate encodings of experience based on some specific brain regions (e.g., hippocampus) into more stable neocortical representations [12] whereas other theories focus on changes in the synaptic connections among neurons [13].

A paradigmatic shift from the historical focus on explicit memories encoding information about specific events or experiences (remembering word lists or lunch yesterday) to more implicit memories demonstrating learned performance, such as playing golf or piano [14] has been important to understanding the role of sleep in learning. As in other approaches to memory research such as neuropsychological patients like HM [15] or non-human animal research [16] the distinction between declarative memory (i.e., describable) and procedural or non-declarative memory (i.e., skill learning, task learning) has provided different kinds of results. This shift from explicit memory for experiences to non-verbal procedures (e.g., perceptual discrimination, motor sequences) however, has changed a number of aspects of the learning situation. These aspects primarily arise because procedural or non-declarative memory tasks marked a shift from learning many things (e.g., lists of words) to learning a single simple task (e.g., repeated finger movements [17] or a single visual pattern discrimination [18]). Given that non-verbal, procedural skills like tennis or telegraphy develop from experiences over time — over days or even years

[19], memories of these experiences must accrue to support learning. Moreover, for skills to generalize to new but related situations, skills must be abstracted from specific experiences. Our view is that a skill is not simply the learning of a single motor pattern (i.e., a sequence of finger movements) or a single visual discrimination, but instead is best conceptualized as a generalized capability to perceive new patterns that share properties or to produce new movement patterns under novel conditions ranging from riding a bicycle to playing chess to becoming a radiologist. But it is also important to note that while declarative and procedural (skill-like) memories have many identified differences, declarative memories are not studied directly. The formation and retrieval of declarative memories is strategic [20] and may be conceptualized as procedural [21], and thus may itself be a kind of skill.

Sleep consolidation of skills

The first studies that showed clear evidence of sleep-dependent memory consolidation were studies of procedural learning (e.g., see [22]) as opposed to declarative memory formation. Learning to discriminate a single visual pattern [23] and learning a single finger-tapping motor sequence [24] showed benefits of sleep in terms of post-sleep enhancements in performance. Indeed, Walker [25] argued that sleep consolidation reflects enhancement over baseline learning whereas time alone can stabilize memory. However, this conclusion is controversial and has been challenged [26–28].

The first clear demonstration that sleep stabilizes skill learning came from training listeners to better understand low-intelligibility computer generated speech in a task in which the same word was never played twice [29•]. Training produced clear evidence of generalized learning. Over a waking retention period following training, performance significantly dropped, presumably due to interference. However, two clear demonstrations of sleep consolidation were reported. If listeners were tested after a retention period that included sleep, performance was similar to that found immediately after training, suggesting sleep restored skill performance that was initially lost via interference. Moreover, if listeners slept before a waking retention period, their performance did not decline, indicating that sleep protected against future interference-related loss. Restoring apparent skill loss and protecting against future skill loss after sleep was also found for generalized sensory-motor learning in a first-person shooter video game, where all the training and testing took place on different visual games and environments [6].

These studies argued strongly that for generalized skill acquisition, sleep does not enhance performance, but rather reduces the effects of interference and protects learning against future loss. Moreover, a comprehensive sleep consolidation study of learning a single finger-tapping sequence [10] replicating prior motor-learning paradigms showed sleep consolidation (*contra* [27]) that follows the same pattern of protecting against interference — rather than enhancement (*contra* [24]). Although a number of studies report that sleep leads to performance enhancement [23,24,30•,31,32•,33•], this conclusion has been questioned. At least in motor tasks, baseline levels of performance may be suppressed [10,27,30•] giving the appearance of post-sleep enhancement when there is really only stabilization [27,28].

Although sleep may not produce enhancement of generalized skill performance, it may be important to produce generalization in skill learning. Training on a large, diverse set of systematically related stimuli as opposed to a small, repetitive set of systematically related stimuli has been demonstrated to lead to greater generalized learning and restoration of skill performance lost via interference [34]. Although sleep performance restoration does not occur following training on small, repetitive training sets [34], small boosts in generalization are still observed following sleep. Evidence of sleep-related generalization is part of a larger body of literature showing that sleep does not merely aid memorization, but leads to qualitative changes in memories, problem-solving, or task performance. For example, sleep promotes insight [35], aids in the development of abstracted representations of learned piano pieces [36], increases the associative connections among learned words [37], alters second-order associations in learning patterns of speech [38], biases the interpretation of ambiguous images [39•], and gives new emotional attributes the ability to capture attention [40]. The commonality between these studies is the finding that sleep promotes the formation of abstractions and connections to previous knowledge that were not present before sleep.

Evidence that non-human animals show similar performance changes as a result of sleep [26] made it possible to test how sleep restores learning due to loss from interference. Training European starlings on two tasks in quick succession resulted in clear proactive and retroactive interference, separately manifest in different conditions [30•]. Rather than reducing the memory of the secondary task to bolster performance on the first, sleep restored performance on both tasks. In other words, separate assessment of the two tasks, a target task and an interfering task, showed that the original task and the interfering task were restored to original levels of baseline performance following sleep. There was no trade-off in task performance between the tasks — both benefited from sleep. Thus sleep appears to reduce interference by reorganizing task representations or the ways in which they are accessed.

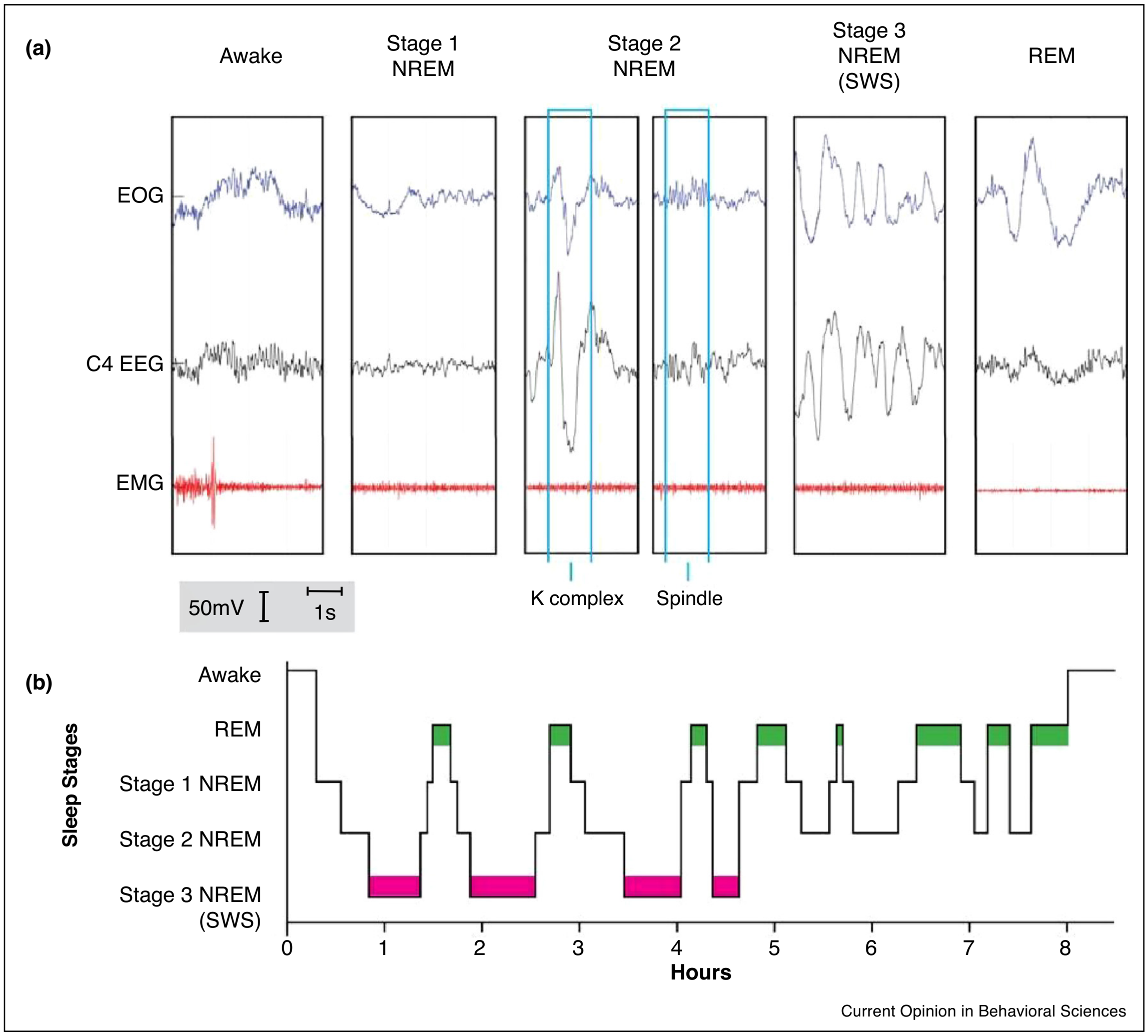
In summary, sleep may play an important role in skill acquisition through stabilization and generalization. Skills practiced in one context can, following sleep, generalize to new situations. If similar skills are learned during the same waking day, sleep can serve to separate and promote the stabilized learning of all skills in spite of interference that might have occurred during learning.

Sleep stages and skill learning

The discovery of sleep stages (see Figure 1) and rapid eye movement (REM) sleep [41] (Figure 1, Panel A) showed that sleep is not homogeneous and varies over time. Scientific interest in REM — and its potential role in learning — intensified with the evidence of an association with dreaming and the resultant perception of REM as the 'psychologically active' sleep stage [42]. However, these results were questioned [4], and research shifted to other stages.

Although some accounts still suggest REM is important for memory consolidation [43–45], recent studies argue

Figure 1



Panel A shows differences in the electrooculography signal (EOG, top trace), the electroencephalogram signal (EEG, middle trace), and the electromyography signal (EMG, bottom trace) in the awake state and the four stages of sleep. Wake is characterized by relatively high chin EMG tone, eye movements corresponding to blinking, reading, or fixating various targets if the eyes are open, and often occipital alpha if the eyes are closed. Generally wake EEG activity is higher frequency than in sleep. Sleep stage 1 is characterized by low-amplitude, mixed-frequency (LAMF) EEG activity, with less than half the 30-second epoch containing occipital alpha, and sometimes with slow, rolling eye movements. Stage 2 contains LAMF activity with K complexes and spindles. Spindles in particular are events of interest as they have been implicated in sleep consolidation, as we will discuss later. Stage 3, also known as slow wave sleep (SWS), occurs when at least 20% of the epoch consists of delta activity (amplitude >75 μV peak to peak, and frequency between 0.5 and 2 Hz). Finally, REM is characterized by low chin EMG tone, LAMF EEG sometimes with sawtooth waves, and distinctive fast eye movements visible in the EOG channels. Panel B shows a hypnogram: a diagram showing sleep stages across a prototypical 8-hour night of sleep. Note that in general, REM (in green) follows SWS (in red). In addition, while SWS typically predominates early in the night, later sleep architecture is more REM-rich.

for the greater importance of slow wave activity (SWA) in skill learning [46,47]. SWA occurs predominantly during stage 3 NREM, which occurs in greater proportion earlier in the night and is characterized by slow, high-amplitude EEG oscillations. Low acetylcholine (ACh) levels in hippocampus during SWA appear to be necessary for memory stabilization during sleep, as blocking ACh breakdown during SWA abolishes consolidation of such memories [48]. This may explain why SWA is important in learning, particularly (but not only) for declarative memories (aging memory decline linked to SWA reduction [49]; electrical enhancement of SWA and memory [50,51•]; auditory enhancement of SWA and memory [52]; localized SWA and implicit motor learning [31]).

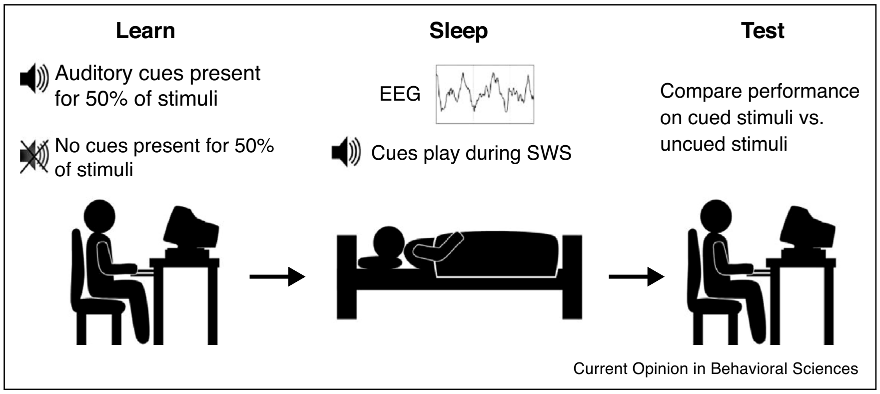
Slow waves or 'slow oscillations' involve widespread synchronous alternation between depolarized (high activity) and hyperpolarized (relatively silent) states in neurons [53–55]. Such coordinated regional activity may support more complex information transfer [14] related to hippocampal sharp-wave ripples or cortical spindles [56–58]. These signals could indicate hippocampal–neocortical interactions, or replay (or reactivation) of hippocampal information [59] thought to be related to memory consolidation [60]. Alternatively, SWA may be crucial for memory consolidation by globally reducing the strength of neural connections, thereby increasing signal-to-noise for important memories ('synaptic downscaling' [61,62]).

Consistent with theories emphasizing SWA in consolidation, local SWA has been shown to increase preferentially in learning-involved brain regions [63–65], with the amount of local SWA positively correlating with post-sleep learning performance [31]. As slow waves travel across cortex in an orderly spatial pattern [66], future work should address the functional importance of the origin, direction and speed of slow wave propagation over cortex in skill learning.

Beyond SWA, sleep spindles, which are bursts of 11–16 Hz thalamocortical oscillations [67•,68] have also been linked to memory consolidation [69]. After motor skill learning, participants show a significant increase in spindle density in NREM 2 over their baseline and further, that this increase is correlated with task improvement such that the larger the increase in spindle activity, the more the learner will improve on the motor task when they wake up. More recently, oscillatory tACS stimulation during sleep has been used to increase spindle count and had demonstrated causal evidence increases in spindle activity leads to larger improvements in motor skill memory consolidation [70•]. It has also been hypothesized that spindles affect hippocampus-dependent memories, particularly by those who argue that declarative memory consolidation involves the transfer of memories from hippocampus to cortex. Given that spindles may co-occur with hippocampal ripples, they may reflect coordination between hippocampus and cortex, which would support memory transfer [60,71•].

Recent work on spindle activity in memory consolidation suggests that there may be a distinction between spindle activity that supports declarative learning (i.e., describable) and spindle activity that supports procedural learning. There are both slow (11–13.5 Hz) and fast (13.5–16 Hz) spindles [72••]; slow spindles predominate over frontal areas and are more common during NREM 3; fast spindles have a centroparietal distribution and predominate during NREM 2 [73]. Recent research [67•,73] suggests that fast spindles support motor skill consolidation, while slow spindles support declarative memory consolidation. More work is needed to clarify whether

Figure 2



Example procedure for a sleep cueing experiment, including an initial learning phase with cues, a nap or full night of sleep with presentation of cues during slow wave sleep (SWS), and finally a post-test to measure improvement. Although this paradigm is characteristic of declarative learning studies, it can be adapted to test the benefits of cueing on more complex tasks such as skill learning, for example as in [72••] which used sleep cueing to enhance motor performance of keyboard melodies.

slow and fast spindles are functionally distinct, and what their respective roles are in consolidating different types of learning.

Cueing during sleep

The argument that sleep consolidation relies on reactivation or replay is often supported by studies that present learning-related stimuli, or cues, during sleep (see [74] for a review, Figure 2). Sleep cues can be associative — for example, odors that were previously paired with visual stimuli during learning could be experienced again during sleep. In one such study [75], Rasch *et al.* presented subjects with a rose odor while they learned the locations of objects in a 2D grid. Subjects who experienced the odor again during SWS recalled significantly more object locations than subjects who experienced an odorless vehicle. Sleep cues can also consist of stimuli directly learned; for example, spoken words from a foreign language could be played softly to sleeping learners after a language learning session (as in [76]). In general, this research has found that presentation of cues during slow wave sleep enhances learning [77•,78].

One possible reason that cueing may support learning is that cues trigger, or at least bias, reactivation of neural activity that was present during initial learning, thereby leading to more replay events for the cued memories than in uncued sleep. Increased replay theoretically strengthens synapses that encoded the memories, possibly facilitating memory restructuring or transfer. For human learners, there is no direct evidence that cueing triggers replay per se (i.e., the same neuronal firing patterns as were active during learning), although animal work supports this account [79]. Studies such as odor-memory cueing [75] demonstrate similar voxel patterns of hippocampal activity in humans using fMRI in response to learning and to cueing during sleep. But similar voxel activity patterns may reflect different neuron responses whereas the same place-coding hippocampal cells can be observed responding during waking and hypothesized replay activity in place-learning nonhuman animals. Given that there is more certainty about the role of hippocampal cells in coding spatial location than the role of the hippocampus in coding odor-association cues, there is still more research needed to directly support the claim about replay in humans.

Although some studies have argued that cueing may only support the consolidation of declarative memories (e.g., [75]) recent research has demonstrated that cueing can also support more complex skill learning [32•,80]. As many real-world skills likely involve both declarative and procedural components, further research is needed to elucidate whether cueing benefits to skill learning are occurring through effects on declarative components, procedural components, or both. Recent research supports the idea that cueing does more than simply boosting declarative memories or preventing forgetting, and there is evidence that both accessibility and memory recovery may occur through sleep [81,82]. Cueing has been shown to promote the generalization of newly learned skills to novel circumstances [83••], and to modulate affective judgments [39•]. Cueing can also affect sleep consolidation of motor skill learning via sleep spindles. Odor cueing of an associated motor task increased frequency, amplitude, and duration of centroparietal NREM 2 sleep spindles, which correlated with performance improvement [33•]. The ability of cueing to enhance skill learning, and the exploration of which neural sleep events underlie cueing effects, are areas that will likely receive much attention in future studies.

Sleep and two-stage learning models

A hallmark of many learning models is that learning occurs in two stages via two memory storage systems: one quick-learning with weak encoding and one slow-learning with stable encoding — thought to be neocortex. In humans, the hippocampus appears essential for the rapid formation of associations that, via a process of consolidation (presumably during an offline period such as sleep), are encoded into neocortical memory systems (e.g., [12]). Although hippocampal based two-stage models deal mainly with declarative memory, the principle of two-stage models may also apply to procedural memories. Ashby and colleagues [84] proposed that a basal ganglia-thalamus circuit serves as a fast-but-labile memory system for categorization, rather than the hippocampus. Indeed, it is possible that this fast-learning system mediates reorganization or consolidation of procedural memories in skill learning. More likely given other findings, it is possible that a network involving hippocampus, striatum, thalamus, and cerebellum is involved in early stages of skill acquisition encoding specific experiences before consolidation into neocortical systems [85–87] and generalized.

Conclusion

Skill learning refers to the acquisition of a generalized ability to perform using the interplay of sensory and motor systems along with knowledge derived from experience. A generalized ability goes beyond a single specific action pattern, but instead, reflects the ability to perform across a variety of settings and differential demands such as playing tennis with different rackets against different opponents. Although cognitive neuroscience distinguishes between declarative and procedural memories, both may be important in skill learning given that there may be explicit recall of particular situations as well as generalized responses involved. How does sleep aid skill learning? First, sleep following learning appears to reduce the impact of both proactive and retroactive interference. With long bouts of practice, performance may start to degrade (due to reactive inhibition, [27]) or due to subsequent experiences but after sleep, performance is improved. This may manifest as performance enhancement or just restoration of pre-interference learning. Second, sleep protects against future loss from interference by making skills robust against forgetting. Third, sleep appears to promote the generalization and abstraction of skills from specific learning experiences.

There are a number of basic scientific questions however that remain to be addressed in sleep consolidation of skill learning. Although there are proposals for synaptic mechanisms to function during sleep consolidation, it is unclear how these operate specifically in the context of a two-stage model of learning. Moreover, how do such mechanisms serve the functions of protecting learning, modifying representations to restore performance after interference, and promoting generalization and abstraction? Furthermore, understanding if and when sleep produces performance enhancement compared to stabilization remains an important question, as does whether such enhancement operates through the same mechanisms as restoration from interference and protection against interference. As new paradigms such as cueing during sleep become directed at understanding generalized skill learning, it may be possible to measure the development and modification of neural representations during sleep giving new insights into both skill acquisition and the mechanisms of sleep consolidation.

Conflict of interest statement

Nothing declared.

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- •• of outstanding interest

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This study provided the first demonstration that generalization in skill learning benefits from sleep consolidation. All training and testing in the study used unique words of difficult-to-understand computer-generated speech. Following training, performance was reduced over a waking retention interval. Sleep restored this loss of performance and sleep protected against future loss.

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This study establishes that cued-reactivation during slow-wave sleep leads to measurable changes in neural activation. Participants learned two visual serial reaction time tasks — one that was cued by high tones, and one that was cued by low tones. During slow-wave sleep, participants were exposed to either the high or low tones. Relative to the uncued task, participants showed enhanced performance (faster reaction times) to the cued task after sleep. Moreover, as assessed through functional magnetic resonance imaging, the cued task showed increased activity in bilateral caudate nucleus and hippocampus. Functional connectivity between these areas was also strengthened for the cued task. These results demonstrate that cued-reactivation during sleep can have important consequences for memory consolidation, as assessed through behavioral and neural markers.

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This study is one of the few examining sleep cueing and motor memory; it differs from many previous studies because cueing occurs during NREM 2 as opposed to SWS. Participants learned a motor sequence task in the presence of associated odors. Later during a night of sleep, the odors were presented as cues to some of the participants during NREM 2. Participants who were cued not only performed better on the task the next day, but had increases in spindle frequency, amplitude, and duration.

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This paper provides evidence that sleep, and potentially memory reactivation during sleep, changes the quality of memories and aids generalization. Participants were presented with photographs depicting scenes with ambiguous valence; individual words were used to disambiguate these scenes and make them positive or negative (e.g., a photograph of children playing instruments could be paired with the word 'applause' (positive) or 'jeer' (negative)). During a subsequent night of sleep, half of these paired words were presented auditorily during stage 2 or 3 sleep. Subsequently, cued pictures were more likely to be interpreted with the valence suggested by the cued words; this effect extended to related but novel pictures.

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This paper addresses sleep spindle frequency as a factor in procedural memory consolidation. The authors found that power in slow spindle frequencies was inversely correlated with the magnitude of memory consolidation for a finger tapping task, suggesting that a predominance of slow spindles might be biasing memory consolidation towards other, non-procedural memories.

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This paper is important to the question of which sleep stages and events are important for memory consolidation, because it is the first study to manipulate sleep spindles in humans with tACS and show a correlated learning effect. After declarative and motor learning tasks, participants slept for a night in the lab. An algorithm detected spindles in real time and applied tACS with a spindle-like waveform for 1 s. The magnitude of the spindle count increase caused by stimulation correlated with motor memory consolidation, providing strong evidence for a link between spindles and sleep consolidation.

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This study provides an important link between hippocampal-dependent memory consolidation, sleep cueing, and sleep spindles. The authors examined patients who had degenerative hippocampal disease. Participants learned associations between nonverbal sounds and words, and half of the sounds were presented as cues during SWS in a full night of sleep. Not only was the benefit of cueing correlated with the volume of intact hippocampus in the patients, but the spindle density during SWS predicted the size of the benefit. Thus, this paper provides evidence that spindles are a mechanism by which hippocampus-dependent memory consolidation occurs.

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This study provides a novel demonstration that sleep spindles can be manipulated by acoustic stimulation during sleep. During a 90-min nap, participants were exposed to two seconds of amplitude-modulated noise at 12 Hz (targeting slow spindles), 15 Hz (targeting fast spindles), or 50 Hz (control), which was followed by eight seconds of non-modulated noise. Relative to the non-modulated noise, the authors found increased slow and fast spindles for the 12 and 15 Hz modulated noises, respectively, but no spindle changes for the 50 Hz modulations. These results suggest that sleep spindles may be able to be non-invasively manipulated, which may have important implications for memory consolidation.

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This study provides important evidence that individual differences in initial (pre-sleep) learning influence the efficacy of targeted memory reactivation. Participants learned to associate several common visual objects with a particular spatial location. As each object appeared, participants also heard a unique sound. During slow-wave sleep, participants were exposed to half of the sounds. The authors found a performance advantage for the visuo-spatial associations that were cued during sleep, but the advantage was greatest for participants who had higher pre-sleep recall accuracy. As such, individual differences in learning may modulate the efficacy of cued-reactivation on sleep-dependent memory consolidation.

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This study is important in the sleep cueing literature because it heralds a new direction for sleep cueing work: the investigation of how sleep cueing might qualitatively change memories. Participants in this study learned grammatical rules of an artificial language through repeated exposure to phrases and rule abstraction (not explicitly seeing the rules). In a subsequent 90-min nap, phrases were presented auditorily as cues, or tones or no cues were presented (control). The phrase cued group showed greater abstraction of grammatical rules than either the tone cues or no cues groups, showing that cueing can promote abstraction or generalization of knowledge.

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