

Sleep Spindles: Timed for Memory Consolidation

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It has long been known that sleep supports memory consolidation. Two recent studies now shed light on how sleep spindles, characteristic 11–16 Hz activity bursts, contribute critically to memory processing during the night.

One of the big remaining questions is why we spend a third of our lives asleep — an unresponsive and seemingly passive state that robs us of our external awareness. Periods of unconsciousness pose a great threat to living organisms, thus the selective pressure to preserve sleep throughout evolution must have been high. One cannot deny our profound need of sleep: already as much as a few hours of sleep loss will leave us feeling emotionally raw, irritated and unable to concentrate. One of the most striking effects of sleep loss, however, may concern memory functions. Not only is it harder to retain new information when we are sleep deprived, we also have difficulties in retrieving existing knowledge. This can be partly attributed to a failure to stably store information that was learned before. Sleep is known to aid the consolidation of newly acquired memories, preventing us from forgetting what we experience during the day and ensuring the long-term accessibility of relevant information. Much recent research has tried to pinpoint how and why sleep benefits cognitive function. Accompanying the loss of consciousness, oscillatory brain activity and communication between brain regions change dramatically as we enter sleep, giving rise to characteristic activity patterns such as slow, high-amplitude waves and the short, spindle-shaped bursts that are sleep spindles. It thus seems likely that the special state that our brains enter during sleep is instrumental in producing the manifold benefits that we can get from a good night's rest. Two exciting new studies reported in *Current Biology* by Cairney *et al.* [1] and Antony *et al.* [2] now demonstrate that sleep spindles indeed have a functional role in nighttime memory reprocessing.

Sleep spindles are one of the hallmarks that define brain activity during non-rapid eye movement (NREM) sleep. These bursts of activity arise from coordinated activity in thalamo-cortical loops and have long been thought to control processing of external sensory information in the sleeping brain [3], thus possibly protecting the sleep state from disturbances. Cairney and colleagues [1] now show that sleep spindles are directly linked to memory processing during sleep (Figure 1). In their study, participants learned to associate spoken words with pictures of either objects or scenes. During NREM sleep, some of the previously learned spoken words were played back to the participants, leading to superior memory compared to words that were not presented during sleep. Interestingly, the sleeping brain responded differently to the presentation of words that were studied during the memory task than to the presentation of other words. When an object or scene association had been learned before sleep, the words elicited more spindle activity, suggesting that sleep spindles might be functionally involved in processing the associated memory content. And indeed, Cairney *et al.* [1] go on to show that it is possible to decode the category of the word-associated images based on this evoked spindle activity (Figure 1C).

It has long been known that we retain new memories better if we sleep after learning [4]. The mechanisms that underlie this effect are still under investigation. A central debate is whether sleep actively supports consolidation or whether the benefits observed after a night of rest arise from other factors that can be attributed to a general change in brain state or a lack of interfering

information [5]. Previous work found that brain activity that is specific to NREM sleep mediates sleep-related advantages for memory [6–9]. Research in both animals and humans shows that memory content is reprocessed during subsequent sleep [10,11]. The finer mechanisms that support this memory processing on the level of brain oscillations, however, have remained elusive. The results by Cairney *et al.* [1] are highly exciting because they attribute an active reprocessing of new memories to temporally precise events: sleep spindles.

Antony and colleagues [2] elegantly address the question of whether sleep spindles also have a causal role in overnight memory consolidation. In a series of experiments, students learned to associate objects with arbitrary sounds and later had to memorize a location for these objects on a spatial field. Similar to the work by Cairney and colleagues [1], some of the object-associated sounds were played again to the participants during the following episode of NREM sleep. Antony *et al.* [2] observed that sleep spindles occur rhythmically every 3 to 6 seconds. With the idea in mind that spindles might be crucial for processing reactivated memory content, they directly tested whether the timing of reactivation cues relative to this inherent spindle rhythm determined their effectiveness (Figure 1C). They reasoned that sounds placed at the right time before a sleep spindle should better leverage the spindle's capacity in information processing. Indeed, only cues that were presented at the optimal distance between spontaneously occurring sleep spindles benefitted memory performance. The studies by Cairney [1] and Antony [2] complement each other in showing that spindles are a critical period



for reactivation-mediated memory consolidation.

The beautiful experimental evidence that reactivation cues are only effective when precisely timed to exploit the natural rhythm of spindle occurrence suggests that targeted memory reactivation, as applied in both studies, utilizes the brain's constantly running reactivation machinery. Though much experimental work has already shown that externally cueing memories during sleep improves retention [12–16], it is not clear whether these effects are mediated by the same mechanisms that underlie spontaneous, endogenous memory reactivation. Such spontaneous memory replay occurring in the hippocampus is thought to trigger activation of associated neocortical memory representations. The interaction between these brain regions seems to be controlled by neocortical slow waves, which in turn time the occurrence of thalamocortical sleep spindles [17]. Interestingly, sharp wave ripples that accompany memory reactivation in the hippocampus are nested into the troughs of these spindle oscillations, indicating that spindles might relay information about memory replay between the hippocampus and neocortex [18]. Work in animals found that reactivation cues can bias the brain towards processing cue-associated material, overriding the inherent processing dynamics [19]. Antony *et al.*'s [2] finding that the brain's inherent rhythm remains unaffected by cueing sounds, together with Cairney *et al.*'s [1] confirmation that sleep spindles carry information about cue-associated memory content, strongly hint at a shared underlying mechanism for targeted and spontaneous memory reactivation.

The two new studies provide further evidence that the effectiveness of cueing critically depends on whether the memory content is processed during thalamocortical spindle oscillations. In fact, especially the role of the thalamus has become a topic of greater interest during recent years. Experiments in rodents show that the thalamus can drive neocortical plasticity during NREM sleep [20]. The current findings add to this idea, demonstrating that thalamocortical interactions during memory consolidation are critical for the behavioral benefit of

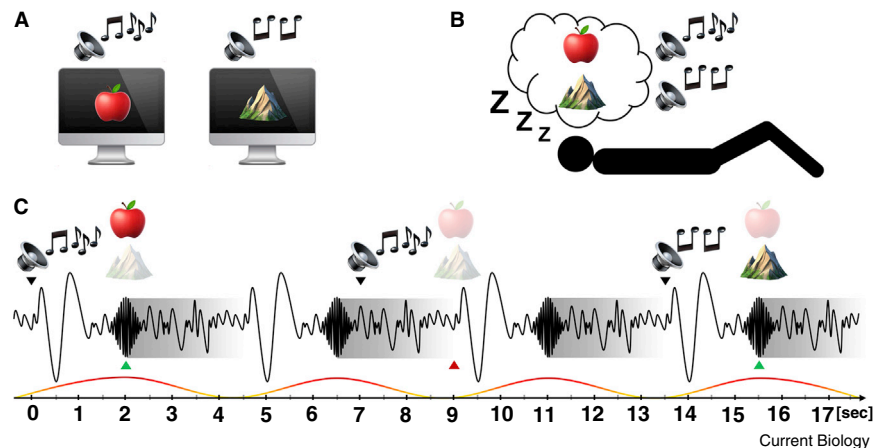


Figure 1. Sleep spindles for memory processing.

(A) In targeted reactivation designs, auditory stimuli are associated with the learning material during encoding. (B) These sounds are later played during sleep to evoke processing of the related material. (C) Sleep spindles are bursts of higher frequency activity (11–16 Hz) that rhythmically occur every 3–6 seconds (schematic EEG trace). The probability for a spindle to occur thus peaks 4.5 sec after the previous spindle (colored line). When a sound is presented to trigger memory processing during sleep (black arrows), increased spindle activity is observed 1.5–2 sec later (green arrows). At times of this spindle activity, the content of the associated memory can be decoded from electrical brain activity. Sleep spindles are followed by a refractory period (grey shading) during which it is unlikely that a further spindle will be elicited. If memory cues are presented during this refractory period, they are less likely to be followed by spindles (red arrow) and thus less effective than when presented at a later point.

reactivation. They also suggest that a strengthening of neocortical representations is central to memory processing during sleep. That sleep spindles provide and restrict opportunities for memory reactivation particularly stresses the role of both the thalamus and the neocortex in controlling how and when information is processed by the sleeping brain.

The new findings by Cairney [1] and Antony [2] open a range of possibilities for future research. Sleep spindles are comparably brief events that can be easily located. A precise knowledge about when learning-related information is processed by the sleeping brain will allow us to study in detail which kind of information is preferentially processed during sleep and to directly relate the reactivation of specific memories and their fate: which memories are retained, which are forgotten? Does sleep-dependent processing determine which memories impact our future behavioral choices? Moreover, the understanding that there are prime opportunities for reactivation will help to better target cue memory reactivation. This can make memory cueing a highly effective strategy to direct information processing during sleep. Given that sleep has been implicated not only in memory consolidation but also in

memory dysfunctions and psychiatric disorders, targeted memory reactivation may in the future gain potential as a strategy for cognitive enhancement as well as a therapeutic intervention.

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Animal Behavior: Social Learning by a Whisker

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Banded mongoose pups learn foraging preferences from unrelated group members rather than their parents, suggesting that cultural transmission maintains behavioral diversity in groups.

“Learning would be exceedingly laborious, not to mention hazardous, if people had to rely solely on the effects of their own actions to inform them what to do”.

Bandura and Walters (1977) [1]

Few things are more important than learning what is safe and nutritious to eat — after all, eat the wrong thing and you may die. For many mammals, all of which are born relatively altricial and in need of early care, offspring usually learn from their mothers what to eat. Dietary preferences can be transmitted through mother’s milk in rats and humans, suggesting that early food preferences are formed from physiological transmission of foraging knowledge [2,3]. However, dietary preferences can also be learned later in life by copying others. Black rat pups, for instance, learn from an adult demonstrator how to acquire food

by stripping pine cones [4]. Rat pups also learn which foods are safe to eat by choosing sites where they see adults feeding [5]. This non-genetic phenomenon, called ‘cultural transmission’, allows learned information to be transmitted across generations and has been demonstrated in apes, dolphins and birds [6–8]. Yet, to convincingly identify learning, and specifically whom animals learn from, it is essential to isolate vertical learning from parents, and horizontal or oblique learning from other group members. One way to understand the relative importance of maternal influence and environmental experiences is to switch animals at birth — for instance when birds’ eggs are cross-fostered by moving them between nests [9] or between species [10]. If an individual exhibits a trait from their parents and not their foster, then the trait can be assumed to be largely genetic or parental in origin, while if they show a trait from their foster

and not their parents, the trait can be assumed to be largely environmental in origin. Cross-fostering is even possible with marsupials, where joeys have been moved between pouches [11] but is more technically challenging for placental mammals in the wild where many young are born in burrows. In this issue of *Current Biology*, Catherine Sheppard, Harry Marshall, Mike Cant and colleagues capitalize on a unique mammalian rearing system of the banded mongoose, which naturally mimics cross-fostering, to convincingly show that the foraging preferences of pups are shaped not by their mothers’ preferences but by exposure to specific non-relatives [12].

Banded mongooses live in groups of approximately 20 adults plus offspring. They are plural breeding cooperative breeders, meaning that many females breed at once and all members of the group contribute to rearing the young.

