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Review Article

Neural reactivation during human sleep

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Sleep promotes memory consolidation: the process by which newly acquired memories are stabilised, strengthened, and integrated into long-term storage. Pioneering research in rodents has revealed that memory reactivation in sleep is a primary mechanism underpinning sleep's beneficial effect on memory. In this review, we consider evidence for memory reactivation processes occurring in human sleep. Converging lines of research support the view that memory reactivation occurs during human sleep, and is functionally relevant for consolidation. Electrophysiology studies have shown that memory reactivation is tightly coupled to the cardinal neural oscillations of non-rapid eye movement sleep, namely slow oscillation-spindle events. In addition, functional imaging studies have found that brain regions recruited during learning become reactivated during post-learning sleep. In sum, the current evidence paints a strong case for a mechanistic role of neural reactivation in promoting memory consolidation during human sleep.

Introduction

After initial learning, newly formed memories undergo a period of *consolidation*, which broadly refers to the strengthening and stabilisation of memory traces over time. Sleep, a state where sensory input is diminished, appears to be conducive to memory consolidation processes [1–5]. Beyond passively protecting memory traces, however, recent work has indicated that sleep plays an *active* role in consolidation [6–8]. The neurophysiological mechanisms underpinning this memory function of sleep have thus been the focus of numerous empirical studies in recent years.

Memory reactivation, especially during non-rapid eye movement (NREM) sleep, has emerged as a leading candidate mechanism underpinning sleep's beneficial effect on memory [9]. Landmark studies in rodents have shown that patterns of neuronal firing observed at learning are replayed during sleep in temporally compressed sequences, primarily in hippocampus but also in coordination with learning-related cortical sites [10–14]. The phenomenon of replay has been linked to post-sleep behavioural performance. Not only are the amount of replay events correlated with pre- to post-sleep memory improvement [12], but techniques such as optogenetics have found that disrupting memory replay leads to a selective disruption of the consolidation of that memory [15–17].

The influential *Active Systems Consolidation (ASC)* framework posits that memory reactivation in hippocampus and neocortex during sleep supports the integration of newly acquired memories into long-term storage [18,19]. This hippocampal-neocortical dialogue is facilitated by a finely tuned interplay of three neural oscillations that characterise NREM sleep: high-frequency (~200 Hz in rodents, ~80–150 Hz in humans) hippocampal ripples, thalamocortical spindles (~10–16 Hz), and global slow oscillations (SOs; ~1 Hz) [9,20] (Figure 1). In hippocampus, ripples encompass reactivation events and are nested into the troughs of spindles, which in turn induce synaptic plasticity in learning-related circuits [21]. A subset of these spindle-ripple events are enwrapped in the excitable rising phase (upstate) of global SOs, which act as a pacemaker for information transfer between hippocampus and neocortex [22].

This hippocampal-cortical dialogue appears to follow a cortical-hippocampal-cortical loop in rodents, with the engagement of task-relevant cortical sites preceding associated reactivation in hippocampus [23–25]. It has been suggested that initiation by cortex ensures that the cortical sites are in a state that is conducive to plasticity [26]. Hippocampal-cortical connectivity is then sustained for a
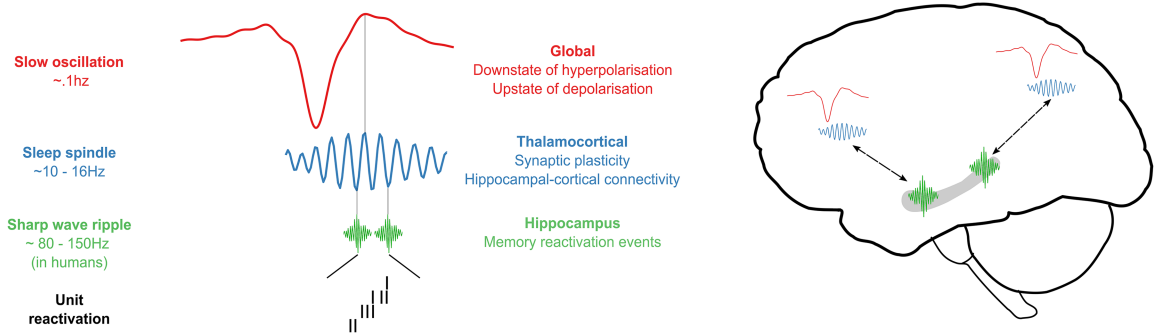
Figure 1. How neural oscillations support memory reactivation during sleep.
Neural sequences coding for specific memories are reactivated during hippocampal sharp-wave ripples. Ripples nest into the excitable trough of sleep spindles: thalamocortical oscillations that facilitate information transfer between hippocampus and neocortex. Spindles in turn couple to the upstate of global slow oscillations, which reflect periods of brain-wide depolarisation, offering a critical time window for this hippocampal-cortical dialogue to occur.

period following hippocampal reactivation, allowing for a spindle-mediated transfer of memory traces from hippocampus back to neocortex [26,27]. These findings emphasise the importance of not just the hippocampus in memory reactivation processes, but also the role that learning related-cortical sites play in initiating a cross-regional dialogue.

Rodent models have made a substantial contribution to our understanding of the neurophysiological mechanisms underpinning sleep-associated memory processing. This review aims to examine recent efforts to translate these findings into humans. We will first consider evidence for the coupling of ripples, spindles, and SOs during human NREM sleep. We will then turn our attention to evidence that the temporal coordination between these neural oscillations promotes memory reactivation and information transfer between hippocampus and neocortex. Finally, we will review evidence that specific brain regions that are involved in learning become reactivated during human sleep.

Coupling of neural oscillations during human sleep

Traditional scalp electroencephalography (EEG) has been widely used to study coupling between cortical SOs and spindles. These studies have consistently shown that a subset of spindles preferentially couple to the rising phase of SOs [28–32]. Correlational studies have reported that the memory benefits of sleep are best when spindles consistently couple to the peaks of SOs [33–40]. Furthermore, these SO-coupled spindles are significantly better predictors of memory than uncoupled spindles [41–44], highlighting the importance of oscillatory coupling in memory consolidation. Moving beyond correlational evidence, electrical and acoustic stimulation has been used to enhance SO-spindle coupling [45,46], leading to improvements in memory [47,48].

Scalp EEG is limited by its spatial resolution, meaning that it is not possible to reliably detect signals coming from deep brain sources such as hippocampus. Therefore the triple-coupling of ripples, spindles and SOs (a key tenet of ASC) cannot be assessed. The only way to reliably detect human hippocampal ripples is via intracranial EEG (iEEG), where depth electrodes are directly implanted into hippocampus. This invasive procedure is only justified in clinical cases, such as assisting in the treatment of medication-resistant epilepsy. Studies in this patient group have confirmed the triple-coupling of ripples, spindles and SOs during human NREM sleep [49,50]. Furthermore, these coupled oscillations drive firing rates of individual hippocampal neurons [51], offering a putative mechanism through which neural oscillations facilitate the reactivation of newly formed memory traces in NREM sleep.

Oscillatory coupling has also been shown to facilitate information transfer during sleep, both within the medial temporal lobe [51] and between hippocampus and neocortex [27,52]. This cross-regional communication appears to be mediated by spindle activity that is locked to hippocampal ripples [27,52], suggesting that spindles serve to synchronise mnemonic processing across cortical and subcortical structures [27,53]. In line with rodent work, it appears that this spindle-ripple mediated, hippocampal-neocortical dialogue is initiated in neocortex, with connectivity sustained until after the ripple has terminated, allowing for the transfer of reactivated memory traces back to cortex [27,52]

A recent breakthrough study was able to causally link these oscillatory dynamics to the behavioural benefits of sleep for memory [54]. Using a deep brain stimulation protocol, the researchers timed the delivery of electrical stimulation in pre-frontal cortex to the excitable upstates of ongoing SOs. Compared with sham stimulation, electrical stimulation increased neuronal spiking during SO upstates and amplified temporal coupling between ripples, spindles, and SOs [54]. Remarkably, upstate stimulation also enhanced picture recognition accuracy the following day, as compared with the sham condition [54]. As an important control condition, the researchers stimulated during the SO downstate, a period of neuronal quiescence that should not be conducive to memory consolidation [9]. This is indeed what they found, with downstate stimulation not leading to any improvement in memory performance. Thus, not only does the triple coupling of ripples, spindles and SOs exist in humans, it directly promotes memory consolidation.

Both scalp and intracranial EEG have verified the presence of oscillatory coupling during human NREM sleep and have linked this to memory consolidation. We next turn our attention to research demonstrating that memory content is reactivated during human sleep.

Electrophysiological evidence for memory reactivation during sleep

In human models, the reinstatement of neural activity that was present at learning is taken as evidence of memory reactivation [55]. As such, machine learning decoding approaches are often used to assess evidence of memory reactivation in the sleeping human brain [56–58]. In such analyses, neural signatures of learning are delineated during wakefulness and this information is used to determine if and when the same content emerges during sleep. For example, suppose EEG is monitored while an individual views images of objects and scenes; the machine learning algorithm can be trained on this EEG data to differentiate neural activity patterns unique to viewing objects and scenes. The machine learning training parameters (obtained from object and scene viewing) can then be applied to sleep EEG data obtained after learning to predict if and when object and/or scene memories are reactivated.

Although there is evidence that sleep-associated memory processing unfolds throughout the night [59], a major challenge for researchers is to determine where to look for memory reactivation. Two approaches have been adopted to address this issue. The first concerns *endogenous memory reactivation*, where researchers look for evidence of memory reactivation that emerges spontaneously. Analyses are focused around the time of ripple-spindle-SO events on the basis that this co-ordinated neural activity represents an electrophysiological correlate of offline memory processing. One challenge of investigating endogenous memory reactivation is that researchers have limited control over which memories are reactivated. This can be addressed with the second approach, known as *targeted memory reactivation* (TMR). With TMR, odours or sounds that are associated with newly learned materials prior to sleep are then re-presented to individuals during sleep in a bid to reactivate specific memories. Both approaches provide a precise timeframe for researchers to isolate evidence of mnemonic processing in sleep.

Endogenous memory reactivation

Studies in rodents have documented reactivation of neuronal firing patterns in temporally compressed sequences during sleep. Extending this finding to humans, a patient case study recently reported evidence of memory reactivation during sleep at the level of single neurons in motor cortex [60]. It was shown that neural sequences associated with motor learning were re-expressed at a rate significantly above chance in sleep, and there was also evidence that memory reactivation was temporally compressed [60].

A recent scalp EEG study employed the machine learning decoding approach outlined above to test for memory reactivation during SO-spindle events. In line with the idea that SO-spindle coupling promotes memory reactivation, category-level features of previously encoded memories (objects or scenes) could be reliably discriminated near the peak of the ongoing SO (Figure 2A). Moreover, the magnitude of this category-level memory reactivation correlated with the precision of SO-spindle coupling and the benefits of sleep for memory retention [61]. Consistent with the putative function of coupled SO-spindle events in memory reactivation during sleep, evidence of category-level reactivation was not observed when the analyses were performed on either spindles or SOs in isolation.

Utilising iEEG, another study reported similar findings within hippocampus [62]. Here, the spontaneous re-emergence of wakeful learning patterns was detected throughout both quiet waking rest and NREM sleep.
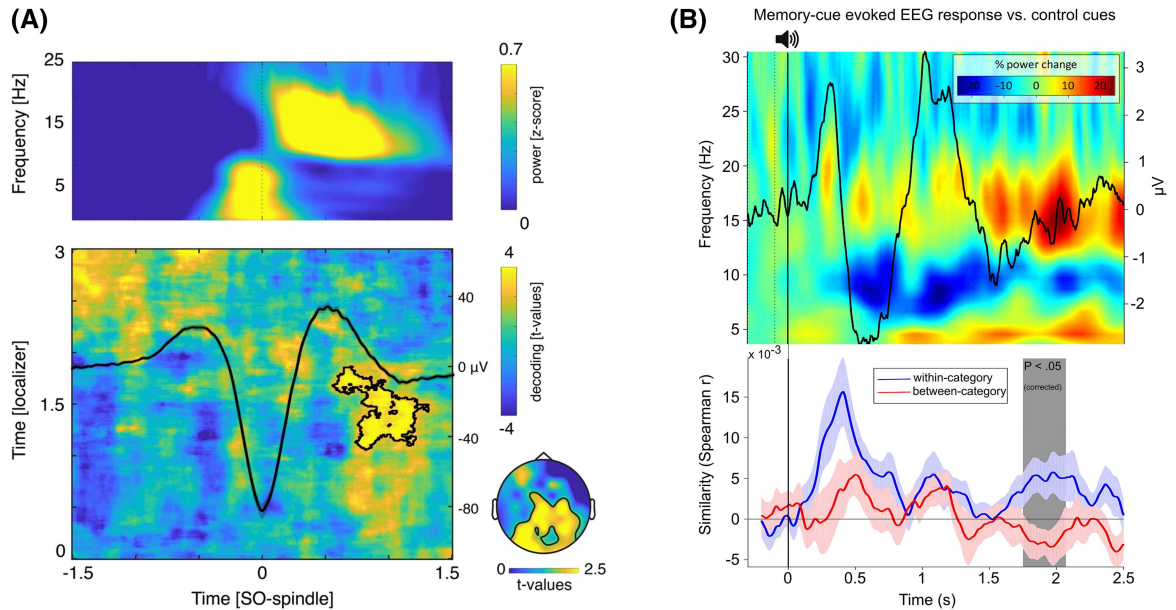
Figure 2. Electrophysiological evidence for memory reactivation in human sleep.
(**A**) Endogenous memory reactivation. Top: Time frequency representation showing that spindle power (yellow blob at ~15 Hz) is maximal around the peak of the SO (black line in bottom panel). Bottom: Machine-learning classification approaches can identify evidence of category-level memory reactivation during NREM sleep. Significant (i.e. above chance level) classification is highlighted with a black contour. Note the close alignment of significant classification to the SO peak [61]. (**B**) Targeted memory reactivation (TMR). Top: Following re-exposure to a memory cue in NREM sleep, there is a larger sleep spindle response than that emerging from previously unheard control cues, consistent with memory reactivation. Bottom: At the same time as this evoked spindle response, evidence of category-specific memory reactivation emerges in the EEG data [71]. All figure reproductions made under a Creative Commons Attribution 4.0 International License.

However, the behavioural benefits of sleep for memory were only correlated with reactivation that occurred during hippocampal ripples in NREM sleep. Together, these findings provide evidence of memory reactivation emerging spontaneously in the sleeping brain, and that reactivation supports overnight memory consolidation.

Targeted memory reactivation

TMR biases memory reactivation towards memories that are associated with a sound or odour cue presented during sleep [63], leading to improved memory for cued relative to non-cued information [64]. TMR cues lead to a robust increase in sleep spindle activity, with the magnitude of this enhanced spindle response predicting the behavioural benefit of TMR [65–70]. This shows that TMR evokes patterns of neural oscillatory activity associated with memory reactivation and consolidation.

Recent studies have combined TMR protocols with machine learning methods to provide evidence of memory reactivation in sleep. This approach is based on the idea that, if a TMR cue elicits reactivation of a specific memory, then the evoked neural patterns should match the learning patterns for that memory, as compared with other memories associated with different cues. Using this approach, it has been demonstrated that categorical features (objects or scenes) of memories cued by TMR can be reliably decoded during the evoked spindle response [71] (Figure 2B). This timing is important, as it provides further evidence that sleep spindles are centrally involved in memory reinstatement processes. The magnitude of this effect also correlated with the behavioural benefit of TMR, thus linking memory reinstatement with behaviour. This basic finding, that memory content can be decoded following TMR cues, has been replicated several times across different domains of memory [72–75].

TMR cues are typically presented without consideration of what is occurring in the background EEG. However, as already discussed, memory reactivation appears to be optimal around the peak of the SO [61], and

electrical stimulation applied during the SO upstate enhances memory, whereas stimulation in the downstate does not [54]. These findings would suggest that memory reactivation evoked by TMR cues should be optimal when TMR cues are presented during the SO upstate, as this is a critical time window for endogenous memory processing. Post-hoc analyses, which compare the behavioural benefit of TMR presented within different SO phases are equivocal on this point. One re-analysis found that only upstate TMR cues improved memory relative to no TMR, however the difference between upstate and downstate TMR was not statistically significant [76]. A different research group concluded that TMR cues presented during the SO downstate were more effective at improving memory compared with cues presented in the upstate [77]. A recent study experimentally manipulated the delivery of TMR cues to either the SO upstate or downstate, and found that neural reinstatement of memory content only occurred when cues were presented during the SO upstate [78]. While this finding is in line with theoretical predictions, it is clear that more work is needed to confirm the relationship between TMR effectiveness and ongoing neural oscillations

In sum, there is accumulating evidence from electrophysiological studies that memory reactivation occurs during human sleep, and this re-emergence of memory content is tightly coupled to SO-spindle-ripple events. In the next section, we turn to evidence from functional imaging methods, including functional magnetic resonance imaging (fMRI), which can more precisely detail reactivation in learning-related brain regions and networks.

Functional imaging evidence for memory reactivation during sleep

Techniques such as fMRI or positron emission tomography (PET) offer unique insights into memory reactivation processes. First, it is possible to non-invasively measure hippocampal activity, which is not possible with scalp EEG. This is important, given the central role of the hippocampus in memory reactivation [9]. Second, rodent studies have emphasised the importance of learning-related cortical sites in both initiating reactivation sequences [24], and the subsequent expression of spindles at those cortical sites for inducing LTP and synaptic plasticity [21,79–82]. Compared with EEG, fMRI can more precisely measure *where* in the brain reactivation is occurring, allowing researchers to confirm whether learning-related sites are reactivated in human sleep.

In a landmark PET study, hippocampal activation observed during spatial navigation was observed again during post-learning sleep [83]. Hippocampal activity during sleep was higher than control groups who either performed no pre-sleep learning task, or engaged in non-hippocampal dependent learning, indicating that the observed hippocampal reactivation was selective for the spatial memories that recruited hippocampus during learning [83]. Many subsequent studies (primarily fMRI), have repeatedly shown that brain regions engaged at learning are re-engaged during subsequent sleep, with the level of re-engagement correlating with the behavioural benefits of sleep for memory consolidation [84–93].

Neuroimaging researchers have also documented reactivation of learning-related cortical regions during sleep. In one experiment where participants consolidated either a face or maze learning task, it was possible to discriminate which task was being consolidated based on reactivation within task-relevant regions [89] (Figure 3A). While both tasks led to reactivation in areas of visual cortex, consolidation of the face task uniquely led to reactivation in the fusiform face area (FFA). In contrast, the maze task promoted reactivation in parahippocampal regions.

A growing number of studies have utilised the power of simultaneous EEG-fMRI recordings to examine fMRI-derived neural reactivation that co-occur alongside sleep spindles detected in the concurrent EEG. This can address the question of whether memory reactivation emerges alongside the neural oscillations that are linked to memory reprocessing during sleep. In one such study, participants learned paired face-scene associates or performed a non-learning control task before sleeping in an MRI scanner with combined EEG recordings [85]. Results showed that activation in specific brain regions associated with processing of faces (FFA) and scenes (parahippocampal place area) re-emerged during sleep spindles. Similar findings have been reported for non-declarative procedural memories, whereby brain regions within a stratio-cerrobello-cortical network that are recruited during a motor sequence learning task are reactivated during post-learning sleep, also time-locked to sleep spindles [86,87].

TMR has also been combined with fMRI to elucidate memory reactivation during sleep. Using an odour-TMR paradigm, researchers paired each of four odours with four distinct categories (buildings, faces, animals, and tools). Two of the odours were re-represented during subsequent NREM sleep [88]. During odour
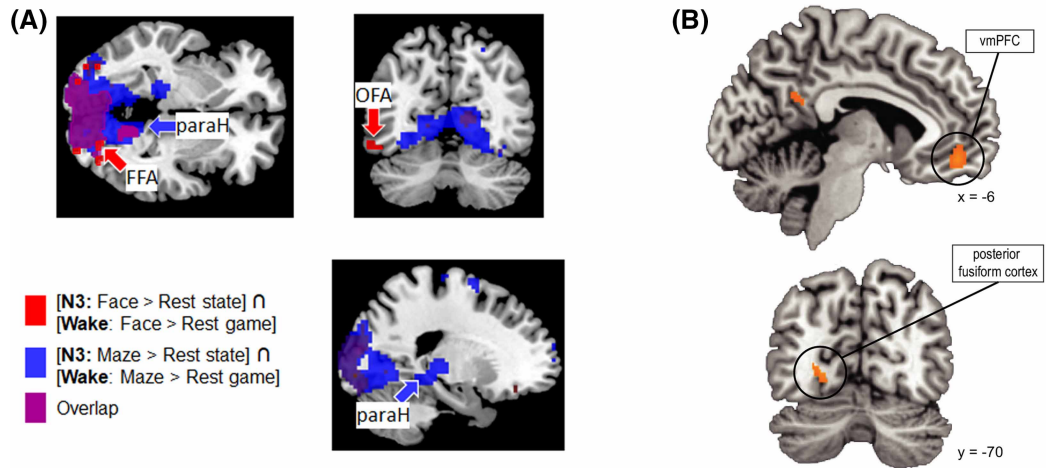
Figure 3. Functional imaging evidence for memory reactivation in human sleep.
(**A**) Selective reactivation of learning-related brain regions during sleep. During the consolidation of a face task, there was selective reactivation of face-related brain areas, such as the fusiform face area. Conversely, during consolidation of a maze task, there was reactivation in brain areas associated with spatial navigation, such as parahippocampal cortex. Both tasks elicited reactivation in visual processing areas [89]. (**B**) Following the presentation of an odour-based TMR cue, category-level reactivation (i.e. discriminating between objects and scenes) was localised to pre-frontal and fusiform cortex regions, implicating these brain regions in the reactivation of category-level memory representations in sleep [88]. All figure reproductions made under a Creative Commons Attribution 4.0 International License.

re-presentation, it was possible to decode the memory category originally paired with the re-presented odour, implying category-level reactivation of the associated memories. Using the high spatial resolution offered by fMRI, they found reactivation occurred most strongly within the ventromedial pre-frontal cortex (vmPFC) and posterior fusiform cortex (Figure 3B). Importantly, category-level discrimination during wake was also localised to vmPFC, again highlighting the close spatial overlap between brain regions involved in learning and brain regions reactivated during sleep. The extent to which the odours reactivated the associated category was also predictive of memory recall performance after sleep, tying neural reactivation to the behavioural benefits of sleep for memory.

This finding of category-level reactivation during sleep is in agreement with findings observed in EEG studies [61,71]. It is important to highlight here how the EEG and fMRI results complement each other. The high temporal resolution and direct recording of neural oscillations available with EEG have demonstrated that memory reactivation is clocked by SO-spindle coupling events, in line with the primary predictions of ASC theory [9]. On the other hand, the high spatial precision of fMRI has confirmed rodent observations of memory reactivation in the learning-related cortical areas [24], pinpointing the brain regions that participate in reactivation with a level of specificity not possible with EEG.

Future directions

Impressive progress has been made in detecting neural reactivation during human sleep. Complementary lines of evidence have confirmed that brain areas involved in memory encoding reactivate during subsequent sleep. Reactivation events occur most strongly during ripple-spindle-SO events, and numerous studies have linked the degree of reactivation to behavioural metrics of sleep-associated consolidation, implying a functional role of reactivation in enhancing memory. Despite this, several open questions remain.

First, work in rodents emphasises the temporally compressed sequential reactivation of learning-related cells in facilitating memory consolidation [10]. In humans, memory reactivation has been detected at broader spatial scales using MVPA techniques (e.g. [60,89]), but the temporal structure of the reactivation is still unknown. Sequential reactivation of single neurons in humans has been demonstrated to be feasible in principle [60], but future studies with multiple participants are needed to link such events to memory improvement. Future

research could also consider employing tasks that have a sequential component to them (e.g. learning a sequence of pictures corresponding to different categories). Utilising a TMR protocol and MVPA analyses, it would be possible to examine sequential reactivation of the sequence following a TMR cue (e.g. if a learning sequence went object → scene → face, evidence for sequential reactivation would be obtained if an MVPA classifier trained on objects peaked first following the cue, followed by a classifier trained on scenes, then finally a classifier trained on faces). Evidence for time compression could also be evaluated by comparing the time courses of the reactivation during sleep with the activation patterns seen during wake, which would speak to the temporal compression seen in rodents.

Second, ASC places a heavy emphasis on oscillatory coupling in promoting memory consolidation. However, in humans at least, only a subset of spindles couple to SOs. The mnemonic function (if any) of uncoupled spindles has yet to be established, and more work is needed to understand the relative contributions of coupled and uncoupled spindles to offline memory processing. Relatedly, theoretical and empirical work has focused on the 'fast' spindle subtype (~13–15 Hz). So-called 'slow' spindles (~10–12 Hz) exhibit distinct topographies and SO-coupling profiles compared with fast spindles [28,30,41]. Although some work has shown that fast spindles are uniquely involved in memory consolidation [41,61], other research has indicated a mnemonic function of slow spindles [94]. Moreover, whereas scalp EEG is agnostic to the generator sources of detected sleep spindles, some iEEG work reported that slow spindles only emerge in cortex [49]. Fast spindles on the other hand occur in both cortical and subcortical structures, including the hippocampus. This preliminary work suggests that only fast sleep spindles exhibit the properties necessary to facilitate the cross-regional dialogue required by active systems consolidation theory. Therefore, the current ASC framework fails to consider the full dynamics of human sleep spindles, and future work is needed to refine our understanding of exactly which neural events best support memory consolidation.

With the growing evidence of memory reactivation in human sleep, a pertinent question is which memories are most likely to be reactivated. It is well known that long-term memory is biased in favour of personally or emotionally salient information [95–98], and some studies suggest that these kinds of memories are prioritised for consolidation during sleep [89,99] (though see [100]). Weakly encoded memories also appear to be reactivated preferentially during quiet wakefulness [101], receive the largest benefit from TMR in sleep [102,103], and are preferentially consolidated during SO-coupled spindles [41,104]. The mechanisms that underlie selectively in consolidation are largely unknown. Based on the current ASC framework, it would be predicted that memory reactivation during SO-spindle events should be biased in favour of certain types of memories. This hypothesis could be tested using machine learning approaches to detect biased reactivation of highly salient information. By using a category-level learning paradigm (e.g. objects and scenes), researchers could tag the object category by informing participants that the retrieval of objects is associated with a high financial bonus. If this biases reactivation in favour of the high-reward category (objects in this example) a classifier should more frequently identify object-specific processing during SO-spindle complexes relative to scene-specific processing.

Relatedly, the hippocampal-cortical dialogue emphasised by ASC would suggest that hippocampal-dependent, associative memories would benefit the most from the mechanisms described by ASC. There is evidence that associative memories receive the largest behavioural benefit of sleep [105], and the degree of memory reactivation correlates with associative, but not recognition, memory performance [61]. These findings are not universal, however. Although recognition memory may benefit less from overnight consolidation, at least one study has linked memory reactivation in sleep to recognition memory performance [78]. Additionally, non-hippocampal procedural memories appear to be strengthened via the same oscillatory coupling mechanisms as declarative memories [42,43], suggesting that hippocampus is involved in memory consolidation even if it is not involved in encoding. Indeed, amnesic patients with hippocampal lesions can successfully learn a non-hippocampal task, but fail to consolidate it [106]. It appears therefore that multiple different memory systems are responsive to memory reactivation during sleep, but more research is required to better delineate potential differences between the consolidation of hippocampal and non-hippocampal forms of memory.

Finally, information transfer from hippocampus to neocortex during sleep is thought to facilitate the integration of related experiences into semantic knowledge, allowing us to draw on past experiences to make predictions about the future. As of yet, however, memory reactivation during human sleep has not been linked to such behavioural outcomes, with researchers primarily focusing on memory strengthening. Interestingly, category-level reactivation during sleep has been localised to vmPFC [88], a brain region which also acts as a hub for memory integration [107,108]. A recent study linked sleep spindles to the restructuring and integration of overlapping memory representations within vmPFC [108]. As such, one possibility is that category-level

reactivation during sleep facilitates the integration of memories with shared categorical features, a process mediated by vmPFC. Such hypotheses should be explored in future work.

Conclusions

The burgeoning literature on neural reactivation in human sleep has largely supported and translated findings from animal studies. Memory reactivation during sleep is facilitated by a finely tuned interplay of hippocampal ripples, thalamocortical spindles, and global SOs. This triple coupling supports a hippocampal-neocortical dialogue, allowing for the co-ordinated reactivation of memory traces in both hippocampus and neocortex, as well as facilitating information transfer in service of long-term storage. Future work should now start to address exciting questions regarding the potential selective nature of memory reactivation, and how memory reactivation sculpts long-term changes in neural memory representations.

Summary

- Overwhelming evidence suggests that sleep benefits memory, leading to a strong interest in understanding the neural mechanisms underpinning this effect.

- Rodent studies have demonstrated memory reactivation to be a key mechanism underlying sleep's beneficial effect on memory, with reactivation occurring in tandem with cardinal non-rapid eye movement sleep oscillations.

- These findings have now started to be translated to humans. A growing number of studies have documented the re-emergence of memory content during sleep, with reactivation being closely linked to slow oscillation-spindle coupling events.

- Similarly, brain regions that are activated during the learning of new information are reactivated again during post-learning sleep, suggestive of learning-related memory reactivation.

- Future work now needs to better understand whether some memories are more likely to be reactivated than others, and what the long-term consequences of memory reactivation during sleep are on wakeful retrieval.

Competing Interests

The authors declare that there are no competing interests associated with the manuscript.

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Author Contributions

D.D. and S.A.C. both contributed to the conceptualisation and writing of the review.

Abbreviations

ASC, active systems consolidation theory; EEG, electroencephalography; FFA, fusiform face area; fMRI, functional magnetic resonance imaging; iEEG, intracranial electroencephalography; NREM, non-rapid eye movement sleep; PET, positron emission tomography; SO, slow oscillation; TMR, targeted memory reactivation; vmPFC, ventromedial pre-frontal cortex.

References

1   Ashton, J.E., Harrington, M.O., Langthorne, D., Ngo, H.-V.V. and Cairney, S.A. (2020) Sleep deprivation induces fragmented memory loss. *Learn. Mem.* **27**, 130–135 https://doi.org/10.1101/lm.050757.119

2   Denis, D., Schapiro, A.C., Poskanzer, C., Bursal, V., Charon, L., Morgan, A. et al. (2020) The roles of item exposure and visualization success in the consolidation of memories across wake and sleep. *Learn. Mem.* **27**, 451–456 https://doi.org/10.1101/lm.051383.120

3   Jenkins, J.G. and Dallenbach, K.M. (1924) Oblivescence during sleep and waking. *Am. J. Psychol.* **35**, 605–612 https://doi.org/10.2307/1414040

4   Plihal, W. and Born, J. (1997) Effects of early and late nocturnal sleep on declarative and procedural memory. *J. Cogn. Neurosci.* **9**, 534–547 https://doi.org/10.1162/jocn.1997.9.4.534

5   Berres, S. and Erdfelder, E. (2021) The sleep benefit in episodic memory: an integrative review and a meta-analysis. *Psychol. Bull.* **147**, 1309–1353 https://doi.org/10.1037/bul0000350

6   Ellenbogen, J.M., Payne, J.D. and Stickgold, R. (2006) The role of sleep in declarative memory consolidation: passive, permissive, active or none? *Curr. Opin. Neurobiol.* **16**, 716–722 https://doi.org/10.1016/j.conb.2006.10.006

7   Paller, K.A., Creery, J.D. and Schechtman, E. (2021) Memory and sleep: how sleep cognition can change the waking mind for the better. *Annu. Rev. Psychol.* **72**, 123–150 https://doi.org/10.1146/annurev-psych-010419-050815

8   Brodt, S., Inostroza, M., Niethard, N. and Born, J. (2023) Sleep—a brain-state serving systems memory consolidation. *Neuron* **111**, 1050–1075 https://doi.org/10.1016/j.neuron.2023.03.005

9   Klinzing, J.G., Niethard, N. and Born, J. (2019) Mechanisms of systems memory consolidation during sleep. *Nat. Neurosci.* **22**, 1598–1610 https://doi.org/10.1038/s41593-019-0467-3

10 Wilson, M.A. and McNaughton, B.L. (1994) Reactivation of hippocampal ensemble memories during sleep. *Science* **265**, 676–679 https://doi.org/10.1126/science.8036517

11 Girardeau, G. and Zugaro, M. (2011) Hippocampal ripples and memory consolidation. *Curr. Opin. Neurobiol.* **21**, 452–459 https://doi.org/10.1016/j.conb.2011.02.005

12 Ramanathan, D.S., Gulati, T. and Ganguly, K. (2015) Sleep-dependent reactivation of ensembles in motor cortex promotes skill consolidation. *PLoS Biol.* **13**, e1002263 https://doi.org/10.1371/journal.pbio.1002263

13 Ji, D. and Wilson, M.A. (2007) Coordinated memory replay in the visual cortex and hippocampus during sleep. *Nat. Neurosci.* **10**, 100–107 https://doi.org/10.1038/nn1825

14 Wierzynski, C.M., Lubenov, E.V., Gu, M. and Siapas, A.G. (2009) State-dependent spike-timing relationships between hippocampal and prefrontal circuits during sleep. *Neuron* **61**, 587–596 https://doi.org/10.1016/j.neuron.2009.01.011

15 Girardeau, G., Benchenane, K., Wiener, S.I., Buzsáki, G. and Zugaro, M.B. (2009) Selective suppression of hippocampal ripples impairs spatial memory. *Nat. Neurosci.* **12**, 1222–1223 https://doi.org/10.1038/nn.2384

16 Gridchyn, I., Schoenenberger, P., O'Neill, J. and Csicsvari, J. (2020) Assembly-specific disruption of hippocampal replay leads to selective memory deficit. *Neuron* **106**, 291–300.e6 https://doi.org/10.1016/j.neuron.2020.01.021

17 Kim, J., Gulati, T. and Ganguly, K. (2019) Competing roles of slow oscillations and delta waves in memory consolidation versus forgetting. *Cell* **179**, 514–526.e13 https://doi.org/10.1016/j.cell.2019.08.040

18 Rasch, B. and Born, J. (2013) About sleep's role in memory. *Physiol. Rev.* **93**, 681–766 https://doi.org/10.1152/physrev.00032.2012

19 Born, J. and Wilhelm, I. (2012) System consolidation of memory during sleep. *Psychol. Res.* **76**, 192–203 https://doi.org/10.1007/s00426-011-0335-6

20 Latchoumane, C.-F.V., Ngo, H.-V.V., Born, J. and Shin, H.-S. (2017) Thalamic spindles promote memory formation during sleep through triple phase-locking of cortical, thalamic, and hippocampal rhythms. *Neuron* **95**, 424–435 https://doi.org/10.1016/j.neuron.2017.06.025

21 Fernandez, L.M.J. and Luthi, A. (2020) Sleep spindles: mechanisms and functions. *Physiol. Rev.* **100**, 805–868 https://doi.org/10.1152/physrev.00042.2018

22 Niknazar, H., Malerba, P. and Mednick, S.C. (2022) Slow oscillations promote long-range effective communication: the key for memory consolidation in a broken-down network. *Proc. Natl Acad. Sci. U.S.A.* **119**, e2122515119 https://doi.org/10.1073/pnas.2122515119

23 Peyrache, A., Khamassi, M., Benchenane, K., Wiener, S.I. and Battaglia, F.P. (2009) Replay of rule-learning related neural patterns in the prefrontal cortex during sleep. *Nat. Neurosci.* **12**, 919–926 https://doi.org/10.1038/nn.2337

24 Rothschild, G., Eban, E. and Frank, L.M. (2017) A cortical–hippocampal–cortical loop of information processing during memory consolidation. *Nat. Neurosci.* **20**, 251–259 https://doi.org/10.1038/nn.4457

25 Sirota, A., Csicsvari, J., Buhl, D. and Buzsáki, G. (2003) Communication between neocortex and hippocampus during sleep in rodents. *Proc. Natl Acad. Sci. U.S.A.* **100**, 2065–2069 https://doi.org/10.1073/pnas.0437938100

26 Rothschild, G. (2019) The transformation of multi-sensory experiences into memories during sleep. *Neurobiol. Learn. Mem.* **160**, 58–66 https://doi.org/10.1016/j.nlm.2018.03.019

27 Ngo, H.-V., Fell, J. and Staresina, B. (2020) Sleep spindles mediate hippocampal-neocortical coupling during long-duration ripples. *eLife* **9**, e57011 https://doi.org/10.7554/eLife.57011

28 Mölle, M., Bergmann, T.O., Marshall, L. and Born, J. (2011) Fast and slow spindles during the sleep slow oscillation: disparate coalescence and engagement in memory processing. *Sleep* **34**, 1411–1421 https://doi.org/10.5665/SLEEP.1290

29 Mölle, M., Marshall, L., Gais, S. and Born, J. (2002) Grouping of spindle activity during slow oscillations in human non-rapid eye movement sleep. *J. Neurosci.* **22**, 10941–10947 https://doi.org/10.1523/JNEUROSCI.22-24-10941.2002

30 Cox, R., Mylonas, D.S., Manoach, D.S. and Stickgold, R. (2018) Large-scale structure and individual fingerprints of locally coupled sleep oscillations. *Sleep* **41**, zsy175 https://doi.org/10.1093/sleep/zsy175

31 Cox, R., van Driel, J., de Boer, M. and Talamini, L.M. (2014) Slow oscillations during sleep coordinate interregional communication in cortical networks. *J Neurosci* **34**, 16890–16901 https://doi.org/10.1523/JNEUROSCI.1953-14.2014

32 Klinzing, J.G., Mölle, M., Weber, F., Supp, G., Hipp, J.F., Engel, A.K. et al. (2016) Spindle activity phase-locked to sleep slow oscillations. *Neuroimage* **134**, 607–616 https://doi.org/10.1016/j.neuroimage.2016.04.031

33 Hahn, M.A., Heib, D., Schabus, M., Hoedlmoser, K. and Helfrich, R.F. (2020) Slow oscillation-spindle coupling predicts enhanced memory formation from childhood to adolescence. *eLife* **9**, e53730 https://doi.org/10.7554/eLife.53730

34 Hahn, M.A., Bothe, K., Heib, D., Schabus, M., Helfrich, R.F. and Hoedlmoser, K. (2022) Slow oscillation–spindle coupling strength predicts real-life gross-motor learning in adolescents and adults. *eLife* **11**, e66761 https://doi.org/10.7554/eLife.66761

35 Halonen, R., Kuula, L., Antila, M. and Pesonen, A.-K. (2021) The overnight retention of novel metaphors associates with slow oscillation–spindle coupling but not with respiratory phase at encoding. *Front. Behav. Neurosci.* **15**, 712774 https://doi.org/10.3389/fnbeh.2021.712774

36 Helfrich, R.F., Mander, B.A., Jagust, W.J., Knight, R.T. and Walker, M.P. (2018) Old brains come uncoupled in sleep: slow wave-spindle synchrony, brain atrophy, and forgetting. *Neuron* **97**, 221–230 https://doi.org/10.1016/j.neuron.2017.11.020

37 Mikutta, C., Feige, B., Maier, J.G., Hertenstein, E., Holz, J., Riemann, D. et al. (2019) Phase-amplitude coupling of sleep slow oscillatory and spindle activity correlates with overnight memory consolidation. *J. Sleep Res.* **28**, e12835 https://doi.org/10.1111/jsr.12835

38 Muehlroth, B.E., Sander, M.C., Fandakova, Y., Grandy, T.H., Rasch, B., Shing, Y.L. et al. (2019) Precise slow oscillation-spindle coupling promotes memory consolidation in younger and older adults. *Sci. Rep.* **9**, 1940 https://doi.org/10.1038/s41598-018-36557-z

39 Niknazar, M., Krishnan, G.P., Bazhenov, M. and Mednick, S.C. (2015) Coupling of thalamocortical sleep oscillations are important for memory consolidation in humans. *PLoS ONE* **10**, e0144720 https://doi.org/10.1371/journal.pone.0144720

40 Kumral, D., Matzerath, A., Leonhart, R. and Schönauer, M. (2023) Spindle-dependent memory consolidation in healthy adults: a meta-analysis. *Neuropsychologia* **189**, 108661 https://doi.org/10.1016/j.neuropsychologia.2023.108661

41 Denis, D., Mylonas, D., Poskanzer, C., Bursal, V., Payne, J.D. and Stickgold, R. (2021) Sleep spindles preferentially consolidate weakly encoded memories. *J. Neurosci.* **41**, 4088–4099 https://doi.org/10.1523/JNEUROSCI.0818-20.2021

42 Mylonas, D., Baran, B., Demanuele, C., Cox, R., Vuper, T.C., Seicol, B.J. et al. (2020) The effects of eszopiclone on sleep spindles and memory consolidation in schizophrenia: a randomized clinical trial. *Neuropsychopharmacology* **45**, 2189–2197 https://doi.org/10.1038/s41386-020-00833-2

43 Solano, A., Riquelme, L.A., Perez-Chada, D. and Della-Maggiore, V. (2022) Motor learning promotes the coupling between fast spindles and slow oscillations locally over the contralateral motor network. *Cereb. Cortex* **32**, 2493–2507 https://doi.org/10.1093/cercor/bhab360

44 Baxter, B.S., Mylonas, D., Kwok, K.S., Talbot, C.E., Patel, R., Zhu, L. et al. (2023) The effects of closed-loop auditory stimulation on sleep oscillatory dynamics in relation to motor procedural memory consolidation. *Sleep* **46**, zsad206 https://doi.org/10.1093/sleep/zsad206

45 Krugliakova, E., Volk, C., Jaramillo, V., Sousouri, G. and Huber, R. (2020) Changes in cross-frequency coupling following closed-loop auditory stimulation in non-rapid eye movement sleep. *Sci. Rep.* **10**, 10628 https://doi.org/10.1038/s41598-020-67392-w

46 Ladenbauer, J., Ladenbauer, J., Külzow, N., de Boor, R., Avramova, E., Grittner, U. et al. (2017) Promoting sleep oscillations and their functional coupling by transcranial stimulation enhances memory consolidation in mild cognitive impairment. *J. Neurosci.* **37**, 7111–7124 https://doi.org/10.1523/JNEUROSCI.0260-17.2017

47 Wunderlin, M., Züst, M.A., Hertenstein, E., Fehér, K.D., Schneider, C.L., Klöppel, S. et al. (2021) Modulating overnight memory consolidation by acoustic stimulation during slow-wave sleep: a systematic review and meta-analysis. *Sleep* **44**, zsaa296 https://doi.org/10.1093/sleep/zsaa296

48 Barham, M.P., Enticott, P.G., Conduit, R. and Lum, J.A.G. (2016) Transcranial electrical stimulation during sleep enhances declarative (but not procedural) memory consolidation: evidence from a meta-analysis. *Neurosci. Biobehav. Rev.* **63**, 65–77 https://doi.org/10.1016/j.neubiorev.2016.01.009

49 Staresina, B.P., Bergmann, T.O., Bonnefond, M., van der Meij, R., Jensen, O., Deuker, L. et al. (2015) Hierarchical nesting of slow oscillations, spindles and ripples in the human hippocampus during sleep. *Nat. Neurosci.* **18**, 1679–1686 https://doi.org/10.1038/nn.4119

50 Jiang, X., Gonzalez-Martinez, J. and Halgren, E. (2019) Coordination of human hippocampal sharpwave ripples during NREM sleep with cortical theta bursts, spindles, downstates, and upstates. *J. Neurosci.* **39**, 8744–8761 https://doi.org/10.1523/JNEUROSCI.2857-18.2019

51 Staresina, B.P., Niediek, J., Borger, V., Surges, R. and Mormann, F. (2023) How coupled slow oscillations, spindles and ripples coordinate neuronal processing and communication during human sleep. *Nat. Neurosci.* **26**, 1429–1437 https://doi.org/10.1038/s41593-023-01381-w

52 Helfrich, R.F., Lendner, J.D., Mander, B.A., Guillen, H., Paff, M., Mnatsakanyan, L. et al. (2019) Bidirectional prefrontal-hippocampal dynamics organize information transfer during sleep in humans. *Nat. Commun.* **10**, 3572 https://doi.org/10.1038/s41467-019-11444-x

53 Antony, J.W., Schönauer, M., Staresina, B.P. and Cairney, S.A. (2019) Sleep spindles and memory reprocessing. *Trends Neurosci.* **42**, 1–3 https://doi.org/10.1016/j.tins.2018.09.012

54 Geva-Sagiv, M., Mankin, E.A., Eliashiv, D., Epstein, S., Cherry, N., Kalender, G. et al. (2023) Augmenting hippocampal–prefrontal neuronal synchrony during sleep enhances memory consolidation in humans. *Nat. Neurosci.* **26**, 1100–1110 https://doi.org/10.1038/s41593-023-01324-5

55 Genzel, L., Dragoi, G., Frank, L., Ganguly, K., de la Prida, L., Pfeiffer, B. et al. (2020) A consensus statement: defining terms for reactivation analysis. *Philos. Trans. R. Soc. B Biol. Sci.* **375**, 20200001 https://doi.org/10.1098/rstb.2020.0001

56 Grootswagers, T., Wardle, S.G. and Carlson, T.A. (2017) Decoding dynamic brain patterns from evoked responses: a tutorial on multivariate pattern analysis applied to time series neuroimaging data. *J. Cogn. Neurosci.* **29**, 677–697 https://doi.org/10.1162/jocn_a_01068

57 King, J.-R. and Dehaene, S. (2014) Characterizing the dynamics of mental representations: the temporal generalization method. *Trends Cogn. Sci.* **18**, 203–210 https://doi.org/10.1016/j.tics.2014.01.002

58 Treder, M.S. (2020) MVPA-light: a classification and regression toolbox for multi-dimensional data. *Front. Neurosci.* **14**, 289 https://doi.org/10.3389/fnins.2020.00289

59 Schönauer, M., Alizadeh, S., Jamalabadi, H., Abraham, A., Pawlizki, A. and Gais, S. (2017) Decoding material-specific memory reprocessing during sleep in humans. *Nat. Commun.* **8**, 15404 https://doi.org/10.1038/ncomms15404

60 Rubin, D.B., Hosman, T., Kelemen, J.N., Kapitonava, A., Willett, F.R., Coughlin, B.F. et al. (2022) Learned motor patterns are replayed in human motor cortex during sleep. *J. Neurosci.* **42**, 5007–5020 https://doi.org/10.1523/JNEUROSCI.2074-21.2022

61 Schreiner, T., Petzka, M., Staudigl, T. and Staresina, B.P. (2021) Endogenous memory reactivation during sleep in humans is clocked by slow oscillation-spindle complexes. *Nat. Commun.* **12**, 3112 https://doi.org/10.1038/s41467-021-23520-2

62 Zhang, H., Fell, J. and Axmacher, N. (2018) Electrophysiological mechanisms of human memory consolidation. *Nat. Commun.* **9**, 4103 https://doi.org/10.1038/s41467-018-06553-y

63 Bendor, D. and Wilson, M.A. (2012) Biasing the content of hippocampal replay during sleep. *Nat. Neurosci.* **15**, 1439–1444 https://doi.org/10.1038/nn.3203

64   Hu, X., Cheng, L.Y., Chiu, M.H. and Paller, K.A. (2020) Promoting memory consolidation during sleep: a meta-analysis of targeted memory reactivation. *Psychol. Bull.* **146**, 218–244 https://doi.org/10.1037/bul0000223

65   Antony, J.W., Piloto, L., Wang, M., Pacheco, P., Norman, K.A. and Paller, K.A. (2018) Sleep spindle refractoriness segregates periods of memory reactivation. *Curr. Biol.* **28**, 1736–1743.e4 https://doi.org/10.1016/j.cub.2018.04.020

66   Farthouat, J., Gilson, M. and Peigneux, P. (2017) New evidence for the necessity of a silent plastic period during sleep for a memory benefit of targeted memory reactivation. *Sleep Spindl. Cortical States* **1**, 14–26 https://doi.org/10.1556/2053.1.2016.002

67   Groch, S., Schreiner, T., Rasch, B., Huber, R. and Wilhelm, I. (2017) Prior knowledge is essential for the beneficial effect of targeted memory reactivation during sleep. *Sci. Rep.* **7**, 39763 https://doi.org/10.1038/srep39763

68   Laventure, S., Pinsard, B., Lungu, O., Carrier, J., Fogel, S., Benali, H. et al. (2018) Beyond spindles: interactions between sleep spindles and boundary frequencies during cued reactivation of motor memory representations. *Sleep* **41**, zsy142 https://doi.org/10.1093/sleep/zsy142

69   Lehmann, M., Schreiner, T., Seifritz, E. and Rasch, B. (2016) Emotional arousal modulates oscillatory correlates of targeted memory reactivation during NREM, but not REM sleep. *Sci. Rep.* **6**, 39229 https://doi.org/10.1038/srep39229

70   Schechtman, E., Antony, J.W., Lampe, A., Wilson, B.J., Norman, K.A. and Paller, K.A. (2021) Multiple memories can be simultaneously reactivated during sleep as effectively as a single memory. *Commun. Biol.* **4**, 25 https://doi.org/10.1038/s42003-020-01512-0

71   Cairney, S.A., Guttesen, A.ÁV., El Marj, N. and Staresina, B.P. (2018) Memory consolidation is linked to spindle-mediated information processing during sleep. *Curr. Biol.* **28**, 948–954 https://doi.org/10.1016/j.cub.2018.01.087

72   Wang, B., Antony, J.W., Lurie, S., Brooks, P.P., Paller, K.A. and Norman, K.A. (2019) Targeted memory reactivation during sleep elicits neural signals related to learning content. *J. Neurosci.* **39**, 6728–6736 https://doi.org/10.1523/JNEUROSCI.2798-18.2019

73   Belal, S., Cousins, J., El-Deredy, W., Parkes, L., Schneider, J., Tsujimura, H. et al. (2018) Identification of memory reactivation during sleep by EEG classification. *Neuroimage* **176**, 203–214 https://doi.org/10.1016/j.neuroimage.2018.04.029

74   Schechtman, E., Heilberg, J. and Paller, K.A. (2023) Memory consolidation during sleep involves context reinstatement in humans. *Cell Rep.* **42**, 112331 https://doi.org/10.1016/j.celrep.2023.112331

75   Liu, J., Xia, T., Chen, D., Yao, Z., Zhu, M., Antony, J.W. et al. (2023) Item-specific neural representations during human sleep support long-term memory. *PLoS Biol.* **21**, e3002399. https://doi.org/10.1371/journal.pbio.3002399

76   Göldi, M., van Poppel, E.A.M., Rasch, B. and Schreiner, T. (2019) Increased neuronal signatures of targeted memory reactivation during slow-wave up states. *Sci. Rep* **9**, 2715 https://doi.org/10.1038/s41598-019-39178-2

77   Batterink, L.J., Creery, J.D. and Paller, K.A. (2016) Phase of spontaneous slow oscillations during sleep influences memory-related processing of auditory cues. *J. Neurosci.* **36**, 1401–1409 https://doi.org/10.1523/JNEUROSCI.3175-15.2016

78   Ngo, H.-V.V. and Staresina, B.P. (2022) Shaping overnight consolidation via slow-oscillation closed-loop targeted memory reactivation. *Proc. Natl Acad. Sci. U.S.A.* **119**, e2123428119 https://doi.org/10.1073/pnas.2123428119

79   Peyrache, A. and Seibt, J. (2020) A mechanism for learning with sleep spindles. *Philos. Trans. R. Soc. B Biol. Sci.* **375**, 20190230 https://doi.org/10.1098/rstb.2019.0230

80   Seibt, J., Richard, C.J., Sigl-Glöckner, J., Takahashi, N., Kaplan, D.I., Doron, G. et al. (2017) Cortical dendritic activity correlates with spindle-rich oscillations during sleep in rodents. *Nat. Commun.* **8**, 684 https://doi.org/10.1038/s41467-017-00735-w

81   Rosanova, M. and Ulrich, D. (2005) Pattern-specific associative long-term potentiation induced by a sleep spindle-related spike train. *J. Neurosci.* **25**, 9398–9405 https://doi.org/10.1523/JNEUROSCI.2149-05.2005

82   Steriade, M. (2003) The corticothalamic system in sleep. *Front. Biosci. J. Virtual Libr.* **8**, d878–d899 https://doi.org/10.2741/1043

83   Peigneux, P., Laureys, S., Fuchs, S., Collette, F., Perrin, F., Reggers, J. et al. (2004) Are spatial memories strengthened in the human hippocampus during slow wave sleep? *Neuron* **44**, 535–545 https://doi.org/10.1016/j.neuron.2004.10.007

84   Peigneux, P., Laureys, S., Fuchs, S., Destrebecqz, A., Collette, F., Delbeuck, X. et al. (2003) Learned material content and acquisition level modulate cerebral reactivation during posttraining rapid-eye-movements sleep. *Neuroimage* **20**, 125–134 https://doi.org/10.1016/S1053-8119(03)00278-7

85   Bergmann, T.O., Mölle, M., Diedrichs, J., Born, J. and Siebner, H.R. (2012) Sleep spindle-related reactivation of category-specific cortical regions after learning face-scene associations. *Neuroimage* **59**, 2733–2742 https://doi.org/10.1016/j.neuroimage.2011.10.036

86   Fogel, S., Albouy, G., King, B.R., Lungu, O., Vien, C., Bore, A. et al. (2017) Reactivation or transformation? Motor memory consolidation associated with cerebral activation time-locked to sleep spindles. *PLos ONE* **12**, e0174755 https://doi.org/10.1371/journal.pone.0174755

87   Boutin, A., Pinsard, B., Boré, A., Carrier, J., Fogel, S.M. and Doyon, J. (2018) Transient synchronization of hippocampo-striato-thalamo-cortical networks during sleep spindle oscillations induces motor memory consolidation. *Neuroimage* **169**, 419–430 https://doi.org/10.1016/j.neuroimage.2017.12.066

88   Shanahan, L.K., Gjorgieva, E., Paller, K.A., Kahnt, T. and Gottfried, J.A. (2018) Odor-evoked category reactivation in human ventromedial prefrontal cortex during sleep promotes memory consolidation. *eLife* **7**, e39681 https://doi.org/10.7554/eLife.39681

89   Sterpenich, V., van Schie, M.K.M., Catsiyannis, M., Ramyead, A., Perrig, S., Yang, H.-D. et al. (2021) Reward biases spontaneous neural reactivation during sleep. *Nat. Commun.* **12**, 4162 https://doi.org/10.1038/s41467-021-24357-5

90   Deuker, L., Olligs, J., Fell, J., Kranz, T.A., Mormann, F., Montag, C. et al. (2013) Memory consolidation by replay of stimulus-specific neural activity. *J. Neurosci.* **33**, 19373–19383 https://doi.org/10.1523/JNEUROSCI.0414-13.2013

91   Vahdat, S., Fogel, S., Benali, H. and Doyon, J. (2017) Network-wide reorganization of procedural memory during NREM sleep revealed by fMRI. *eLife* **6**, e24987 https://doi.org/10.7554/eLife.24987

92   van Dongen, E.V., Takashima, A., Barth, M., Zapp, J., Schad, L.R., Paller, K.A. et al. (2012) Memory stabilization with targeted reactivation during human slow-wave sleep. *Proc. Natl Acad. Sci. U.S.A.* **109**, 10575–10580 https://doi.org/10.1073/pnas.1201072109

93   Rasch, B., Büchel, C., Gais, S. and Born, J. (2007) Odor cues during slow-wave sleep prompt declarative memory consolidation. *Science* **315**, 1426–1429 https://doi.org/10.1126/science.1138581

94   Lustenberger, C., Wehrle, F., Tüshaus, L., Achermann, P. and Huber, R. (2015) The multidimensional aspects of sleep spindles and their relationship to word-pair memory consolidation. *Sleep* **38**, 1093–1103 https://doi.org/10.5665/sleep.4820

95   Cowan, E.T., Schapiro, A.C., Dunsmoor, J.E. and Murty, V.P. (2021) Memory consolidation as an adaptive process. *Psychon. Bull. Rev.* **28**, 1796–1810 https://doi.org/10.3758/s13423-021-01978-x

96   Dunsmoor, J.E., Murty, V.P., Davachi, L. and Phelps, E.A. (2015) Emotional learning selectively and retroactively strengthens memories for related events. *Nature* **520**, 345–348 https://doi.org/10.1038/nature14106

97   Sharot, T. and Yonelinas, A.P. (2008) Differential time-dependent effects of emotion on recollective experience and memory for contextual information. *Cognition* **106**, 538–547 https://doi.org/10.1016/j.cognition.2007.03.002

98   Payne, J.D., Stickgold, R., Swanberg, K. and Kensinger, E.A. (2008) Sleep preferentially enhances memory for emotional components of scenes. *Psychol. Sci.* **19**, 781–788 https://doi.org/10.1111/j.1467-9280.2008.02157.x

99   Denis, D., Sanders, K.E.G. Kensinger, E.A. and Payne, J.D. (2022) Sleep preferentially consolidates negative aspects of human memory: well-powered evidence from two large online experiments. *Proc. Natl Acad. Sci. U.S.A.* **119**, e2202657119 https://doi.org/10.1073/pnas.2202657119

100 Davidson, P., Jönsson, P., Carlsson, I. and Pace-Schott, E. (2021) Does sleep selectively strengthen certain memories over others based on emotion and perceived future relevance? *Nat. Sci. Sleep* **13**, 1257–1306 https://doi.org/10.2147/NSS.S286701

101 Schapiro, A.C., McDevitt, E.A., Rogers, T.T., Mednick, S.C. and Norman, K.A. (2018) Human hippocampal replay during rest prioritizes weakly learned information and predicts memory performance. *Nat. Commun.* **9**, 3920 https://doi.org/10.1038/s41467-018-06213-1

102 Cairney, S.A., Lindsay, S., Sobczak, J.M., Paller, K.A. and Gaskell, M.G. (2016) The benefits of targeted memory reactivation for consolidation in sleep are contingent on memory accuracy and direct cue-memory associations. *Sleep* **39**, 1139–1150 https://doi.org/10.5665/sleep.5772

103 Creery, J.D., Oudiette, D., Antony, J.W. and Paller, K.A. (2015) Targeted memory reactivation during sleep depends on prior learning. *Sleep* **38**, 755–763 https://doi.org/10.5665/sleep.4670

104 Schmidt, C., Peigneux, P., Muto, V., Schenkel, M., Knoblauch, V., Münch, M. et al. (2006) Encoding difficulty promotes postlearning changes in sleep spindle activity during napping. *J. Neurosci.* **26**, 8976–8982 https://doi.org/10.1523/JNEUROSCI.2464-06.2006

105 Studte, S., Bridger, E. and Mecklinger, A. (2015) Nap sleep preserves associative but not item memory performance. *Neurobiol. Learn. Mem.* **120**, 84–93 https://doi.org/10.1016/j.nlm.2015.02.012

106 Schapiro, A.C., Reid, A.G., Morgan, A., Manoach, D.S., Verfaellie, M. and Stickgold, R. (2019) The hippocampus is necessary for the consolidation of a task that does not require the hippocampus for initial learning. *Hippocampus* **29**, 1091–1100 https://doi.org/10.1002/hipo.23101

107 Tompary, A. and Davachi, L. (2017) Consolidation promotes the emergence of representational overlap in the hippocampus and medial prefrontal cortex. *Neuron* **96**, 228–241.e5 https://doi.org/10.1016/j.neuron.2017.09.005

108 Cowan, E., Liu, A., Henin, S., Kothare, S., Devinsky, O. and Davachi, L. (2020) Sleep spindles promote the restructuring of memory representations in ventromedial prefrontal cortex through enhanced hippocampal–cortical functional connectivity. *J. Neurosci.* **40**, 1909–1919 https://doi.org/10.1523/JNEUROSCI.1946-19.2020