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Cairney, Scott Ashley orcid.org/0000-0002-1135-6059 and Horner, Aidan James orcid.org/0000-0003-0882-9756 (2024) Forgetting Unwanted Memories in Sleep. Trends in Cognitive Sciences. ISSN 1364-6613

https://doi.org/10.1016/j.tics.2024.07.011

Trends in
Cognitive Sciences

CellPress
OPEN ACCESS

Forum

Forgetting unwanted memories in sleep

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Memories are sometimes best forgotten, but how do our brains weaken unwanted details of the past? We propose a theoretical framework in which memory reactivation during sleep supports adaptive forgetting. This mnemonic rebalancing underpins the affective benefits of sleep by ensuring that our memories remain aligned with our emotional goals.

The need to forget

Forgetting plays an important role in maintaining a healthy brain. We cannot remember every detail of our past (nor would we likely want to) and must instead rely on memory systems that ensure the remnants of recent experience are aligned with our future needs. One way this adaptive forgetting occurs is through **inhibitory control** (see Glossary) processes that override habitual responses conflicting with our cognitive and emotional goals [1]. When environmental cues guiding retrieval activate other memories in addition to the one we seek, inhibitory control is often required to overcome distraction from competing memories. Extensive research has shown that selectively retrieving a target memory triggers forgetting for its competitors, a phenomenon known as **retrieval-induced forgetting (RIF)** [1]. Hence, memories can be forgotten because they share a reminder cue with other memories that are retrieved consistently.

Sleep promotes the flexible use of memory by reactivating and thereby strengthening newly acquired memories [2]. We propose a theoretical framework in which memory reactivation during sleep facilitates adaptive forgetting by weakening unwanted components of prior experience, akin to RIF. Memory reactivation and adaptive forgetting in sleep are supported by **sleep spindles**, which prompt conflict detection during retrieval competition, leading to the weakening of competing memories. We argue that adaptive forgetting in sleep is not only part of a healthy memory system, but that it is integral to emotion regulation. Specifically, mutually dependent processes during **slow-wave sleep** and **rapid eye movement (REM) sleep** strengthen behaviorally-relevant mnemonic content while weakening both unwanted content and the emotional tone of salient memories.

Sleep promotes adaptive forgetting

Our framework proposes that memory reactivation during sleep weakens competing, unwanted memories, which we refer to as reactivation-induced forgetting in sleep (RIFiS). Evidence supporting this idea has been obtained via an innovative memory cueing technique known as targeted memory reactivation (TMR). In a typical TMR paradigm, auditory cues (e.g., spoken words or sounds) are paired with new memories at learning. A subset of these cues is replayed during sleep to reactivate and strengthen the corresponding memories [3]. We recently showed that TMR not only enhances retrieval of the target memories, but also induces forgetting for their competitors [4]. This suggests that memory reactivation in sleep prompts retrieval competition that results in the weakening of competitors, consistent with RIFiS.

But how do our brains determine what is remembered and forgotten during sleep? Together with **slow oscillations** and **sharp-wave ripples**, sleep spindles are thought to promote memory reactivation and localized plasticity in slow-wave sleep [2]. Indeed, replaying memory cues during slow-wave sleep (relative to playing previously unheard control cues) prompts a transient increase in spindle activity [5]. Moreover, endogenously generated spindles are most pronounced over cortical sites engaged in prior learning, with the extent of this learning-spindle overlap predicting the mnemonic benefits of sleep [6]. Interestingly, the occurrence of sleep spindles is associated with increased activation in anterior cingulate cortex (ACC), a brain region implicated in conflict detection during retrieval competition in wakefulness (with spindle amplitude correlating with ACC activity) [7]. We propose that spindles strengthen target memories while engendering conflict detection in ACC, triggering the weakening of their competitors.

Evidence from animal and human models points to a causal role of prefrontal cortex (PFC) in initiating the top-down inhibitory control signal that induces wakeful RIF [1]. Similar inhibitory control mechanisms

Glossary

Autobiographical memory: a memory system consisting of experiences recollected from one's lifetime.

Inhibitory control: the ability to actively suppress a habitual response to achieve a goal.

Rapid eye movement (REM) sleep: a distinct phase of sleep characterized by quick eye movement, low muscle tone, and electrophysiological similarities to wakefulness.

Retrieval-induced forgetting (RIF): a memory phenomenon where practicing retrieval causes forgetting of non-retrieved memories associated with the same reminder cue.

Sharp-wave ripples: electrophysiological events of ~80–100 Hz (in humans) that are most frequently observed in hippocampus during slow-wave sleep.

Sleep spindles: transient bursts of ~11–16 Hz activity that occur across widespread cortical areas during slow-wave sleep.

Slow oscillations: <1 Hz brain rhythms of slow-wave sleep that reflect coordinated activity of large neuronal populations.

Slow-wave sleep: the deepest stage of sleep that is characterized by distinct electrophysiological events, namely slow oscillations, sleep spindles, and sharp-wave ripples.

Theta oscillations: ~4–7 Hz brain rhythms that have been linked to various aspects of cognition and behavior.

may occur during slow-wave sleep to directly weaken competitor memories. While selective retrieval tasks that trigger wakeful RIF engage lateral PFC [1], reactivating visual object-location memories via TMR in slow-wave sleep enhances connectivity between visual (occipital) cortex and dorsomedial PFC [8]. Whether lateral PFC plays a similar (currently unobserved) inhibitory role during slow-wave sleep, or if this dorsomedial PFC connectivity is related to a sleep-related inhibitory control mechanism, is unclear. It is also possible that RIFiS occurs in the absence of prefrontal-controlled inhibition. Recent work has shown that conscious memory reactivation during wakefulness benefitted the target memories and weakened their semantic associates, whereas unconscious reactivation during wakefulness (achieved by presenting memory cues subliminally) produced nonselective benefits for both the targets and their associates [9]. The authors argued that unconscious reactivation entails less prefrontal-controlled inhibition than conscious reactivation, permitting more widespread activation. Understanding the neurocognitive mechanisms of RIFiS, and how these differ from those underpinning wakeful RIF, is thus an important avenue for future research (Box 1) and speaks to broader debates concerning the unique role of sleep relative to idle wakefulness in offline memory processing.

Emotion regulation relies on adaptive forgetting in sleep

Sleep is inextricably linked to emotion regulation. Another component of our framework predicts that adaptive forgetting in sleep supports affective wellbeing. Cognitive reappraisal is an established emotion regulation strategy that people can use to reframe emotionally scarring experiences in a more positive light. We argue that the reactivation of positively reappraised memories in sleep invokes plasticity-promoting spindles, which serve to both stabilize new positive associations and weaken older negative associations via conflict detection and inhibition. Hints that RIFiS may promote emotion regulation in this way can be seen in recent work linking sleep spindles to the reduced tendency to recall emotionally negative aspects of prior experience following cognitive reappraisal [10]. It is also worth noting that RIF effects during wakefulness have consistently emerged in remote **autobiographical memory** [1], demonstrating that even well-consolidated memories (such as those pertaining to emotionally aversive experiences) can be modified through an adaptive rebalancing of mnemonic strengths.

Our framework also links with existing theories on the role of REM sleep in emotional memory processing [11]. Supported by **theta oscillations** in hippocampus and amygdala, REM sleep is thought to strengthen the central components of emotionally negative memories while simultaneously weakening their affective charge. We argue that spindle-mediated memory reactivation during slow-wave sleep could strengthen behaviorally relevant targets from an aversive experience, while initiating processes that allow for weakening of competitors from the same experience. The strengthened target components could be 'tagged' for further processing in subsequent REM sleep, where their emotional charge is stripped away (Figure 1). Conflict detection in ACC during slow-wave sleep may also generate a 'tag' for the competitor memories, allowing for further weakening of other mnemonic details during REM sleep (aligning with extant models that link REM sleep to forgetting [12]). Such synergistic mnemonic processing in slow-wave and REM sleep would result in a concise, behaviorally relevant memory representation that can adaptively guide future decision making. Consistent with this view, recent work has shown that sleep spindles are predictive of memory retention, but only when they are followed by REM sleep [13].

Box 1. Predictions for future research

- Does RIFiS emerge from inhibitory control processes? If memory reactivation during slow-wave sleep promotes forgetting via competitor inhibition, then neural activity patterns evoked by TMR should become progressively more similar to activity patterns corresponding to target memories and less similar to activity patterns corresponding to competitor memories.
- What is the role of PFC in RIFiS? Competitor inhibition arising from TMR during slow-wave sleep should engage PFC, with the magnitude of PFC engagement declining as retrieval competition is resolved over TMR events.
- Do sleep spindles contribute to RIFiS? The magnitude of TMR-evoked spindle activity should correlate with conflict detection responses in ACC, inhibitory control signals in PFC, and competitor forgetting after sleep.
- Can RIFiS offer new perspectives on the link between sleep and emotion regulation? Cueing a reappraised memory in sleep (via TMR) should strengthen the new positive interpretation of that memory and weaken the older negative interpretation.
- Do mnemonic operations in slow-wave sleep and REM sleep work in concert to support mental health and wellbeing? The affective benefits of reactivation-induced forgetting in slow-wave sleep should be amplified when it is immediately followed by REM sleep.

Concluding remarks

We have outlined a neurocognitive framework to explain how sleep supports the flexible use of memory via the strengthening and weakening of mnemonic content and affect. First, we proposed that memory reactivation in slow-wave sleep induces a spindle-mediated conflict signal in ACC that leads to weakening of competitor memories. Second, we outlined how this weakening could be driven by direct inhibitory control mechanisms during slow-wave sleep, akin to those involved in wakeful RIF. Third, we argued that RIFiS can support reappraisal-based learning in service of emotion regulation and might represent a causal mechanism underpinning the well-known link between sleep and mental health. Finally, we outlined how RIFiS during slow-wave sleep may work synergistically with mnemonic operations in later

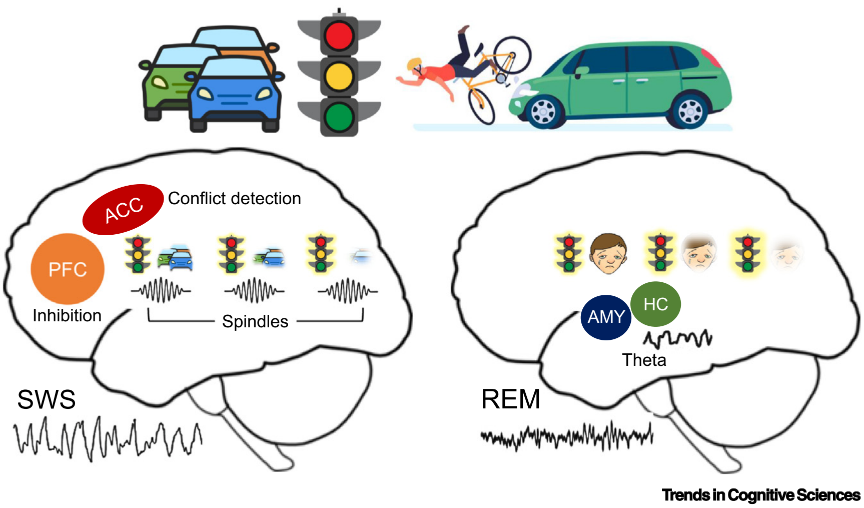

Figure 1. Integrated view of reactivation-induced forgetting in sleep (RIFiS). Memories of an unpleasant experience (cycling accident) are reactivated during slow-wave sleep (SWS). Spindles serve to reactivate the future-relevant target memories (traffic light) and engender conflict detection in anterior cingulate cortex (ACC) as a result of retrieval competition from other mnemonic details (bystanders' cars), potentially prompting inhibition by prefrontal cortex (PFC). Consequently, the target memories are strengthened during SWS, whereas their competitors are weakened. In later rapid eye movement sleep (REM), theta oscillations in hippocampus (HC) and amygdala (AMY) support further reactivation of the target memories and unbind their affective charge. One can then recall details about the traffic light on future cycling trips without being consumed by distressing emotions about their cycling accident.

REM sleep to ensure that emotionally salient memories are retained in a manner that is aligned with our behavioral and emotional needs. In sum, RIFiS could provide critical insight into how sleep strengthens and weakens existing memories to shape the autobiographical narrative of our lives.

Acknowledgments

A.J.H. receives funding from the Economic and Social Research Council (ES/X00791X/1) and Leverhulme Trust (RPG-2023-003).

Declaration of interests

The authors declare no competing interests.

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https://doi.org/10.1016/j.tics.2024.07.011

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