



Recurring memory reactivation: The offline component of learning

Ken A. Paller

Northwestern University, Department of Psychology, Evanston, IL, 60208, USA

ARTICLE INFO

Keywords:

Learning
Memory
Reactivation
Consolidation
Sleep
Slow-wave sleep
Dreaming
Memory replay
Sleep learning

ABSTRACT

One can be aware of the effort needed to memorize a new fact or to recall the name of a new acquaintance. Because of experiences like this, learning can seem to have only two components, encoding information and, after some delay, retrieving information. To the contrary, learning entails additional, intervening steps that sometimes are hidden from the learner. For firmly acquiring fact and event knowledge in particular, learners are generally not cognizant of the necessity of offline consolidation. The memories that persist to be available reliably at a later time, according to the present conceptualization, are the ones we repeatedly rehearse and integrate with other knowledge, whether we do this intentionally or unknowingly, awake or asleep. This article examines the notion that learning is not a function of waking brain activity alone. What happens in the brain while we sleep also impacts memory storage, and consequently is a critical component of learning. The idea that memories can change over time and become enduring has long been present in memory research and is foundational for the concept of memory consolidation. Nevertheless, the notion that memory consolidation happens during sleep faced much resistance before eventually being firmly established. Research is still needed to elucidate the operation and repercussions of repeated reactivation during sleep. Comprehensively understanding how offline memory reactivation contributes to learning is vital for both theoretical and practical considerations.

1. Introduction

Memory researchers have addressed the question of how memory works through a steady progression of insights. A chief focus has been on elucidating mechanisms of the input/output stages of encoding and retrieval. Neuroimaging and studies with event-related brain potentials have heavily emphasized neural activity at these two time-points. The dominance of this orientation has sometimes overshadowed the in-between stage. Encoding and retrieval are certainly essential. However, this input/output focus could encourage an unstated assumption that brain activity at encoding is sufficient for transforming experience into a long-lasting memory (Paller and Wagner, 2002).

Some types of encoding are certainly too weak to produce enduring memories. In the levels-of-processing approach, processing verbal input superficially, focusing on orthographic or phonological features, was acknowledged as inferior to focusing on meaning (Craik and Lockhart, 1972). Depth of processing is rightfully taken to be key to later remembering. The notion of elaboration provides another heuristic for the most effective types of encoding. But is deep or elaborative encoding all that's needed for memory storage to be successful?

Memory researchers also figured out that the test used to subsequently assess memory is also crucial (Tulving and Thomson, 1973;

Morris et al., 1977). The encoding-specificity principle and the related idea of transfer-appropriate processing called attention to the impact of retrieval needs on determining which type of encoding would be effective. These principles provoked a flurry of advances as researchers delved into various aspects of effective memory encoding and effective memory retrieval, along with the agenda of understanding how they map onto each other. This orientation carried through to the present era when we use all sorts of behavioral and neurophysiological observations in memory experiments.

Experimental results in memory research, as well as theories, potentially impinge on many sorts of practical considerations, from recommended learning strategies to educational policies to clinical treatments. Consider the difficulty of remembering names. Who hasn't experienced the stress of realizing that you've already forgotten the name of the person you've just met. What strategies should be used to avoid the potential embarrassment of flubbing a person's name at a later time? Although elaborative encoding helps, concerted practice retrieving the name is even better (Willingham, 2021). The ideal practice might be retrieving the name upon seeing the face. Likewise, students aiming to ace an upcoming exam can implement suitable memorization techniques of repeated practice in accordance with the exam format. Repeatedly remembering presumably engages beneficial

E-mail address: kap@northwestern.edu.

<https://doi.org/10.1016/j.neuropsychologia.2024.108840>

Received 30 October 2023; Received in revised form 19 February 2024; Accepted 25 February 2024

Available online 28 February 2024

0028-3932/© 2024 Elsevier Ltd. All rights reserved.

neural processing, though we don't yet know how to precisely measure what changes in the brain.

The principle of repeated practice to achieve one's memorization goals may apply for all types of memory. Skill learning is the epitome of arduous and gradual learning, encompassing perceptual skills, motor skills, and cognitive skills. People have mastered a variety of musical, athletic, and other talents through intensive practice. Contrast those situations with the way a computer picks up and stores new information; when one drags a file to the hard drive, memory storage is seemingly instantaneous and permanent.

Whereas some types of learning, like skill learning, require considerable practice, maybe others don't. Immediately effective encoding is arguably emblematic of episodic memory. We can remember the specifics of one episode in its unique spatiotemporal context. Sometimes a singular event can be remembered accurately years later, even without any efforts to memorize it.

2. Instant karma

Can encoding be so optimal that a single episode has the full power to establish a long-lasting memory at that moment? Many people would endorse the idea that transforming an experience into a lasting memory could entail just one efficacious encoding trial. The epitome of one-shot episodic learning is the classic flashbulb-memory phenomenon, whereby an episode of very high importance and emotional impact seems to be instantly ingrained in the brain (Brown and Kulik, 1977; Schmolck et al., 2000; Hirst et al., 2009).

The prototypical example of a flashbulb memory is when people vividly recall when they first heard the news of a presidential assassination. Robert Livingston (1967) proposed that the gravity of a momentous news event can engage what he termed a "now-print" mechanism, whereby the important facts along with the context at that moment are instantly imprinted in a memorial perma-store.

An alternative to this traditional interpretation of flashbulb memories is that what happens in the brain at that initial emotional moment is not the operative reason for why they can be remembered so amazingly well. Rather, it is because of what happens subsequently: repeated rehearsal. In other words, these special memories are preserved thanks to offline consolidation.

A person might object to this reinterpretation by claiming to have remembered a past event without even once retrieving that information during the intervening time. This objection is easily countered — retrieval may occur repeatedly during the intervening time without the individual knowing it. A strand of research central to this point reinforces the view that memory reactivation during sleep supports later remembering (Paller et al., 2021).

By this view, remembering a specific episode from the past can be based on a singular experience, but the requisite learning is not complete at the time the episode is encoded. An extended learning process is required; learning continues during sleep. This view calls into question the often-implicit assumption that learning can be complete when newly acquired information is encoded well (e.g., Paller and Wagner, 2002). Although offline consolidation might be considered a mainstream idea today, a recent account put forward by Yonelinas et al. (2019) instead stressed contextual binding. This account de-emphasized offline consolidation and instead favored the position that sleep is beneficial for memory merely due to "reduced encoding of interfering information" during sleep rather than reactivation during sleep (Yonelinas et al., 2019, p. 368). Offline consolidation is not a universally accepted principle.

In what follows I briefly summarize the view that long-lasting memory storage is a consequence of learning that continues during offline periods of sleep (Fig. 1). The idea of offline consolidation has a long history (as summarized in the next section). Despite how much memory research emphasized two stages — first forming a memory and later retrieving a memory — there is more to effective learning.

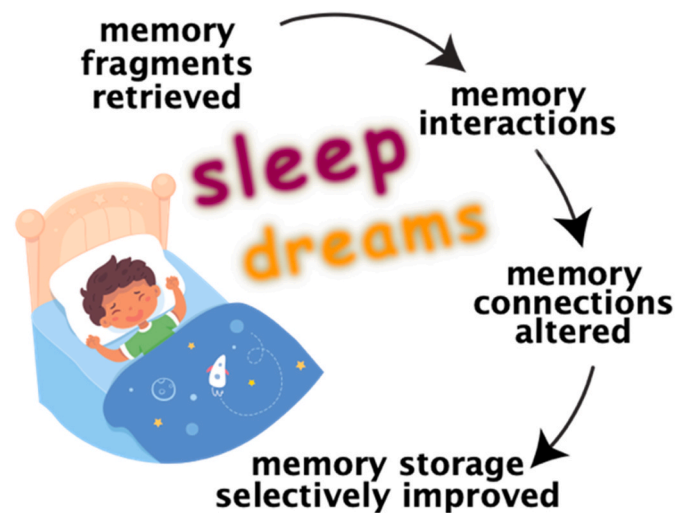


Fig. 1. An illustration of the general scenario championed here whereby memory storage is altered offline during sleep (adapted from Paller and Voss, 2004). Following initial memory acquisition, consolidation occurs when memory fragments are retrieved to enable changes in storage based on relationships worked out among the fragments, both during wake and during sleep (sleep is emphasized here). Dreams are a prominent feature of sleep from the first-person perspective. Yet, dream narratives seldom recapitulate recent episodes (Fosse et al., 2003). Some theories nevertheless posited a critical role for dreams (e.g., Paller and Voss, 2004; Zadra and Stickgold, 2021; Winson, 1985), but the empirical literature has not yet produced convincing evidence to implicate a role for dreaming in sleep-based mechanisms of memory consolidation. Dreams seem to be primed to be forgotten — most are not remembered, and it is striking how readily a dream can be subject to forgetting at the moment of awakening. The present article focuses on sleep-based consolidation without taking a position on its possible dependence on dreaming, but hopefully future research will bring progress in answering this question.

3. Offline consolidation

An early landmark study of memory consolidation was Müller and Pilzecker's (1900) demonstration that a period of sleep following acquisition seemed to advantage memory retrieval. Studies of retrograde amnesia, both in neurological patients and experimentally produced in rodents, also implicated offline consolidation, but without highlighting sleep. These studies suggested that memory storage gains stability during a prolonged period after initial acquisition (Squire et al., 1984). A three-stage view has thus been standard — that information is acquired during a learning episode, stored effectively via consolidation, and ultimately retrieved. By this view, progressive memory consolidation mediates storage whereas certain types of brain damage or disruptive electrical stimulation can interfere with consolidation (Paller, 2009; Dudai, 2012). Two types of consolidation have been distinguished, synaptic consolidation on a shorter time scale and systems consolidation on a longer time scale. Both can be considered as steps of memory stabilization. Naturally both types entail changes in neural connectivity, but systems consolidation occurs conjointly in multiple brain regions such that critical plasticity occurs across networks (Marr, 1971; McClelland et al., 1995).

Is making a memory like sculpting some clay into a particular shape (encoding) and then firing it in a kiln (consolidation) so that it gradually hardens into a permanent piece of art? Consolidation could be a series of biochemical steps, a chain reaction that proceeds steadily and methodically in a predestined manner. On the other hand, the hardening process for a memory may be unlike that of sculpture. Systems consolidation is not inexorable, nor is it a one-shot process, nor does it lead to an unchangeable final form. It depends instead on optional processing steps — intermittent memory reactivation during offline periods.

Neuropsychological studies have thoroughly documented selective

deficits in amnesic patients (Mayes, 1988). Memory impairments can appear against a background of preserved memory functions and are centered on the ability to recall and recognize facts and events. This ability, known as *declarative memory*, undergirds the ability to consciously remember prior experiences. A principle widely accepted by contemporary memory researchers is that different types of memory function differently. Avoid assuming that all types of memory are mechanistically the same — that is the prime directive of an expedition in memory research (paralleling the prime directive of a Star Trek expedition to avoid interference with an alien culture). A distinctive mechanistic feature of declarative memory is a consolidation process critically dependent on hippocampal-neocortical interaction along with a less-well specified diencephalic contribution. Other types of memory may be subject to other types of consolidation.

A patient can present with retrograde amnesia in different ways. Perhaps the most common retrograde deficit concerns remembering difficulties for information acquired during a discrete period before the onset of amnesia. The period does not include their entire lifetime, but rather covers hours, days, or months. A disruption in consolidation is often inferred to explain these retrograde deficits (Squire et al., 1984; Paller, 2002). Storage of declarative memories cannot be maintained, according to this idea, because consolidation cannot fully secure the memories even though they were acquired when the patient did not yet have amnesia.

Some memory deficits have remained difficult to understand. One such problem is known as *accelerated long-term forgetting*. It has been described in people with the diagnosis of transient epileptic amnesia (Atherton et al., 2016; Butler et al., 2019; Cassel and Kopelman, 2019; Mayes et al., 2019). In these cases, learning may seem normal for up to a few hours, but after longer delays there are impairments. An intriguing possibility under active investigation is that deficits could be caused by overnight memory consolidation gone awry (Fig. 2).

Insights from the neuropsychology of amnesia are consonant with the advances experimental psychologists made in investigating methods to optimize learning. Desirable difficulty and expanding retrieval practice promote effective consolidation (Bjork and Bjork, 2020). The testing effect highlights the related finding that repeated retrieval produces superior remembering compared to repeated re-exposure to what one hopes to learn (Roediger and Karpicke, 2006). Such strategies reinforce the storage of newly acquired information. The underlying cognitive transactions, as with effective encoding strategies, need not be intentional. Note that retrieval is uniformly explicit when it occurs in the context of retrieval practice; people know they are retrieving the information they want to memorize.

Similar strategies can be engaged without the intention to alter memory storage. Unintentional retrieval practice can also be effective, and it could occur without either the prior intention to retrieve or

explicit knowledge of retrieving. In other words, covert retrieval practice could contribute to offline consolidation. In this sense, offline memory processing should be considered part of effective learning.

4. Sleep-based consolidation is a post-acquisition component of learning

Offline memory processing is now widely seen as part of an extended process of learning facts and events. Following initial acquisition, more is required for an experience to be stored in a long-lasting way.

Sleep may have provided various adaptive benefits in a long evolutionary trajectory, beginning well before mammalian evolution (Mayes, 1983). The benefit most relevant to the present discussion is that, during sleep, human memories may be reactivated, re-evaluated, and related to current goals (Cartwright, 2010; Winson, 1985). Connections can be formed between the newly acquired information from one unique episode and already-stored episodic and factual memories. These connections are the very same connections that allow an event to be meaningful, to be understood, to have a context, to have relevance for the future, and to be worth remembering. Strengthening these connections is tantamount to stabilizing the new memory.

Importantly, this stabilization is not simply solidifying a new sculpture in the mind to join a huge number of other mental sculptures in the collection. Rather, this processing encompasses integrating the new information together with existing information, leading to further adjustments (as in Piaget's description of accommodation and assimilation). Transformation is inherent to consolidation. Consolidation entails establishing relationships with other knowledge, adding new facets, and sometimes altering existing knowledge. It can include both the retention of specifics and a progression to generalized knowledge. Many experimental paradigms in contemporary memory research revolve around a set of to-be-remembered items, even though storing single memories in isolation is probably the exception rather than the rule. Offline learning may be particularly advantageous for exactly the sorts of memory interactions that involve complex interrelationships among many pieces.

How can we begin to characterize neural processing during sleep that supports consolidation? When we sleep, our brains remain busy. We may not be dead to the world, even figuratively, but the brain faces fewer challenges with respect to taking in sensory inputs and anticipating what will happen next (Andrillon and Kouider, 2019). Electroencephalographic (EEG) recordings confirm that the brain is not turned off, although neuronal activity can be quite minimal for ultra-short periods. These are the so-called down-states of slow waves, lasting less than half a second, most common during slow-wave sleep. The moment when the down-state is ending and neurons are resuming their firing, as the up-state begins, appears optimal for memory processing. At this

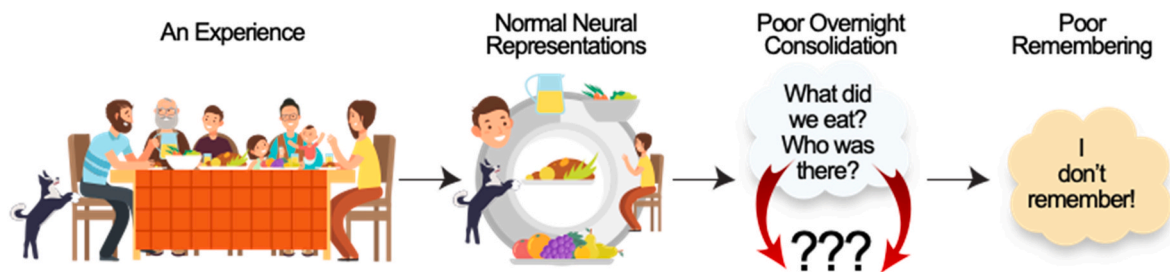


Fig. 2. Problems stemming from dysfunctional overnight memory reactivation, as shown in one schematic example. After one night of poor sleep, the toll on consolidation may be small, aside from impairments due to drowsiness, but multiple bad nights could be more deleterious. Such patterns of forgetting have not always been on the radar of clinical neuropsychology, which generally relies on memory testing after delays no longer than 30 min. To detect typical amnesia, such short delays are highly effective, but remembering what happened on prior days can be very important in daily life. In some cases, a person's retrieval abilities may be disproportionately deficient after multi-day delays. Memory reactivation and consolidation during sleep may be disrupted due to intermittent epileptiform brain activity, for example, resulting in memory contamination and reduced accuracy of recall (Creery et al., 2019). Problems with overnight memory processing may also be operative in other populations, contributing to psychiatric issues conjointly with troublesome memory symptoms, as suggested by various findings (Harrington et al., 2018; Wassing et al., 2019).

time, another prominent electrophysiological signal, the sleep spindle (a brief 11–15 Hz oscillation) can emerge. Many recent studies have linked spindles with memory reactivation (e.g., Antony et al., 2018; Cairney et al., 2018). Spindles are generated by cortico-thalamic networks, such that specific regions of the cortex can communicate with one another, as they have simultaneously transitioned to the up-state due to the widespread synchronization of slow waves. These events may mark the participation of critical cortical and thalamic regions in consolidation, and intriguingly, may also be relevant for explaining diencephalic amnesia (Aggleton and Saunders, 1997). We previously speculated that the central role of the thalamus in generating spindles and corresponding replay events may be at the heart of both sleep-based consolidation and the classic symptoms of amnesia after certain configurations of diencephalic damage (Paller et al., 2020).

Conjectures about declarative-memory consolidation often emphasized neocortical-hippocampal interactions (Marr, 1971). Evidence for the hippocampal side of the interaction can be seen in another sleep oscillation known as the sharp-wave ripple or SWR (Rothschild et al., 2017; Ngo et al., 2020). SWRs are not limited to sleep and have been linked with the recapitulation of waking patterns of hippocampal place cells in a novel environment, the neuronal patterns of hippocampal replay (Pfeiffer, 2020). The extensive literature on hippocampal replay at the single-unit level, however, does not focus on exactly how stored representations are changed to be remembered differently afterwards.

EEG oscillations during sleep represent only a small part of the full story of consolidation, but they provide valuable hints about the engagement of networks in the hippocampus, cortex, and thalamus that contribute to consolidation during sleep (Klinzing et al., 2019). Invasive methods such as intracranial EEG recordings may be best for interrogating interactions across these brain regions in humans. The evidence to date backs the conclusion that memories are reactivated during sleep and that this reactivation changes memory storage (e.g., Creery et al., 2022; Duan et al., 2024).

What is the best evidence that memory consolidation progresses during human sleep? Historically, the most common sort of evidence consisted of demonstrations of superior memory after a nap compared to after an equal period remaining awake, or after a full night of sleep versus after overnight sleep deprivation. Such results are not convincing for the following reasons. These results need not implicate sleep because performance could be impacted not by sleep per se, but indirectly by excessive sleepiness or the stress of sleep deprivation. Even if arguments are raised to counter these problems and possible time-of-day confounds, a serious problem that always remains is that wakefulness may entail more interference than sleep. Comparing memory after delays including versus not including sleep does not convincingly implicate the sleep contribution to learning, though stronger conclusions are warranted when sleep physiology adds correlational support. Evidence that is generally not subject to critiques of arousal confounds, time-of-day confounds, and differential interference has come from methods for modifying sleep.

How can we experimentally hack into sleep? The method of targeted memory reactivation (TMR) is one way to show that retrieval can be improved for memories that have been reactivated during sleep (Paller et al., 2021). Generally, a stimulus such as an odor or a sound can serve as a reminder cue during sleep, precipitating reactivation of some recently learned information. A meta-analysis covering 91 TMR experiments confirmed the replicability of relative memory improvements produced with this method (Hu et al., 2020). In one TMR study, for example, participants attempted to learn 80 names, each associated with a different face, so that they could recall each name when shown the corresponding face (Whitmore et al., 2022). Following a short period of training and repeated practice, memory was tested and then the participants were invited to have an afternoon nap. When a participant reached slow-wave sleep, as indicated by concurrent polysomnographic recordings, the experimenter delivered a subset of the spoken names from the learning session. After awakening, participants viewed each

face again, one at a time, and attempted to recall the name for each face. Name recall was superior for the names that had been presented during sleep than for those not presented during sleep. In another TMR study, participants memorized 90 object locations, some of which were reactivated during sleep using corresponding object sounds (Schechtman et al., 2021). Results suggested that sleep reactivation could improve memory for the distinctive spatial locations of a set of objects all linked to the same sound (Fig. 3).

Cues presented during sleep in TMR experiments often do not include the information to be remembered later, but rather provoke retrieval of the critical information during sleep. Further studies have sought to understand the brain events accompanying reactivation and how they may contribute to consolidation and improved memory storage (e.g., Schönauer et al., 2017; Schreiner et al., 2018; Wang et al., 2019; Abdellahi et al., 2023). We have much more to learn about offline consolidation and its role in learning. Nevertheless, we now have a wealth of empirical perspectives on the intermediate stages in a memory's trek from initial acquisition to eventual retrieval.

5. Memory entanglement

What is a person but a sum of their memories!

This line was delivered by an unusual embodiment of memories in the fictional universe of *Star Trek Deep Space 9*. A Trill in this universe is someone who retains memories over multiple lifetimes by virtue of an implanted symbiont creature that resides within a progression of humanoid hosts. The symbiont and the host share a single mind. When the host dies, the symbiont can be transferred to another host and live on, carrying the memories from each host's lifetime and somehow keeping them all separate. To what extent can our brains keep our memories separate?

Memories are generally not stored in the human brain in isolation from other memories. Each memory is not contained in a distinct memory orb (e.g., as figuratively shown in the 2015 animated film *Inside Out*). There are some exceptions when memories may seem exceedingly compartmentalized. In psychogenic amnesia and dissociative identity disorder, people have developed something like a new identity. How this new identity behaves may vary considerably from patient to patient because it is governed by the way they've conceptualized how memory works (Kritchevsky et al., 2004). Once we enter the realm of these sorts of disorders, as in a science-fictional universe, all bets are off.

Under typical circumstances, though, how are our memories entangled? Let's consider episodic memories first. Each is unique, as it was experienced at a unique time, but to make sense of an experienced episode, we rely on many aspects of knowledge (semantic memory). In addition, episodes tend to have a context connected to other episodes. More generally, our new experiences make sense through connections to previously acquired knowledge, and in that sense, memories are not isolated. We understand facts and episodes by virtue of both how they are related to other bits of knowledge and how they are different. Not only is this entanglement critical for comprehension, but it applies to considerations of memory storage. Comprehension and retrieval are fundamentally accomplished via these interrelationships, and there are benefits and costs of these interrelationships.

Relationships among memories are a potential source of interference and forgetting. Attempting to retrieve one memory can bring along closely related memories, and confusion among the options can then prevent the correct memory from being accessed. Inhibition in such contexts can be studied in various ways (e.g., Storm and Levy, 2012). Reactivation of a memory can entail interactions with other memories, and reactivation may differ for conscious reactivation versus unconscious reactivation (Tal et al., 2024). Storing a memory effectively demands clarity with respect to how that memory is connected to related memories.

Ken Norman and colleagues (2005) hypothesized that REM sleep can

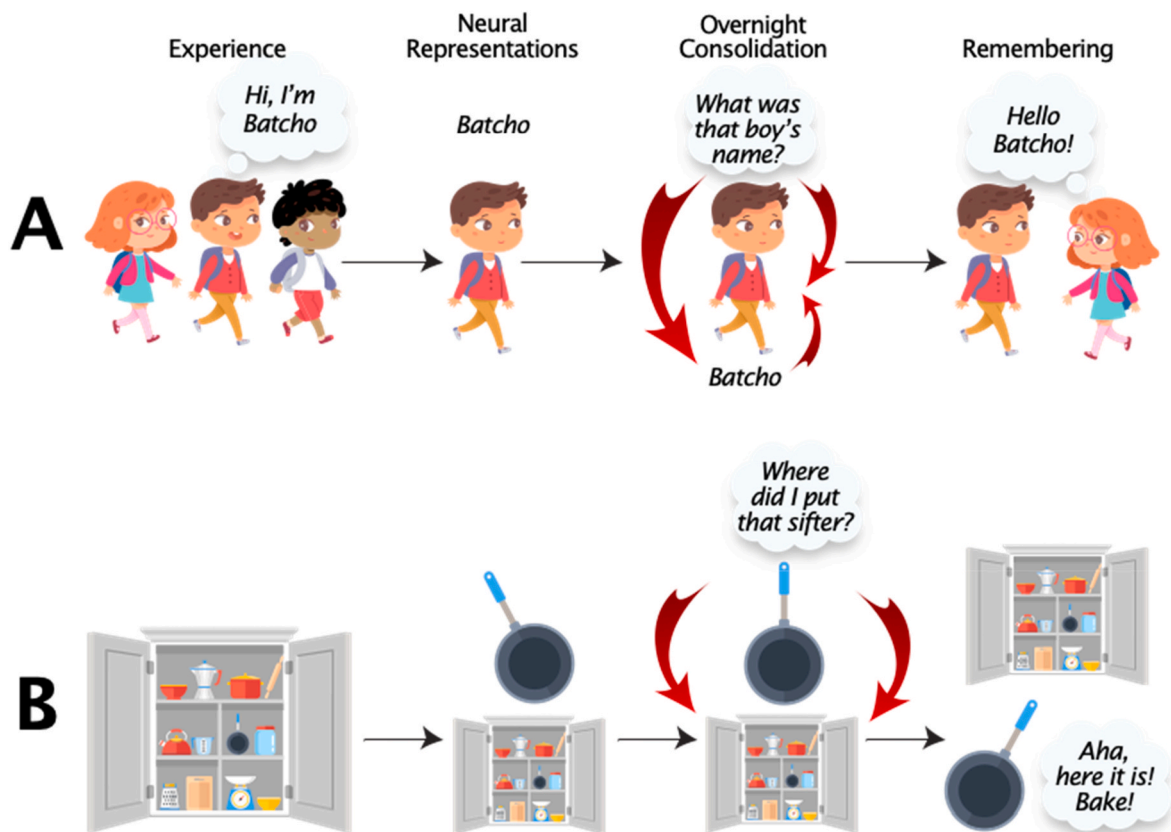


Fig. 3. Examples of learning studied using methods of targeted memory reactivation during sleep. (A) Learning face-name associations. Whitmore et al. (2022) showed that memory reactivation during sleep could improve name recall. (B) Learning object-location associations. Schechtman et al. (2021) investigated how recall of object locations was influenced by memory reactivation during sleep when multiple memories were simultaneously reactivated. The term “sleep learning” has conventionally been restricted to mean acquiring new information from environmental input during sleep, but because overnight consolidation makes valuable contributions to learning, overnight consolidation could be considered a valuable form of *Sleep Learning*.

allow for interleaved reactivation of memories and their potential relationships, thereby offsetting the problem of incorporating new information into networks without disrupting existing knowledge. Storage alterations could go two ways: (i) related memories could become linked in a way that mutually supports their storage, or (ii) memories could change so that they become more clearly differentiated from each other. Further tests are needed to determine whether this sort of processing occurs during REM sleep, or during sleep generally, though the idea continues to be entertained (González et al., 2020; Lewis et al., 2018).

To the extent that new memories are not isolated from other memories, memory consolidation can work by modifying these various interconnections. Some interconnections are formed at encoding, as part of acquisition. But there is potential for a new memory to gain more meaning when additional interconnections are developed later, offline.

6. The memories we keep

*Let's forget about all the things that we've done wrong
Just remember all of the things that we've done right*
- Songwriter Ray Davies (1971)

Our personal recollections of the past can be biased toward the positives or the negatives in our lives. Positive reminiscence versus perseverative negative rumination could have opposite effects on memory storage, brought to extremes in obsessive-compulsive disorder and suicidal depression. What we choose to recollect likely biases which memories are stored most effectively. Overnight consolidation may either probe new ground in a creative fashion or stick with existing biases in a conservative fashion (Fig. 4).

What are the requirements for forming an enduring memory? Certainly not the intention to remember, as we so often remember (and forget) things we'd rather not. True to age-old wisdom, practice is key. But not only intentional practice — also the practice we don't intend and the practice we don't even seem to know about. Although sleep-based reactivation was emphasized here, improvements in memory storage are also driven while we are awake, even when we don't realize it (Tambini and D'Esposito, 2020). During sleep, we may also remain unaware of mechanisms that contribute to synaptic homeostasis by weakening connections, which facilitates new learning the next day (Tononi and Cirelli, 2014), but such mechanisms are readily distinguished from the reactivation-based changes in storage emphasized here.

Principles of memory developed through the years include valuable insights about elaboration, repetition, and actively engaging retrieval. Even for episodic information acquired during a single unique event that we experience just the once, repeated reactivation may be central to maintaining that memory for the long term (Paller et al., 2020). Knowledge of brain mechanisms of memory consolidation for complex episodic memories is still rudimentary and not surveyed here. The medial temporal region and a variety of neocortical areas would be certainly critical depending on the type of episodic information involved. Hippocampal-cortical interactions have been part of this story since Marr (1971) and delineating the relevant physiological steps during sleep continues to be an exciting research focus (Girardeau et al., 2009; Maingret et al., 2016).

Future research on sleep-memory connections may provide insights useful for treating those with disordered sleep as well as other people. Recurrent nightmares in people with post-traumatic stress disorder seem

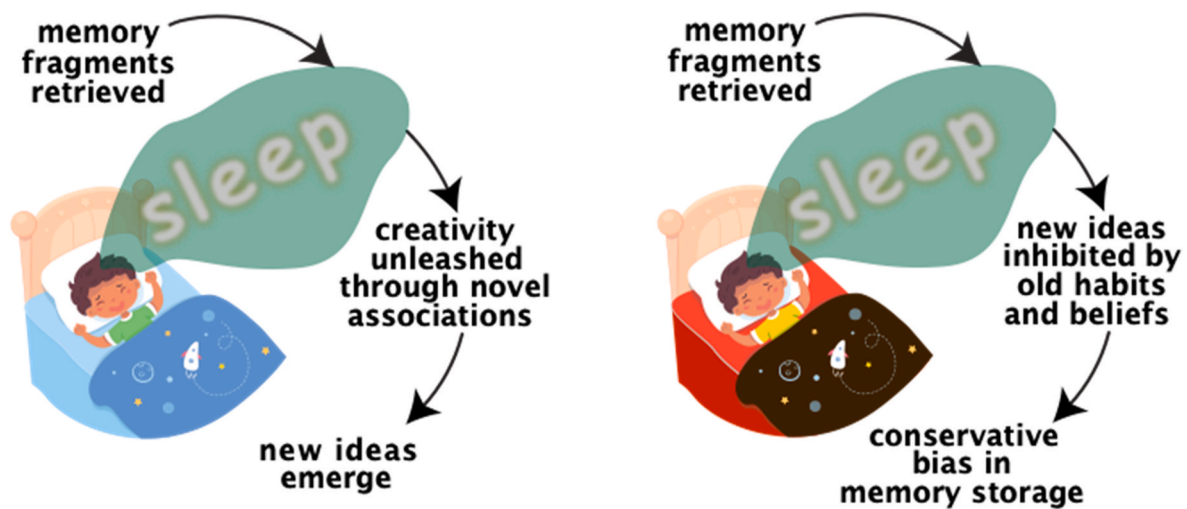


Fig. 4. Is overnight consolidation creative or conservative? New research is needed to address this question. Given that memory interrelationships are critically relevant for consolidation, memory storage is guided by the unique collection of memories each of us have stored to this point in our lives, which includes an influential conglomeration of beliefs and goals. As shown on the left, consolidation could be particularly beneficial when it affords a chance for new associations to be discovered. A recent event may initially be restricted to a recent context, but eventually make contact with knowledge from long ago that puts it in a new light. The dramatic creativity often evident in dreams tells us that sleep is capable of opening the door to a wealth of novel ideas. The creative potential of sleep is indeed supported by experimental evidence (Horowitz et al., 2023; Lacaux et al., 2021; Sanders et al., 2019). Another possibility, shown on the right, is that sleep-based consolidation can suppress creativity. A conservative tendency may be operative when each day's memorable experiences are reactivated and consolidated. Ingrained habits and beliefs may be operative during sleep-based consolidation, acting to protect the status quo in the sense of maintaining consistency with deeply held views. This force may interfere with the ability to take on new ideas that do not harmonize with long-held habits. This question about sleep-based consolidation may have wider relevance. Andrew Mayes put forward a set of ideas for societal change to assure a safe planet for the future (Mayes, 2024). He argued that wise decisions are needed to weather the political challenges and struggles of modernity, including the need to change our ways and avoid a global climate disaster. If one's habits of freely using resources that have always seemed ample or unlimited are operative during consolidation, these habits may interfere with taking on board the idea that strategic action is needed to counteract climate change on Earth. Perhaps a helpful step is to recognize both (a) our natural tendency to be comfortable when things remain the same, and (b) our capacity to gain new habits that can improve well-being and allow new ideas to take root. To overcome conservative tendencies, concerted effort may be needed to resist the ingrained paths our minds tend to follow, especially when the dire shortcomings of well-worn paths become obvious.

to be associated with failures to consolidate traumatic memories effectively. Yet, there is a glaring gap in our understanding when it comes to questions about dreaming and its potential benefits. Advances in methods for asking dreamers about their experiences while they are still asleep (Konkoly et al., 2021) have opened the door to new strategies for determining the extent to which dreaming entails changes in memory storage. The persistent mystery of dreaming highlights how much more remains to be learned about the neurocognitive mechanisms of memory reactivation during sleep.

CRediT authorship contribution statement

Ken A. Paller: Conceptualization, Funding acquisition, Methodology, Project administration, Resources, Visualization, Writing – original draft, Writing – review & editing.

Data availability

No data was used for the research described in the article.

Acknowledgements

This article is a tribute to the powerful influence of Andrew Mayes on my thinking about memory and my orientation as a scientist. The ideas presented here reflect the scientific training I received from him when I was a PhD student, a few years later when I was a postdoc in his lab, and subsequently in collaborative research that continued until his untimely passing. Some of the ideas expressed here were also described in our 2020 book chapter (Paller et al., 2020). Many other individuals also provided inspiration and beneficial conversations on these topics, including John Batcho, Daniela Montaldi, and Marcia Grabowecy.

Thanks to Lynn Pearson for illustrations. Research support from NSF, NIH, the Mind Science Foundation, the McKnight Foundation, and the Mind and Life Institute is gratefully acknowledged.

References

- Abdellahi, M.E.A., Koopman, A.C.M., Treder, M.S., Lewis, P.A., 2023. Targeting targeted memory reactivation: Characteristics of cued reactivation in sleep. *Neuroimage* 266, 119820.
- Aggleton, J.P., Saunders, R.C., 1997. Relationships between temporal lobe and diencephalic structures implicated in anterograde amnesia. *Memory* 5, 49–71.
- Andrillon, T., Kouider, S., 2019. The vigilant sleeper: neural mechanisms of sensory (de) coupling during sleep. *Current Opinion in Physiology* 15, 47–59.
- Antony, J.W., Piloto, L.R., Wang, M., Pacheco, P., Norman, K.A., Paller, K.A., 2018. Sleep spindle refractoriness segregates periods of memory reactivation. *Curr. Biol.* 28, 1736–1743.
- Atherton, K.E., Nobre, A.C., Lazar, A.S., Wulff, K., Whittaker, R.G., Dhawan, V., Lazar, Z. I., Zeman, A.Z., Butler, C.R., 2016. Slow wave sleep and accelerated forgetting. *Cortex* 84, 80–89.
- Bjork, R.A., Bjork, E.L., 2020. Desirable difficulties in theory and practice. *Journal of Applied Research in Memory and Cognition* 9, 475–479.
- Brown, R., Kulik, J., 1977. Flashbulb memories. *Cognition* 5, 73–99.
- Butler, C., Gilboa, A., Miller, L., 2019. Accelerated long-term forgetting. *Cortex* 110, 1–4.
- Cairney, S.A., Guttesen, A.Á.V., El Marj, N., Staresina, B.P., 2018. Memory consolidation is linked to spindle-mediated information processing during sleep. *Curr. Biol.* 28, 948–954.
- Cartwright, R., 2010. *The Twenty-Four Hour Mind: the Role of Sleep and Dreaming in Our Emotional Lives*. Oxford.
- Cassel, A., Kopelman, M., 2019. Have we forgotten about forgetting: a critical review of 'accelerated long-term forgetting' in temporal lobe epilepsy. *Cortex* 110, 141–149.
- Craik, F., Lockhart, R., 1972. Levels of processing: a framework for memory research. *J. Verb. Learn. Verb. Behav.* 11, 671–684.
- Creery, J.D., Brang, D.J., Arndt, J.D., Bassard, A., Towle, V.L., Tao, J., Wu, S., Rose, S., Warnke, P., Issa, N.P., Paller, K.A., 2022. Memory reactivation during slow-wave sleep elicits electrophysiological activity in the human hippocampus to support memory consolidation. *Proceedings of the National Academy of Sciences USA* 119, e2123430119.
- Creery, J.D., Brang, D., Patel, M., Towle, V.L., Tao, J., Wu, S., Paller, K.A., 2019. Hippocampal epileptic activity during sleep disrupts memory consolidation. *In:*

- Poster Presented at the 26th Annual Meeting of the Cognitive Neuroscience Society. San Francisco.
- Duan, W., Xu, Z., Chen, D., Wang, J., Lui, J., Xian, X., Wang, M., Paller, K.A., Axmacher, N., Wang, L., 2024. Memory consolidation during human sleep depends on cortical reactivation and hippocampal-cortical dynamics. Manuscript under review.
- Dudai, Y., 2012. The restless engram: Consolidations never end. *Annu. Rev. Neurosci.* 35, 227–247.
- Fosse, M.J., Fosse, R., Hobson, J.A., Stickgold, R.J., 2003. Dreaming and episodic memory: a functional dissociation? *J. Cognit. Neurosci.* 15, 1–9.
- Girardeau, G., Benchenane, K., Wiener, S.I., Buzsáki, G., Zugaro, M.B., 2009. Selective suppression of hippocampal ripples impairs spatial memory. *Nat. Neurosci.* 12, 1222–1223.
- González, O.C., Sokolov, Y., Krishnan, G.P., Delanois, J.E., Bazhenov, M., 2020. Can sleep protect memories from catastrophic forgetting? *Elife* 9, e51005.
- Harrington, M.O., Johnson, J.M., Croom, H.E., Pennington, K., Durrant, S.J., 2018. The influence of REM sleep and SWS on emotional memory consolidation in participants reporting depressive symptoms. *Cortex* 99, 281–295.
- Hirst, W., et al., 2009. Long-term memory for the terrorist attack of September 11: flashbulb memories, event memories, and the factors that influence their retention. *J. Exp. Psychol. Gen.* 138, 161–176.
- Horowitz, A.H., Esfahany, K., Gálvez, T.V., Maes, P., Stickgold, R., 2023. Targeted dream incubation at sleep onset increases post-sleep creative performance. *Sci. Rep.* 13, 7319.
- Hu, X., Cheng, L., Chiu, M.H., Paller, K.A., 2020. Promoting memory consolidation during sleep: a meta-analysis of targeted memory reactivation. *Psychol. Bull.* 146, 218–244.
- Klinzing, J.G., Niethard, N., Born, J., 2019. Mechanisms of systems memory consolidation during sleep. *Nat. Neurosci.* 22, 1598–1610.
- Konkoly, K.R., Appel, K., Chabani, E., Mangiaruga, A., Gott, J., Mallett, R., Caughran, B., Witkowski, S., Whitmore, N.W., Mazurek, C.Y., Berent, J.B., Weber, F.D., Türker, B., Leu-Semenescu, S., Maranci, J.B., Pipa, G., Arnulf, I., Oudiette, D., Dresler, M., Paller, K.A., 2021. Real-time dialogue between experimenters and dreamers during REM sleep. *Curr. Biol.* 31, 1417–1427.
- Kritchevsky, M., Chang, J., Squire, L.R., 2004. Functional amnesia: clinical description and neuropsychological profile of 10 cases. *Learn. Mem.* 11, 213–226.
- Lacaux, C., Andrillon, T., Bastoul, C., Idir, Y., Fonteix-Galet, A., Arnulf, I., Oudiette, D., 2021. Sleep onset is a creative sweet spot. *Sci. Adv.* 7, eabj5866.
- Lewis, P.A., Knoblich, G., Poe, G., 2018. How memory replay in sleep boosts creative problem-solving. *Trends Cognit. Sci.* 22, 491–503.
- Livingston, R., 1967. Reinforcement. In: Quarton, G.C., Melnechuk, T., Schmitt, F.O. (Eds.), *The Neurosciences: A Study Program*. Rockefeller, pp. 568–576.
- Maingret, N., Girardeau, G., Todorova, R., Goutierre, M., Zugaro, M., 2016. Hippocampal-cortical coupling mediates memory consolidation during sleep. *Nat. Neurosci.* 19, 959–964.
- Marr, D., 1971. Simple memory: a theory for archicortex. *Phil. Trans. R. Soc. Lond. B* 262, 23–81.
- Mayes, A.R., 1983. *Sleep Mechanisms and Functions in Humans and Animals: an Evolutionary Perspective*. Van Nostrand Reinhold.
- Mayes, A.R., 1988. *Human Organic Memory Disorders*. Cambridge University Press.
- Mayes, A.R., 2024. *Improving Human Futures*. Unpublished manuscript.
- Mayes, A.R., Hunkin, N.M., Isaac, C., Muhlert, N., 2019. Are there distinct forms of accelerated forgetting and, if so, why? *Cortex* 110, 115–126.
- McClelland, J.L., McNaughton, B.L., O'Reilly, R.C., 1995. Why there are complementary learning systems in the hippocampus and neocortex: insights from the successes and failures of connectionist models of learning and memory. *Psychol. Rev.* 102, 419–457.
- Morris, C.D., Bransford, J.D., Franks, J.J., 1977. Levels of processing versus transfer-appropriate processing. *J. Verb. Learn. Verb. Behav.* 16, 519–533.
- Müller, G.E., Pilzecker, A., 1900. Experimentelle beiträge zur lehre vom gedächtnis. *Z. Psychol. Ergänzungsband* 1, 1–300.
- Ngo, H.-V., Fell, J., Staresina, B., 2020. Sleep spindles mediate hippocampal-neocortical coupling during long-duration ripples. *Elife* 9, e57011.
- Norman, K.A., Newman, E.L., Perotte, A.J., 2005. Methods for reducing interference in the Complementary Learning Systems model: Oscillating inhibition and autonomous memory rehearsal. *Neural Network.* 18, 1212–1228.
- Paller, K.A., 2002. Cross-cortical consolidation as the core defect in amnesia. In: Squire, L.R., Schacter, D.L. (Eds.), *The Neuropsychology of Memory*, third ed. Guilford, pp. 73–87.
- Paller, K.A., 2009. Memory consolidation: systems. In: Squire, L.R. (Ed.), *Encyclopedia of Neuroscience*. Academic, pp. 741–749.
- Paller, K.A., Creery, J.D., Schechtman, E., 2021. Memory and sleep: how sleep changes the waking mind for the better. *Annu. Rev. Psychol.* 72, 123–150.
- Paller, K.A., Mayes, A.R., Antony, J.W., Norman, K.A., 2020. Replay-based consolidation governs enduring memory storage. In: Poeppel, D., Mangun, G.R., Gazzaniga, M.S. (Eds.), *The Cognitive Neurosciences*, sixth ed. MIT, pp. 263–274.
- Paller, K.A., Voss, J.L., 2004. Memory reactivation and consolidation during sleep. *Learn. Mem.* 11, 664–670.
- Paller, K.A., Wagner, A.D., 2002. Monitoring the transformation of experience into memory. *Trends Cognit. Sci.* 6, 93–102.
- Pfeiffer, B.E., 2020. The content of hippocampal "replay". *Hippocampus* 30, 6–18.
- Roediger, H.L., Karpicke, J.D., 2006. Test-enhanced learning: taking memory tests improves long-term retention. *Psychol. Sci.* 17, 249–255.
- Rothschild, G., Eban, E., Frank, L.M., 2017. A cortical-hippocampal-cortical loop of information processing during memory consolidation. *Nat. Neurosci.* 20, 251–259.
- Sanders, K.E.G., Osburn, S., Paller, K.A., Beeman, M., 2019. Targeted memory reactivation during sleep improves next-day problem solving. *Psychol. Sci.* 30, 1616–1624.
- Schechtman, E., Antony, J.W., Lampe, A., Wilson, B., Norman, K.A., Paller, K.A., 2021. Multiple memories can be simultaneously reactivated during sleep as effectively as a single memory. *Commun. Biol.* 4, 25.
- Schmolck, H., Buffalo, E.A., Squire, L.R., 2000. Memory distortions develop over time: recollections of the OJ Simpson trial verdict after 15 and 32 months. *Psychol. Sci.* 11, 39–45.
- Schönauer, M., Alizadeh, S., Jamalabadi, H., Abraham, A., Pawlizki, A., Gais, S., 2017. Decoding material-specific memory reprocessing during sleep in humans. *Nat. Commun.* 8, 15404.
- Schreiner, T., Doeller, C.F., Jensen, O., Rasch, B., Staudigl, T., 2018. Theta phase-coordinated memory reactivation reoccurs in a slow-oscillatory rhythm during NREM sleep. *Cell Rep.* 25, 296–301.
- Squire, L.R., Cohen, N.J., Nadel, L., 1984. The medial temporal region and memory consolidation: a new hypothesis. In: Weingartner, H., Parker, E. (Eds.), *Memory Consolidation*. Erlbaum, pp. 185–210.
- Storm, B.C., Levy, B.J., 2012. A progress report on the inhibitory account of retrieval-induced forgetting. *Mem. Cognit.* 40, 827–843.
- Tal, A., Schechtman, E., Caughran, B., Paller, K.A., Davachi, L., 2024. The reach of reactivation: effects of consciously triggered versus unconsciously triggered reactivation of associative memory. *Proceedings of the National Academy of Sciences USA* 121, e2313604121.
- Tambini, A., D'Esposito, M., 2020. Causal contribution of awake post-encoding processes to episodic memory consolidation. *Curr. Biol.* 30, 3533–3543.
- Tononi, G., Cirelli, C., 2014. Sleep and the price of plasticity: from synaptic and cellular homeostasis to memory consolidation and integration. *Neuron* 81, 12–34.
- Tulving, E., Thomson, D.M., 1973. Encoding specificity and retrieval processes in episodic memory. *Psychol. Rev.* 80, 352–373.
- Wang, B., Antony, J.W., Lurie, S., Brooks, P.P., Paller, K.A., Norman, K.A., 2019. Targeted memory reactivation during sleep elicits neural signals related to learning content. *J. Neurosci.* 39, 6728–6736.
- Wassing, R., Lakbila-Kamal, O., Ramautar, J.R., Stoffers, D., Schalkwijk, F., Van Someren, E.J.W., 2019. Restless REM sleep impedes overnight amygdala adaptation. *Curr. Biol.* 29, 2351–2358.
- Whitmore, N.W., Bassard, A.M., Paller, K.A., 2022. Face-name learning benefits from targeted memory reactivation during ample and undisturbed slow-wave sleep. *NPJ Science of Learning* 7, 1.
- Willingham, D.T., 2021. Remembering Names Can Be Tricky. *The Washington Post*. https://www.washingtonpost.com/health/tricks-for-remembering-names/2021/08/20/e889beda-f566-11eb-9738-8395ec2a44e7_story.html.
- Winson, J., 1985. *Brain and Psyche: the Biology of the Unconscious*. Anchor/Doubleday.
- Yonelinas, A.P., Ranganath, C., Ekstrom, A.D., Wiltgen, B.J., 2019. A contextual binding theory of episodic memory: Systems consolidation reconsidered. *Nat. Rev. Neurosci.* 20, 364–375.
- Zadra, A., Stickgold, R., 2021. *When Brains Dream: Exploring the Science & Mystery of Sleep*. Norton.