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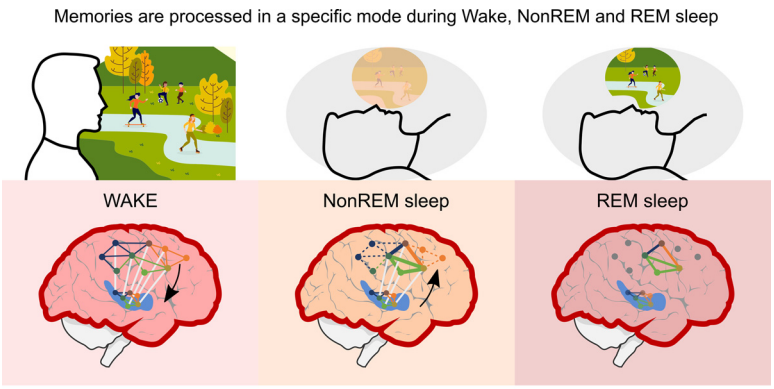

During NonREM sleep a dialogue between the hippocampus and neocortex leads to a neocorticalization of the representation, which is further shaped during REM sleep

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KEY WORDS

abstraction; consolidation; memory; reactivation; sleep

CLINICAL HIGHLIGHTS

- Sleep plays a critical role in memory consolidation, directly influencing daily functioning by enhancing the retention and organization of learned information. A better understanding of how sleep aids memory consolidation can foster awareness of the importance of sleep, which is particularly crucial given the high prevalence of disordered sleep and related issues worldwide.
- The decline in sleep quality with aging, particularly of slow-wave sleep, contributes to memory impairments, emphasizing the need for targeted sleep-related interventions to support cognitive health in older adults.
- Disturbed sleep in insomnia significantly affects memory processing, with the review summarizing key findings on its detrimental cognitive effects.
- Research on sleep and memory in humans has advanced the development of innovative techniques, such as non-invasive brain stimulation during sleep or targeted memory reactivation, offering promising new approaches to enhance sleep and cognitive performance in clinical conditions, beyond pharmacological treatment.

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REVIEW ARTICLE

SLEEP'S CONTRIBUTION TO MEMORY FORMATION

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Abstract

The brain state of sleep contributes in a specific way to the formation of long-term memory. Over the past 10 years, research on the psychological and neuronal mechanisms underlying this process has rapidly increased, including studies in humans and rodents across early and late life. Intended to comprehensively cover this research, our review reveals that the majority of findings are consistent with the concept of long-term memory formation during sleep as an active systems consolidation process that concurs with widespread synaptic downselection. In this concept, the repeated neuronal replay of encoded representations, particularly in the hippocampus, in conjunction with brain oscillations hallmarking non-rapid eye movement (non-REM) sleep, provide mechanisms for regulating information flow across brain networks. This interplay drives the consolidation of newly encoded memory into neocortical long-term stores, whereby this neocorticalization of representations goes along with a transformation of memories into more abstract representations. The findings, however, remain controversial as to the nature of memory transformation: What kind of information is eventually consolidated into neocortical networks and how is storage of this information achieved at the synaptic level? Furthermore, the roles of REM sleep in consolidation of, in particular, emotional memory and in shaping representations at the synaptic level are unclear. Future research also needs to elaborate on how consolidation during sleep differs from that during wakefulness, as well as on the changes in sleep-dependent consolidation across the life span. A promising new area arising from this research pertains to brain stimulation techniques developed to enhance memory consolidation during human sleep.

abstraction; consolidation; memory; reactivation; sleep

1. INTRODUCTION

Sleep is a ubiquitous phenomenon in the animal kingdom. Its main characteristics are behavioral inactivity and a greatly reduced arousability to environmental stimuli, in conjunction with a specific regulation of nervous system activity, and humans experience a more or less profound loss of consciousness while sleeping. Although capturing the whole organism, sleep is generated in the brain, and there is quite detailed knowledge about the neurobiological mechanisms mediating the onset and maintenance of sleep (1–3). However, rather than the mediating mechanisms, this review focuses on the function of sleep, a question that is closely related to what evolutionary benefit sleep offers. Given the vulnerability to predators due to inattentiveness to environmental stimuli, why has sleep remained so well preserved throughout evolution and become particularly differentiated in humans?

Just as breathing not only serves the exchange of carbon dioxide and oxygen in the lungs but also enables speech, sleep may serve multiple functions, such as supporting growth and anabolic metabolism, clearing metabolic waste from the brain, and conserving energy, with memory formation being perhaps its most crucial role, as it allows experiences to be transformed into lasting memories during sleep. We need these long-term memories to effectively adapt to our environment and ultimately also for establishing consciousness as it is experienced in the wake state. For example, to consciously recognize the computer screen in front of us, we need to have a

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concept, an abstracted memory, a neuronal representation of what a computer screen is. From this perspective, it could be speculated that the memory function of sleep may be the only reason that can explain why we lose our consciousness when we fall asleep (see Ref. 4 for related thoughts).

Sleep is a multifaceted phenomenon. That sleep serves multiple functions implicates that not every feature of sleep necessarily serves each of these functions. When, for example, research about the relationship between rapid eye movements (REMs) during REM sleep and memory formation provides mixed results, this could, in principle, also mean that REMs do not play a meaningful role in long-term memory formation. Our focus in this review is on sleep features for which a contribution to memory processing is well established. The review is an update of our previous review published in 2013 (5), and accordingly concentrates on research during the last decade. The previous review focused on the active role that sleep plays in (quantitatively) stabilizing newly encoded declarative memory based on hippocampal neuronal reactivations during slow-wave sleep (SWS; see sect. 3.1) as well as on topics like the coexistence and compatibility of active systems consolidation and synaptic renormalization processes during SWS (sect. 2), i.e., fundamental ideas that, indeed, are now widely acknowledged. Against this backdrop, the present review mainly covers recent developments in the field aiming at clarifying how systems consolidation during sleep (qualitatively) transforms newly encoded memories and also at a finer analysis of the neuronal mechanisms underlying the consolidation process. The present review also covers areas that showed a particular growth during the last 10 years, such as the research of sleep-associated memory consolidation during early life and aging (sect. 5), and the development of techniques, like "target memory reactivation" (TMR), that might be used for enhancing sleep-dependent memory consolidation in clinical and educational settings (sect. 7). The present review, like the previous one, highlights findings in humans, with confirmatory evidence from studies in animal models, mostly in rodents.

1.1. History of Sleep and Memory Research

The history of experimental research on the memory function of sleep started almost in parallel with the beginnings of experimental memory research. Rosa Heine (the later Rosa Katz), a student of the German psychologist Georg Elias Müller, was the first to publish a detailed analysis of the effects of sleep after learning sequences of syllables in her 1914 dissertation entitled (translated into English) *About Recognition and Retroactive Inhibition* (6), which was based on a total of 67 trials tested in six participants. The participants learned the syllables either shortly before nocturnal sleep or at a specific time in the morning or afternoon, and recall was tested 24 h later. Learning before nocturnal sleep consistently produced a better retention of the syllable sequence than the daytime learning control conditions. In a later seminal study, Jenkins and Dallenbach (1924) (7) confirmed these findings by testing the retention of syllables across intervals between 1 and 8 h in two participants. They found that recall performance was significantly better when the participants slept during the retention interval in comparison with retention intervals of the same length spent awake (7). The enhancing effect of sleep in this early work was explained based on the concept of memory consolidation as proposed by Müller and Pilzecker in 1900 (8), assuming that the consolidation of encoded materials into long-term memory results from activity induced in the brain by the recently learned stimuli, which perseverates some time after encoding. This consolidation process is easily disrupted by retroactive interference, for example when briefly after the encoding of syllables other stimuli are to be learned. In this view, sleep after encoding provides a period passively protecting ongoing consolidation of the newly encoded stimuli, as no further information is encoded and processed. Accordingly, Heine (1914) (6) had already speculated that the enhancing effect of post-encoding sleep on memory could be diminished when vivid dreams occurred.

The concept of sleep passively protecting the consolidation process from retroactive interference has been supported by numerous later findings and still provides the basis of recent accounts of the memory function of sleep. For instance, the "opportunistic theory" of memory consolidation by Mednick et al. (2011) (9) assumes that memories benefit from sleep as a period of reduced interference during which no new memories are formed, and indeed this view receives support from many recent

experiments (e.g., Refs. 10–13). This concept became particularly valuable when, after the discovery of REM sleep by Aserinsky and Kleitman in 1953 (14), research shifted the focus to differentiate functions of REM sleep from those of non-REM sleep. In the early 1970s, Ekstrand and coworkers (15–17) performed a series of studies that compared the retention of lists of word pairs across retention periods that covered either the early part of nocturnal sleep or the late part of nocturnal sleep, with the early part containing most of the night's slow-wave sleep (SWS) and the late part containing most of the night's REM sleep. Notably, retention of the word pairs was consistently found to be inferior over the REM sleep-rich late night interval than over the early SWS-rich interval, which was assumed to be a consequence of the activated brain during REM sleep producing greater retroactive interference with ongoing consolidation processes.

Until the 1970s, studies on the effects of sleep on memory consolidation exclusively examined learning of verbal (declarative) materials. The field of sleep and memory advanced by the discovery of different memory systems, centrally based on studies of patient H.M., who because of severe epilepsy underwent bilateral surgical resection of large parts of the hippocampus (18, 19). This research led to the differentiation of a hippocampus-dependent declarative memory system comprising episodic and semantic memories and a more heterogeneous nondeclarative system mainly comprising procedural skill memory that was thought to be independent of a functioning hippocampus. Beginning with the late 1990s, studies of sleep in humans not only extended the beneficial effect of sleep on memory consolidation to nondeclarative procedural skills (20) but also provided clues that sleep may act differently on the consolidation of declarative and nondeclarative memories. Comparing the consolidating effects of early SWS-rich and late REM-rich periods of nocturnal sleep on different kinds of declarative (e.g., word pairs) and nondeclarative (e.g., procedural mirror tracing skills) memory, Plihal and Born (21, 22) revealed that declarative memories showed a greater benefit from SWS-rich sleep whereas nondeclarative memories showed a greater benefit from REM-rich sleep. These and related findings motivated the "dual process" concept, assuming that non-REM and REM sleep serve different and rather independent roles in memory consolidation (sect. 3.3.1). Moreover, the beneficial effects of REM sleep specifically on nondeclarative types of memory challenged the view that protecting consolidation from retroactive interference represents the only way in which sleep supports consolidation processes.

Although the research on sleep and memory was dominated for decades by purely behavioral and psychological studies, since the 1990s a growing number of neurobiological studies have focused on uncovering the neural mechanisms of memory consolidation during sleep in animal models. A significant breakthrough occurred when Bruce McNaughton and coworkers (23, 24) demonstrated in several rat studies that newly acquired spatial memories are replayed at a neuronal level during subsequent periods of SWS (sect. 3.1.1). Specifically, firing patterns of hippocampal place cell ensembles that emerged while the rat navigated a maze to receive a food reward reemerged in the same sequential order during SWS periods following the learning experience. Subsequent studies have supported the causal role of these neuronal reactivations in memory consolidation during sleep in both rats and humans (25–27). The discovery of neuronal memory replay not only translated the original concept of the consolidation process by Müller and Pilzecker (1900) (8) as based on "reverberating activity" into a neurobiological mechanism but also stimulated the view that, in addition to "passively protecting" memory consolidation, sleep actively contributes to the consolidation process by reactivating neuronal representations (28). Building on this active role of sleep in memory consolidation, recent developments in the field are characterized by a rapidly growing body of research on techniques that can be used to enhance (or disrupt) ongoing consolidation processes during sleep (sect. 7).

1.2. Brief Introduction to Memory and Sleep

Sleep makes up about one-third of human life and is defined as a reversible state of relative inactivity, in which the individual adopts a characteristic body posture and shows reduced responsiveness to external stimuli, accompanied, at the subjective level, by a more or less profound loss of consciousness (5, 29–31). Sleep is regulated homeostatically and by the circadian clock. Virtually all animals investigated to date exhibit the core criteria of sleep, i.e., increased arousal threshold, rapid reversibility, and homeostatic rebound after sleep deprivation, including mammals, birds, reptiles, as well as invertebrates (Refs. 31, 32, but see Ref. 33). Because sleep exposes us to external threats, one of the biggest mysteries in neuroscience concerns the adaptive function of sleep: What is sleep for (34–38)? Sleep has been associated with saving and restoration of energy resources (39, 40), metabolic regulation (41–43), and regulation of immunological and inflammatory responses (44, 45). The loss of consciousness, in particular, suggests that sleep is critically important for the brain (46, 47), with one major function being the formation of long-term memory (5, 28, 48). BOX 1 offers an overview of core concepts on memory systems and how memories are formed (see also **FIGURE 1**). BOX 2 provides a summary of electroencephalographic (EEG) and neuromodulatory factors that define the different stages of sleep (see also **FIGURE 2**).

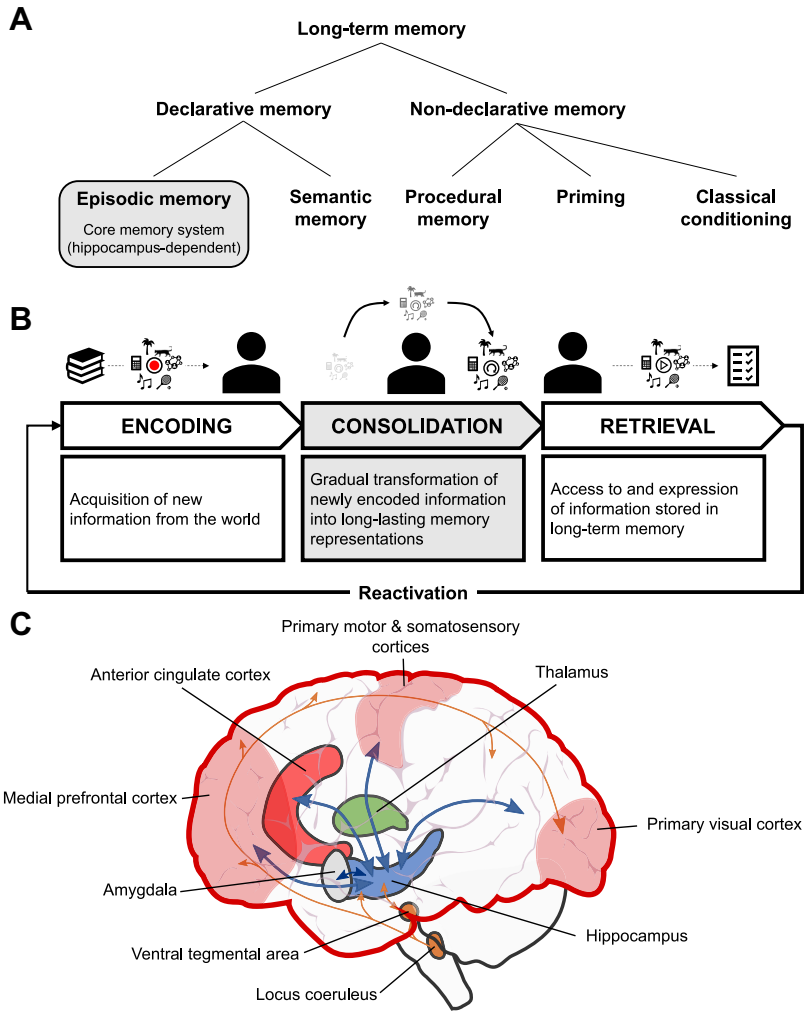

FIGURE 1. Memory systems. *A*: long-term memory is classically divided into declarative and nondeclarative memory systems. Declarative memory is further subdivided into episodic and semantic memory. Nondeclarative memory constitutes a heterogeneous class of phenomena, including procedural memory, priming, and classical conditioning. *B*: memory processing comprises the subprocesses of encoding (or acquisition), consolidation, and retrieval (or recall). Newly encoded memory representations are initially instable, and the information is prone to forgetting. Consolidation refers to the process of transforming newly encoded memories into long-lasting representations. Long-term representations can be accessed and expressed during retrieval. Retrieval involves a reactivation of the stored representation, which entails a labilization and potential updating of the representation and, similar to the encoding of new information, a (re)consolidation of the representation. *C*: brain structures involved in memory formation. The hippocampus and neocortex represent the main structures of the episodic memory system, with the interplay between these regions partly relayed via the thalamus. Representations of semantic memory are assumed to be widely distributed in the neocortex. The primary visual and motor cortices contribute to procedural memory for respective perceptual and motor skills. Structures of the medial prefrontal cortex (mPFC), like the anterior cingulate cortex (ACC), appear to be particularly relevant for abstracting gist memory during sleep-dependent consolidation. The amygdala is central for emotional memory formation and the ventral tegmental area (VTA) for reward learning. The brain stem locus coeruleus (LC) modulates memory formation during sleep and wakefulness. Note that all of these regions are strongly connected and integrated with the hippocampal/neocortical axis forming the episodic memory system.

2. CONCEPTS OF MEMORY FORMATION DURING SLEEP

Newly encoded memories are labile and prone to forgetting and thus need to be consolidated to be stored for the long term. Whereas we encode and retrieve memories during wakefulness, sleep is arguably best suited for memory reprocessing and consolidation. The two most influential theories to explain effects of sleep on memory formation are the active systems consolidation (ASC) concept and the synaptic homeostasis hypothesis (SHY), which have been elaborated in several previous reviews (5, 28, 79, 107–114) and are briefly described in the following.

2.1. Active Systems Consolidation

Although initially it was assumed that sleep improves memory retention only passively by protecting an ongoing consolidation process from retroactive interference (11, 115), a growing body of evidence indicates that sleep forms memory by an active process (79). In this context, the active systems consolidation (ASC) concept was proposed, evolving from the standard consolidation theory, with a particular focus on memory processing during sleep (28, 79, 108, 109, 116, 117). The concept assumes that during encoding the hippocampus binds the different components of an experience into a unique spatiotemporal episodic memory. These memories, initially, are thus strongly dependent on the hippocampus and only weakly represented in neocortical networks, which are, however, critical for long-term storage. Central to the consolidation process is that hippocampal memory representations are repeatedly reactivated during sleep, thereby gradually strengthening the distributed neocortical representations through activation of associated memory networks, which ultimately results in a "corticalization" of the respective representations. Evidence for memory reactivation during sleep has accumulated in recent years (Refs. 26, 118, 119; see sect. 3.3.1). Furthermore, extrahippocampal, mainly neocortical networks are activated more strongly during later retrieval of a memory when subjects have slept after initial encoding, supporting the hypothesis of a sleep-dependent corticalization (120–123). In humans, for instance, napping following encoding of face-location associations led to changes in hippocampal and

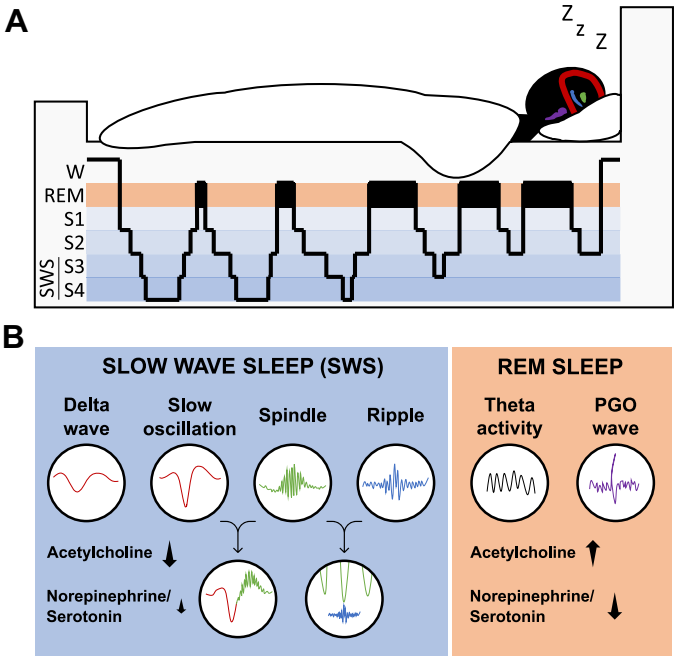

FIGURE 2. Sleep stages, EEG characteristics, and neuromodulatory factors. *A*: macroarchitecture of human nocturnal sleep. W, wake. *B, left*: underlying microarchitecture of field potential oscillations in slow-wave sleep (SWS): delta waves, neocortical slow oscillations, thalamo-cortical sleep spindles, and hippocampal ripples and the phase-amplitude coupling into slow oscillation-spindle and spindle-ripple events. *Right*: in rapid eye movement sleep (REM sleep): theta activity and ponto-geniculo-occipital (PGO) waves. *Bottom*: levels of acetylcholine, norepinephrine (NE), and serotonin during SWS and REM sleep are indicated (arrows) with reference to levels during wakefulness. Colors in *B* correspond to sleep stages (SWS and REM sleep) in *A*.

prefrontal cortex (PFC) activity over the course of 3 mo, with a decrease in the hippocampal contribution to memory recall but an increase in the prefrontal contribution over time (122). Notably, the transformation and corticalization of representations is often a very gradual process evolving over several months (120).

A key aspect of the ASC concept is the assumption that the transmission of reactivated memory information during sleep from the hippocampus to extrahippocampal sites is accompanied and facilitated by particular brain oscillations that occur during SWS (**FIGURE 3*A***; see sect. 3.1). Specifically, hippocampal SW-Rs, which drive reactivations of newly encoded representations in the hippocampus, are coalescing with sleep spindles originating from the thalamus to support the bottom-up transfer of the reactivated memory information to extrahippocampal regions. In addition, slow oscillations (SOs) that originate from neocortical networks exert a top-down control to synchronize spindles, ripples, and hippocampal reactivations to their excitable up-state. This particular constellation of brain oscillations with ripples nesting into the oscillations of spindles and spindles nesting into the excitable up-states of SOs during SWS provides the means of

BOX 1
Memory systems

Until the late nineteenth century, memory was considered as one single faculty (49). This notion has been challenged by experiments conducted on patients with lesions to the hippocampus, particularly the famous patient H.M., whose hippocampus and medial temporal lobe were largely bilaterally removed in an attempt to control epileptic seizures (50). These experiments revealed the existence of two major systems, the declarative and nondeclarative memory systems (51) (**FIGURE 1*A***), with only the former depending on the hippocampus. Declarative memory, sometimes also referred to as explicit memory (52–55), is defined as "knowledge available as conscious recollection" that can be "brought to mind as remembered verbal or nonverbal material" (e.g., ideas, sounds, images, sensations, odors, or words) (51, 55). Declarative memory is further subdivided into episodic and semantic memory (56), with episodic memory being defined as detail-rich memory of episodes, i.e., unique (personal) events occurring in a specific spatiotemporal context, and semantic memory being related to general knowledge (facts, ideas, concepts, etc.). Nondeclarative memory, on the other hand, represents a heterogeneous class of memory phenomena that are not consciously accessible (i.e., implicit memory), such as procedural memory (skills, habits), priming, and classical conditioning (49, 51, 52, 57–61). Although declarative and nondeclarative memory systems are considered independent, they can also cooperatively contribute to knowledge acquisition to optimizing behavior (49, 62). Note that since any learning occurs in an episode, i.e., as an event within a specific spatiotemporal context, the hippocampus-dependent episodic memory system can be considered a core system that supports formation of other kinds of memory. Thus, in semantic memory a concept of "school" may derive from the multiple episodes a person has experienced in a school. The episodic memory system can likewise support formation of nondeclarative memory, e.g., motor skills through the embedded encoding of the training episodes into hippocampus-anchored episodic representations.

Learning is the "biological process of acquiring new knowledge about the world," whereas memory is the "process of retaining and reconstructing that knowledge over time" (63). During learning, new information is encoded into an initial storing system (sometimes termed "short-term memory") with limited capacity, which, in the case of explicit learning and the encoding of episodic memories, involves the medial prefrontal-hippocampal system (49, 64, 65). Much of the encoded information is rapidly forgotten. The transformation of instable memories from the initial storage into a more stable state in long-term memory is called memory consolidation (**FIGURE 1*B***). This transformation depends on processes at the systems level (systems consolidation) as well as the synaptic level (synaptic or cellular consolidation). Systems consolidation refers to the gradual redistribution of initially encoded episodic representations from short-term storage systems, depending on the hippocampus as a fast-learning system, to the slow-learning long-term storage systems, represented mainly by neocortical regions (55, 66). That is, although experiences are encoded in both the hippocampus and neocortex during learning, the newly encoded representations are reorganized and transformed over time, with a more permanent, less hippocampus-dependent, memory gradually evolving in distributed neocortical regions (55). Synaptic consolidation, on the other hand, is based on plasticity-dependent long-term strengthening of synapses and is thought to be completed within hours after encoding (67). Synaptic consolidation processes, however, are also considered to occur as "subroutines" during systems memory consolidation, given that reprocessed representations during systems consolidation are modified by plasticity-dependent mechanisms at the synaptic level (62, 68). Notably, systems consolidation processes can extend over considerable time intervals, from several hours up to years (55, 69, 70), rendering these processes particularly susceptible to influences of daytime wakefulness and nighttime sleep. The study of memory formation of very long intervals is technically challenging and, indeed, an often overlooked aspect in sleep studies (see also **FIGURE 11**).

BOX 2
The macro- and microarchitecture of sleep

Sleep in humans is commonly divided into non-REM sleep stages and REM sleep (REM for rapid eye movement; **FIGURE 2*A***). Non-REM sleep is subdivided into four stages (S1–S4, according to Rechtschaffen and Kales, Ref. 71), with S3 and S4 representing the deepest stages of non-REM sleep, termed slow-wave sleep (SWS). [The classification system of the American Academy of Sleep Medicine (AASM) discriminates only 3 non-REM sleep stages, N1–N3, with N3 corresponding to SWS (Ref. 72; see also Ref. 73).] When falling asleep, we first enter S1 sleep (typically <7 min), which is characterized by <50% alpha activity (8–12 Hz) in the electroencephalogram (EEG) and a decrease in electromyogram (EMG) activity. The following S2 sleep stage usually accounts for ~50% of a typical night (30). This sleep stage is characterized by sleep spindles, i.e., bursts of short waxing and waning oscillatory activity generated in the thalamic reticular nucleus (**FIGURE 2*B***), and K-complexes, i.e., a brief surface negative high-voltage peak that is followed by a slower positive complex, often co-occurring with a spindle. There are slow (9–12 Hz) and fast (12–15 Hz) spindles, reaching maximum power over frontal and centro-parietal cortical brain areas, respectively (74, 75). Whereas S3 is scored when the EEG shows >20% high-amplitude slow-wave activity (SWA, 0.5–4 Hz), S4, the deepest form of non-REM sleep, contains >50% of SWA. Fast spindles are similarly distributed across S2–S4 sleep, whereas slow spindles preferentially occur during SWS (74). A hallmark of SWS is the so-called slow oscillations (SOs, <1 Hz; **FIGURE 2*B***). SOs primarily originate in the neocortex and consist of up- and down-states that are associated with synchronized widespread membrane depolarization or hyperpolarization, respectively, of cortical pyramidal cell networks (76–78). In addition, SWS is associated with the dominant occurrence of so-called sharp-wave ripples (SW-Rs) in the hippocampus, i.e., brief high-frequency oscillatory ripple events of >80 Hz, occurring superimposed with fast depolarizing sharp waves (79, 80) (**FIGURE 2*B***). Although SOs, spindles, and ripples can occur independently, they tend to co-occur in a coordinated manner, with (fast) spindles nesting into the excitable SO up-states and ripples nesting into the excitable spindle troughs, thus forming coupled "SO-spindle" and "spindle-ripple" events (**FIGURE 2*B***; see also sect. 3.1). SWS is also characterized by a specific neuromodulatory milieu mainly comprising minimum levels of acetylcholine and norepinephrine (NE) levels that fluctuate at an intermediate level (28, 81). Note that non-REM sleep stages S1 and S2 cannot be discriminated in rodent sleep. Accordingly, studies of non-REM sleep in rodents refer to SWS, whereas in humans such studies typically refer to S2–S4 (omitting S1 as a rather transient period of nonconsolidated non-REM sleep). Accordingly, here in the context of human studies, we use the term SWS only when studies specifically analyzed sleep stages S3 and S4 (or N3).

REM sleep constitutes ~20–25% of total sleep time and is characterized by "rapid, jerky, and binocularly symmetrical" eye movements (14) as well as muscle atonia (82–85). REM sleep in humans is characterized by a low-amplitude mixed-frequency EEG with only occasional theta (4–8 Hz) bursts. Because of the similarity of the EEG to that during attentive wakefulness, REM sleep is also referred to as "paradoxical sleep" (30). Field potentials and unit activity during phasic REMs were found to resemble those observed during image presentation in awake humans (86). In rodents, theta is the prevailing rhythm during tonic REM sleep (87) (**FIGURE 2*B***). REM sleep in rodents, moreover, is characterized by so-called ponto-geniculo-occipital (PGO) waves (88), which are short, intense bursts (3–5 Hz, 300–500 ms) of synchronized activity that originate in the pontine brain stem and propagate to the lateral geniculate nucleus and the occipital cortex (89) (**FIGURE 2*B***). PGO waves appear to be driven by coherent theta activity between the hippocampus and amygdala and are not reliably detected in humans (but see Ref. 88). PGO bursts occur at a higher rate at transitions into REM sleep (90). This period preceding REM, in which the EEG often displays also high spindlelike activity, likely constitutes an independent sleep stage in rodents and cats, termed intermediate state or pre-REM (91–93). The neuromodulatory milieu during REM sleep is characterized by maximum levels of acetylcholine that can exceed even levels during wakefulness, whereas levels of NE and serotonin are minimal (28, 81). Since the discovery of REMs in 1953, this sleep stage has often been associated with dreaming (14, 94). However, although awakenings from REM sleep yield the highest rate of dream reports (80–90%), dreams are also reported in up to 70% of awakenings from other sleep stages, although these dreams are less vivid and shorter than dreams reported after awakenings from REM sleep (95, 96).

Apart from oscillatory EEG features, sleep stages also differ in nonoscillatory "aperiodic" activity, which is higher during REM than during non-REM sleep. Aperiodic EEG activity can be considered an estimate of the level of cortical excitation and, as such, appears to be also linked to memory processing during sleep (97, 98).

Non-REM and REM sleep alternate in an ultradian cycle, with four to six non-REM-REM sleep cycles per night, each cycle lasting ~100 min (30, 99, 100). Across a full night, the time in SWS decreases while REM sleep increases. Consequently, SWS dominates the first and REM sleep the second half of the night. In parallel, plasma cortisol concentrations reach a minimum during the first half of the night, because of a suppressive action of SWS on activity of the hypothalamus-pituitary-adrenal (HPA) axis (101). Cortisol levels distinctly increase during the second half of the night to reach a maximum at around the time of morning awakening (102). SWS and REM sleep cannot always be considered as separate entities. For instance, the hippocampus often shows signs of REM sleep while cortical areas are still in SWS (103, 104). Similarly, SWA occasionally intrudes into ongoing REM sleep (105, 106). The discovery of the macroarchitecture of sleep as defined by the basic temporal pattern of sleep stages, together with the underlying microarchitecture of EEG oscillations, has greatly advanced the field of sleep research, with >4,000 articles per year (in the last 10 years) that include "sleep" in the title. Of those, >400 articles per year relate to the memory function of sleep.

a hippocampal-neocortical dialogue to gradually transform and redistribute the original, hippocampally anchored, episodic representation into long-lasting neocortical representations (e.g., Refs. 79, 125–130). Within cortical networks, the strengthening of representations relies on synaptic consolidation processes, thereby supporting the integration of newly encoded memory information into preexisting memory networks (107). As a result of this active systems consolidation process during sleep, at a later retrieval test the neocortical representations can be used to reinstate a more or less complete representation by activating only parts of the memory trace (131). Notably, the gradual corticalization of representations during sleep-dependent consolidation goes along with a qualitative transformation that supports processes of higher-level abstraction and generalization, with the cortical long-term representation preferentially containing schemalike and invariant information from overlapping experiences (Refs. 132–134; see sect. 4.2).

According to the ASC concept, sleep preferentially benefits episodic memories that depend on hippocampal processing. However, the hippocampus may also be involved in the consolidation of memories that can, in principle, be acquired and retrieved in the

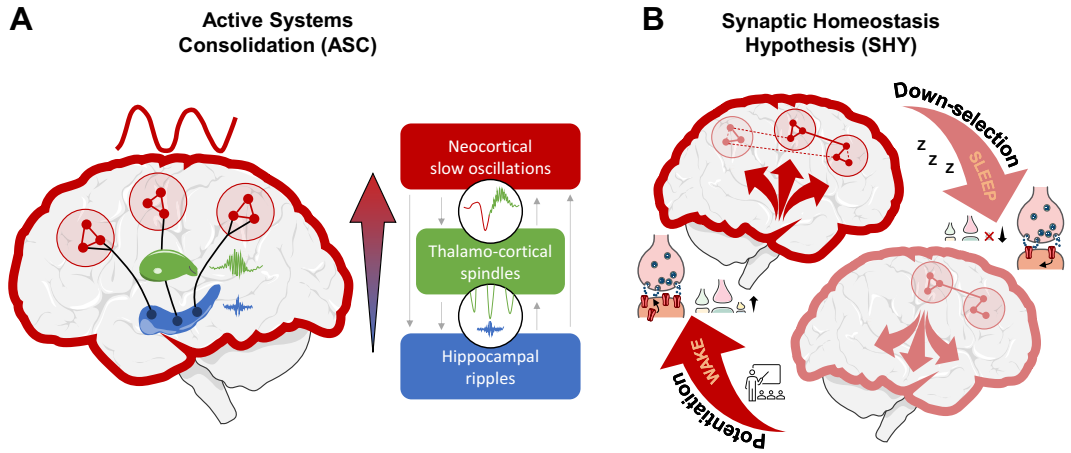

FIGURE 3. Active systems consolidation (ASC) and synaptic homeostasis hypothesis (SHY). *A*: ASC focuses on hippocampus-dependent episodic memory representations. During SWS, newly encoded hippocampal representations are repeatedly reactivated, which drives the gradual redistribution of representations, eventually residing mainly in extrahippocampal, cortical structures serving as long-term stores. The gradual redistribution of representation is mediated by the fast hippocampal-to-neocortical transmission of reactivated memory information that is facilitated by the triple nesting of hippocampal ripples (blue) into the excitable troughs of thalamo-cortical spindle (green) that themselves tend to nest into the excitable up-states of neocortical SOs (red). *B*: SHY focuses on the synaptic connectivity in brain networks that is homeostatically regulated across the sleep-wake cycle. The encoding of information during the wake period is associated with widespread "synaptic potentiation," i.e., strengthening of network connectivity, involving the synaptic recruitment of AMPA receptors, which progressively saturates the ability to encode new information. Sleep, by a process of "downselection," renormalizes the net synaptic strength (e.g., Ref. 124). Downselection is driven by SWS and includes the internalization of AMPA receptors, which desaturates synapses and recovers the brain's ability to encode new information. Synaptic downselection, by preferential impact on weakly potentiated synapses encoding "noise," increases the signal-to-noise ratio in the networks and thereby enhances accessibility of respective memories after sleep. Although it is not clear how exactly synaptic weakening targets some synapses more than others, several molecular candidate mechanisms have been characterized (112, 114). See GLOSSARY for additional abbreviations.

absence of a functioning hippocampus (see also BOX 1). This is because any learning occurs in a spatiotemporal context, which in the intact brain is encoded by the hippocampal system. As a result, the consolidation of extrahippocampal representations can benefit from hippocampal reactivations. This has been demonstrated in two studies showing in humans and rats, respectively, that the consolidation process during sleep involves the hippocampus also for enhancing types of memories that do not require the hippocampus at encoding (Refs. 135, 136, see Refs. 62, 137, 138 for related results; **FIGURE 4**). The study in rats (135) employed a novel object recognition (NOR) task. Sleep after encoding on the task enhanced the rat's long-term NOR memory in comparison with a postencoding wake control condition, and this enhancement was highly correlated with spindle activity during postencoding SWS. Importantly, the memory benefit from postencoding sleep was nullified when hippocampal activity was pharmacologically suppressed during the postencoding sleep period. Confirming these findings in rats, the study in humans (136) showed that patients with lesions to the hippocampus, unlike healthy control subjects, did not improve on a procedural finger sequence tapping task when the training was followed by sleep. Findings like these indicate that the ASC concept can be extended to memories that are classically considered "non-hippocampus dependent."

2.2. Synaptic Homeostasis Hypothesis

The synaptic homeostasis hypothesis (SHY) is based on the idea that synaptic potentiation and the growth of synapses in the brain's neuronal networks are homeostatically regulated. Encoding of any information during wakefulness is associated with widespread upscaling of synaptic networks, i.e., the potentiation of synapses and growth of dendritic spines, and during subsequent sleep the potentiated synapses are downregulated ("synaptic downselection"), as part of a homeostatic regulation of network synaptic strength across the sleep-wake cycle (Refs. 112, 113, 124, 139, 140; **FIGURE 3*B***). Encoding of information during wakefulness is thus associated with a strengthening of glutamatergic synapses and synaptic connectivity throughout the brain, including neocortical as well as hippocampal networks, which progressively saturates these networks and thereby diminishes their ability to further encode new information (141). Sleep, on the other hand, renormalizes the net synaptic strength, which in turn desaturates the networks, thereby increasing their ability to encode new information and to learn. Widespread synaptic upscaling during wakefulness, in addition, increases the brain's energy and space demands, which are countered by synaptic renormalization during sleep as well. In this framework, memories, to be maintained for the long term, profit from synaptic renormalization as they are represented by synaptic ensembles with above-average

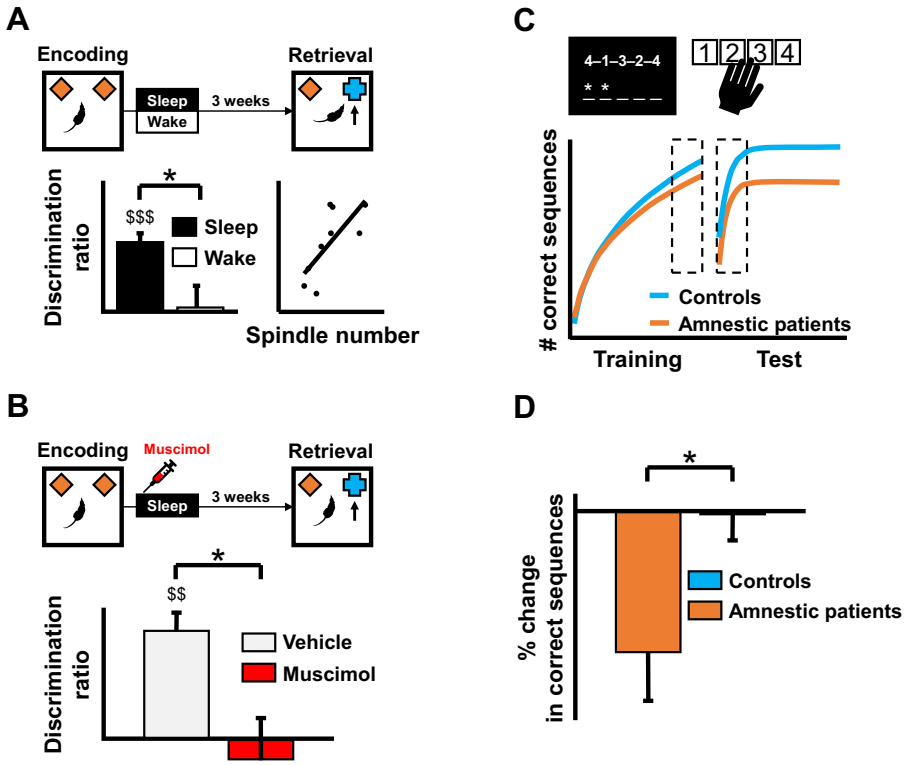

FIGURE 4. Hippocampal involvement in nonhippocampal memory formation during sleep. *A*: in a novel object recognition (NOR) task, during encoding rats explored 2 identical objects in an arena, which was followed by a 2-h interval of sleep or wakefulness. During retrieval of remote memory 3 wk later, the rats explored the arena, in which 1 of the 2 objects was replaced by a novel object (arrow). The time spent to explore the novel object compared with the familiar object (discrimination ratio) indicates a measure of recognition memory. *Bottom*: mean and SE of discrimination ratios during the first minute of exploration at the remote retrieval test. NOR memory benefited from postencoding sleep but decayed in the wake condition. In the sleep condition, NOR performance was further correlated with the number and duration of spindles during SWS. *$P < 0.05$ group difference; $$$P < 0.001$, $$P < 0.01$ for *t* tests against chance level. *B*: to pharmacologically suppress hippocampal activity during sleep, muscimol was bilaterally infused into the dorsal hippocampus. Hippocampal inactivation during postencoding sleep abolished remote NOR memory compared to vehicle injection, demonstrating that the hippocampus is crucial for forming nonhippocampal long-term memory during sleep. *C*: patients with medial temporal lesions (including the hippocampus) and healthy human control subjects were trained on a motor task that required them to repeatedly tap with the fingers of the nondominant left hand a particular sequence (e.g., 4-1-3-2-4) as fast and as accurately as possible. *Bottom*: curve fits to average performance of amnestic patients and control subjects during training and test. There was no difference in initial learning between the groups. However, whereas control subjects performed at the same level at the beginning of the test as at the end of training, amnestic patients exhibited a decline in performance. *D*: mean and SE of % change in correct sequence performance (comparing the last 3 training blocks with the first 3 test blocks, as marked in *C*) show a significant difference between amnestic patients and healthy control subjects, indicating that the hippocampus is necessary for consolidation of a task that does not require the hippocampus for initial learning. *$P < 0.05$, *t* test. Figure parts in *A* and *B* are based on Sawangjit et al. (Ref. 135). Reprinted with permission by the author's copyright. Figure parts in *C* and *D* are based on Schapiro et al. (Ref. 136). Copyright 2019 by John Wiley and Sons. Reprinted with permission.

synaptic strength. Widespread synaptic downselection is assumed to decrease and nullify all "spurious" connections (noise) that accumulate during wakefulness, while strongly potentiated synapses that significantly contribute to memories are downregulated to a lesser degree, overall increasing the signal-to-noise ratio and thus enhancing the accessibility of the respective memory representations (139).

There is ample evidence supporting SHY. Sleep compared with wakefulness reduced the overall number of synapses in cortical areas (142, 143), decreased the area of contact between axon terminals and dendritic spines in the cortex of mice (142), and also reduced α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptor levels in neocortical networks, overall proving, at the morphological and functional levels, a reduction in network synaptic connectivity and strength (124, 144, 145). A gain of synapses during wakefulness versus sleep pressure-dependent loss of synapses during sleep was likewise demonstrated for excitatory synapses at the single-neuron level in zebrafish (140). Interestingly, this modulation was robustly observed in some (type 2 and type 4) but not all (type 3) neuron types, consistent with a synaptic downselection process (rather than a global downscaling), as proposed by SHY (113). Similarly, compared with wakefulness, sleep reduced phosphorylation levels of cortical AMPA receptors (146) and neuronal firing rates in the neocortex and hippocampus in rodents (Refs. 147–155, but see Ref. 156) as well as indicators of cortical excitability in humans (157–159). It is, however, questionable whether functional parameters like a decrease in firing rates are necessarily a consequence of synaptic downscaling or rather a shift in

the balance between excitation and inhibition induced by other factors in the course of sleep (79, 160).

Synaptic potentiation and downselection have been associated with slow-wave activity (SWA) as a marker of sleep need that increases during wakefulness, and particularly with extended wake periods during sleep deprivation as well as decreases during SWS (112, 144). SHY assumes that the homeostatic regulation of sleep need reflects changes in network synaptic strength, which implicates a critical role of SWA and SWS in synaptic renormalization. Supporting this view, molecular and electrophysiological assessments indicated a decrease in excitability in larger cortical networks across SWS periods in rodents and humans (144, 161). Total sleep deprivation, but not selective REM sleep deprivation, prevented the widespread downregulation of cortical and hypothalamic AMPA receptors (162, 163), further corroborating a major role of SWS for downselection processes. Conversely, some evidence exists that SWS even promotes the formation of new spines (164) and that long-term potentiation-like augmentation of cortical neuronal responses occurs during SWS (165). Overall, these findings agree with the view that downselection during SWS does not equally pertain to all synapses in neocortex but spares selected ensembles that contribute to to-be-maintained memories. Apart from SWS, there are also clues of REM sleep adding to synaptic downselection processes. Neuronal firing rates during sleep decreased more strongly during REM sleep than SWS epochs in both the hippocampus and neocortex (148, 166), and in developing mice REM sleep promoted synaptic pruning and spine elimination after the animals were exposed to conditions enhancing experience-driven plasticity, like fear conditioning and monocular deprivation (167, 168).

The SHY and ASC concepts highlight different but compatible processes underlying memory formation during sleep, with SHY focusing on global synaptic downscaling and ASC focusing on systems-level consolidation involving synaptic consolidation and upscaling (113). Both processes appear to coexist. Structural imaging of synapses in the neocortex revealed a general decrease in both the number of synapses and the area of synaptic contact during sleep, alongside localized increases in synapse numbers and the formation of new spines (142, 145, 164, 168). An assessment of AMPA receptors containing the GluA1 subunit, i.e., a specific marker of synaptic potentiation, in the motor cortex of mice indicated that those spines in which prior motor learning led to the largest increase in GluA1 expression have a relative advantage, as they appeared to undergo less downselection during posttraining sleep (124). Evidence, mainly from in vitro studies, suggests several potential molecular mechanisms, including Homer1a-dependent synaptic renormalization in combination with increased Arc expression, phosphorylation of GSK3beta, and/or GluA1 at Ser845, that could implement the selective downscaling of targeted synapses (112, 114).

3. ROLE OF SLEEP STAGES IN MEMORY FORMATION: SYNAPTIC, CIRCUIT, AND SYSTEMS-LEVEL MECHANISMS

Different sleep stages and accompanying sleep oscillations are assumed to play different roles in memory consolidation (BOX 2 provides an overview of sleep stages and their properties). Here, we explore at the synaptic, circuit, and systems levels the neurophysiological mechanisms supporting memory formation during non-REM sleep and SWS on one hand and during REM sleep on the other hand. We also discuss complementary roles of SWS and REM sleep in memory processing.

3.1. Non-REM Sleep

Non-REM sleep, particularly SWS, has often been proposed to be the sleep stage that is most important for memory consolidation (169–171). Yet this does not necessarily mean that memory consolidation improves with more time spent in SWS (172). Along this line, light non-REM sleep (S2 sleep) and SWS in humans have been suggested to differentially contribute to memory formation, with S2 supporting active consolidation processes and SWS supporting processes of synaptic downscaling (173) (sect. 2.2). Given that down-states of SOs are likely associated with a widespread breakdown of connectivity in cortical neuronal networks and synaptic plasticity is reduced during SWS, non-REM sleep overall might even be unfavorable to memory consolidation (174). In rodent and human studies, positive as well as negative correlations have been found between time spent in SWS after encoding of episodic types of memory and the retention of these memories (175–178). Rather than the mere time spent in non-REM sleep or SWS, select mechanisms associated with this sleep stage are probably more decisive for effective consolidation. Of these mechanisms, reactivation of neural ensembles that occurs during SWS and is often temporally coupled with SOs and spindles appears to be most critical for memory consolidation.

3.1.1. Neuronal ensemble reactivations and ripples.

Current theories (see, e.g., Refs. 79, 80, 108; sect. 2.1) assume that during non-REM sleep, and particularly during SWS, memory representations encoded in the hippocampus are repeatedly activated, thereby gradually strengthening the distributed extrahippocampal representations through activation of associated memory networks,

particularly of highly salient (e.g., reward associated) and novel (179–181) information (sects. 4.2 and 4.3). Such neuronal reactivations are observed in hippocampal place cells of rats and resemble neural firing patterns of previous encoding (23, 118, 182), i.e., they replay new information in the same temporal order as previously acquired (79), but compressed in time by a factor of 5–20 (Refs. 118, 183; **FIGURE 5, *A* AND *B***). The term "replay" is used specifically when ensemble firing reoccurs in the same temporal sequence as during encoding (184). Memory replay in the hippocampus is accompanied by ripples, i.e., brief high-frequency oscillatory events of >180 Hz in rodents and 80–100 Hz in humans, that often occur superimposed with a fast depolarizing sharp wave (79, 80, 185, 186). Such SW-Rs are independently generated in the left and right hippocampus and propagate within the respective hemisphere to support memory reactivation locally (187). The importance of ripples for memory reactivations and consolidation has been primarily investigated in rodents. For example, CA3 place cells representing novel waking experiences were preferentially reactivated during SW-Rs in sleeping rats (188). Similarly, a role of CA2 SW-Rs was demonstrated for (nonspatial) social memories in rats (189). Consequently, disruption of hippocampal SW-Rs in rats, with optogenetic stimulation of septal cholinergic neurons or optogenetic silencing of CA1 principal neurons, impaired memory retrieval (25, 190). Furthermore, an assembly-specific disruption of specific reactivation events following the training on a task that required animals to locate goals at fixed locations in different environments revealed a selective recall deficit that was restricted to the spatial environment whose reactivation was disrupted (191). Vice versa, memory performance was enhanced when spontaneously occurring ripples were prolonged by closed-loop optogenetic stimulation after maze learning in rats (192). At the synaptic level, effects of ripples involve KIBRA, which is a memory-associated protein regulating AMPA receptor trafficking (193). The increase in activity associated with hippocampal ripples and associated memory replay appears to be counter-regulated by long barrages of action potentials arising from CA2 pyramidal neurons that project to cholecystokinin-expressing (CCK+) basket cells in CA1, providing a potential mechanism to balance activity in hippocampal networks during memory reactivations and to avoid excess connectivity in repeatedly reactivated ensembles (194). Although neuronal memory reactivations have been mostly investigated in rodents, they also occur in other species such as zebra finch and *Drosophila*, demonstrating the universality of this phenomenon (195, 196).

Differing from rodent studies, studies in healthy humans can only provide indirect evidence of memory reactivations and underlying mechanisms during sleep.

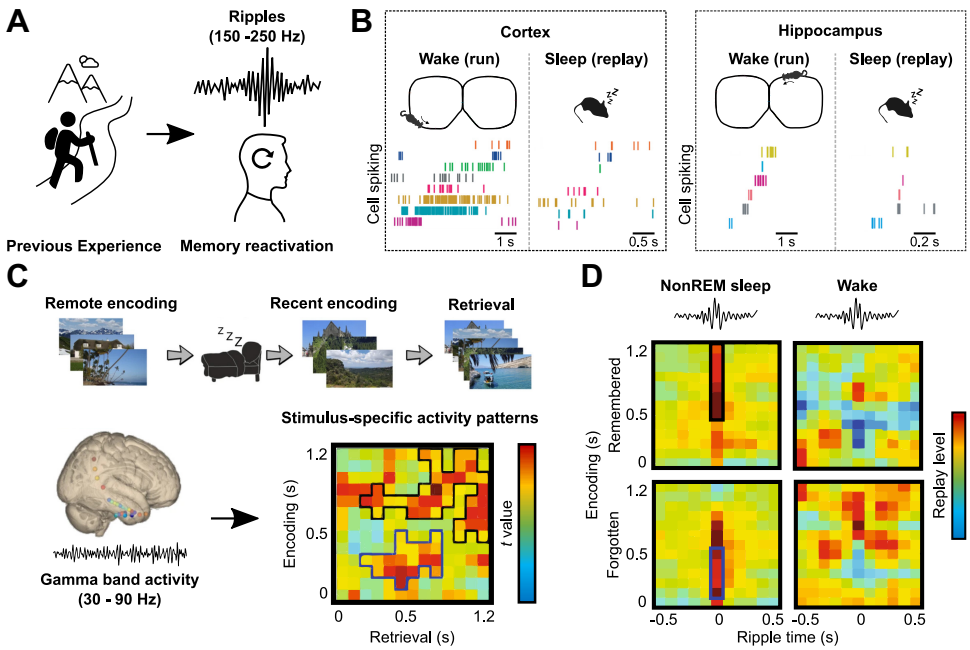

FIGURE 5. Sleep-associated memory reactivation. *A*: illustration of memory reactivation as a fundamental mechanism for memory consolidation, orchestrated by ripples. *B*: spatially tuned neurons in the visual cortex (*left*) and hippocampus (*right*) fire in a sequential pattern specific to a rat's current position in a figure-8 maze. During subsequent sleep this pattern is replayed, though compressed by a factor of 5–20. Adapted from Ji and Wilson (Ref. 118). Copyright 2006 by Springer Nature. Reprinted with permission. *C*: in human epilepsy patients, representational similarity analyses of intracranial EEG gamma activity between encoding and retrieval (of pictures showing landscapes and buildings) revealed stimulus-specific neural representations. An early cluster (100–500 ms, blue frame) was correlated with forgotten items and a later cluster (500–1,200 ms, black frame) with remembered items. *D*: replay of stimulus-specific clusters of gamma activity was locked to sharp-wave ripples during non-rapid eye movement (REM) sleep, but not wakefulness, regardless of whether items were remembered or forgotten. Adapted from Zhang et al. (Ref. 119) with permission under CC-BY license.

Nevertheless, such studies likewise demonstrate a critical role of reactivation for memory consolidation, using noninvasive techniques to assess activity over widespread cortical areas. For instance, in magnetoencephalographic (MEG) recordings in healthy volunteers, visuomotor learning elicited a pattern of long-range cortico-cortical synchronization of slow (0.1 Hz) fluctuations in beta-band power (12–30 Hz), which spontaneously reappeared in delta-band power (1–3.5 Hz) fluctuations during subsequent sleep (197). Notably, the individual strength of these reactivations, as measured by their correlation with the synchronization pattern during training, predicted overnight memory improvement. Using multivariate pattern classification to decode electrical brain activity in healthy volunteers, another study (198) revealed that specific patterns of learning-related processing were reactivated during subsequent non-REM as well as REM sleep. Here, the strength of reprocessing during sleep also predicted later memory performance, a relationship that was specific to SWS and not observed for REM sleep. These studies not only show that memory reactivation can, with some limitations, be investigated with noninvasive techniques in humans but also suggest that such reactivations can be assessed from large-scale cortical network activity (see Ref. 199 for a discussion of methods to detect reactivations in standard sleep recordings).

Signs of local neuronal reactivations in humans can only be assessed in patients who are implanted with intracranial electrodes, studying local field potential (LFP) recordings from multiple cortical and hippocampal sites of such patients (119, 200, 201). Zhang et al. (119) used representational similarity analyses to reveal a stimulus-specific reactivation of neuronal patterns in the gamma-band range during ripples in postencoding sleep (**FIGURE 5, *C* AND *D***). Before sleep, the patients were asked to distinguish between pictures showing landscapes and buildings by pressing one of two buttons. Landscape- versus building-specific gamma (30–90 Hz) activity during early (100–500 ms) and late (500–1,200 ms) poststimulus intervals after picture presentation onset was spontaneously reactivated during both wakefulness and sleep, but replay levels were independent of later memory performance. Ripples that occurred during non-REM sleep, but not ripples occurring during wakefulness, were associated with reactivated gamma activity from the late 500–1,200 ms encoding window, and this relationship was found only for the pictures that were remembered at the test after sleep. Contrary to gamma activity during the late 500–1,200 ms encoding window, gamma activity during the early 100–500 ms encoding window was more strongly reactivated for pictures that were forgotten at the test after sleep, which is consistent with the view that ripples, beyond reactivating hippocampal memories, might simultaneously downregulate hippocampal representations (113, 202). In another study in epilepsy patients (200), sequences of population firing peaks ("motifs") that occurred during wake experiences in large-scale neocortical networks reappeared during non-REM sleep following (but not preceding) the wake period. Importantly, these motifs were coupled to hippocampal SW-Rs as well as neocortical sleep spindles and SO down-to-up-state transitions (see below).

Reactivations during non-REM sleep can also be experimentally triggered by reinstating a reminder cue that has previously been associated with the learning experience. This technique, termed "targeted memory reactivation" (TMR), has been successfully employed using olfactory (e.g., Ref. 26) and auditory (e.g., Ref. 203; sect. 7.2) cues. Together, the findings corroborate a critical role of reactivations of newly encoded neuronal representations, and associated hippocampal ripple oscillations, for memory consolidation during sleep.

3.1.1.1. REACTIVATIONS DURING NON-REM SLEEP VS. WAKEFULNESS. Reactivations of neuron ensembles that are accompanied by hippocampal ripples are also observed during wakefulness, specifically during quiet rest and intermittent rest periods while the animal is performing on a task (204–209). Also in humans, signs of reactivations have been revealed during waking rest (119, 210–212). Unlike sleep replay, which occurs after an event in a forward direction, wake reactivations can also occur in reverse order ("reverse replay") and in anticipation of an event ("preplay") (207, 213–217), overall suggesting that wake reactivations benefit the flexible retrieval of stored representations to support adaptive behaviors like decision-making and planning (218). Reactivations and replay during sleep and wakefulness display largely similar features (219), including the factors that select which content is reactivated (204, 207, 220), such as reward (179, 208, 221–223). However, wake replay was also found to be biased toward representations associated with less rewarded outcomes (224, 225). Like sleep reactivations, wake reactivations have also been associated with an enhanced subsequent recall performance (226–229). Furthermore, optogenetic silencing of CA1 pyramidal neurons in mice during SW-Rs occurring during learning of new goal locations impaired memory formation (230).

However, sleep and wake reactivations also differ. For example, in rats trained on a spatial alternation task, associated wake replay during initial learning was stronger than during subsequent sleep, while also being characterized by a stronger synchronization of hippocampal (in CA1) and prefrontal cortical firing, more structured activity, and distinct excitation-inhibition patterns (231). Although these and related findings (205, 232, 233) suggest that reactivations during wakefulness, like during sleep, support memory consolidation, postencoding suppression of

hippocampal reactivations in awake rats enhanced rather than impaired subsequent retrieval testing on an NOR task (234). Similarly, in rats and humans the experimental reactivation of conditioned fear memory enhanced the memory when reactivations were induced during SWS but weakened fear memory strength when induced during wakefulness (235, 236). To reconcile these seemingly discrepant findings it has been proposed that wake reactivations support consolidation only if it occurs in the same spatiotemporal context and in close proximity to the encoding phase, whereas later awake reactivations in a different context may rather cause retroactive interference (108). Beyond this, these studies show that memory consolidation, in certain conditions, occurs also during wakefulness, albeit through mechanisms different from those during sleep (108, 212, 234, 237–239).

The general superiority of offline reactivations occurring during sleep over wake reactivations in promoting long-term memory formation (108, 209, 240) may also be owing to the fact that during sleep reactivations in terms of ripple-associated replay of hippocampal ensemble firing patterns are most consistently observed during SWS (79, 183, 241) and thus in a neuromodulatory milieu very different from that during wakefulness (see BOX 2 and sect. 7.3.2). In particular, the high levels of acetylcholine present during wakefulness (and also REM sleep) suppress hippocampal output from CA1 neurons to extrahippocampal brain regions (242, 243). Accordingly, whereas during wakefulness the information flow is predominantly from the neocortex to the hippocampus, facilitating the encoding of novel experiences, during SWS the information flow is in the opposite direction, from the hippocampus to the neocortex and other extrahippocampal networks (like the amygdala and striatum), facilitating consolidation processes (243–246). Supporting this view, combining resting-state functional magnetic resonance imaging (fMRI) with electrocorticography, a study in humans revealed that higher (0.5–4 Hz)- and lower (<0.1 Hz)-frequency oscillatory activity propagate in opposite directions between cortex and hippocampus, with these directions being reversed during SWS compared to wakefulness (247).

3.1.1.2. REACTIVATIONS OUTSIDE THE HIPPOCAMPUS. Although reactivations in the form of a replay of neuronal firing patterns have been closely associated with ripples in the hippocampus, simultaneous recordings from multiple brain regions revealed signs of neuronal reactivations also in extrahippocampal cortical and subcortical regions, which occurred in parallel with or independently of hippocampal replay. These areas include the PFC (248–250), parietal cortex (251), motor cortex (252–254), occipital/visual cortex (118, 255, 256), entorhinal cortex (257, 258), striatum (259, 260), amygdala (244), and the ventral tegmental area (VTA) (261, 262). Reactivations in the striatum and neocortex occurred with a temporal delay of ~40–50 ms after reactivations in the hippocampus (118, 259, 260, 263), suggesting that reactivations of firing patterns preferentially originate in hippocampal networks and then propagate to extrahippocampal networks, thereby strengthening the connectivity within these extrahippocampal ensembles. Ripples have also been detected outside the hippocampus, e.g., in the neocortex, where they occurred predominantly during non-REM sleep and temporally fine-tuned with hippocampal ripples (264–268). Within the neocortex, reactivations of neuronal firing patterns and associated ripples can occur in synchrony across multiple neocortical areas, indicating a high level of coordination and communication during the consolidation process at the neocortical level (269).

3.1.2. Spindles.

Spindles play a key role in regulating the dialogue between the hippocampus and neocortex and in the hippocampal-to-neocortical transfer of reactivated memory information during non-REM sleep (79, 80, 130, 270–277), as hippocampal ripples and memory replay tend to nest in the excitable troughs of spindles, forming “spindle-ripple” events, whereas in the neocortex spindles tend to nest in the excitable up-state of SOs, forming “SO-spindle” events (BOX 2). Spindles are generated in a recurrent GABAergic inhibitory network mainly comprising the thalamic reticular nucleus (TRN) and thalamo-cortical projections (79). They reach the entire neocortex via widespread thalamo-cortical connections as well as hippocampal networks via the thalamic nucleus reuniens or the entorhinal cortex (278–280). Within the hippocampal CA1 region spindles organize the spatiotemporal occurrence of ripples (278). Indeed, the synchronization of activity in different cortical and subcortical networks seems to be critical for the enhancing effect of spindles on memory consolidation. For example, combined EEG and fMRI in humans revealed a spindle-related enhancement of motor memories that was associated with increased synchronization of spindle activity (11–17 Hz) in a hippocampo-striato-thalamo-cortical network known to be implicated in motor memory consolidation (281).

Within the thalamus, spindles are accompanied by a suppression of sensory inputs to the cortex through the inhibition of relay nuclei, creating a temporal window where thalamo-cortical networks become unresponsive to external signals (282–284), with auditory processing possibly representing an exception to this gating effect (285). Simultaneously, the information flow originating from hippocampal reactivations shifts toward preferential thalamo-cortical gating. There is evidence that the same GABAergic TRN neurons gate information flow toward the neocortex activity during selective attention in wakefulness and during sleep spindles (282, 286–

290). This mechanism presumably involves prefrontal control over GABAergic TRN neurons gating the information flow via feedforward inhibition of thalamo-cortical projection neurons (282, 286, 287). For instance, sensory-projecting TRN neurons with axon terminals primarily reaching sensory thalamic nuclei synchronize their firing activity not only to alpha rhythms during attentive wakefulness but also to spindle oscillations during sleep (282). In contrast, activity of limbic-projecting TRN neurons, which exert inhibitory control over anterior thalamic nuclei (ATNs) and are assumed to mediate interactions between the hippocampus and PFC, is not modulated by sleep spindles or attention. However, their activity is strongly suppressed during SWS (282), presumably facilitating interactions between the structures in a nonspecific manner. Accordingly, spindle power in this study was positively correlated with the firing rates of sensory-projecting TRN neurons and negatively correlated with those of limbic-projecting TRN neurons.

Thalamic spindle generation is additionally controlled by noradrenergic activity of the brain stem locus coeruleus (LC). LC neurons fall silent shortly before the onset of a spindle and only fire during the spindle waning phase (291), supposedly leading to the suppression of spindle generation through the depolarizing action of NE on thalamo-cortical neurons (292). In fact, optogenetically stimulating LC neurons in rats resulted in a significant decrease in sleep spindle occurrence, and this was associated with impaired consolidation of spatial food-location memories (293).

3.1.2.1. SPINDLES IN CORTICAL NETWORKS. Although present in the entire neocortex, fast spindles show a dominance over posterior cortical areas. Microarray recordings in epileptic patients revealed two different sources of spindles, generated by pyramidal cells in supragranular layers and in deeper, infragranular, layers, possibly involving matrix and core thalamo-cortical afferents, respectively (294, 295). Cortical spindles are local phenomena inasmuch as they are increased over those areas that were engaged in prior learning (e.g., Refs. 296, 297) or areas that were previously stimulated, e.g., with transcranial direct current stimulation (tDCS; Ref. 298). Correlations between parameters of spindle activity and memory retention are typically highest for the areas that are most strongly involved during learning (297, 299–307). For instance, after visual perceptual task learning, participants showed increased spindle power during non-REM sleep stage S2 over trained versus untrained primary visual cortex (V1) areas, which was positively correlated with performance gains in the trained task (303, 305). Furthermore, the EEG spindle amplitude during sleep after encoding of spatiotemporal information was maximally correlated with subsequent retrieval performance at temporo-parietal sites (307). For more complex tasks multiple cortical sites may be involved, as it has been shown that cortical gamma-band EEG power, as an indicator of memory processing in local networks, was found to be locked to the phase of EEG spindles at different cortical sites (308). The findings overall corroborate the view that topographically restricted increases in spindle activity over cortical areas reflect the reprocessing of specific memory representations, with the spindles serving to synchronize memory processing in distributed cortical networks (296).

The effects of spindles on cortical mechanisms of neuronal plasticity have been mainly studied in animal models. In anesthetized cats, stimulation with a spindle-associated pattern of spike trains induced *N*-methyl-D-aspartate (NMDA) receptor-dependent short-term potentiation (STP) and a calcium channel-dependent long-term potentiation (LTP) in cortical neurons (309). Two-photon calcium imaging of cortical (layer 2/3) pyramidal neurons in naturally sleeping mice revealed increases in calcium activity in the apical dendrites of these cells during sleep spindles (310). Simultaneously, spindles are accompanied by an increased activity of parvalbumin-positive interneurons (basket cells) that, by inhibiting the soma of the pyramidal cells, are expected to produce an effective suppression of axonal firing output from these cells (284, 311, 312). Different from the overall populations of cortical pyramidal cells, pyramidal cells with increased calcium activity during spindles upregulate their activity across SWS periods (313). These studies suggest that cortical spindles are associated with an ongoing memory processing in specific cortical neuronal ensembles, in conditions that favor synaptic plasticity, in the apical dendrites of the contributing pyramidal cells.

Consistent with this view, in healthy humans pharmacologically increasing sleep spindle density by administration of the $GABA_A$ receptor agonist zolpidem enhanced sleep-dependent consolidation of emotional memory (Ref. 314; sect. 4.3). Also, increases in fast spindle activity after application of a TMR procedure were predictive of subsequent recall of the targeted stimulus category (315).

3.1.3. Slow oscillations.

Slow oscillations (SOs) are generated in cortical networks and primarily originate from prefrontal brain regions, traveling over the scalp in an antero-posterior direction, but they can also emerge as local phenomena over more restricted cortical areas. SOs are also observed in multiple subcortical structures including the thalamus and hippocampus (316–324) and may likewise arise from ascending arousal systems (106, 325). They are characterized by alternations between "down-states" and "up-states" that originate from the synchronized widespread

hyperpolarization and depolarization of the contributing pyramidal cell networks, respectively (76–78). SOs are thought to play a central role in driving systems consolidation processes and underlying plasticity during sleep (79, 326). The SO up-state following the negative SO down-state peak appears to be particularly important, as it signifies a period of enhanced large-scale communication within the cortex (174) as well as between cortex and multiple subcortical regions. Memory reactivations predominantly occur during the SO up-state, as reflected by the tendency of spindles as well as hippocampal ripples to nest into this depolarizing state (125, 128, 130). In humans, upon presentation of a memory cue (in a TMR procedure) memory-related reactivation patterns were observed to spontaneously reemerge at a rate of ~1 Hz, suggesting a temporal coordination of reactivations by succeeding SOs (327). Also, hippocampo-prefrontal synchronization in the gamma frequency band is enhanced during the SO up-state, pointing to an enhanced communication between these regions during this period (328). Experimentally increasing SO activity during postencoding SWS, e.g., by noninvasive brain stimulation (sect. 7.1), enhanced memory performance in human participants (e.g., Refs. 329–331), proving a causal role of SO in memory consolidation. Research on SOs in the medial prefrontal cortex (mPFC) of rats additionally points to the existence of two subtypes of SO up-states, i.e., with shorter and longer durations being associated with reactivations of recent and remote memories, respectively (332).

3.1.3.1. SOs VS. DELTA WAVES. Whereas <1-Hz SOs have been rather consistently found to support sleep-dependent memory consolidation, neocortical delta waves covering the neighboring 1–4 Hz frequency band may have even opposite effects, i.e., weakening rather than strengthening newly encoded memories (see also sect. 4.4). Kim et al. (333) trained rats to control firing of neurons in the motor cortex. When reactivations of the target cells were optogenetically disturbed during SO up-states, task performance decreased at a test after sleep. By contrast, task performance was improved at the test when cell reactivations were disturbed during delta waves. Possibly, this differential effect was partly mediated by changes in the temporal coupling of spindles, as the optogenetic disruptions during delta waves produced a relative increase in spindles nesting into SO up-states. Contrasting with these findings, others found delta waves in mPFC of rats to be associated with improved consolidation of spatial location memories (334). The seemingly diverging results can be partly explained by the definition of delta waves in this study, basically considering these waves as equivalent to the down-state of SOs.

Indeed, the confusing picture as to a differential role of SOs and delta waves in memory processing appears to be linked to problems in accurately defining and separating the two kinds of oscillations. For discriminating SOs from delta waves in the original work in cats, Steriade et al. (335) combined local field potential recordings with recordings of single cells. The slower SOs differed from delta waves mainly in their much more pronounced down-state with almost complete ceasing of firing of thalamo-cortical neurons. Delta waves, on the other hand, could occur during the depolarizing up-state of an SO in these recordings. But, unlike SOs, they did not seem to systematically nest spindles. Recordings of cortical multiunit activity likewise suggest that only the down-states of the slower SOs are associated with a robust decrease in firing activity (e.g., Refs. 270, 336–338). However, contrasting this view of separable events, delta waves have also been considered to represent the down-state of SOs or as oscillation with the same down- and up-states and the same tendency to nest spindles in their up-state as SOs, only quantitatively differing in amplitude and frequency (339).

Despite these basic difficulties in discriminating SOs and delta waves, there have been continuing efforts to distinguish their functions in memory processing in humans. Relying on surface EEG recordings, the distinction between the two oscillatory activities based on frequency and amplitude criteria inevitably remained somewhat noisy (340). Nevertheless, these studies of the surface EEG in humans, too, have provided first clues that delta waves may weaken memories and downregulate cortical synaptic connections. Thus, different from more widespread and larger slow waves with a steeper slope (termed Type I waves in this study), more local deltalike slow waves with a lower amplitude (Type II waves) displayed a clear homeostatic regulation across sleep, gradually decreasing in amplitude and in their slopes toward the end of the nocturnal sleep period (105, 106). This homeostatic regulation pattern suggests that these deltalike Type II waves are specifically involved in processes of global synaptic downregulation during sleep. Deltalike waves may also more closely mimic the conditions of slow waves observed during urethane anesthesia in mice, which likewise weakened synaptic connections (341).

3.1.3.2. SO-SPINDLE EVENTS. The depolarizing up-state of the neocortical SO promotes the generation of thalamic spindles, leading to the formation of SO-spindle events (Refs. 76, 79, 80, 130, 284, 342–345; BOX 2). This process begins with the SO down-state hyperpolarizing spindle-generating networks of the TRN followed by a depolarizing phase triggering the recruitment of spindles in thalamo-cortical projections (76, 346). Although this scenario suggests a cortical origin of SO-spindle events, intrathalamic recordings from epilepsy patients indicate that ATN may also initiate these events,

with SO down-states and subsequent spindles recorded in ATN preceding those recorded over frontal cortex by 50–100 ms (347). The anterior thalamus likely plays a key role in coordinating hippocampal memory replay with thalamo-cortical activity (125, 130, 348).

Although SOs exert a top-down control over spindle generation, this influence appears to be nonspecific, facilitating spindle emergence across various cortical locations rather than determining which specific local network produces spindles (320, 342). The impact of SOs on ripples and reactivations seems likewise to be only of permissive nature, with the SO up-state-associated increase in hippocampal ripple activity being primarily controlled by thalamic spindles (127, 128).

There is a growing body of evidence that links sleep-dependent memory consolidation to the occurrence of SO-spindle events (79). In rats, SO events during motor memory reactivations in the motor cortex, coupled with bursts of spindle activity, were positively correlated with improved motor skills (349). In humans, visuomotor learning enhanced SO-spindle coupling during subsequent SWS (350), and less precise coupling of SO-spindle events, as seen, e.g., in older people or children, was associated with poorer memory retention (Refs. 351–353; sect. 5). Intracranial recordings in human PFC, indeed, suggest that rather than the mere co-occurrence of SO up-state and spindle events, it is the temporally precise phase-locking of the spindle event into the SO up-state peak that is of central importance for hippocampal-neocortical information transfer during sleep (Ref. 354; see Refs. 128, 355 for similar results in rodents), and this coupling appears to also enhance large-scale brain communication in general (Ref. 174; see also Refs. 356, 357). The precise phase-amplitude coupling between fast (12–15 Hz) spindles and SOs was confirmed as a factor most closely linked to consolidation of both hippocampus-dependent and -independent forms of memory in a recent meta-analysis of human studies (358). Associations involving slow spindles (9–12 Hz), typically emerging at the up-to-down-state transition of SOs, were much more variable, underlining that slow spindles serve distinct functions in memory processing.

Studies experimentally manipulating SOs and spindles likewise suggest a critical role of coupled SO-spindle events for memory consolidation. Techniques like tDCS and auditory closed-loop stimulation (CLAS) that aim to enhance SOs typically produce an increase in spindle activity that is phase-locked to the up-states of the stimulated SOs, and this increase in coupled SO-spindle activity is connected to an enhanced memory consolidation, e.g., for word pairs (Refs. 330, 359; sect. 7.1.2). In mice, thalamic spindles improved context-conditioned fear memories as well as spatial object-location memories only when they were optogenetically induced during SO up-states (360). Spindles induced in the absence of SO up-states did not affect memory consolidation, although these spindles grouped hippocampal ripple events to the spindle troughs in the same way as spindles induced during the SO up-state. A possible explanation comes from two-photon imaging of neocortical microcircuits in mice, which revealed that SO-spindle events are associated with a pronounced increase in calcium activity of cortical pyramidal cells in comparison with spindles or SOs that occurred in isolation (311, 312). The strong increase in pyramidal cell activity concurred with a strong perisomatic inhibition but a release of dendritic inhibition of the cells, i.e., conditions known to be favorable for dendritic synaptic plasticity within local cortical circuits (e.g., Ref. 361).

3.1.3.3. SO-SPINDLE-RIPPLE EVENTS AND COUPLING STRENGTH BETWEEN OSCILLATORY EVENTS. Given that spindles nest hippocampal ripples and SOs nest spindles, there is also evidence for the occurrence of triple-nested SO-spindle-ripple events (125, 128, 130, 360, 362). The significance of such triple-coupling of oscillatory events has been demonstrated in these studies with spectral power-based estimates of spindle and ripple activity during SO events as well as event-based analyses (128). Coupling between events occurs only intermittently, i.e., SO, spindle, and ripple events each may occur also in isolation. Absolute values of coupling strength between the events cannot be provided because such values strongly depend on the exact criteria used for defining the respective event (and the resulting event density, i.e., events/min). Nevertheless, rough estimates can be obtained from such analyses. During SWS, where SO density is much higher than spindle density, ~7–15% of cortical SOs coincide with a spindle and, conversely, ~50–80% of the spindles co-occur with a SO event (128, 277). During human sleep stage N2, where SOs occur less frequently and couple with spindles in form of visible K-complexes, the rate of SOs nesting a spindle appears to be similarly high as during full-blown SWS (362). The percentage of SOs and spindles, respectively, co-occurring with hippocampal ripples during SWS has been specified with ~70% and 10% (128). Triple nesting of SOs, spindles, and ripples in event-based analyses is rare (<5% of cortical SOs are linked to both spindle and ripples). But, in light of the local nature of ripple events, this likely reflects an underestimation, as the respective analyses accounted for ripples at only a single hippocampal recording location (128).

3.1.3.4. A HIPPOCAMPAL-NEOCORTICAL LOOP. Although the majority of findings in humans and animals indicate a more or less specific top-down influence, such that neocortical SO up-states drive the occurrence of thalamic spindles that, in turn, prime the occurrence of ripples and memory reactivations in hippocampal networks, there is also evidence for the converse bottom-up influence of ripples and spindles on the emergence of SOs. Thus,

hippocampal ripples might promote the emergence of SOs by triggering the SO down-to-up-state transition (128, 363). Other findings suggest that hippocampal ripples can directly prime the occurrence of cortical SO down-states by activating inhibitory cortical networks, especially in PFC (128, 364–366). Electrical stimulation of cortical networks in rats, time-locked to the occurrence of hippocampal sharp-wave ripples, induced SOs followed by spindles and in turn improved object-location memories encoded before sleep (365).

Spindles might also trigger SOs (360, 367). In human studies, especially slow spindles were suspected to contribute to the emergence of SOs, as they systematically occur during the up-to-down transition of SOs (74, 368). However, the experimental findings remained overall inconclusive. Although in specific optogenetic stimulation conditions spindles may contribute to SO generation, this rarely happens in natural conditions (128). Thus, SOs drive spindles but not the other way around, a view that also aligns with evidence that spindle-generating networks go into refractoriness distinctly faster than SO-generating networks (369, 370).

Overall, these findings are in line with the notion of a hippocampal-neocortical loop where cortical SOs provide a globally acting top-down signal, with the hyperpolarizing down-state setting the temporal frame for thalamic spindles and hippocampal ripples during the subsequent depolarizing SO up-state. Spindles reaching hippocampal networks synchronize ripples to the excitable troughs of the spindle. Hippocampal ripples, in turn, facilitate the occurrence of SO-spindle events in thalamo-cortical networks, promoting the transfer of reactivated hippocampal information to neocortical networks (108, 129). This looplike process may also extend to the content of the information that is reactivated, as activity in cortical regions predicts the content of hippocampal reactivations (371) and hippocampal reactivations, in turn, predict reactivations in cortical regions (260, 371, 372). Novel experience appears to activate this hippocampal-neocortical loop. In rats trained on a motor skill, hippocampal ripples only initially coupled with SOs (detected in the 0.1–4 Hz range) in the primary motor cortex during post-training SWS, but this coupling sharply decreased once motor performance stabilized (373). In humans, memory reactivations after motor sequence learning were time-locked to SO-spindle complexes only in the hemisphere that was actively involved in learning the task (374).

3.1.4. Infraslow rhythm and breathing.

In addition to ripples, spindles, and SOs, infraslow rhythms of activity can be identified during non-REM sleep, which may further contribute to effective memory consolidation (375, 376). In mice and humans, spindle rates oscillate in a coordinated infraslow rhythm at a frequency of ~0.02 Hz, dividing non-REM sleep epochs into 20- to 25-s epochs of enhanced alertness to external stimuli and epochs of internal memory processing (376). The rhythm also captures hippocampal ripple activity, spindle activity, and heart rate and likely reflects a rhythmic modulation of noradrenergic LC activity (377, 378). In humans, the strength of this infraslow oscillation in fast spindle activity predicted postsleep memory recall in an episodic "what-where-when" task (376) and less temporal clustering of spindles was associated with impaired declarative memory consolidation in Parkinson patients, possibly due to disrupted noradrenergic modulation during sleep (379, 380). Also in humans, peaks in the infraslow fluctuations of heart rate were regularly preceded (by ~5 s) by increases in SO, delta, and spindle activity, and the more such infraslow heart rate peaks occurred during non-REM sleep, the better was the participant's recall of previously encoded memories for words and images (381). A study in mice (382) demonstrated a link between the infraslow oscillations in pupil diameter during non-REM sleep (known to be coupled to fluctuation of acetylcholine and noradrenaline; Ref. 383) and the hippocampal replay of recently versus previously acquired memories. Specifically, optogenetic inhibition of hippocampal SW-Rs impaired consolidation of recent memory when applied during phases of pupil contraction. In contrast, pupil dilation during non-REM sleep was associated with replay of older memories, suggesting that non-REM sleep microstructure may organize memory replay to minimize interference between recent and remote memories. Taken together, the few studies of infraslow rhythms so far point to contributions of brain stem mechanisms, like LC noradrenergic activity, that synchronize autonomous nervous system activity with brain oscillatory activity during non-REM sleep, and thereby enhance memory consolidation.

Brain oscillations during sleep also interact with breathing-related activity as another kind of infraslow rhythm. Specifically, breathing during sleep modulates the emergence of SOs in humans (384) as well as the coupling of hippocampal sharp-wave ripples and cortical SO down-to-up-state transitions in mice (385), with a systematic increase in SOs, spindles, and SO-spindle events toward inhalation peaks (384). The strength of this coupling between respiration and SO-spindle events was positively correlated with the extent of memory reactivations. Although this coupling was not significantly correlated with behavioral measures of memory recall, the findings identify breathing as a potential additional modulator of the efficacy of memory consolidation during sleep.

3.2. REM Sleep

Traditionally, REM sleep has been thought of as the central sleep stage for the cognitive reprocessing of wake experiences and memory consolidation because of its relation to reports of vivid dreaming and the wakelike

EEG activity characterizing this sleep stage (386). Initial experimental evidence indicating an involvement of REM sleep in memory consolidation was mainly based on effects observed after the selective deprivation of this sleep stage, and these findings were often questioned because selective REM sleep deprivation is known to induce confounding stress effects (387, 388). Over the last decade, relatively few studies have focused on the potential role of REM sleep in memory consolidation compared to the extensive research on non-REM sleep. The findings on REM sleep altogether provide a rather mixed picture, suggesting that some specific physiological features of this sleep stage, in particular theta activity, may support specific aspects of memory consolidation (Refs. 389, 390; BOX 2).

3.2.1. Theta activity.

Theta activity, i.e., synchronized oscillations in the 4–8 Hz frequency band, is the most prominent feature of REM sleep in rodents. In human REM sleep, theta is less prominent and typically occurs in transient bursts. Intracranial recordings in epileptic patients suggest that the continuous hippocampal theta rhythm seen in rodents may correspond more closely to the slower delta frequency activity observed more continuously during REM sleep in these patients (391). Theta activity is also increased in specific wake states. In rodents, it is prominent during active spatial exploration and in humans over prefrontal cortical areas during focusing of attention and the encoding of new information (392–396). In rodents, the main source of theta activity during REM sleep, as well as during wakefulness, is the septal-hippocampal system (397–402). However, the theta rhythm can capture a wide network including subcortical structures such as the VTA and the amygdala, as well as the neocortex (403–406). Differences between features of hippocampal theta activity during REM sleep and wakefulness appear to be marginal, with REM sleep theta showing a slightly lower frequency (407). Theta activity in the hippocampus can increase synaptic LTP when cells fire during the up-state of the theta cycle, whereas firing during the down-state favors synaptic long-term depression (LTD) (408–410). Accordingly, it has been proposed that local hippocampal theta activity during REM sleep supports synaptic consolidation in reactivated neuron ensembles, specifically when the reactivation is locked to a theta up-state (28, 148, 408, 411–415). Conversely, there is also evidence supporting the view that theta activity during REM sleep mainly serves to downscale synapses that were potentiated during prior wakefulness and are irrelevant to long-term memory formation (148, 168, 416).

An enhancing effect of REM sleep theta activity on memory consolidation is also suggested by findings in rats indicating an increased nesting of gamma-band activity and high-frequency oscillations (up to 160 Hz) in theta peaks in the hippocampus and neocortex during REM sleep (417). During wakefulness, increased gamma-theta phase-amplitude coupling is typically associated with enhanced accuracy of task performance (418). Silencing GABAergic septo-hippocampal projections during REM sleep impeded theta-phase coherence and theta-gamma coupling (419) as well as memory consolidation during sleep (420). Theta coupling between the hippocampus and retrosplenial cortex in REM sleep has been likewise found to be critical to the consolidation of context fear conditioning memory, based on analyses of Granger causalities in rats (421).

In regard to memory content, it has been proposed that theta activity particularly facilitates the processing of emotional memory (87). After fear conditioning in rats, REM sleep theta activity was increased in the hippocampus, amygdala, and cortical circuits of adult rats that had been stressed (by maternal separation) during infancy (422). Conversely, a reduction in theta power during the transition into REM sleep was linked to impaired fear-associated memory processing in a rodent model of posttraumatic stress disorder (PTSD) (423), and similar changes were found in a rat model of insomnia (424). Also in rats, a direct link was revealed between REM sleep theta and consolidation of cued fear conditioning memories (425). In this study, theta oscillations in the ventral hippocampus, lateral amygdala, and medial PFC strongly synchronized during REM sleep following fear conditioning. Importantly, fear memory recall was most closely related to a specific phase difference in theta oscillations between the lateral amygdala and ventral hippocampus, marking the fine-tuning between these structures. Optogenetically inducing hippocampal theta rescued deficits of fear memory consolidation caused by sleep deprivation in mice (426), and, conversely, optogenetically suppressing hippocampal theta during REM sleep impaired the consolidation of contextual fear memories as well as NOR memories (420). Altogether, these findings highlight the causal role of REM sleep theta in memory consolidation.

A link between REM sleep theta activity and (emotional) memory consolidation was likewise revealed in human studies. For instance, memory for discrete features of emotional events was found to be positively correlated with theta power over right frontal cortical regions during postencoding REM sleep (427), with this right lateralization of the effect fitting the commonly observed right lateralization of theta activity during encoding of emotional materials in the wake state (428–431). Stress may be a modulator of the impact of REM theta. For instance, REM sleep theta power predicted memory for positive emotional items, particularly in stressed participants with a

high cortisol response during learning (432). Another modulating factor might be the participant's dominant EEG alpha frequency, as correlations between theta power and emotional memory consolidation were found to be stronger in participants with a lower individual alpha frequency (433). Traitlike dominant alpha frequency (in the 8–12 Hz range) is known to affect a variety of memory and attentional processes during wakefulness (434) and is thus an interesting candidate mechanism in the interaction with theta-based consolidation during REM sleep. Positive associations between enhanced REM sleep theta activity and memories for emotional and traumatic experience have also been observed in patients suffering from PTSD and autism spectrum disorder (431, 435, 436). The extent of this benefit was correlated with theta power in frontal and central regions during REM sleep. Overall, the findings point to a supporting influence of REM sleep theta activity on emotional memory consolidation in humans. However, Durrant et al. (437) also observed that theta power during REM sleep is linked to the consolidation of newly encoded memories that fit into preexisting knowledge (i.e., "schema-conformant" memories), suggesting a role for theta activity beyond emotional memory processing that warrants further investigation.

3.2.2. Ponto-geniculo-occipital waves.

Ponto-geniculo-occipital (PGO) waves refer to short, intense bursts (3–5 Hz, 300–500 ms) of synchronized activity that originate in the pontine brain stem and propagate to the lateral geniculate nucleus and occipital cortex (BOX 2). Their emergence is closely linked to the theta-generating mechanisms during REM sleep. In rats, PGO bursts in the pons and theta waves in the hippocampus are correlated (438), and spontaneous as well as tone-elicited PGO waves were found to occur phase-locked to hippocampal theta peaks during REM sleep (439). The emergence of PGO waves may be driven by periods of increased coherence in theta activity in hippocampal-amygdalar circuitry (440). In humans, the presence of PGO waves is questionable (441–443); however, PGO-like waves have been observed to precede the onset of phasic REMs, and the pattern of these waves predicted the direction of the subsequent phasic REM (444). Phasic REMs are associated with a diminished processing of meaningful (verbal) stimuli presented during sleep (445). Multistructural recordings in macaque monkeys revealed PGO-like waves coupled to hippocampal theta as well as ripples, with both types possibly favoring memory reactivations, especially when preceding phasic REMs (446).

Overall, these findings suggest a role of PGOs in memory processing (447, 448). Early work in rats from the Datta laboratory (449) indeed showed a significant increase in PGO wave density in the first episodes of REM sleep after conditioned avoidance learning (vs. no-learning). Activating the phasic pontine wave generator cells by carbachol microinjection improved avoidance memory performance (450) and prevented memory-impairing effects of postlearning REM sleep deprivation (451). Vice versa, neurotoxic lesions of the phasic pontine wave generator cells impaired memory retention (452). Also, PGO wave activity during REM sleep was found to be linked to fear extinction memory in these studies (389), with this effect critically involving the dorsal nucleus subcoeruleus, i.e., a brain stem region comprising PGO wave-generating cells (453). Further studies pointed to contributions of the pontine oculomotor nucleus (454) as well as hippocampal CA3 in mediating the memory effects of PGO waves during REM sleep (455, 456). Evidence from human studies is rare, but a case study in a patient with lesions to pontine brain stem areas (critical to PGO wave generation in rodents) did not reveal any memory impairments, although normal signs of REM sleep were almost completely missing in the patient (388). Although the research on animals so far indicates a distinct contribution of PGO waves to REM sleep-associated memory processing, it is presently unclear to what extent these contributions overlap with functions of REM sleep theta activity and how they translate to humans.

3.2.3. Neuronal ensemble reactivations.

Neuronal replay of memory has been mainly observed during SWS, with little evidence for its occurrence during REM sleep. Although some rodent studies revealed indirect signs of memory reactivations in LFP recordings during REM sleep (182, 408, 413, 446, 457), and despite computational models suggesting its possibility (458), most studies failed to provide evidence of ensemble firing pattern replay occurring during REM sleep (e.g., Refs. 459, 460). Only recently, in a study of motor skill learning in rats, it was demonstrated that reactivations of ensemble sequential firing can occur during postencoding REM sleep (Ref. 461; **FIGURE 6**). In this study, rats were trained daily on a skilled single-pellet reaching task while firing activity of neurons in the motor cortex was recorded during training sessions and interleaving rest periods. Reactivations of sequential firing patterns occurred during both epochs of SWS as well as in REM sleep following the training. In rats that acquired the skill rapidly, SWS and REM sleep reactivations were observed on the same day between training sessions, with REM sleep replay occurring more often before the next training session and SWS replay occurring more often after the last training session. Both REM sleep and SWS reactivations appeared to be coordinated with

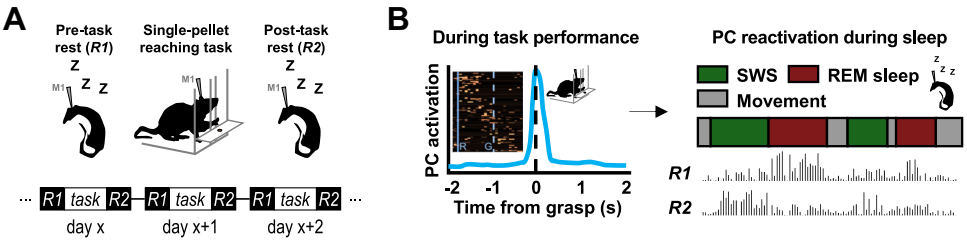

FIGURE 6. Reactivations of ensemble firing during REM sleep. *A*: single units were recorded from the forelimb region of the primary motor cortex (M1) while the rats were trained daily on the single-pellet reaching task, as well as during 3-h pre- and posttask rest periods (*R1* and *R2*). *B*: based on sequential firing patterns during task performance, principal components (PCs) were calculated for each rat. These PCs showed strong activation during reach behavior (*left*) and were reactivated during sleep (illustrative example time course of PC activation during *R1* and *R2*, *right*). Reactivation strength was highest during *R1* REM sleep and *R2* SWS. See GLOSSARY for abbreviations. Figure based on Eckert et al. (Ref. 461). Copyright 1990 by The Royal Society (U.K.). Reprinted with permission.

muscle activity during sleep, suggesting a functional role for the reactivation in learning the motor skill. Indeed, the focus on motor skill learning and firing activity in motor cortex may explain why this study succeeded in identifying replaylike neuronal activity in REM sleep, in contrast to many other studies focusing on hippocampal ensemble firing, where fast synaptic rearrangements after a learning period may prevent the detection of ensemble reactivation occurring at a later time during REM sleep.

Signs of memory reactivations occurring spontaneously during REM sleep have also been identified in a few studies in humans (198, 462). Using positron emission tomography (PET) during training of participants on a serial reaction time task (SRTT) and during subsequent sleep, an early study revealed an increased reactivations of several brain areas (bilateral cuneus, left premotor cortex, thalamus, and mesencephalon) during REM sleep after training (462). A more recent study, using multivariate pattern classification for decoding of high-density EEG signals during sleep after learning pictures (faces vs. houses), revealed distinct activity patterns (across participants) during both non-REM and REM sleep that discriminated the two picture categories (198). The frequencies relevant for the reactivated patterns differed between non-REM and REM sleep, and only reprocessing strength during SWS but not during REM sleep was correlated with later memory performance. Additional evidence for memory reactivations during REM sleep comes from a number of human EEG studies using TMR to experimentally induce such reactivations by presenting reminder cues during REM sleep, which, furthermore, indicates that experimentally induced reactivations can benefit the consolidation of the memory (Refs. 463–467; sect. 7.2). Overall, the picture arising from this research indicates that reactivations, even in the form of a sequential replay of firing patterns, also occur during REM sleep, more likely in cortical than in hippocampal networks. However, their functional relevance for consolidation processes needs to be further studied.

3.3. *Complementing Functions of SWS and REM Sleep*

The role of non-REM sleep and REM sleep in memory consolidation has been explored from two distinct conceptual perspectives. On one hand, the dual process hypothesis assumes that non-REM sleep and REM sleep serve different aspects in memory consolidation, which are largely independent from each other. On the other hand, the sequential hypothesis (468, 469) assumes that non-REM and REM sleep serve complementary functions, since in natural sleep non-REM and REM sleep epochs follow a fixed sequence, such that REM sleep is entered only after an epoch of non-REM has occurred.

3.3.1. The dual process hypothesis.

This concept arose mainly in the context of purely behavioral studies in humans that supported the view that non-REM sleep consolidates declarative memory (e.g., Refs. 21, 26, 470, 471) whereas REM sleep consolidates procedural skill memory (e.g., Refs. 21, 462, 472–474). Although there is an ever-growing number of studies supporting a crucial role of non-REM sleep in the consolidation of declarative memories, in light of more recent findings this hypothesis has to be abandoned.

First, although declarative memory, according to the dual process view, specifically profits from non-REM sleep (e.g., Ref. 475), some studies point to a role for REM sleep as well. REM sleep deprivation in healthy humans, for instance, impaired recall of spatial and temporal information in an episodic what-where-when task (476), and in another study (132) the time spent in REM sleep was positively correlated with high-confidence "remembering" of abstract visual shapes presented at different screen locations. Second, the assumed role of REM sleep specifically enhancing procedural memories has received little support (477). There is strong evidence that procedural skills can also benefit from non-REM sleep. Correlation analyses in human studies yielded mixed results, with both

REM (e.g., Refs. 478–480) and non-REM (e.g., Refs. 305, 481–485) sleep parameters being inconsistently associated with the formation of procedural skills. For instance, sleep-related gains in motor sequence skills and parallel increases in striatal activity were positively correlated with the duration of posttraining SWS (472) and spindle activity (303, 305, 482, 483). Additionally, the assumed beneficial role of REM sleep for procedural memory formation has been questioned by findings of unchanged motor skill memories after selective REM sleep deprivation (486). Pharmacological suppression of REM sleep even improved rather than impaired finger tapping skill memory (Ref. 487, see also Refs. 138, 488–490).

Beyond procedural memory, emotional and social memories have been proposed to specifically benefit from REM sleep (Refs. 491–495; sect. 4.3). Groch et al. (496), for instance, reported a differential contribution to memories for neutral and aversive pictures for SWS and REM sleep, with REM sleep particularly enhancing emotional item memory and SWS aiding (color) context memory for neutral items (see Refs. 427, 497 for similar results), consistent with the view that REM sleep integrates amygdala-dependent emotional processing into episodic memory processing within the hippocampal-mPFC loop (Ref. 498; for related results, see Refs. 499–501). Indeed, given that both declarative and procedural memory can be more or less emotional, the effect of REM sleep could be restricted to modulating the emotional tag of a memory, although there are also findings conflicting with this view (Ref. 493; see sect. 4.3 for a detailed discussion).

3.3.2. The sequential hypothesis.

This view is consistent with the great body of findings in healthy humans overall indicating that the retention of any kind of memory can be positively correlated with both non-REM and REM sleep parameters. However, it is unclear whether, as assumed by this hypothesis, the succession within a sleep cycle, with non-REM sleep preceding REM sleep, is critical for effective memory consolidation, which is difficult to test experimentally. Whereas in healthy humans REM sleep strictly follows non-REM sleep, patients with central hypersomnolence disorder (including patients with narcolepsy) frequently enter REM sleep right after sleep onset and before any non-REM sleep epochs occur. Investigating sleep-dependent memory consolidation in such patients, Strauss et al. (502) demonstrated that the succession of non-REM followed by REM sleep epochs is indeed important for the consolidation process. Comparing naps starting with REM sleep followed by non-REM sleep with non-REM-REM sleep naps in these patients revealed that non-REM sleep spindles contributed to the formation of visual perceptual memory only across non-REM-REM sleep naps and not in REM-non-REM sleep naps, indicating a supporting role of REM sleep in the consolidation process only when it occurs after non-REM sleep.

Against this backdrop, it has been proposed that REM sleep generally stabilizes representations across memory systems, as they are still in a labile state after memory transformation during prior SWS (28, 503). Thus, REM sleep following SWS may trigger local processes of synaptic consolidation, which strengthen the memory representations that already underwent transformation and systems consolidation during SWS, thereby entailing an optimal benefit on memory consolidation from the sequential occurrence of both SWS and REM sleep. Such sequential processing would likewise affect memories as different as motor skills and object representations. Additionally, the sequence of SWS-associated transformation and REM sleep-associated stabilization could differentially affect newly encoded representations depending on how well the encoded information fits into preexisting knowledge. Information fitting well with preexisting knowledge and schemalike representations may not require SWS-dependent transformation but could be quickly mapped into neocortical long-term storage sites, where they especially benefit from REM sleep-associated stabilizing effects (Refs. 504, 505; see also Refs. 506, 507). In this view, procedural skill learning could be considered a type of learning where schemalike representations are readily available and thus REM sleep is particularly beneficial. The iterative cycling between non-REM and REM sleep and associated memory reactivations has been proposed, in a similar manner, to boost the formation of complex knowledge frameworks and creative problem-solving (508).

3.3.2.1. UP- AND DOWNREGULATION OF NEURONAL ACTIVITY DURING SWS VS. REM SLEEP. A sequential view with SWS transforming memory and subsequent REM sleep stabilizing this memory also agrees with findings from studies focusing on neuronal activity underlying memory processing during sleep. Calcium imaging of cortical networks in naturally sleeping mice revealed that a subpopulation of pyramidal cells, opposite to a global decrease in activity, upregulates calcium activity during SWS epochs (313). This subpopulation was defined by the cells that showed highest activity during spindles and was thus most likely comprised of cells engaging in memory processing during sleep. Different from SWS, REM sleep epochs were associated with a general downregulation of pyramidal cell activity, which persisted into subsequent wake epochs and also included the subpopulation of spindle-active pyramidal cells. Comparable activity dynamics across SWS and REM sleep epochs were also observed in multiunit activity in hippocampal networks (148), where pyramidal cell firing rates generally increased during SWS epochs

in parallel with a decrease in the recruitment of spiking during ripples. The firing rate increase within SWS epochs was counteracted by a larger decrease of firing rates across triplets of SWS-REM-SWS epochs, with this decrease being stronger the higher theta power was during the interleaved REM sleep epoch. Moreover, the occurrence of spindles and ripples during SWS strongly predicted subsequent REM sleep-related decreases in hippocampal firing rates (149), altogether suggesting a sequential up- and downscaling of neural activity during SWS and REM sleep.

3.3.2.2. A COMPLEMENTARY ROLE OF SWS AND REM SLEEP IN SYNAPTIC CONSOLIDATION. Performing in vivo two-photon structural and functional calcium imaging of postsynaptic dendritic spines in primary motor cortex, a series of studies in mice provided direct evidence for sequentially complementing functions of SWS and REM sleep in synaptic consolidation processes underlying sleep-dependent memory formation (164, 167, 168). Sleep after training of mice on a rotarod motor learning task promoted the formation of spines on a subset of branches of individual layer 5 pyramidal neurons, with new spines being formed on different sets of dendritic branches in response to a different task version (164). The effect was mediated by SWS, inasmuch as the same neurons activated during training were reactivated during subsequent SWS, and disrupting this neuronal reactivation prevented branch-specific spine formation. Vice versa, REM sleep after motor task learning pruned newly formed dendritic spines in layer 5 pyramidal neurons (168), with this general pruning facilitating spine formation during subsequent learning of a new motor task. Importantly, in parallel with a general pruning of synapses, REM sleep also strengthened and maintained a subset of spines newly formed during prior motor training.

3.3.3. Conclusion.

Increasing evidence supports sleep's active role in memory formation, with ripples, spindles, delta waves, and SOs critical for systems consolidation during non-REM sleep and theta and PGO waves involved in (synaptic) memory consolidation during REM sleep. Research in the last decade points toward the involvement of both non-REM and REM sleep in the consolidation of both declarative and procedural memory, contradicting the long-held view that different types of memory are exclusively strengthened during specific sleep stages. Open questions are whether and how the succession of non-REM and REM sleep is a critical feature of the consolidation process and whether memory reactivations outside the hippocampus or during wakefulness fulfill functions similar to hippocampal reactivations during non-REM sleep.

4. THE BALANCE BETWEEN MEMORY ABSTRACTION AND FORGETTING

4.1. Capacity Limits in Memory Formation

Memories are not an exact copy of the past but change in quality during the process of consolidation, with much of the original information being forgotten over time (509, 510). This highly dynamic nature of memory is commonly considered a consequence of limited memory capacities of the brain (511). Memories may be forgotten simply to make space for the storage of new information. In addition to a finite storage capacity, these limitations may also stem from constraints in the processes of memory formation and retrieval. We rely on past memories to guide present behavior. In a memory system that stores every detail, relevant information may not be quickly accessible for current situations. It is hence generally assumed that

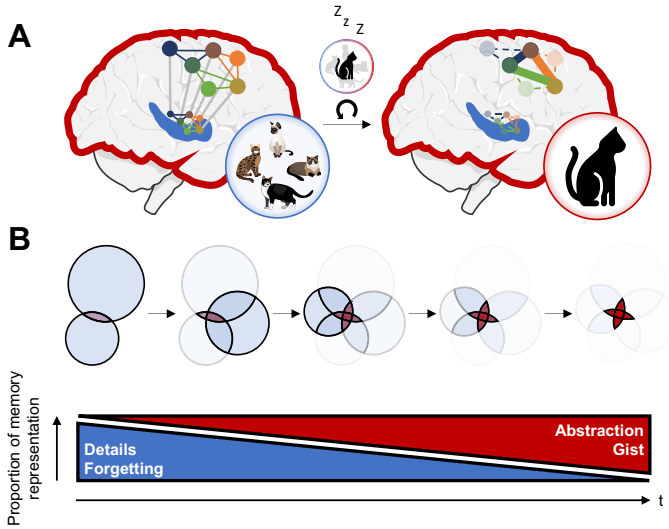

FIGURE 7. Memory abstraction and forgetting. During encoding, overlapping memories (differently colored networks, e.g., associated with individual cats in *A*; blue circles in *B*) are stored as individual representations that are rich in episodic details and strongly depend on hippocampal networks (*A*). The invariant overlapping information is most strongly represented, as this representation is repeatedly activated multiple times during encoding. In this way, individually encoded experiences (e.g., of different cats) accumulate to form an abstract schemalike "gist" representation that is retained in neocortical networks. This process is specifically enhanced during SWS through the repeated reactivations of the newly encoded representations originating from hippocampal networks and possibly also during REM sleep through as yet unknown mechanisms (emerging network between nodes of individual representations in *A*; red shaded area in *B*). At the same time, the encoded (irrelevant) details are slowly forgotten (dashed lines between nodes in *A*; fading blue shaded areas in *B*), rendering the initially detailed episodic memory a more and more schemalike gist representation (e.g., of a cat in *A*). Note that individual overlapping representations are usually encoded at different points in time (*B*), thus allowing for the new memory traces to be gradually integrated into existing memory networks and fostering an abstraction of invariant features in neocortical representations. See GLOSSARY for abbreviations.

to be effective, a memory system needs to form more abstracted representations that contain the most essential information across many experiences, i.e., representations that contain the gist of multiple experienced episodes (512, 513). Indeed, it has been proposed that such abstracted, schemalike representations containing the gist of multiple episodes are formed as part of the systems consolidation process taking place during sleep (28, 79, 134, 509). Against this backdrop, many studies (discussed in the following sections) have examined the role of sleep in forming abstracted representations containing any kind of gist of prior experiences, as well as in the forgetting of irrelevant information. Only a few studies, however, addressed the more fundamental question, i.e., to what extent sleep-dependent memory formation is limited by capacity constraints.

Two studies in humans suggest capacity limitations for the formation of declarative word memories during sleep (514, 515). In the first, young adults learned lists of either 40, 160, or 320 word pairs before nocturnal sleep or sleep deprivation, followed by retrieval testing 36 h later, after all subjects had a night of undisturbed sleep. Postlearning sleep enhanced retention for the 160-word pair condition, but this effect completely vanished for the 320-word pair condition, where recall after postencoding wakefulness appeared to be even slightly better than after sleep. The authors speculated that with increasing information loads during encoding sleep may favor forgetting over consolidation (see also sect. 4.4). In a second study (515), participants learned an increased number of 640 word pairs across an entire day, with interspersed breaks of quiet rest. As in the first study, participants had well encoded the word lists before the retention interval. At the test after the retention interval, recall performance was similar for the sleep and wake groups, and this negative outcome was confirmed with visual materials (object images) (516), contradicting the hypothesis that with high encoding load postencoding wakefulness, rather than sleep, would favor retention. Overall, these findings indicate a limited capacity for sleep-dependent memory consolidation. Given this, memory consolidation processes likely include mechanisms to selectively favor certain information over others, with the latter perhaps subjected to an active forgetting process.

4.2. Memory Abstraction during Sleep

That memories are transformed during consolidation, and in this process change in quality, is a basic tenet of current theories of memory systems consolidation, like the multiple trace theory (66, 69, 517, 518). These theories, in this regard, go essentially beyond harbinger concepts, all rooting in the standard consolidation theory assuming that consolidation acts on a "fixed" trace, with the quality and content of a memory not being changed even if transferred between different brain networks (519–522). Specifically, multiple trace theory assumes that the consolidation process transforms a detail-rich episodic representation that anchors in hippocampal networks into a more abstract schemalike representation that predominantly resides in extrahippocampal, mainly neocortical, networks and is more likely to be retained for the long term, whereas details of encoded information are more and more forgotten. Concepts like ASC (28, 79) (sect. 2.1) and "information overlap to abstract" (iOtA) (134) add to these theories by emphasizing the role of sleep for the transformation process, as originally proposed by David Marr (523) based on computational models of consolidation. The iOtA concept, for example, assumes that the abstraction of invariant features across different episodes results from the repeated reactivation of overlapping hippocampal representations during sleep, whereby the overlapping parts of representations are strengthened at the expense of nonoverlapping parts that are weakened and synaptically "downselected" (112, 113) (**FIGURE 7**; sect. 2.2).

The abstraction process during consolidation is generally thought to go along with a neocorticalization of the representations. And in accord with this assumption, studies in humans and rodents showed that when encoding of memories is followed by sleep long-term recall of the encoded materials is associated with enhanced activation of specific neocortical areas, like subareas of the PFC and (in humans) the precuneus, in comparison with wake control conditions (120, 122, 123, 276, 390, 524–530). For example, Samanta et al. (526) observed in human fMRI recordings at a delayed recall of spatial memories (virtual water maze) increased activity in multiple cortical areas including the medial and lateral frontal cortex as well as the visual cortex when encoding was followed by a nap versus daytime wakefulness. In complementary experiments on rats, expression of immediate early genes (*Arc*, *Fos*, and *Zif268*) indicated a likewise increased activity in prefrontal cortical as well as striatal areas at a delayed recall test in a real water maze when encoding was followed by sleep. In mice, neuronal activity as assessed by the expression of *Zif268* was found to be reduced in superficial layers of the anterior cingulate cortex (ACC) together with impaired recall performance at a retrieval test 30 days after REM sleep deprivation following contextual fear conditioning (529). By contrast, the hippocampus and basolateral amygdala showed increased gene expression at retrieval (for a review of effects of REM sleep on memory corticalization, see Ref. 390).

Building on the effect of sleep supporting the neocorticalization of long-term memory, numerous studies have sought to characterize how sleep facilitates memory abstraction. The studies typically address two questions: i.e., whether

sleep enhances the consolidation of abstracted memory representations and what kind of memory information is preferentially abstracted during sleep. "Gist" refers to the salient (core) information selected for consolidation. However, the term as used often leaves undefined what specific features of encoded experiences are abstracted during sleep (512, 531–533). Abstracted gist information can refer to "schema" memories, which represent invariant and repeating information about regularities and rules inherent to multiple experienced episodes. Importantly, gist abstraction can also pertain to emotional salient information in a single episode (sect. 4.3). Gist abstraction processes may differ depending on the stimulus domain (e.g., verbal, nonverbal) and modality, as well as the memory system. Human sleep studies have used diverse tasks to examine abstraction processes. In the following, we review these studies by classifying the employed task designs into tasks assessing gist as a semantic theme abstracted from presented items (sect. 4.2.1), tasks assessing transitive inference and memory for nonadjacent associations (sect. 4.2.2), tasks assessing the abstraction of categories and rules (sect. 4.2.3), and task paradigms used to study the contextual dependency of learned materials (sect. 4.2.4) (534). As virtually all of the studies of interest here relied on declarative types of tasks, we complete the section by discussing studies investigating memory abstraction in the nondeclarative procedural system (sect. 4.2.5) and studies of gist abstraction in rodent models (sect. 4.2.6).

4.2.1. Gist as a semantic theme: the Deese-Roediger-McDermott paradigm.

The Deese–Roediger–McDermott (DRM) paradigm has been the most commonly used task to investigate abstraction processes during sleep-dependent consolidation. In the verbal version of the task, participants learn several lists of semantically related words. For example, a list might include the words "bed," "rest," "awake," etc. Crucially, the word most strongly associated with all other words in the list, known as the "critical lure" (i.e., "sleep") is deliberately omitted during encoding. During recall, participants often falsely and confidently remember this critical lure alongside the actual words presented (535, 536). The critical lure thus represents the list's overarching theme, and its recall is referred to as "gist memory" or "false memory," in contrast to the "veridical memory" of the words actually presented.

Although early studies (175, 537) reported an increase in gist memories after sleep compared to wakefulness, later results were mixed (e.g., Refs. 538–540; see Ref. 541 for a meta-analysis). The overall outcome suggests that whether sleep enhances gist memories in the DRM task depends on several modulating factors such as the type of retrieval and the individual baseline performance level. When participants were asked to freely recall the learned word lists instead of merely recognizing them, gist memory was more dependent on sleep (176) (e.g., Refs. 537, 541). Moreover, gist memory in the DRM task seems to be more sleep dependent for participants who are generally less good at recalling (low performer) the learned lists (176, 537), as well as for more weakly (vs. strongly) encoded information and for gist memories that participants are very confident to recall (131, 542–546). This pattern is consistent with the view that sleep primarily acts to facilitate the accessibility of memories rather than strengthening underlying traces (547). Another modulating factor seems to be the semantic order in which the words were presented during encoding. For example, in one study, sleep increased gist memory only when the words were presented during learning in a descending order of semantic proximity to the critical lure, as typically done in the standard DRM task version (548). Also, shorter word lists (8–10 words) yielded greater sleep benefits than longer lists (12–15 words) (541, 549), and sleep had also a stronger effect on gist memory formation when words were presented to the left rather than the right visual field, indicating hemispheric differences (550). Age is also a modulator: Whereas sleep increased recognition of gist memories in young adults, sleep had a reducing effect in older adults (551) (sect. 5.2). Importantly, in addition to these modulating factors, several studies indicate that sleepiness and attentional deficits during memory retrieval, often a consequence of prior sleep deprivation, can confound the findings, with more sleepiness associated with higher gist memory recall (552–558).

The verbal version of the DRM task might also be confounded by mnemonic strategies participants use when explicitly memorizing verbal materials. This concern has stimulated the use of visual versions of the task, where instead of words sets of abstract shapes are presented. Similar to the verbal task version, evidence for a sleep effect on gist memories with the visual version is mixed. Noteworthy here, the effect in several studies appeared to be more pronounced with longer retention intervals, lasting up to 1 yr (55, 62, 69, 132, 519).

In the verbal DRM task, gist abstraction is essentially based on preexisting semantic knowledge. To study sleep effects on such semantic knowledge-based abstraction, several other tasks have been employed. In the "semantic coherence task," for instance, participants judge the coherence of word triplets (e.g., salt, deep, foam), with gist abstraction being assessed by how many correct common associate words (e.g., ocean) are identified. Similarly, in the "compound remote associates" task participants search for a solution noun (e.g., day) that meaningfully connects a triplet of nouns (e.g., dream, break, light). Another approach involves having participants listen to a short story, with gist abstraction assessed by the recollection of plausible details that were never actually included in the story. However,

none of these tasks yielded consistent evidence that sleep supports abstraction of gist memory (559–561). Notably, a study by Ashton et al. (562) may provide one explanation for this. In this study, participants learned noun-color pairings (e.g., elephant-red) and rated each pairing as plausible or implausible before entering a 12-h retention interval of overnight sleep or daytime wakefulness. Sleep generally enhanced the memory for noun-color pairs; however, this effect was much stronger for implausible pairs. Thus, sleep might preferentially promote the consolidation of information that does not conform to preexisting semantic knowledge compared to strongly conformant information (Refs. 437, 563; see Ref. 564 for similar results with respect to motor memory consolidation). Notably, information is encoded differently depending on whether it aligns with preexisting knowledge, and these differences may influence subsequent consolidation.

The mixed behavioral evidence for gist abstraction during sleep in DRM-like tasks is likewise reflected by related physiological findings of event-related potential (ERP) responses. For instance, the amplitude of the P300 component was higher for the recognition of gist compared to veridical memory, regardless of sleep (565). Another memory-related ERP component, the late positive potential (LPP), decreased to gist memory recall only after wakefulness. At the same time, LPP amplitude, in comparison with wakefulness, decreased after sleep to veridical memory accompanied by a decrease in veridical memory performance, with this pattern indeed pointing to a specific enhancing effect of sleep on gist memory consolidation. However, correlational analyses focusing on sleep parameters linked to systems consolidation are heterogeneous. Spindle and SO occurrence were only inconsistently correlated with gist abstraction (175–177, 550, 566). The duration of SWS, SO amplitude, and SO-spindle coupling, in some studies, were even negatively associated with gist memory (Refs. 176, 177, 538; see also Refs. 567, 568). Indeed, the findings overall suggest that oscillatory activity, linked to hippocampal memory reactivations during sleep, is not crucial for the gist abstraction in DRM-like tasks. This conclusion is further supported by early evidence showing that wake-associated consolidation after encoding can also enhance gist memory abstraction in DRM-like tasks, even when controlling for confounding factors at retrieval and encoding (e.g., Refs. 538, 539). Whether gist abstraction during wakefulness involves the same mechanisms as during sleep is unclear.

4.2.2. Transitive inference and memory for nonadjacent associations.

Several studies have demonstrated that sleep enhances transitive inference, i.e., the ability to infer the relationships between nonadjacent items after learning a set of premise pairs (131, 569–574). For example, after learning pairs of abstract shapes that were embedded in a hierarchical structure, participants showed better understanding of second-degree nonadjacent pairs after sleep compared to wakefulness (569). Similar results were found with different stimuli such as faces, scenes, or pictures of galaxies, although how long the benefit persisted differed between studies (572, 575). Additionally, a combination of nocturnal sleep and a daytime nap improved performance when testing how sleep affects updating a learned hierarchy by adding new items or restudying it (576). This benefit could be attributed to increased SWS and higher density of fast spindles.

Other studies examined nonadjacent associations by having participants spontaneously reproduce these associations rather than relate them hierarchically (131, 574, 577). For example, Lutz et al. (131) investigated the effects of postencoding nocturnal sleep versus wakefulness (both followed by a night of undisturbed sleep) on word memories in an associative learning task. In this task, words were presented according to a complex associative structure, allowing the dissociation of strongly, weakly, and indirectly encoded associations. Sleep was found to enhance memory recall for the weak and indirect (i.e., nonadjacent) associations, whereas strongly encoded associations remained unaffected. Improved transitive inference performance for second-degree nonadjacent associations after sleep was likewise observed with TMR applied upon SO up-states during SWS (573).

4.2.3. Abstraction of categories and rules.

The acquisition of categories and rules is commonly considered a central function of the prefrontal cortical-hippocampal system (578, 579). Drawing mainly on the study of single-cell activity, hippocampal circuitry, and computational models of sparse coding, the role of the hippocampus in this process has been linked to processes of pattern separation and pattern completion, enabling the distinct activation of representations for similar individual experiences and of holistic representations for multiple similar experiences, respectively (523, 580–583). How sleep affects category formation and rule learning on a behavioral level has been studied with rather different tasks (584, 585). Simple versions, such as grouping of different stimuli (e.g., visually presented objects) into classes based on their perceived similarity, have often been used in studies with children. These studies consistently show that postencoding sleep significantly enhances category formation (e.g., Ref. 586; sect. 5.1). In adults, often more complex tasks have been used, involving complex deterministic or probabilistic rules hidden in the stimulus materials, with overall less consistent results.

One of the first studies in adults employed the number reduction task, which required the detection of an invariant sequence of response numbers, hidden in multiple series of digits presented to the participants. Compared with different wake control conditions, nocturnal sleep after encoding distinctly enhanced the participants' insight into the hidden rule (587). Similar facilitating effects of sleep on insight into hidden sequential rules were observed in later studies, partly using rather short naps (305, 509, 588–610). Beneficial effects of sleep were likewise revealed with category learning tasks (132, 133, 586, 611–614). For example, participants trained to classify abstract dot patterns into two different categories showed a distinctly improved classification performance after nighttime sleep compared with daytime wakefulness (611). This improvement extended not only to the trained patterns but also to similar, related patterns, indicating that sleep facilitated the generalization of embedded regularities to new dot patterns not previously encountered. In some studies, sleep-dependent improvements were positively correlated with measures of non-REM sleep, such as sleep spindle activity and SOs, consistent with the view that benefits from sleep on such tasks are a consequence of reactivations of overlapping representations (133, 297, 586, 590, 591, 610, 614–616). One study also identified the transition into sleep as a critical factor facilitating insights into hidden rules (605).

However, there are also a number of studies that failed to show beneficial effects of sleep on the recognition of hidden rules and sequence, also using tasks like the number reduction task (617, 618), or on category learning tasks (619–623). In a study by Sweegers and Talamini (619), for example, participants were able to detect regularities in encoded face-location information and to generalize them to novel stimuli. However, no differences were observed between tests after 4-h consolidation periods that included either a nap or wakefulness. Similarly, a novel category learning paradigm (620) revealed no sleep effect but did find a time-of-day effect, with better performance in the morning versus the evening, independent of sleep. Participants even performed worse on a task requiring the formation of abstract categories based on complex probabilistic rules when sleep followed encoding, compared to a wake period, in one other study (621).

Interestingly, tasks designed to differentiate processes of pattern completion and pattern separation revealed that sleep can benefit both pattern completion, i.e., the process facilitating the detection of commonalities underlying the identification of rules and categories, as well as pattern separation, with this twofold effect offering a possible explanation for the inconsistent effects of sleep observed in many rule and category learning tasks. Hanert et al. (624) used a mnemonic similarity task (MST) in which the participants encoded visually presented everyday objects and were tested on recognition performance for the encoded objects as well as for novel objects that were more or less similar to the objects presented at encoding. Compared with daytime wakefulness, nighttime sleep enhanced the false recognition of objects that were most similar to the originally presented old target stimuli, consistent with an enhancing effect of sleep on pattern completion processes supporting similarity-based formation of categories. However, a reversed pattern was observed for objects with low similarity to old target stimuli, which indeed were better correctly recognized after sleep than after wakefulness, indication that sleep supports pattern separation underlying the recognition of distinct individual events (for related results, see Ref. 625). Hints toward a supportive effect of sleep on both pattern completion and pattern separation during sleep-dependent memory processing have been likewise provided by studies using other tasks, such as multielement association tasks, where sleep improved not only individually cued elements but also the joint remembering of a whole set of associations based on a single cue (Ref. 131; see also Ref. 626). However, for both types of tasks, results on the effect of sleep are not entirely coherent (Refs. 516, 574; see also Ref. 627).

The findings overall point to an enhancing effect of sleep on forming abstracted memory representations for categories and hidden rules, although the precise conditions for this effect to occur need to be clarified. The emergence of such an effect has been mostly found to be linked with non-REM sleep-related signatures of memory reactivation like spindles. Noteworthy, studies using TMR have provided evidence for an additional involvement of REM sleep in forming such abstracted memories, e.g., for face categories or spatial rules (628–630).

4.2.4. Gist as context-independent representation.

Learning happens within a context; in an experimental situation this often refers to features that remain constant across the entire experiment (such as the experimenter and the experimental room) or across experimental blocks and trials, in contrast to the to-be-learned stimuli that change from trial to trial. Along this line, gist abstraction can be more broadly seen as a process that enables a person to apply acquired knowledge to novel circumstances, i.e., in a different context. This type of contextual generalization has been investigated in numerous studies and led some to propose that a major function of sleep-dependent consolidation processes is to transform episodic experience, i.e., events occurring in a unique spatial-temporal context, into context-independent memories that represent a more abstract knowledge that can be

flexibly used in multiple situations (107). However, the respective studies greatly differ in the way "context" was experimentally varied, and, overall, the findings do not unequivocally support this view.

Indeed, an early study (631) revealed an increased binding of memory for events into their specific context after sleep. The participants learned lists of words presented in two different contexts, i.e., words of one list were presented (on a screen) while the participants saw a specific poster placed at eye height at the wall in front. For learning the second word list, the participants were turned 180° and sat on the opposite side of the room facing a different unique poster placed at eye height. Six hours later, first the recognition of the words was tested, and, if correctly identified as an "old" word, the memory for the context (poster) in which it had been presented was tested as well. Memory for the words (item memory) did not benefit from the subsequent nap, but memory for the context in which a recognized word had been presented was enhanced, suggesting that sleep, rather than promoting a decontextualization of memory, strengthens their contextual binding. Slightly different results were revealed in a study in ~10-yr-old children tested on a rather similar task comprising the learning of two word pair lists (Ref. 632; see also Ref. 633). To make the learning context distinct, presentation of the words of the first list was introduced by presenting "List 1" and of the second list by presenting "List 2" on the screen and, additionally, learning of the two lists were separated by a 1-h interval. Compared with a daytime wake interval, nocturnal sleep enhanced separate recall of both word pairs and the lists per se, whereas the combined recall of correct word pair and the list it had appeared in remained unaffected by sleep, which is in line with a dissociating influence of sleep on event and context memory (for related results, see Ref. 634 and sect. 5.1). Along this line, several recent studies point toward a decontextualizing effect of sleep on episodic memories also in adults (Refs. 602–604, 635–642; however, see also Refs. 643–646), whereas others suggest that sleep strengthens the binding of an event into its context (427, 475, 496, 647–658).

A decontextualizing effect of sleep has also been observed with problem-solving tasks (Ref. 659; for related results, see Refs. 660–670). For example, when participants were presented with different kinds of problems before sleep and wake periods, only after sleep did they show enhanced problem-solving capabilities on tasks with a similar problem structure, although the surface features of the task problems, taken here as the context, were entirely different from that used during the encoding session (659). The sleep-induced enhancement of these analogical transfer capabilities reflects a generalization of the underlying problem structure and, notably, was not due to improvements in memory for the features of the original task problems. It is worth noting that these experimental approaches are unique in that the task required attention to surface features, making context an essential part of problem-solving. This aligns these paradigms with tasks involving the detection of categories and hidden rules within diverse stimulus materials (see sect. 4.2.5 and Ref. 640 for related approaches).

Altogether, the studies show that sleep can promote the decontextualization of memory in certain conditions. However, the current picture remains inconclusive, partly reflecting that the psychological definition of what a context is is not sufficiently precise (671).

4.2.5. Gist abstraction in the procedural memory system.

Gains in procedural skill, in terms of enhanced speed and accuracy of performance and underlying shaping of sensorimotor circuits, can be also thought of as a memory abstraction process that profits from sleep. Many studies on the effects of sleep on procedural skills have concentrated on simple tasks of perceptual and motor skills, i.e., the texture discrimination task and the finger sequence tapping task, respectively (20, 672–675). The standard texture discrimination task requires the participant to discriminate the orientation (vertical or horizontal) of a structure of lines embedded in a context of similar lines, whereby the presentation time of each pattern is kept close to the perception threshold and is followed by the presentation of a mask stimulus at varying intervals (stimulus to mask onset asynchrony) to prevent discrimination based on afterimages. The finger sequence tapping task typically requires the participant to repeatedly tap as fast and as accurately as possible (within 30-s blocks) a specific five-element sequence of taps on a keyboard with the fingers of the nondominant hand. Performance levels on both kinds of tasks are higher after a posttraining period of sleep compared to postencoding periods of wakefulness (for more recent studies, see Refs. 297, 305, 481, 528, 601–604, 608, 636, 676–704). Importantly, some of these studies also confirmed a gain of skill after sleep, in comparison with the levels at the end of the training session (281, 472, 479, 483, 484, 528, 601, 607, 610, 615, 636, 678–680, 682, 685–687, 689–698, 700–702, 704–726), supporting the view of an active consolidation process that shapes underlying synaptic circuitry. However, there are exceptions (618, 727–745). For example, posttraining improvements were less consistent in the motor adaptation task (479, 685, 697, 731, 746–750). In addition, there are also findings questioning that posttraining sleep indeed produces a gain in finger sequence tapping performance compared with skill levels at the end of the experimental training (480, 615, 734, 736, 740–742, 745, 751–762). For example, postsleep gains in

finger tapping were eliminated when confounding factors were minimized, such as task fatigue (by reducing the duration of training blocks) and time-of-day effects (by using 24-h instead of 12-h delays between training and test) (753). When the baseline level in the motor skill is assessed some minutes after training, rather than immediately at the end of training (as it was done in most early studies), a substantial gain in skill is typically revealed already at this delayed assessment, possibly reflecting what is sometimes called "synaptic fatigue," i.e., a diminished skill performance toward the end of a training session, which recovers within a 10- to 30-min break (480, 734, 745, 762). Notably, compared with skill levels at such delayed baseline assessment, a subsequent sleep period does not further improve the skill, overall suggesting that sleep, rather than producing a gain, merely stabilizes skill performance in comparison with a posttraining wake period. Recent meta-analyses (740, 741), moreover, point to a pronounced publication bias and no consolidation-based absolute performance gain in motor sequence learning tasks following sleep (see also Refs. 736, 754).

Compared with posttraining wakefulness, enhancing effects of sleep on procedural skills were revealed also for more complex skills, such as the SRTT, with more elements and hidden probabilistic sequence structures (305, 509, 587–604). Many of these studies tested not only for the skill as trained before sleep but also for the transfer of skill into another context. For example, posttraining sleep specifically improved the interocular transfer of texture discrimination skills (602), and in another study (603) the extent of the cross-modal transfer of statistical information from the auditory to the visual modality was predicted by the time the participants spent in SWS after training. In a visuomotor SRTT, sleep improved the transfer of the skill from the trained deterministic sequence with long interstimulus intervals to a sequence with shorter interstimulus intervals (Ref. 604; see also Ref. 763). Interestingly, sleep in parallel often increased signs of explicit knowledge about the sequence structure underlying SRTTs, which participants are typically not aware of at the end of the training session (Refs. 591, 592, 606–610; see also Ref. 618). Such gain in explicit knowledge about hidden sequence structures was consistently associated with posttraining SWS (591) and non-REM spindle activity (297, 590, 615, 616), as well as with non-REM-REM and light sleep-SWS transitions (610), and has also been produced by administering TMR during SWS (584, 706, 764).

Research indicates that the consolidation of procedural skills during sleep involves the hippocampus, even though these skills are typically considered independent of hippocampal function, mainly relying on extrahippocampal areas such as the striatum in the case of motor skills. In early fMRI studies by P. Maquet's group, both hippocampal and striatal activations during oculomotor sequence training were found to predict performance gains observed after sleep but not after wakefulness (758). The positive correlation between striatal and hippocampal responses at the test after sleep was taken to suggest that sleep turns the competitive interaction between these structures observed during training into a cooperative synergistic interaction, a view that was confirmed in a follow-up study (528). In that study, sleep at the test session produced an increased activation in the hippocampus-mPFC system, whereas striatal and cingulate cortex regions showed a stronger increase when training was followed by a wake period (but see Ref. 749; for a review, see Ref. 765), with this pattern of changes being overall stronger in young than old participants (483, 766). The sleep-dependent increase in hippocampal activation appeared to be particularly pronounced with a finger tapping task including a strong spatial component (137). Sleep-dependent benefits on cross-modal transfer of statistical sequence knowledge, on the other hand, were associated with a shift toward increased striatal activity (603), consonant with a transfer of statistical knowledge to striatal regions during sleep (705). Applying TMR during SWS after training a SRTT increased both hippocampal and striatal responses at later retest (472). In fact, the hippocampal contribution is even critical to sleep-dependent gains in skill, as patients with hippocampal lesions failed to show any such gains in finger tapping (136, 767).

4.2.6. Abstraction of gist-like memory in rodents.

Memory abstraction processes have been less extensively studied in rodent models at the behavioral level, largely because of the complexity of the required learning paradigms. Nevertheless, rodents are able to abstract rules and schemalike representations from multiple experiences (768–770), and there are, in fact, a few studies that have explored effects of sleep on either the abstraction of rules from multiple experiences or the generalization of learned information from one context to another.

A first study in rats (771) used the Y maze-based alternative choice task that requires the abstraction of a simple sequence rule, as the animal on each subsequent trial has to choose the other arm of the Y maze to receive food reward. Rats training on such a task showed a peak in theta coherence between prefrontal and hippocampal theta activity when they reached the choice point of the Y maze, most strongly after task rule acquisition, and the medial prefrontal cell assemblies activated during these theta coherence peaks were preferentially reactivated during subsequent SWS, concurrent with sharp-wave ripples in hippocampal networks. The findings fit the view that sleep supports consolidation of rule memories, although in these experiments there was no demonstration of a behavioral gain in rule memory across sleep.

This missing behavioral evidence for a role of sleep was provided by more recent studies. Abdou et al. (772) established a complex spatial learning task in mice to show that sleep benefits transitive inference. The task comprised an arena of five different compartments ("contexts"). First, the mice were trained over 8 days on pairs of the contexts to prefer one of the two contexts as it was rewarded, with this procedure aiming to establish a hierarchical order of the contexts, such that context A was preferred over context B, B over C, C over D, and D over E. To test whether, beyond the presented pairings, they had learned the entire hierarchy of associations, they were later given a choice between context B and context D, which was never presented during training. Accordingly, a preference for context B over D at this test would indicate transitive inference, i.e., that the mice had learned the overall hierarchical reward structure underlying the contexts. Whereas the animals did not show knowledge of the hierarchy in a test 30 min after completing the training, they did so in a test 24, 48, and 72 h later when sleep occurred during the 4-h interval after the last training. Further evidence pointed to the importance of the mPFC, specifically the ACC, in this process, as optogenetic inhibition of the ACC during both non-REM and REM sleep abolished the animals' preference for context B at the test.

Some rodent studies have also focused on the question of whether sleep facilitates the generalization of learned information to new contexts (e.g., Refs. 234, 639). Overall, these studies, however, suggest that sleep strengthens context dependency of memory rather than facilitating the generalization to other contexts. Accordingly, rats that slept after the encoding phase of an NOR task exhibited less memory for the familiar object 1 wk later when tested in a new context (with new proximal and distal cues and a different experimenter). Conversely, NOR memory was stronger than in a wake control group when the rats were tested in the same context as during encoding (234), indicating that sleep strengthens object-in-context binding. In another study, mice were first trained over multiple daily sessions on a "reach-to-grasp" motor task (373). Rats rapidly improved in the task during this period, which was associated with an increase in the coupling between sharp-wave ripples in the hippocampus and SOs in the prefrontal and primary motor cortices that, however, faded as performance stabilized, suggesting a disengagement of the hippocampus. Yet there was a reengagement of the hippocampal-neocortical system in conjunction with destabilized motor performance when the rats were exposed to the same task but required to use the opposite paw. The findings are also consistent with the view that the coupling of hippocampal ripples with cortical SOs during SWS strengthens the binding of, in this case, skill memories into a new context.

The majority of rodent studies investigating the generalization of learned information to new contexts, however, employed contextual fear conditioning and respective extinction learning (e.g., Refs. 235, 249, 773; see sect. 4.2.6). Rats fear conditioned in a "shock box" showed less generalization of fear at a later test in a different "safe box" when conditioning was followed by sleep in comparison with a wake control condition (773). The effect of sleep was abolished by intrahippocampal injection of corticosterone after conditioning. However, whether sleep prevents or facilitates contextual fear generalization depends on the similarity of the contexts. That is, a stronger generalization of the conditioned fear response after sleep was observed when testing took place in a context similar to that during training (249). The generalization effect of sleep, in these experiments, critically depended on the coreactivation of relevant neurons in the ACC, which during posttraining sleep were activated via neuron ensembles in the retrosplenial cortex. Altogether, these studies show that also in rodents sleep can aid the formation of abstracted schemalike memory and the generalization of such memory to new contexts, but only when these are similar to the original learning environment. The ACC appears to be a main contributor to these processes.

4.2.7. Conclusion.

Over the past decade, the focus of research has shifted from a now established active role of sleep in stabilizing memories to the role sleep plays in the qualitative transformation of memories during systems consolidation. The relatively few studies in rodents, indeed, point to a supporting effect of sleep, and particularly of SWS-related memory reactivations, on the formation of abstracted memory representations, in which mPFC structures like the ACC play a central role. In contrast, the large body of studies in humans provides an overall mixed picture, with some studies showing beneficial effects of sleep while many others also report negative results. This may not come as a surprise, considering the great variety of task paradigms used in this research. Effects of sleep in purely verbal tasks like the verbal version of the DRM task show little consistence across studies, and findings appear to be even more diverse in studies that aim to show decontextualizing effects of sleep on episodic memory. More robust effects were obtained with tasks testing the strength of nonadjacent associations in a previously learned hierarchy and tasks requiring the abstraction of rules, especially when embedded in spatial/motor requirements, as in the SRTT. The reasons for the divergencies are presently not clear, but the timing of retrieval testing might be one factor as, depending on the task, the abstracted representation emerges more or less rapidly. Also, the terms "abstraction" and "gist" we use here are rather broad, and future studies

might benefit from working out more precise definitions and concepts of the underlying processes to guide the development of task paradigms. Independently of the employed task, the studies overall suggest that abstraction processes during memory consolidation are more closely linked to spindles than to SOs.

4.3. The Role of Emotions and Reward

Against the backdrop that sleep-dependent consolidation favors the abstraction of salient gist information, it has been proposed that sleep preferentially enhances memory for emotional experiences and information associated with reward, as such memories are of greater relevance for the individual's future adaptation (774, 775). A principal problem in studies on the consolidation of emotional and reward-associated memories arises from the fact that stimuli that are associated with strong (negative or positive) affective response are already differently encoded, i.e., activating amygdalar and dopaminergic striatal circuitry to a much greater extent than emotionally neutral stimuli. Consequently, emotional materials are generally better remembered than neutral materials, even when encoding is followed by wakefulness, a phenomenon termed "emotional enhancement in memory." The qualitative differences in the encoded representations hamper direct comparison between the respective following consolidation processes, as the conditions at encoding may specifically interact with circuitries relevant to emotional memory formation (e.g., Ref. 776). The interpretation of results from these experiments is further complicated by evidence indicating that the processing of emotional stimuli at encoding and retrieval is influenced by the quality of prior sleep (651, 777–781). Nevertheless, as an approximate approach to these problems, studies in humans typically compared retention of emotional versus neutral stimuli, with the focus on the question of to what extent sleep augments the emotional enhancement in memory, as assessed during the encoding phase before the retention interval.

4.3.1. Memory for emotionally aversive information.

The majority of human studies have compared processing of emotionally aversive versus neutral information and, indeed, observed that sleep increases the emotional enhancement in memory. Thus, in an early study (782), REM sleep-rich late nocturnal sleep particularly benefited memories obtained from reading negative emotional texts, compared with neutral texts, and the sleep benefit for these emotional memories could be seen even years later (783). Although these findings were questioned by more recent reports (e.g., Ref. 784), studies with large sample sizes of >250 participants strongly supported a preferential consolidation of emotionally salient information during sleep, especially with negative valence (785). This preferential consolidation of emotionally negative memories was observed in young as well as middle-aged (46–65 yr) participants (Ref. 491; but see also Ref. 786), appeared to be little affected by experimental manipulations of encoding strength (787), emerged also when the participants at encoding were explicitly instructed to later remember the materials (492), and was found to be positively correlated with non-REM sleep-associated parameters like the percentage of SWS and spindles, as well as REM sleep-associated parameters (e.g., Refs. 491, 492, 788, 789). Asking the participants to cognitively reappraise the emotionally negative stimuli at encoding (i.e., to try to increase or decrease their emotional response to the respective stimuli) did not change the effect of sleep on consolidation of the emotional stimuli (790).

Fear conditioning and extinction paradigms are also often used for the study of sleep effects on emotional memory in humans (500, 791–805) (for reviews, see Refs. 806, 807). A representative example is a study by Menz et al. (500) using Pavlovian fear conditioning, where participants were shown a picture of a living room with various visual stimuli, some of which (conditioned stimuli; CS+) were paired with an 80% chance of receiving a mild electric shock (unconditioned stimulus; US). During a subsequent extinction phase, one of the CS+ ("CS+Ext") was presented in a different "extinction context," in the absence of the shock. Then, nocturnal sleep or wakefulness and an additional recovery night followed. At a test, sleep improved conditioned fear recall, as evidenced by stronger skin conductance responses (SCRs) to the CS+ that was not extinguished, a stronger activation of the basolateral amygdala in the fMRI, and a stronger perceived anxiety, with the increased SCR being positively correlated with the time in REM sleep during the postconditioning night. Confirming the association with REM sleep, an increased fear response was likewise observed when conditioning was followed by late nocturnal REM-rich sleep, paralleled by a reduced activation of the ventromedial PFC and amygdala and an enhanced discrimination between the extinguished CS+Ext stimulus and a neutral stimulus (793, see also Ref. 808). The ventromedial PFC is known to be involved in both fear acquisition as well as extinction, and its functional connectivity with the amygdala is indeed reduced when participants are sleep deprived before fear acquisition (Ref. 802; for related findings, see Refs. 796, 801, 804, 809–811). Activity of the ventromedial PFC during fear conditioning was also associated with time in subsequent REM sleep, which was in turn associated with increased subsequent fear recall (799).

Although these findings overall point to an enhancing effect of sleep, in particular REM sleep, on both the overnight consolidation of fear and safety memories, there are also conflicting findings: For example, one study (812) did not find a link between fear extinction and the subsequent amount of REM sleep, another study (794) did not find an effect of sleep depriving participants after extinction learning (see also Refs. 795, 809, 813, 814), and a third (815) even suggested that fear memory consolidation depends on time rather than on sleep (791).

Studies using TMR, on the other hand, have provided hints that sleep might also have a weakening effect on fear memories (Refs. 236, 816–819; see sect. 7.2). In these studies, typically the conditioned stimulus (CS+) is repeatedly presented during sleep after conditioning, but in the absence of the unconditioned stimulus, thereby basically establishing an extinction procedure during sleep. Indeed, in two studies (816) repeated presentation of the CS+ during SWS enhanced fear extinction, which was accompanied by pre- to postsleep reductions of hippocampal activity and a change in amygdala ensemble activation patterns in the fMRI response (see also Ref. 820). The fear-reducing effects being specific to cue presentation during SWS points to additional contributions of SWS to fear memory processing. However, studies in rodents in particular have yielded contradicting results, with CS+ presentations during sleep increasing rather than weakening fear memory (e.g., Refs. 235, 821; see below).

Taken together, these studies suggest a rather consistent benefit of sleep on the consolidation of aversive memory, including fear conditioning and extinction memory, with an emerging role of amygdala-ventromedial PFC interactions in the consolidation of fear during REM sleep, whereas findings on the role of non-REM sleep are less consistent.

4.3.2. The role of context information.

Mainly driven by the clinical relevance of the topic, studies of (aversive) emotion processing have aimed at dissociating effects of sleep on the memory for the event and the context in which it happened. Bennion et al. (822) presented participants with pictures of scenes composed of a negative or neutral object on a neutral background. At a test 12 h later, objects and backgrounds were presented separately and were to be judged as either old, i.e., presented at encoding, or new. Retrieval of the background cues itself did not differ between postencoding sleep and wake conditions. However, increased functional connectivity between the middle occipital gyrus and the hippocampus for correctly retrieved backgrounds that were associated with negative objects during encoding after postencoding sleep pointed toward a strengthening effect of sleep on contextual memory embedding negative events. Sleep likewise selectively stabilized spatial contextual aspects for negative event memories in a task requiring the participant to recall the location where an emotionally negative (vs. neutral) object had been presented during encoding (642). Noteworthy, these effects of sleep on consolidation of object-context associations do not appear to depend on the emotional valence of the context itself (638, 653). Diverging from these findings, sleep deprivation after encoding of negative, positive, and neutral film clips generally impaired memory for the clips (at a test after recovery sleep) but did not affect memory for contextual details, which depended on the emotional valence of the clip (651, 823). A specific effect on contextual memory was observed only when the participants were sleep deprived before encoding, with this effect likewise being independent of the emotional valence of the film clip.

4.3.3. Emotionally positive vs. negative information.

Interestingly, of the growing number of studies comparing negative versus positive memories, some yielded a stronger benefit of sleep for positive emotional memory processing. An afternoon nap, for instance, enhanced consolidation of pleasant and neutral, but not unpleasant, memory of pictures in comparison with a wake control condition (824). When participants were explicitly instructed to learn negative, neutral, and positive words before a nap (vs. wakefulness) and at a later test these words were used as cues in an “associational breadth” task to assess spreading of activation in semantic networks, participants after the nap produced more uncommon associations for emotional than neutral cue words, with this effect being significantly stronger for the positive cue words (825). This suggested that sleep-dependent consolidation of positive information goes along with a greater breadth of associative strengthening in semantic networks. As the effect only emerged in a subgroup of participants who exhibited increased REM sleep during the nap, REM sleep may play an important role in this process. Similar to these findings are studies of dream reports (e.g., Ref. 826) that indicate an increased incorporation of personally relevant details from waking life into REM sleep dreams compared with dreams reported after non-REM awakenings (see Refs. 827, 828 for reviews on dreaming and emotional processing). Furthermore, the bias toward processing of positive memories appears to be more pronounced in conditions of disturbed SWS, i.e., after experimental disruption of SWS in young participants (829) and in older adults (Refs. 830, 831; sect. 5.2).

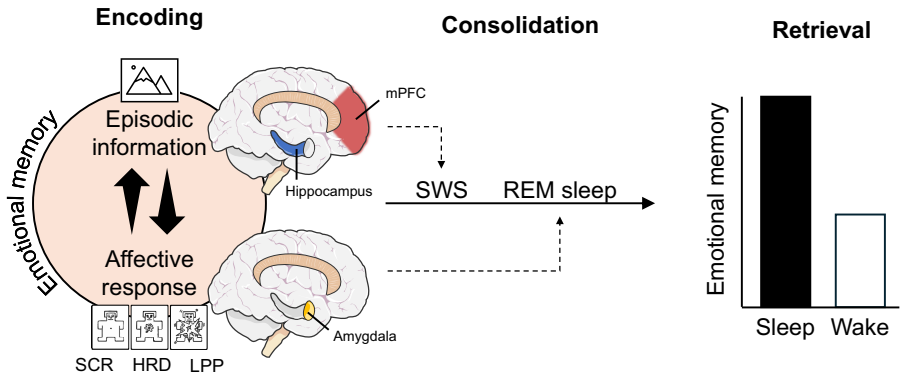

FIGURE 8. Emotional memory consolidation during sleep. Emotional memory consists of a contextual episodic component mainly represented by the medial prefrontal cortex (mPFC)-hippocampal system and an affective response mainly represented by the amygdalar system, which are preferentially enhanced by SWS and REM sleep, respectively, eventually leading to enhanced retrieval of the emotional memory after sleep. Beyond an assessment of amygdala activity in the fMRI, affective responses are typically measured using arousal ratings (e.g., self-assessment manikins), skin conductance responses (SCRs), heart rate deceleration (HRD), or the late positive potential (LPP) of the EEG. See GLOSSARY for additional abbreviations.

4.3.4. Distinct roles for non-REM and REM sleep.

The processing of emotional memory has been traditionally linked to REM sleep (87, 500, 788, 825, 832–836), although there are also accounts linking the consolidation of emotionally valenced memory to oscillatory markers of memory reactivation during non-REM sleep (837). However, many studies found no evidence for a particular role of REM sleep in emotion processing and no difference in the consolidation of emotional versus neutral information following sleep periods containing more or less REM sleep (789, 824, 838–841). Conversely, an involvement of non-REM sleep in emotional memory consolidation is supported by findings indicating memory for salient emotional information to be associated with non-REM sleep-related signatures of memory processing, like the percentage of SWS, EEG delta power (492, 789), and spindle activity (Ref. 491; however, see Ref. 842). In a TMR study, the facilitating effect of TMR on memory for negative picture-location associations was predicted by both SWS duration and spindles during postencoding SWS (Ref. 493; sect. 7.2). A particular benefit on emotional memory consolidation was also found after pharmacologically increasing sleep spindle density by zolpidem administration (Ref. 314; sect. 7.3).

Experiments using selective sleep stage deprivation procedures provided more evidence for a major role of REM sleep for emotional memory consolidation, though. In one study (497), selective SWS deprivation improved consolidation of negative (vs. neutral) pictures, with picture memory in this condition being positively correlated with the amount of REM sleep. A comparison of 3-h periods of early-night SWS-rich and late-night REM-rich sleep revealed that late-night REM-rich sleep specifically improved memory for the emotional event, i.e., the aversive pictures (496), whereas SWS-rich sleep specifically improved memory for contextual stimulus aspects, i.e., the color of the frame in which the (neutral as well as aversive) pictures were presented (see Refs. 427, 843 for comparable results). REM-rich sleep, moreover, produced a corresponding increase in the LPP of the ERP response to correctly recognized emotional pictures (844). Such differential effects of SWS-rich and REM-rich sleep on emotional memory appear to depend on the participant's mood, e.g., reported depressive symptoms (845, 846), and were completely overridden by reward-related effects, i.e., when memory for the stimuli was additionally associated with a reward to enhance their salience (465). Interestingly, in a clinically oriented study (847), compared with wakefulness sleep after an experimental trauma exposure (watching a film including fictional violence) resulted in fewer and less distressing intrusive trauma memories, with this effect being particularly evident 1 wk after the exposure. Intrusive trauma memory was positively correlated with the duration spent in non-REM S2 sleep as well as spindle density but was negatively correlated with density of REMs during the experimental sleep period. Finally, fMRI data indicated that the consolidation of negative memories during SWS leads to reduced activity in the hippocampus, but increased activity in the mPFC, at retrieval, whereas REM sleep might increase connectivity in networks additionally integrating amygdalar circuitry (498, 848, 849).

Overall, the findings argue against the view of a single sleep stage, like REM sleep, comprehensively regulating emotional memory consolidation. Rather, both non-REM and REM sleep appear to have different but complementing functions. This may not surprise, considering that conceptually there is no purely emotional memory but emotional memories, particularly as investigated in most studies, represent hippocampus-dependent

episodic memories with an emotionally negative or positive tone. Furthermore, emotional procedural memories are only rarely investigated. Accordingly, the observation that both non-REM and REM sleep contribute to particularly enhancing emotional memory might be related to the fact that such memories comprise an affective response that is associated with the respective episodic (or procedural) content. REM sleep might particularly enhance emotional memory through an impact on the affective response, whereas the contribution of SWS might pertain to the episodic content of the emotional memory (**FIGURE 8**).

4.3.5. Effects of sleep on the affective response to emotional stimuli.

Emotional memory comprises an affective response, which may be represented in separate systems from the episodic memory content. Accordingly, studies have aimed to specifically assess effects of sleep on this affective component that is characterized (for aversive stimuli) by an increase in amygdala activity and subjectively experienced arousal in combination with an aversive feeling, as well as by physiological responses such as heart rate deceleration (HRD) or SCR. Subjective arousal and affective valence responses, assessed by subjective ratings, were found to decrease across intervals of sleep in comparison with wakefulness (642, 850), even in the absence of memory differences for the respective groups (but see also Ref. 851). A sleep-dependent decrease was likewise observed for the amygdalar activation to emotional stimuli, with this effect positively correlating with the time the participant spent in REM sleep after the encoding session, whereas restless REM sleep, a characteristic of insomnia patients, impeded the amygdalar adaptation (852, 853). The amygdala response to aversive events encoded before sleep could be further reduced and "updated" toward more positive affective judgments in postsleep tests through a TMR procedure, in which the cues presented during sleep to reactivate the negative memoires were associated with positive words (854). Generally, poor sleep quality (or sleep deprivation) is well known to disinhibit negative emotion expression and to reduce positive affective responses (855, 856).

SCR and HRD responses to negative stimuli have been found to decrease across periods of sleep (857, 858). Larger SCRs and HRD responses at encoding were further positively correlated with memory for negative objects and scenes in the sleep but not the wake groups of these experiments (858). Moreover, changes in the emotional response occurred faster: Comparing responses at a test shortly after sleep versus 1 wk later revealed that the sleep-dependent downregulation of the emotional HRD response to aversive pictures, in parallel with a decrease in (negative) valence ratings, is established already shortly after sleep, whereas the improvement in memory for the aversive scenes emerged only 1 wk later (for comparable results see Ref. 859). Notably, in a clinically oriented study (860) a cognitive "rescripting" procedure that aimed to diminish the negative valence of the participants' autobiographical memories and was introduced before sleep was associated with a stronger decrease in heart rate, together with diminished signs of subjective distress after sleep. Instructing the participants before sleep to forget the aversive memories yielded a similar decrease in the SCR (861), overall pointing to an interaction of the emotional response with cognitive processing during sleep (see also Refs. 862, 863). The sleep-dependent dynamics of the emotional response appear to be different in children (Ref. 864; sect. 5.1).

Beyond SCRs and HRD responses, cortisol levels were assessed (in saliva) as a measure of distress. Enhanced cortisol during encoding enhanced the sleep-dependent benefit for memory of negative arousing pictures but not after wakefulness (Ref. 865; see also Ref. 432). Note that enhanced glucocorticoid levels accompanying encoding may extend into the postencoding sleep period with distinct effects on the sleep-dependent consolidation process. Indeed, exogenous administration of glucocorticoids during postencoding sleep, while reducing consolidation neutral episodic memory (Refs. 866–868; see also Ref. 773), seems to also enhance the difference between recall of negative emotional versus neutral memory (869).

4.3.6. Emotion and the reorganization of episodic memory.

Emotional features might specifically contribute to the reorganization of episodic memory during sleep (for a review, see, e.g., Ref. 870). Alger and Payne (871) used two sets of object-face picture pairs with the same objects in both sets to study direct (within set) associations and indirect "relational" associations, i.e., between faces associated with the same object in the two sets. Compared with a wake condition, postencoding sleep facilitated memory for both the direct and indirect associations. Importantly, a postencoding nap enhanced relational associations only when they comprised emotional (but not neutral) faces, with the time in REM sleep being positively associated with relational memory formation (871). These emotion effects could be replicated when encoding was followed by a nocturnal sleep period rather than a nap (872).

A question of great clinical relevance in this context is whether sleep promotes the generalization of conditioned fears and their extinction (Refs. 792, 797, 873–877; for reviews see Refs. 832, 874). In a study by Lerner et al.

(877), sleep indeed promoted the generalization of (shock) conditioned SCR responses to new contexts, with this effect linked to increased amounts of REM sleep and increased ventromedial PFC activity at recall testing. Sleep has been likewise observed to support the generalization of the conditioned SCR response to other stimuli that were similar to the conditioned stimulus (876). However, there are also conflicting results that indicate no effect of sleep on fear generalization (875), and in one study fear generalization was even higher after wakefulness (797). Regarding fear extinction, an early study (873) revealed a sleep-dependent generalization of conditioned SCR to the unconditioned stimulus, i.e., at the test following postextinction sleep the SCR response was reduced not only to the conditioned stimulus but also to a control stimulus that was not used for fear conditioning, compared with a wake condition. Similar results were found in subsequent studies (792, 878), which also indicated interactions between effects of sleep and time of day.

Altogether, these findings indicate that emotional processing contributes to the assumed reorganization of memory representations during sleep, likely through an interaction with the hippocampus-dependent episodic memory system.

4.3.7. Reward-associated memory and future relevance.

Reward-associated memory can be considered a special kind of emotional memory where the to-be memorized stimulus is associated with an actual or expected reward, i.e., an incentive that elicits a pleasant emotional response together with increased motivation. Processing of reward is associated with activation of a well-characterized dopaminergic system comprising a hippocampus-ventral-striatum-VTA-hippocampus feedback loop, where dopaminergic input from the VTA to the hippocampus functions as a neuromodulatory reward signal that enhances neuroplasticity and effectively gates information selection for possible long-term memory formation during sleep (879, 880). There is evidence for sleep replay in reward structures like the VTA (see below). However, it has also been suggested that dopaminergic input tags highly relevant memories during encoding in the wake state, with this tagging enhancing memory replay during sleep, without further involvement of the dopaminergic system (for related reviews see Refs. 881–884).

Studies of reward effects often compare memory for stimuli that, at encoding, are presented together with different incentives indicating whether correct recall of the respective stimulus at a later test leads to high, low, or no reward (e.g., in money). With such a reward manipulation, sleep-dependent benefits for high- versus low-rewarded word pairs have been observed in many studies (e.g., Refs. 179, 885–888; however, see also Refs. 652, 889). These effects seem to be accompanied by signs of enhanced memory processing. For example, a positive correlation between spindle density during postencoding sleep and memory performance after sleep was observed only for high- but not low-reward word pairs (885), and in another study (179) rewarded (vs. nonrewarded) events were found to be prioritized for spontaneous neural reactivations during sleep. Combining fMRI with a brain decoding approach, this study also revealed that brain activity patterns observed at encoding during wakefulness spontaneously reemerged during SWS, with a preference for reactivating patterns linked to a rewarded task. Moreover, the reactivated patterns were positively correlated with subsequent memory performance. In children (8–12 yr), enhancing SO activity by CLAS during SWS particularly improved consolidation of high-reward memory items (886). Presenting, in a TMR procedure, reward-associated cues (i.e., the spoken name of a familiar, valued snack item) during a postencoding nap, but not during wakefulness, enhanced the preference for that item at a later choice test, further corroborating the notion that reprocessing of reward-associated memories during sleep implicates the additional reactivation of respective reward circuitries (888). Challenging this view, however, activation of dopamine D2-like receptors (by the receptor agonist pramipexole) during postencoding sleep did not enhance but eliminated preferential consolidation of high- versus low-rewarded memories (882, 887) (see also Ref. 890).

Rather than through reward, the salience and future relevance of a memory can be increased in human studies also by instructions, e.g., simply by informing the participants that the recall of the respective memories would or would not be tested at a later test. Typically, before actual retrieval testing, the original instruction about whether or not retrieval of the memory is tested is revoked to allow for an unbiased test of all memories. Using this approach, early research showed consistently stronger sleep-dependent benefits for declarative as well as procedural memories expected to be tested later on in comparison with memories not expected to be tested (Refs. 774, 891, but see also Ref. 892).

Addressing the future relevance of a memory, more recent studies have adopted the "prospective memory" framework (893–921). Prospective memory specifically refers to memory for future intentions and plans and appears to be mainly supported by regions in the anterior PFC (e.g., BA10). In the encoding phase of prospective memory experiments, the participants typically learn specific action plans (e.g., to cover the table for a dinner in a certain way), which are to be completed after the experimental sleep versus wake period or before sleep.

With such tasks, quite robust beneficial effects of sleep were observed (893–902). For example, Diekelmann et al. (894) found that after nighttime sleep significantly more participants executed the action plan compared with nighttime wakefulness (followed by an additional recovery night in both groups). Notably, sleep enhances the memory for the plan only when it is kept active across the entire postencoding interval. This means that sleep did not enhance memory for the plan when the participants completed the plan 2 h after encoding, but still before the sleep period, and sleep was also not effective when the plan was reinstated after it was completed (895, 899). A comparison between early nocturnal SWS-rich and late REM-rich sleep revealed a superior plan execution when the implementation of the intention was followed by SWS-rich early-night sleep (894). An association of the benefit in prospective memory with SWS was likewise revealed in other (897), but not all (898), studies. A superior execution of plans after postencoding sleep is also seen when the detrimental effects of sleep deprivation on attention and executive functions are controlled for (900–902). Studies in older people and patients validated the importance of sleep for prospective memory (903–920). For example, older people suffering from sleep disruptions showed a smaller sleep benefit in prospective memory performance than younger participants (e.g., Refs. 903–908; sect. 5.2). Also, prospective memory performance is generally worse in patients with insomnia and obstructive sleep apnea (OSA) disorder (e.g., Refs. 909–912), although the picture appears to be more complex in patients with chronic insomnia (e.g., Refs. 913, 914; sect. 6). Impaired prospective memory performance has been observed also in patients with idiopathic REM sleep behavior disorder (RBD) (915–917), pointing to an involvement of REM sleep-related dopaminergic activity in striatal networks in mediating prospective memory (see also Refs. 911, 918–920).

The overall picture indicates that future relevance, be it induced by an increased anticipated reward or by invoking plans for the future, plays a key role in selecting memories for sleep-dependent consolidation that appears to outweigh the contribution of emotionality (922). Most robust effects of sleep are observed on prospective memory, which in healthy people are conveyed by mechanisms active during SWS (921).

4.3.8. Fear-related memory in rodents.

Studies on rodents that investigate the role of sleep in emotional memory consolidation have focused on fear conditioning and extinction paradigms and overall indicate an enhancing effect of sleep on these memories (167, 425, 529, 923–934). The experiments administered cued fear conditioning [where, e.g., a tone (CS) is associated with an electrical shock (US)] and context fear conditioning procedures (where the shock is delivered in a specific context serving as CS) separately or in combination. Behaviorally, the fear memory is typically assessed by the animal's freezing in response to the CS presentation alone. Context conditioning more strongly depends on hippocampal function than cue conditioning. For example, compared with sleeping mice, mice that were sleep deprived after conditioning showed less freezing in response to a specific context (conditioning chamber) that was conditioned to an electric foot shock at a later test (926). Reduced freezing was likewise observed in rats when sleep after context conditioning was disturbed by a circadian desynchronization protocol, inducing fragmentation of non-REM and REM sleep (935). Sleep compared with a 3-h period of sleep deprivation that followed extinction training also enhanced contextual fear extinction memory in mice when tested 24 h later (925). The effects of sleep were independent of the circadian phase.

Fear conditioning and extinction memories appear to particularly profit from REM sleep (167, 422, 447, 448, 936–949). In mice, REM sleep deprivation following tone-shock conditioning applied in a specific chamber (context) diminished both cue and context conditioned freezing responses at a test 22 h later (936). Notably, these effects may be stronger in male than female animals (945). In parallel with the decrease in freezing, REM sleep deprivation diminished signs of synaptic consolidation, i.e., a reduced expression of AMPA receptors containing the GluR1 subcomponent as well as a decrease in frequency and amplitude of miniature excitatory postsynaptic currents (mEPSCs) in the thalamic-amygdalar pathways. The impairing effect of REM sleep deprivation on behavioral fear memory and associated mEPSC activity could be reduced by intraperitoneal injections of leptin (see also Ref. 950). The synchronization of theta activity was enhanced in the ventral hippocampus and the lateral amygdala during post-fear conditioning REM sleep, with theta phase shifts between the regions predicting cued fear memory recall after sleep (425). Activation of PKA in hippocampal regions was found to be critical to the formation of contextual fear memory during sleep (927). Notably, in mice impaired context conditioned fear memory after REM sleep deprivation at a remote test (30 days later) was accompanied by increased *Zif268* (a marker of neuronal activity) expression in several regions known to be involved in emotional processing, including the CA1 subregion of the ventral hippocampus, the basolateral amygdala, and the ventral orbitofrontal cortex (529). Similar increases in neuronal activity patterns were found with total sleep deprivation following fear conditioning (930), altogether suggesting that REM sleep

serves to downregulate emotional processing upon recall of fear memory at the test. In parallel, REM sleep may contribute to enhancing activity in regions that are not specifically involved in the processing of emotional aspects of the memory, like the dorsal hippocampus, during context fear conditioning (951).

Findings on the effect of REM sleep deprivation have been questioned, as many of these studies used the so-called "flowerpot" technique, which induces stress potentially and may confound memory processing. With this technique, the animals are put on a small platform surrounded by water that prevents them from completely relaxing their muscles, which would result in falling from the platform and waking. However, diminishing effects of REM sleep deprivation on context conditioned freezing responses and associated sings of synaptic consolidation (e.g., impaired LTP induction) have also been revealed with less stressful procedures of REM sleep deprivation like "gentle handling," where the experimenter only slightly knocks at or inclines the animal cage to keep the animal awake (951).

A role of REM sleep in fear consolidation is also suggested by evidence that, although not entirely consistently, points to a promoting effect of fear conditioning on subsequent REM sleep (389, 926, 938, 942–944, 952–956). For example, an increase in REM sleep was found following foot shock conditioning compared with nonshocked control animals, with REM sleep also being predictive of developing PTSD-like symptoms 1 mo after foot shock exposure (Ref. 937, see also Ref. 423). Increased REM sleep in conjunction with an increased density of PGO waves has also been observed following context fear extinction training, especially in the rats showing successful extinction (389). Although increases in REM sleep may partly be a consequence of a nonspecific stress response to the aversive shock stimulation, this seems to support subsequent memory consolidation. Using an escapable shock procedure in which mice were trained to escape from a foot shock in one chamber by moving to another through an opening door, Machida et al. (938) observed more REM sleep episodes following training in mice that had successfully learned to escape compared with mice that had failed to learn to escape. In line with this, other findings indicate that stress itself, as induced, e.g., by inescapable shocks, is followed by decreased REM sleep (939, 941–944, 957–960). Conversely, the encoding of fear and fear extinction memory can promote SWS (953). For example, Kumar and Jha (953) observed an increase in SWS after cued fear conditioning in rats. Interestingly, this SWS increase could be prevented when synaptic consolidation processes were disrupted by amygdalar microinjections of the protein synthesis inhibitor anisomycin or by blocking glial-neuronal glutamate transmission by administration of DL-α-amino-adipic acid. Also, contextual fear conditioning increased neuronal firing in the hippocampal CA1 region during subsequent SWS and stabilized the functional connectivity pattern in these networks (assessed by spike-timing clusters), although these changes did not seem to be restricted to SWS (923). There is also evidence from experiments combining behavioral experiments with in vitro whole cell patch-clamp recordings in amygdala slice preparations from rats, showing that cued fear memory recall is linked to network slow oscillation power (0.1–3 Hz) (932).

A different line of research used stimulation techniques, mainly optogenetic stimulation in mice, to manipulate sleep rhythms (like REM sleep theta) or to neuronally reactivate emotional representations during sleep (235, 255, 420, 426, 501, 821, 933, 949, 961–965). For example, optogenetically enhancing or decreasing hippocampal theta activity during REM sleep consistently produced respective enhancing and decreasing effects on subsequent context and cue conditioned fear memory (426). Effects appeared to be independent of whether changes in theta were induced through optogenetic silencing of GABAergic neurons in the medial septum as a main generator of hippocampal theta (420) or via stimulation of the basolateral amygdala (963). Amygdalar stimulation was associated with an activation of basolateral amygdala projections to hippocampal CA3 excitatory as well as inhibitory neurons (for related results, see Ref. 501). An enhancement of fear extinction memory was likewise observed in rats following chemogenetic stimulation of the dorsal hippocampus during REM sleep after extinction training (933), whereas stimulation of hippocampal afferents to the supramammillary nucleus during wakefulness impaired fear extinction. In a discriminative auditory fear conditioning task, optogenetic silencing of vasoactive intestinal peptide-positive (VIP^+) interneurons in the dorsal PFC during REM sleep after conditioning diminished the difference in freezing responses to the conditioned stimulus (CS+) and the nonconditioned safety stimulus (CS−), i.e., the mice showed a generalized freezing response to both kinds of stimuli (949). Silencing parvalbumin-positive (PV^+) interneurons, conversely, increased this difference. The effects appeared to be linked to the generally increased activity of both types of interneurons during REM sleep leading to a somato-dendritic decoupling of cortical pyramidal cells (as PV^+ interneurons inhibit the soma and VIP^+ cells mainly produce a disinhibition of the dendrites of these cells). A study by Kumar et al. (961) linked the REM sleep-dependent formation of context conditioned fear memory to hippocampal neurogenesis. In these experiments, young adult-born neurons in the dentate gyrus spontaneously reactivated during REM sleep following fear conditioning. Optogenetically silencing these neurons during REM sleep altered the structural

remodeling of their dendritic spines and impaired fear memory recall. Enhancing effects on conditioned fear memory were likewise observed following optogenetic manipulations of cortical representations (255, 965). Using a TRAP (targeted recombination in active population) that allows genetic labeling of neurons activated during encoding for subsequent optogenetic stimulation, Clawson et al. (255) showed that the optogenetic reactivation during sleep of primary visual cortex (V1) neurons that encoded the cue of a visually conditioned fear memory produced an increased cue representation in V1, whereas optogenetic inhibition during postconditioning sleep disrupted fear memory consolidation. Also, optogenetically suppressing pyramidal neurons in the infralimbic medial PFC, a key region that mediates fear extinction memory, impaired fear extinction of an auditory-cued fear memory when applied during REM sleep after training (948, 966). In combination, these findings support the view that fear-related memory is strengthened by REM sleep as well as by neuronal reactivations of the respective representations in REM or non-REM sleep.

4.3.9. Reward-associated memory in rodents.

Most studies on the role of sleep in reward-associated memory consolidation in rodents have employed variants of operant conditioning tasks and indicate overall beneficial effects of sleep on these memories (181, 261, 639, 967–972). Importantly, these studies also provided insights into how reward during wake encoding could prioritize the respective memories for undergoing consolidation during subsequent sleep. Yang et al. (967) trained mice on an 8-shaped maze where they received a water reward for alternating between runs through the left or right circle (**FIGURE 9**). During training, the mice exhibited reactivation of the current spatial experience whenever they reached the goal to drink the water, i.e., during reward consumption approximately one-third of detected hippocampal sharp-wave ripples were found to be accompanied by replay of place cell ensembles that were activated in the current run. Importantly, during posttraining sleep sharp-wave ripples primarily reactivated those events that were most often replayed during sharp-wave ripples at reward consumption, suggesting that the SW-Rs accompanying firing replay represent a mechanism tagging the respective representation for enhanced reactivation and consolidation during subsequent SWS. Corroborating these findings, disturbing cholinergic inputs to the hippocampus by optogenetic stimulation of septal neurons during reward consumption in mice that were trained on a reward-based navigation task not only impaired behavioral memory performance on the task but also reduced the occurrence of sharp-wave ripples both during reward consumption at training as well as during subsequent sleep (Ref. 968; for a related review, see also Ref. 973). In addition to sharp-wave ripples, dopaminergic release in response to reward may contribute to determining which cell assemblies are reactivated during subsequent sleep (241, 881).

Although reward at training enhances memory consolidation during sleep by increasing respective replay of rewarded memory, it is currently less clear whether the sleep-dependent consolidation of reward-associated memories also requires the reactivation of neurons representing the reward. Initial studies found replay of neuronal firing in hippocampal networks to precede replay in the VTA, suggesting that the hippocampus drives replay in reward-related regions (260, 974). In rats, hippocampal SW-Rs accompanied the reactivation of reward-related neurons in the nucleus accumbens during postencoding sleep as well as during wakefulness (970). In addition, the sleep-dependent consolidation of food reward-associated memory was found to be associated with increased activity of dopaminergic neurons in the VTA during periods of SWS and quiet wakefulness after learning (261).

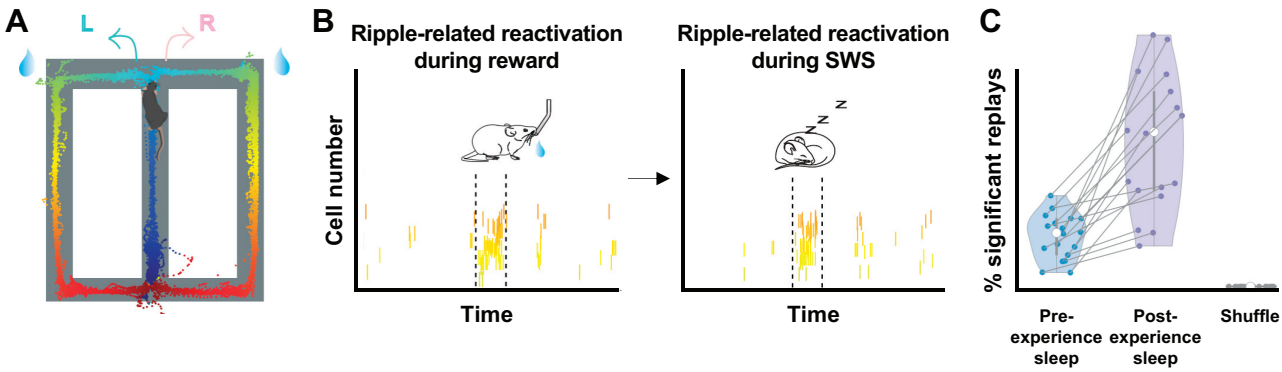

FIGURE 9. Sleep-dependent replay of reward-associated memories. *A*: in an 8-shaped maze task, mice alternated between left (L) and right (R) arms for water reward (blue droplets). *B*: raster plots of neuronal spikes, showing sharp-wave ripple (SW-R)-related reactivation that occurred when the animal stopped for water reward (*left*). This ripple-related reactivation during reward was a strong predictor for ripple-related reactivation during postexperience sleep (*right*). *C*: proportion of replays during pre- and postexperience sleep compared with shuffled data. Adapted from Yang et al. (Ref. 967). Copyright 2024 by The American Association for the Advancement of Science. Reprinted with permission.

Interestingly, in the latter study, mildly aversive stimuli (food pellets containing 2% quinine) that did not demotivate the starved animals were reactivated more often than positive stimuli in the VTA, possibly related to amygdalar interactions (e.g., Ref. 975). However, there is also evidence that reward-related memory reactivations in VTA neurons are diminished during posttraining SWS in comparison with quiet wakefulness (261).

Noteworthy in this context is a study by de Lavilléon et al. (181) showing that during SWS activation of reward-related neurons in the medial forebrain bundle (MFB), another key region mediating reward (976, 977), is sufficient to form reward-associated spatial memories. The authors first demonstrated that MFB stimulation applied during increased firing of putative place cells in hippocampal CA1 while mice explored an arena can induce reward-associated spatial memories, i.e., the mice preferentially visited the arena locations associated with the respective place cells in a subsequent test. In a second experiment, the authors transferred this approach to sleep. This means that the MFB during sleep was stimulated whenever activity of a target place cell (identified during prior wake recordings) exceeded a specific threshold. This procedure led to a marked four- to five-fold increase in the time the mouse spent in the reward-associated place field of the arena during a test after sleep. The majority of these paired MFB stimulations during sleep were triggered upon place cell activation in SWS, with more than one-third occurring during SW-Rs, altogether suggesting that reward-associated memories created during sleep are sufficient to form reward-associated memories that guide behavior during wakefulness (see also Ref. 978).

Overall, these studies indicate that reward enhances SWS-associated consolidation processes, specifically by enhancing neuronal reactivation of hippocampal and associated reward-related circuitries. However, there are also hints, like increased REM sleep following reward-associated learning (979), suggesting that REM sleep could also contribute to reward memory processing in sleep, although findings are inconsistent in this regard (980–982).

4.3.10. Conclusion.

Findings in humans and rodents converge to support the view that sleep critically contributes to the consolidation of emotional and reward-associated memory. This effect pertains to memory both for aversive information, including conditioned fear and extinction memory, as well as for information of positive valence. In humans, prospective memories, related future plans, and intentions as well as anticipated reward show particularly robust benefits from sleep.

Both human and rodent studies also converge in indicating a central role for REM sleep in the consolidation of emotional memory, although more recent findings point to contributions of non-REM as well, which likely reflects the nature of emotional memory as a composite of contextual episodic content and an associated emotional response that are preferentially processed during non-REM and REM sleep, respectively. Context conditioned fear memory, for example, appears to profit from neuronal reactivations of its context aspects in hippocampal networks during non-REM sleep and with regard to the associated emotional response from amygdalar reactivations during REM sleep. The consolidation of reward-associated memories appears to be similarly mediated by an enhanced neuronal reactivation of the episodic content in hippocampal networks during SWS, whereas the role of reactivations of reward-related circuitry, e.g., in the VTA, as well as the role of REM sleep in the consolidation process are currently not clear. The study of reward-associated memory has identified hippocampal sharp-wave ripples and associated neuronal replay at learning during wakefulness as one mechanism tagging memories for subsequent reactivation and consolidation during sleep. It is conceivable that SW-Rs accompanying wake replay also mediate the preferential consolidation of emotional memory during sleep.

4.4. Sleep-Dependent Forgetting

In psychological terms, forgetting refers to the decay of memory traces over time or to retroactive interference. Retroactive interference refers to the fact that older memory traces are not accessible anymore for retrieval because the encoding of new, more or less similar, information has produced traces that superimpose, damage, or even erase the respective old memory traces. Indeed, the enhancing effect of sleep on memory consolidation has been initially explained by sleep protecting newly encoded memories from retroactive interference (7, 11, 115), and there is no doubt that part of the enhancing effect of sleep on memory is due to the fact that sleep is a period of largely diminished encoding of new information that potentially interferes with the consolidation of information encoded before sleep (9, 983). In this vein, numerous studies have shown that sleep, in comparison with wakefulness or any kind of sleep restriction, protects memory from forgetting (e.g., Refs. 984–992) or even leads to an "inverse forgetting" (i.e., it makes episodes that were weakly encoded more accessible; e.g., Ref. 993). In addition, research of the last three decades has accumulated evidence that sleep, beyond passively protecting new memories from interference, actively promotes the consolidation of these newly encoded memories, with the neuronal replay of newly encoded representations representing the core

mechanism supporting such an active systems consolidation process (28, 108). Accordingly, sleep was proposed to "sculpt" memory by concurrent processes of consolidation and forgetting (511, 994–997). Although the gist of experienced episodes is consolidated, the memory for details might be actively erased (134). Thus, the question arises whether sleep, alongside actively strengthening some memories, also actively contributes to the weakening and forgetting of others. Indeed, that sleep favors an active forgetting of irrelevant and "noisy" information encoded during the wake period is also an assumption derived from SHY, posing that sleep downregulates and "renormalizes" synapses, in particular those that were rarely activated during prior wakefulness (112, 113).

4.4.1. Behavioral studies.

Although the idea of sleep supporting an active forgetting process appears conceptually compelling, there is so far little behavioral evidence supporting it. Assuming that sleep-dependent forgetting may particularly occur in conditions of high memory load, a study in humans tested memory for large numbers of word pairs to be learned before periods of sleep or wakefulness (514). Indeed, whereas a sleep-dependent benefit on word pair memory was revealed after learning 160 word pairs, recall after sleep tended to be even worse than after wakefulness when the participants had learned 320 word pairs. However, a subsequent experiment testing memory for even more, i.e., 640, word pairs did not confirm a forgetting effect of sleep, inasmuch as recall was closely comparable between the sleep and wake conditions (Ref. 515, see also Ref. 541). Very similar results were obtained with the DRM paradigm. If sleep induced an active forgetting of episodic details in favor of strengthening the gist, sleep would be expected to lead to a reduced recall of veridical memories for the many words to be learned in this paradigm. However, with some exceptions, most studies using this or similar paradigms did not find the recall of veridical memory to be significantly worse when encoding was followed by sleep in comparison with a wake control condition (132, 175, 176, 537–540, 547–549, 551, 565).

With regard to procedural memory, a daytime nap was found to deteriorate motor adaptation skills on a complex gross motor task, i.e., riding a bicycle with an inverse steering device (748). The accuracy of slalom riding was significantly reduced when the training was followed by a nap in comparison with a wake period. However, this impairing effect of sleep on the same gross motor adaptation task was not confirmed in a follow-up study testing the effects of nocturnal sleep (rather than a nap) in adults and adolescents (746, 747). Overall, these few behavioral findings do not support the view that sleep contributes to an active forgetting of explicitly learned declarative or procedural tasks.

4.4.1.1. FORGETTING OF EMOTIONAL AROUSAL. The putative forgetting function of sleep might pertain to specific aspects of memory, like its emotional tone. The "sleep to remember, sleep to forget" (SRSF) hypothesis proposes that, rather than promoting the forgetting of details of individual experienced episodes, sleep reduces the emotional arousal associated with an episode, with this downtoning of the emotional response mainly taking place during REM sleep (998). Accordingly, impairments of REM sleep and associated decoupling of the emotional reactivity associated with an episodic memory are expected to favor the development of chronic anxiety and PTSD. In line with the SRSF hypothesis, overnight sleep, for example, reduced facial blushing when participants watched a previously recorded video of their own singing in a karaoke paradigm (999). Also, TMR of emotional memories during REM sleep, but not SWS, selectively suppressed arousal associated with the emotional memories (464). There is also evidence that sleep can reduce the dependency of memories on the state of mood in which they were acquired (Ref. 645; see related Refs. 635, 646, 1000). However, contrary to the "sleep to forget, sleep to remember" hypothesis, there are also a substantial number of studies that failed to show that sleep diminishes psychophysiological measures of the emotional response to aversive or positively valenced stimulus materials (1001) (see sect. 4.3 for an in-depth discussion).

4.4.1.2. DIRECTED FORGETTING. "Directed forgetting" can be considered a special type of forgetting with distinct underlying physiological mechanisms. In this paradigm, participants are simply instructed to forget or retain information that was encoded before. Two methods are typically used: In the "list method," after presentation of a list (e.g., of words) participants are asked to remember or forget the list. In the "item method," participants are instructed to remember or forget particular items immediately after their presentation. There is ample evidence that directed forgetting indeed reduces retrievability of to-be-forgotten memories in comparison with to-be-remembered memories (1002–1004). When participants were instructed to remember one half and forget the other half of a word pair list, an early study failed to show an enhancing effect of postencoding sleep on the forgetting of to-be-forgotten memories (1005). On the contrary, late nocturnal REM-rich sleep even improved recall of to-be-forgotten word pairs in comparison with early SWS-rich sleep. Subsequent studies comparing experimental sleep versus wake conditions overall remained inconclusive with regard to a possible enhancing effect of sleep on the forgetting of to-be-forgotten memory (492, 645,

653, 871, 1006–1008), and the same holds true for studies combining directed forgetting with TMR approaches (1009–1011). Note that the interpretation of these overall mixed results is further complicated based on theoretical issues: The directed forgetting paradigm, beyond learning of the item associations, requires the memorization of the task instruction, as a form of prospective memory. Accordingly, the paradigm does not allow for clearly dissociating effects of sleep on the memory for the task from that for the item associations.

4.4.2. SWS-associated mechanisms of forgetting.

Although behavioral evidence supporting an active role of sleep in processes of forgetting is scarce, a number of mechanisms have been proposed that could promote forgetting during SWS as well as REM sleep. At the neuronal level, spontaneous forgetting is assumed to be primarily driven by the depotentiation or erasure of synapses in ensembles that used to store the respective memories.

A contribution of non-REM sleep to forgetting is suggested by results in human studies that indicated a positive correlation between sleep spindle activity and decreases in recall performance across experimental sleep periods (492, 653, 748, 1006). Also, in patients with accelerated forgetting due to epilepsy, unlike in healthy control subjects, the time spent in SWS was positively correlated with the decrease in overnight retention of word pairs (1012). In rats, increases in SWS observed after training on a "delayed non-match to place" working memory task (requiring the animal to maintain a position in space acquired during the sample phase for only 15 s) with minor long-term memory demands were taken to suggest that non-REM sleep and SOs are involved in the forgetting of irrelevant information required only for short-term decisions (1013). By contrast, training on a reference memory task, requiring the animal to retain spatial memories over several days, produced an increase in spindles and REM sleep in this study.

According to these correlational findings, all of the three oscillatory events hallmarking SWS, i.e., SWA, spindles, and ripples, could contribute to forgetting. For spindles, however, a direct causal role in forgetting is unlikely in light of evidence that, rather than with synaptic depotentiation, spindles are associated with signs of synaptic potentiation and enhanced plasticity as well as an increased excitation in respective neocortical circuits (165, 284, 310–313). In fact, mechanisms causing forgetting and synaptic depotentiation during SWS appear to be primarily linked to slow oscillatory activity. Accordingly, the SHY proposes that SWA during non-REM sleep mediates a widespread downregulation of synapses that manifests itself primarily in a decrease in excitatory glutamatergic AMPA receptor signaling including, beyond a profound decease in AMPA receptors containing the GluA1 subunit, also structural changes such as the shrinking and erasure of synaptic buttons (Refs. 112, 113; sect. 2.2). A comparison of effects of total sleep deprivation and selective REM sleep deprivation indicated that the decrease in synaptic AMPA receptor expression is induced by SWS, with no additional contributions by REM sleep (162, 163). However, it is presently not clear whether and how the electrical activity associated with SWA translates into the molecular changes underlying the reduction in synaptic AMPA receptor expression: Immediate early genes, particularly *Homer1* and *Arc*, as well as type 1 metabotropic glutamate receptor 1/5 (mGluR1/5) signaling are important scaling factors implicated in weakening synapses during sleep to restore synapse homeostasis (145, 1014–1017). During wake, *Homer1* and *Arc* are expressed in neurons in response to increased firing activity. Whereas homer1a is prevented from entering synaptic buttons during wake, because of high noradrenaline levels, it binds to mGluR1/5 at the synapse during sleep and thus initiates a sleep-type signaling that promotes broad synaptic downscaling. Specific patterns of phosphorylation at the individual synapse, in combination with *arc* expression, may offer a mechanism that selectively influences the strength of single synapses. However, it is unclear how these possible mechanisms relate to specific sleep stages and their brain activity patterns.

Another unresolved issue arises from contrary findings indicating that SOs, in particular when they nest spindles in their up-state, are associated with signs of increased excitation and synaptic plasticity (e.g., Refs. 311, 312, 1018) and, in humans, have been found to predict increased memory strength rather than forgetting (174, 352, 357). These opposing findings have led to the suggestion of the presence of two different kinds of slow oscillatory waves in the 0.5–4 Hz frequency band, one supporting memory consolidation as reflected by the classical >1-Hz SO and another one, with perhaps a slightly higher frequency content, that supports depotentiation and forgetting (105, 106). This idea of competitive functions of two kinds of slow waves on the consolidation and forgetting of memory is strongly supported by a study in rats by Kim et al. (Ref. 333; see also Ref. 1019; **FIGURE 10**). The authors trained rats on a brain-machine interface (BMI) reward-learning task to control the activity of one or two target neurons in the motor cortex. During the 1-h period of sleep following training, they recorded the reactivations of those motor neuron ensembles that encoded the task at training. Importantly, to disturb these neuronal reactivations, closed-loop optogenetic stimulation was applied whenever the online analysis of the recording identified an up-state (i.e., the depolarizing phase of the oscillation) of either a SO or a delta wave, with delta waves defined by a lack of the pronounced negative down-state

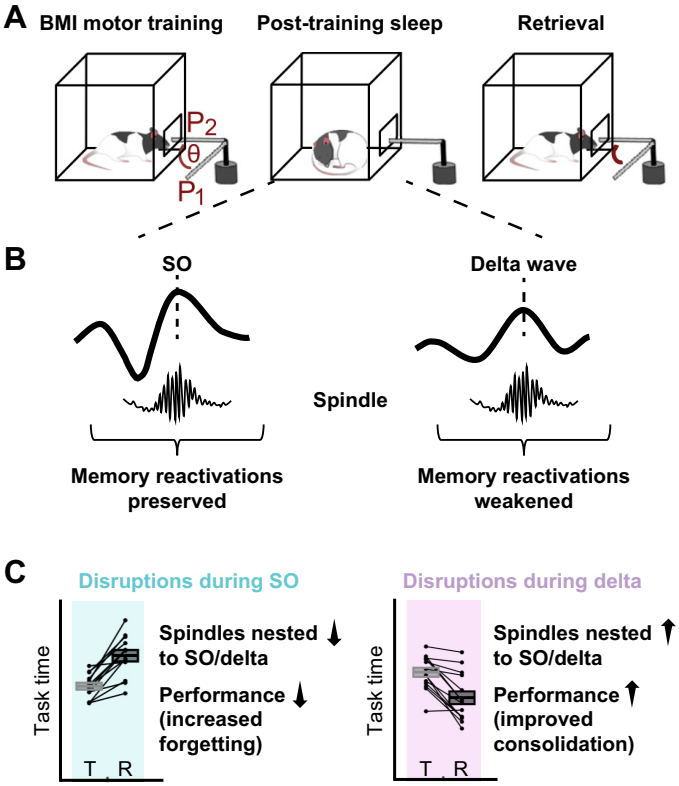

FIGURE 10. Slow oscillations (SOs) support consolidation; delta waves support forgetting on a brain-machine interface (BMI) motor task. *A*: BMI motor task. Rats learned direct neural control of a feeding tube. Successful trials required movement from P_1 to P_2 (via the angle θ) within 15 s. After posttraining sleep, retrieval performance was tested. *B*: up-states of SOs and delta waves both nest spindles and are associated with reactivations of firing patterns in motor cortex neuron ensembles. The strength of reactivations decreased when they occurred during delta waves but was preserved when they occurred during SOs. *C*: in the experiments, reactivations were disrupted either during SO or delta wave up-states. Disruptions of reactivations during SO up-states reduced the proportion of spindles nested to SOs relative to spindles nested to delta waves and subsequently diminished BMI task performance [increase in task time from training (T) to retrieval (R)]. Conversely, disruption of reactivations during delta waves increased the proportion of spindles nested to SOs relative to spindles nested to delta waves and subsequently increased BMI task performance. Adapted from Kim et al. (Ref. 333). Copyright 2019 by Elsevier. Reprinted with permission.

peak that is typical for SOs. Compared with no stimulation or random stimulation as control conditions, disturbing the firing activity during SO up-states decreased overall neuronal reactivations during sleep and, at a postsleep test, impaired BMI task performance. By contrast, disturbing activity during the up-state of delta waves increased the number of reactivations during sleep and increased BMI task performance at the subsequent test. The findings thus link SO-associated firing activity to the consolidation of the acquired memory and delta wave-associated firing to the forgetting of the memory.

A contribution of hippocampal sharp-wave ripples to forgetting has been suggested by experiments in mice where ripples during SWS triggered a long-lasting synaptic depression in CA1 neuron ensembles as indicated by reduced slopes of excitatory postsynaptic potentials (EPSPs) to single-pulse electrical field stimulation (202). This spontaneous synaptic depression did not occur after optogenetically silencing the sharp-wave ripples. Interestingly, silencing hippocampal sharp-wave ripples in mice during sleep following the encoding phase of a standard object-place recognition (OPR) task did not improve, but impaired, recall of the spatial memories at the later test phase, indicating that the ripple-triggered synaptic depression in hippocampal ensembles does not translate into forgetting of the spatial memory on the behavioral level. The finding of a ripple-triggered synaptic depression seemingly conflicts also with evidence indicating that hippocampal spatial representations reactivated during ripples are particularly stable over time (1020, 1021). However, an assessment of place-field and object-related firing during an OPR task in rats revealed that extended periods of SWS following OPR encoding were associated with an increased occurrence of hippocampal ripples and, consequently, led to a stronger decorrelation of firing activity in hippocampal place cells. As a result, this enhanced the degree of remapping in hippocampal place cells during the test phase of the OPR task, triggered by the novel spatial arrangement of the two objects in this phase (1021). Thus, the ripple-triggered synaptic depotentiation and decorrelation of activity in hippocampal place cell ensembles seem to enhance the flexibility of hippocampal networks for encoding novel spatial information. A tempting speculation is that hippocampal ripples accompanying place cell reactivations, on one side, enhance systems consolidation by supporting the transmission of reactivated memory information toward extrahippocampal, mainly neocortical, sites serving as long-term store for these memories. On the other side, ripples through synaptic depression may contribute to the decay of the memory representation, specifically in hippocampal networks, thereby enhancing the network's flexibility to encode new information.

4.4.3. REM sleep-associated mechanisms of forgetting.

REM sleep has been proposed to be involved in so-called "targeted" forgetting, which refers to the depotentiation and erasure of synapses to enable the incorporation of new information into established cognitive schemata (996). Such updating of schema memory has in fact been found to be associated with increased time spent in REM sleep in several studies in humans (e.g., Refs. 437, 628). The concept of targeted forgetting derived from early studies in rodents showing that hippocampal place cells

are reactivated during REM sleep in the peaks of the theta oscillation as long as the encoded environment is novel but reactivations shift to the troughs of the theta oscillation once the environment becomes familiar. The reactivations during theta troughs are assumed to depotentiate synapses and thus to weaken respective memory (408, 410, 1022). In this view, the transfer of memory information mainly during spindle-rich periods of non-REM and, in rodents, pre-REM sleep helps establish representations outside the hippocampus, with the hippocampal representation fading in parallel because of the reactivation of correlated firing patterns during the throughs of the theta cycle. These effects of REM sleep on the hippocampus may additionally depend on input from melanin concentrating hormone (MCH)-producing neurons in the lateral hypothalamus that are specifically active during REM sleep (495, 1023). Activating (or inhibiting) a subpopulation of these MCH neurons projecting to the dorsal hippocampus impaired (or enhanced) hippocampus-dependent memory on a NOR task in mice (1023). The forgetting effect appeared to be mediated by an increased inhibition of dorsal hippocampal pyramidal cell firing.

Another important precondition of synaptic depotentiation occurring during theta activity in hippocampal circuitry is the minimum norepinephrinergic activity with periods of sustained silence of the LC, which is unique to REM sleep (996, 1024–1026). Indeed, periods of LC silence in combination with ongoing theta activity may not only support synaptic depotentiation in hippocampal circuitry keeping spatial representations but likewise contribute to the weakening of emotional response associations mediated via amygdalar circuitry (416, 852, 853). And they might also play a role in shaping cortical circuitry: In juvenile mice, auditory-cued fear conditioning as well as monocular deprivation caused rapid spine elimination in layer V pyramidal cell dendrites in primary visual and frontal cortex areas, respectively, which was distinctly reduced after total sleep deprivation as well as after selective REM sleep deprivation (167). The effect on spine elimination appeared to be mediated through dendritic calcium spikes that substantially increased during REM sleep and could be blocked by administering the NMDA receptor blocker MK801. Similarly, REM sleep in mice increased elimination of new dendritic spines in layer V motor cortex neurons that were formed during prior training on a rotarod motor task (168). REM sleep in these experiments did not affect the elimination rate of old spines that were present already before training. The increased elimination of newly formed spines during REM sleep appeared to facilitate subsequent formation of new spines when the training was shifted to a different motor task (from backward to forward running on the rotarod).

4.4.4. Conclusion.

During both non-REM and REM sleep, mechanisms are at work that mediate synaptic depotentiation and erasure of spines. The mechanisms associated with SWA appear to act globally, inducing depotentiation in widely distributed networks, whereas the mechanisms associated with hippocampal ripples and REM sleep theta activity appear to be more "targeted," pertaining to the weakening of synapses and the elimination of spines that were newly formed during a prior learning period. This overall robust evidence for mechanisms serving the global or targeted downregulation of synapses during sleep stands in stark contrast with the lack of any behavioral evidence for an active forgetting function of sleep. This might be owing to the administration of insufficient behavioral paradigms that do not sensitively reflect any forgetting of "noisy" information. However, in light of the heterogeneity of behavioral paradigms applied so far, it might likewise be justified to conclude that sleep simply does not contribute to forgetting, in behavioral terms (see also Ref. 1027). Given this, it is probably misleading to simply equate behavioral forgetting with a more or less extended weakening of synaptic connections. Rather, processes of synaptic pruning appear to primarily help maintain and shape the newly encoded memories and integrate them with preexisting memories, and such shaping may be optimally achieved during sleep [see Sara response to Poe (2017), Ref. 1026]. Note that in this view memory consolidation and strengthening during sleep also do not necessarily equate to a linear upscaling of contributing synapses.

5. SLEEP AND MEMORY FORMATION ACROSS THE LIFE SPAN

Over the past decade, the number of publications addressing the link between sleep and memory across early development and aging has grown remarkably. This partly reflects the great relevance of the topic for society, which started to perceive sleep as a means to enhance memory function, e.g., in school settings during early life, and to preserve memory function in later life. However, studies at both ends of the life span can also contribute to the basic understanding of the link between sleep and memory, in showing to what extent the development of memory during early life depends on a parallel development of sleep and its memory-relevant features. Similarly, such studies may show that memory failure during aging is critically linked to the loss of specific signatures of sleep, and in this way validate the functional importance of these signatures for memory formation.

5.1. Sleep and Memory during Early Development

During infancy and childhood humans, like other mammals, spend much more time asleep than during adulthood. In parallel, they also form an incredible amount of new memories that eventually guarantee effective adaptation to complex environmental conditions in later life. This apparent parallelism in the amounts of sleep and learning has stimulated the idea that sleep in children may be a particularly sensitive model to analyze the function of sleep for forming memory (108). Implicitly, this idea assumes that sleep-dependent memory formation during early life is the same as in adults but stronger, i.e., directly comparing children and adults is expected to reveal a stronger enhancing effect of sleep on memory in children. Beyond quantitative differences, however, sleep and memory processes likely also differ in quality as well, especially since sleep physiology in infancy is quite different from that of older children and adults.

5.1.1. Development of sleep and oscillatory signatures of memory processing.

Sleep as a brain state distinct from wakefulness is not present from early on but gradually develops in parallel with the emergence of synchronized activity in cortical and hippocampal networks (1028). Human infants before the age of 3 mo do not display consolidated periods of non-REM and REM sleep. Indeed, REM sleep is quite difficult to discriminate in human infants at this age as it occurs often right after sleep onset, including also low-frequency EEG waves, with less pronounced muscle atonia, and often interrupted by small movements and muscle twitches (1029). Reflecting these qualitative differences, sleep stage classification in humans at this age based on polysomnography differentiates between "quiet" and "active" sleep as precursor states of non-REM and REM sleep, respectively. In subsequent life periods sleep also undergoes massive changes. Total sleep time decreases, and there is a change from polyphasic to monophasic distribution of sleep phases, with humans typically stopping napping during the day around the age of 3 yr (1030–1032). In parallel with total sleep time, the time in non-REM and REM sleep also decreases from infancy to early adulthood, with REM sleep commonly thought of as a state particularly involved in the regulation of synaptic plasticity during early life (168, 1033).

The EEG signatures putatively mediating processes of memory consolidation likewise show distinct and partially protracted developmental trajectories during early life, with these trajectories being roughly comparable between humans and rodents (108, 1034–1036). Sleep spindles appear first and, in humans, typically before the third week after birth. Spindles at this time may also intrude into REM-like periods of active sleep (1037, 1038). At roughly the same age, brushes of slow oscillatory activity occur, with mature forms of consolidated SWA and SOs, not emerging until 4–5 mo of age. During the subsequent development, both spindles and SWA show different trajectories, with spindle density reaching an intermediate minimum between the age of 1.7 and 3.0 yr (1037, 1039) whereas SWA shows an inverted U-shaped trajectory with peak values reached at early adolescence. The trajectory of SWA likely reflects parallel changes in cortical synaptic connectivity and white matter microstructure (1040–1043). Importantly, although spindles and SOs emerge already early during infancy, these early activities do not constitute mature, adultlike kinds of the oscillatory events (1042). Thus spindles show, within the first year, a topographical shift from frontopolar to central regions, then shift again toward anterior regions during childhood, and reach their adultlike predominance over central-parietal cortical areas only during adolescence (1044). SO activity during the first 1.5 yr, unlike in older children and adults, appears to dominate over posterior cortical regions, whereas slow-wave amplitudes over frontal cortical regions are rather low (1045–1049). The precise phase-coupling of spindles into the up-state of the SO is another EEG oscillatory signature that has been linked to effective memory consolidation during sleep in adults and adolescents (352, 353, 356). In light of the distinct developmental trajectories of spindles and SWA during sleep, it might surprise that a significantly enhanced SO-spindle co-occurrence has been detected already in 6-mo-olds (1050) although not in 3-mo-olds (Ref. 1049; **FIGURE 11**). However, the spindles co-occurring around SO events at this early stage are not precisely phase-locked to the SO up-state, and thus probably less effective in consolidating memory.

The development of hippocampal SW-Rs has been exclusively studied in rodents. In the hippocampus, "sharp wave burst" can be detected at the end of the first postnatal week in rats as a first organized harbinger event, whereas SW-Rs in combination with place cell firing reactivation patterns do not emerge before the end of the second postnatal week (1051–1053). During early development, i.e., before weaning [at postnatal day (PD)21], the activity of place cells during SW-Rs mainly reflects single locations that the animal had recently visited. Only later in development (PD32), at an age roughly corresponding to midchildhood in humans, does the activity of place cells during SW-Rs become more complex and capable of "stitching" separate locations together into ordered trajectories in space (1051). The coordinate replay of sequential firing patterns in hippocampal place cell ensembles in the presence of SW-Rs during sleep appears to be one of the

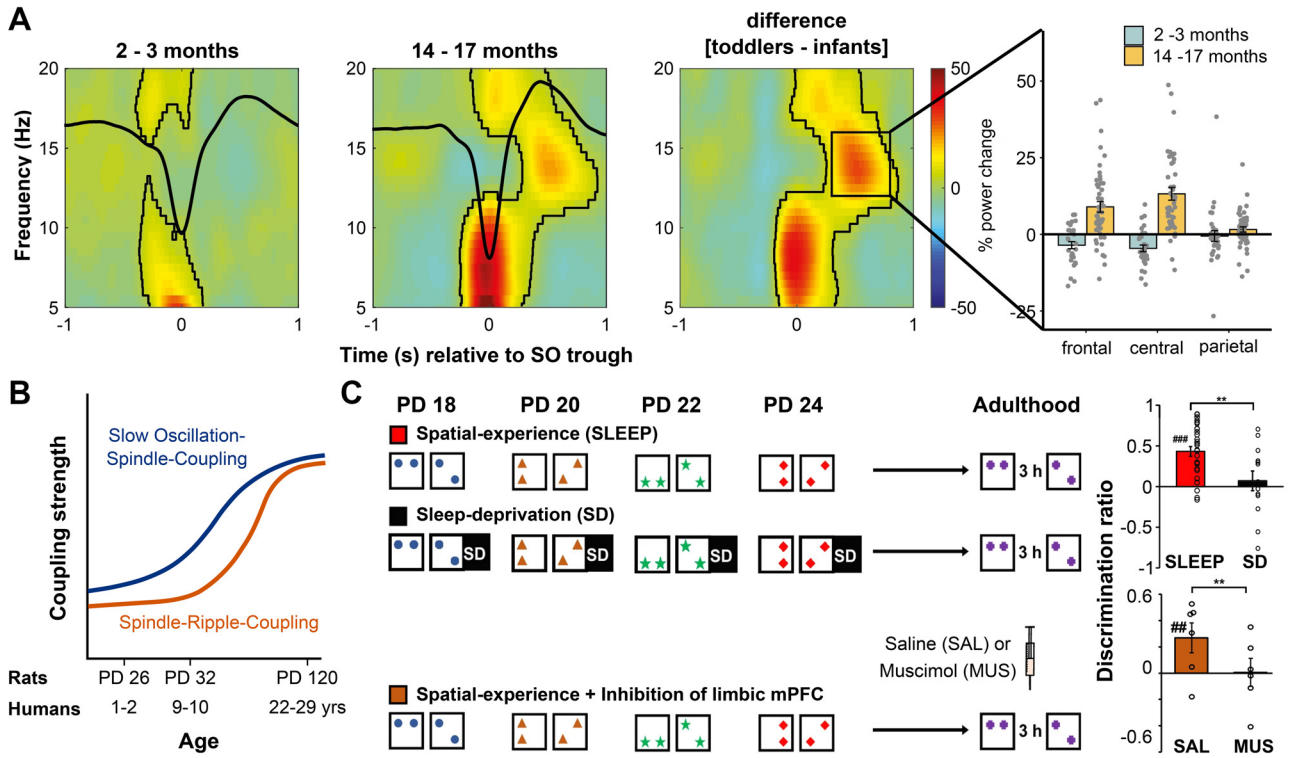

FIGURE 11. Memory formation during early life. *A*: time-frequency representations (TFRs) of EEG power (at Cz) time-locked to SO events in infants (*left*) and toddlers (*center left*) and difference TFR (*center right*), indicating the presence of significant phase-amplitude coupling of 12–16 Hz spindle activity to the SO up-state (300–800 ms) in toddlers but not in infants over frontal and central regions [*right*; adapted from Kurz et al. (Ref. 1049). Reprinted with permission by the author's copyright]. *B*: developmental trajectory of SO-spindle coupling of spindles with hippocampal ripples as obtained from studies in rats, indicating that spindle-ripple coupling develops only during adolescences. Ages roughly comparable to humans are additionally indicated on *x*-axis [adapted from Fechner et al. (Ref. 1046). Reprinted with permission by the author's copyright]. PD, postnatal day. *C*, *top*: rat pups exposed to discrete spatial experiences during their early childhood (PD18, PD20, PD22, PD24) show improved memory performance on an object place recognition (OPR) task when tested during adulthood. The improvement is abolished when the rats are sleep deprived (SD) for 2 h after the childhood experiences or activity of the limbic region of the mPFC is suppressed at adulthood OPR testing (*bottom*). This indicates that postencoding sleep during childhood supports formation of a contextual spatial memory representation in mPFC, $###P < 0.001$, $##P < 0.005$, *t* test against chance level, $**P < 0.005$ for differences between groups [adapted from Contreras et al. (Ref. 525). Reprinted with permission by the author's copyright]. See GLOSSARY for additional abbreviations.

latest emerging signatures of hippocampal activity during early development, possibly reflecting the late postnatal maturation in excitatory synaptic plasticity in hippocampal networks (1054, 1055). Fitting with these findings, significant phase-amplitude coupling of hippocampal ripples to the excitable troughs of the spindle oscillation was not present in rats at PD26 and PD32, i.e., times roughly corresponding to early (1–2 yr) and later (9–10 yr) human childhood, but only in adult animals (Ref. 1046, **FIGURE 11*B***). This lack of precise ripple-spindle phase-coupling suggests that the transfer of replayed hippocampal memory information to extrahippocampal regions is still not optimally functioning during childhood (108, 360). However, the rat pups at both time points, PD26 and PD32, exhibited significant phase-coupling of spindles to the SO up-state, altogether suggesting that childhood sleep affects memory representations more strongly through the synchronized processing within thalamo-cortical networks than through the synchronization of memory information replayed in hippocampal networks.

5.1.2. Development of memory systems.

Research on how memories develop during early life has traditionally focused on the episodic memory system. This is partly owed to the phenomenon of "infantile amnesia," meaning that adults normally cannot remember individual episodes they experienced before the age of 3–4 yr. However, there is also evidence suggesting that infantile memories can be reinstated after they are forgotten later in life by presenting appropriate reminders (1056–1059). In humans, the presence of harbingers of episodic-like memory has been demonstrated in infants as young as 9 mo (1060–1062). However, during infancy the temporal and spatial resolution of such memories as well as their persistence are rather low. The task paradigm most often used to assess episodic-like memory in infants is the deferred imitation task, which assesses the infant's ability to reproduce a puppet's actions previously performed by an experimenter. On this task, 12-mo-olds, but not 6-mo-olds, were able to reproduce a sequence of three actions

shown by the experimenter after a significant delay (1063). The presence of allocentric spatial memory, another harbinger of episodic memory, has been demonstrated in toddlers before the age of 2 yr, who were able to find hidden objects based on distal environmental cues (1064, 1065).

The diminished capability of forming episodic long-term memory during early childhood has been mainly ascribed to the protracted maturation of major contributing structures, i.e., the hippocampus and the PFC (1066). Myelinization of neuron axons in these regions continues into adulthood (1067). Neurogenesis, i.e., the recruitment of young neurons, is at a very high level in hippocampal networks, reaching minimum levels only some time after infancy (1068–1070). Soon after birth, GABA-A receptors, forming the major inhibitory system of the mature brain, show a gradual functional switch from conveying membrane depolarization to hyperpolarization, which appears to go in parallel with the emergence of ripples in hippocampal networks (1051, 1071). Glutamatergic excitatory NMDA receptors, which are widespread in the brain and essential for the induction of synaptic long-term potentiation and synaptic plasticity, undergo distinct changes in their composition of subunits, with the GluN2B subunit being predominant during infancy and the GluN2A subunit becoming predominant later (1072–1074). Such changes are presumably linked to qualitative changes in memory processing and how representations are formed during infancy and early childhood. They may also mark "critical periods," i.e., time windows at certain stages of development during which plasticity in response to experience is heightened in specific brain circuits to enable maturation and the formation of longer-lasting adaptive representations (1075, 1076). Accordingly, the switch toward predominant expression of NMDA receptors with the GluN2A subunit marks the closure of the critical period for ocular dominance plasticity during infancy (1077, 1078). Furthermore, the switch may be likewise implicated in a critical period of hippocampal plasticity during which it gains capabilities to form long-term memory (1057, 1079, 1080). Overall, these changes suggest that sleep-associated memory consolidation during the early postnatal period, i.e., human infancy and toddlerhood, also differs in quality from that during later childhood and adulthood.

5.1.3. Episodic memory and sleep during development.

5.1.3.1. INFANTS AND TODDLERS. To characterize the effect of sleep on the consolidation of episodic memory, Seehagen and colleagues (1081–1084) performed a series of studies using different versions of a deferred imitation paradigm. They assessed memory for a puppet's actions modeled by the experimenter in 6- and 12-mo-old infants. Only infants who had napped (i.e., >30 min of continuous sleep) in a 4-h retention interval showed a significant memory at testing, i.e., imitated more target actions after cuing than control infants who had not napped (1081). The effects of postlearning napping were observed at a 24-h delay and independently of the infant's age. A test at a 4-h delay in the 12-mo-old infants with a novel puppet differing (in color) from that used during the demonstration phase revealed signs of enhanced memory generalization in the infants of the nap group (1082), and the same sleep-dependent enhancement in memory generalization was observed with a slightly different learning procedure (using instead of 1 puppet 3 different puppets) (634). The enhancing effect of a nap on deferred imitation was confirmed in another study in 9-mo-olds who habitually took two naps, a morning and an evening nap (1085). The study compared memory retention in two conditions, one in which the infants had their habitual morning and afternoon naps (Nap-Nap) and the other in which they stayed awake during the time of the morning nap and napped unrestricted during the afternoon (Wake-Nap). Imitation memory tended to be lower after the morning wake interval, and also retention across the afternoon nap was worse after the missing morning nap. SWA during the afternoon nap positively predicted memory retention across this nap in the Nap-Nap condition but not in the Wake-Nap condition. Altogether this suggests that not only a nap itself but also the distribution of naps across daytime plays a role in the memory effect of sleep during infancy. A study in older infants aged 15 and 24 mo showed that imitation memories depend on anticipated relevance and reward (1084). During the learning phase, the experimenter first demonstrated an action on an experimental device that was irrelevant for achieving a desirable outcome (accessing a toy) and then an action that was relevant for achieving it. At the test 24 h later, the relevant actions were imitated more often than irrelevant actions and the 24-mo-olds imitated more than the 15-mo-olds. However, contrary to expectations, napping here did not enhance imitation memory, possibly because of the generally high rates of action imitation and associated ceiling effects.

5.1.3.2. CONFOUNDS. In studies of infants, sleep is typically not directly manipulated but learning and consolidation periods are adapted to the habitual sleep schedule such that the learning phase occurs either before ("nap condition") or after ("no-nap" condition) the infant's habitual napping time, i.e., a procedure possibly confounding effects of (prior) sleep on encoding with those of (postencoding) sleep on consolidation. Such a confound, however, was excluded by studies concentrating on the effects of sleep on encoding. For example, high sleep quality (i.e., a low number of short awakenings) on the

night before the demonstration phase in a deferred imitation task was positively associated with a high reproduction of target actions on a test immediately following the experimenter's demonstration in 6-mo-olds and not in 12-mo-olds (1083). This effect suggests that prior sleep supports memory encoding, and in a no-nap control condition of an experiment testing consolidation effects it would likely enhance rather than diminish the consolidation of imitation memories.

Habitual sleep is another potential confound of infant studies, especially when the nap and no-nap control groups are separated on the basis of a minimum postencoding nap duration (>30 min). Indeed, longer habitual sleep duration was positively associated with memory recall in a deferred imitation task in 6-mo-olds (Ref. 1086; for similar results, see Ref. 1087). In 10-mo-old infants, the frequency of nocturnal awakenings during the week before testing was negatively and the duration of daytime naps positively correlated with the generalization of a modeled event sequence to an analog version of the sequence that was perceptually distinct from, but functionally identical to, the modeled sequence (1088). In ~21-mo-olds, forgetting of imitated actions over a period of 1 mo correlated with poor sleep quality as reported by the parents (1089). Despite the unique difficulties of experimentation with infants, the overall evidence supports the view of an enhancing effect of postencoding sleep on episodic memory representations as assessed in deferred imitation tasks.

5.1.3.3. PRESCHOOLERS AND SCHOOL CHILDREN. Studies in children used a greater variety of tasks and revealed overall more mixed results. Often, they were performed in laboratory conditions but some also in more natural preschool and school settings. In 3- to 5-yr-old preschoolers, in comparison with a wake control condition, in-class naps distinctly enhanced the retention of spatial memories for the location of pictures presented on a grid (1090), and similar nap-dependent enhancements were found at this age for recognition memories of objects and animals (1091). Memory benefits were greatest for children who napped habitually (1090). Significant associations between habitual napping, sleep duration, as well as hippocampal volume and the capability to retain contextual memory (about whether certain facts were taught by a teacher or a puppet) over 1 wk were likewise found in 4- to 6-yr-old preschoolers (1092).

As in preschoolers, a benefiting effect of postlearning sleep on episodic kinds of memory has also been consistently revealed in school-aged children, for longer naps in natural school settings (1093, 1094) as well as in laboratory conditions (1095–1097) (for a review, see Ref. 1098). In 7- to 12-yr-olds, nocturnal sleep significantly enhanced the consolidation of associations between (drawings of) artificial "nonobjects" and their functions (e.g., "with this object you can open any door") (1096). Notably, the sleep effect in children was more robust than in adult control subjects, who did not show significant memory enhancement after sleep compared with a daytime wake condition (for related results, see Refs. 1099, 1100). MEG recordings in children of similar age (8–12.5 yr) tested on basically the same learning task revealed signs of a rapid memory reorganization induced by sleep after encoding (1101). New learning of the associations initially triggered enhanced magnetic responses in hippocampal and parahippocampal regions. However, retrieval after a postencoding 90-min nap was accompanied by increased responses from prefrontal and parietal cortices. In contrast, retrieval after a wake control condition continued to primarily involve hippocampal and parahippocampal regions. Similar signs of sleep promoting the redistribution of memory representations toward cortical and, in particular, prefrontal cortical regions have been observed in adults (e.g., Refs. 120, 122). In comparisons with those findings, however, the sleep-dependent neocorticalization of memory representations in children appeared to proceed at a distinctly faster pace.

The notion of a rapid reorganization of memory representations during sleep in children is also supported by findings by Wilhelm et al. (608). They trained children (~10 yr of age) on a SRTT requiring them to press, repeatedly and as fast as possible, an eight-element sequence of buttons (each lighting up when to be pressed). Training followed an implicit order, i.e., the children did not know the order of buttons to be pressed and when asked immediately after the training they were still largely unaware of the underlying button press sequence. However, when asked after a posttraining period of nocturnal sleep, almost all children showed explicit knowledge of the entire eight-element sequence, whereas no such gains in explicit sequence knowledge emerged after a postencoding daytime wake interval. The sleep-dependent gains of explicit sequence knowledge in children were significantly greater than in sex-matched adult control subjects. Moreover, explicit sequence knowledge at retrieval was positively correlated with EEG SWA during posttraining sleep, which was much higher in the children than the adults. fMRI of the children at retrieval testing revealed that the sleep-dependent increase in sequence knowledge involved enhanced activity in posterior hippocampal as well as neocortical regions, i.e., the superior frontal gyrus and cuneus.

In contrast to these findings, there are also studies showing comparable benefits of sleep for children and adults or even superior benefits for adults (1102, 1103). In 8- to 12 yr-olds, sleep-dependent consolidation of episodic memory on a what-where-when task was comparable to that in adults when retrieval of the original episode was tested, i.e., of exactly the event (in this

case, individual faces) as experienced in a specific spatiotemporal context (1095). Sleep-dependent gains in this study also did not differ between children and adults for a separate assessment of the spatial component (correct "where" responses) of episodic memory and were unrelated to postencoding SWS. Overall, these findings suggest that benefits of sleep on episodic memory in children are not superior to those in adults when retrieval involves genuinely episodic aspects, such as binding the memory of an event to its unique spatiotemporal context. However, children may outperform adults when retrieval specifically involves aspects of memory generalization emerging from the hypothesized transformation of the representation during sleep, which is thought to unbind event features from the hippocampally represented context of the experienced episode (533). Indeed, functional imaging data (608, 1096, 1101) suggest that the transformation of episodic memories during sleep in schoolchildren is associated with the redistribution of the representation toward neocortical, particularly prefrontal cortical, regions and is linked to SWS. It is thus similar to that in adults but, overall, appears to be more effective.

5.1.3.4. COMPARABLE MEMORY AFTER SLEEP AND WAKEFULNESS. Notably, there are also an increasing number of studies in children that failed to reveal a superior effect of postencoding sleep on declarative memory when performance was compared with an equivalent postencoding period of wakefulness (567, 568, 1104, 1105). For example, in 5- to 9-yr-old healthy children and age-matched children with primary snoring and OSA, cued recall of spatial memories did not differ between the postencoding nighttime sleep and daytime wake conditions (1104). Spindle power during N2 of the nocturnal sleep period was positively correlated with memory consolidation in the sleep condition but also in the wake condition. Similarly, in 7- to 11-yr-old children, recall of object-location memories (for card pairs showing the same object) was improved after postencoding nocturnal sleep, in comparison with a daytime wake interval, only when these memories were associated with a high reward. Such negative findings do not necessarily exclude a specific role for sleep in memory formation but suggest that memories can also be consolidated during wakefulness, although through different mechanisms (e.g., Refs. 234, 568). The mechanisms specifically acting during wake consolidation are presently unclear but may also be more effective in children than adults.

5.1.4. Language-related memory.

A number of studies have addressed the question of to what extent sleep supports language learning during development. In theory, language learning during infancy is thought of as a process sharing basic features with the acquisition of declarative memory, where more generalized semantic categories and grammatical rules are abstracted across multiple episodes of audiovisual language experience the infant is exposed to. However, once language representations are well established, the processing of purely verbal stimuli may predominantly rely on language centers of the brain and may lose its strong reference to the basic hippocampus-dependent episodic memory system, putting the individual's experience into a unique spatiotemporal context. Thus, whereas in infants and toddlers recall of memories from a verbal task may strongly engage the hippocampal memory system (e.g., Ref. 1106), in older children and adults hippocampal engagement may be very transient and the recall of verbal materials primarily engage extrahippocampal areas (238, 1107).

To investigate the influence of sleep on language-related memory formation in a very early developmental stage, specifically in 3-mo-olds, Bastian et al. (1108) compared an EEG evoked mismatch response to the word "baby" spoken by an unfamiliar female voice with that to the same word spoken by the mother. The study was based on the assumption that infants at this age already possess long-term memory for their mother's voice. Although in the beginning both voices evoked strongly different mismatch responses, the response to the novel voice became similar to that to the mother's voice when the infants had been familiarized with the novel voice (by reading a story) and subsequently slept for, on average, 64 min. Specifically, after sleep, the response to the familiarized voice, similar to the response to the mother's voice, exhibited a pronounced frontocortical late positivity ~850 ms after stimulus onset. This response may suggest that a more persistent memory representation for the novel voice had been formed. Interestingly, not only nap duration but also spindle activity during the nap were positively correlated with the increase in similarity between both kinds of mismatch responses after sleep.

Studies in older infants and toddlers most often tested the retention of words, nouns and verbs, and their meaning and consistently found a benefit from sleep (1109–1111). In studies involving nouns, children were typically presented with pairs of visually displayed objects and acoustically presented words during encoding. Multiple similar objects were associated with a single word, effectively labeling a category. Recall testing evaluates whether familiar object-word associations are correctly recognized and, in addition, whether the recognition response generalizes to novel object exemplars of a category that the child had not seen during the encoding session. With such an approach, the examination of ERPs and eye movement responses ("preferential looking") showed that a postencoding nap not only enhanced memory for the

familiar object-word associations that were presented during encoding, in infants between 6 and 16 mo, but also enhances the generalization of words to novel object exemplars. In 6- to 9-mo-old infants, only those who napped for >30 min during a 1.5-h retention interval after encoding showed ERP signs of generalization, i.e., an enhanced N400 component to the novel object exemplars. This semantic generalization was linked to an increased sleep spindle activity during the postencoding nap. A similar association between spindle activity and semantic generalization was observed in slightly older infants (9–16 mo) (133). Moreover, enhanced central-parietal spindle activity was also observed during a nap following the encoding of new object-word associations in infants (586), indicating an adjustment of sleep spindle activity to new learning similar to that in adults (1112).

5.1.4.1. TODDLERS. Sleep likewise supports the formation of word categories in toddlers. Werchan and coworkers (569, 1113) examined the effects of daytime naps in combination with subsequent nocturnal sleep in 29- to 36-mo-olds on forming new word-object categories. Of note, during the encoding session of this study the different object exemplars for a category word were presented, on each occasion, in a different context (background color, isolated or in combination with other objects). Accordingly, successful word category abstraction tested at retrieval required not only generalization across similar objects but also an abstraction of the similar objects from the different contexts in which they were experienced, which is difficult at this age (1114). Thus, when asked at a test immediately after the encoding session to identify novel exemplars for a given category, the toddlers did not succeed. They did, however, show successful generalization of a category word to novel object exemplars when tested after a 24-h retention interval including the postencoding nap and nighttime sleep. Word category generalization at this test was superior to that in toddlers who did not nap after encoding but still had normal nighttime sleep. Similar results were obtained in studies of 3- to 4-yr-old preschoolers using nouns instead of verbs (613). These findings overall support the view that naps, in conjunction with a period of nighttime sleep, are most effective in forming generalized semantic long-term representations for words and their meanings (Ref. 471; but see Ref. 623).

Paradoxically, directly comparing the effects of only a single postencoding nap during a 4-h retention interval, Werchan and Gomez (569) found that only toddlers who stayed awake were able to generalize learned word-object associations to similar new object exemplars, pointing to the presence of consolidation processes also during the wake state. Such wake consolidation, relying to a lesser extent on hippocampal reactivations than consolidation during sleep (1106), might strengthen memories for an event independent from the contextual background in which it is experienced (135, 234, 237, 1107) and thereby facilitate the generalization across objects experienced in different contexts. In contrast, sleep, as seen in the nap study by Werchan and Gomez (569), may initially hinder the separation of an object from its context by reactivating and strengthening the hippocampus-dependent contextual background features on which the objects had been presented. This reinforcement could, in turn, impair the ability to generalize to similar objects successfully. Indeed, consolidation during sleep may involve two waves of plasticity, with a first wave acting locally in the hippocampus to confer context specificity and a second acting to stabilize abstracted generalized memory representations in neocortical regions (1115). This concept could well explain that successful generalization of category words to new object exemplars is achieved in toddlers only during nocturnal sleep that follows a midday nap (1113) as well as findings suggesting that napping itself preferentially strengthens the context-bound episodic memory for word-object associations in toddlers (1116). Indeed, napping may preferentially strengthen contextual episodic over more generalized representations already in younger infants (1117).

5.1.4.2. GRAMMAR LEARNING. A few studies have explored how sleep affects grammar learning in young children, mainly building on early findings by Rebecca Gomez's group. These studies demonstrated that in 15-mo-olds, naps following exposure to language (auditory strings of artificial words) promoted memory for the abstract grammatical relationship between the first and last word of the strings. Remarkably, infants were able to generalize to strings that maintained a similar structure but contained different words (1118, 1119). The same group showed in 6.5-mo-olds that sleep, after listening to continuous speech in an artificial language, enhanced the infants' capabilities to abstract and retain words from this language based on the transitional probabilities of the words (1120). Retention correlated, among others, with greater fronto-central SWA. Using ERP responses in conjunction with artificial strings of words, similar to those used by Gomez et al. (1118, 1119), another study demonstrated that 6-mo-olds showed capabilities to abstract memories for nonadjacent grammatical dependencies from similar artificial word strings (1117). However, in this study, the effect was independent of whether the infants had napped or stayed awake after exposure to the strings, consistent with the notion that, in a first wave, consolidation during a nap may mainly act hippocampally to confer contextual specificity and in turn hampers the generalization across different contexts (1115).

5.1.4.3. OLDER CHILDREN. Studies in older preschoolers and schoolchildren provided hints toward enhancing effects of sleep on various aspects of language learning, including forming memories for grammatical rules in spoken sentences of a foreign language (1121) and supporting multisensory-motor training designed to improve reading fluency (1122). However, the bulk of these studies focused on the effect of sleep on learning novel words and their meanings and integration into preexisting lexical networks. Based on the learning of object-word associations, these studies overall confirmed an improving effect of sleep after learning on explicit knowledge of words (1123–1126). Henderson et al. (1126), for example, used a more naturalistic approach in which 5- to 7-yr-olds were read a story containing 12 novel words with illustrations by their parents, either at bedtime or 3–5 h before. The children's memory for the words was tested immediately after reading the story and on the following morning with a cued recall procedure, i.e., prompting the child to recall the word by providing the initial syllable as a cue (test of word production), and a recognition task where the child was presented with the spoken word and had to select out of four different pictures the one illustrating the associated object (test of word comprehension). In comparison with immediate recall performance, the children showed overnight improvements in both word production and comprehension tests, with the improvements being larger for reading 3–5 h before than immediately before bedtime. Overnight improvements in word production and word comprehension were likewise observed in 8- to 12-yr-old children (1127). How these memory benefits were linked to EEG signatures of memory processing during postencoding sleep remained obscure, with one study reporting a positive correlation with spindle density (1123) and others with SWA and REM sleep duration (1124, 1125). In 5- to 7-yr-olds, the beneficial effect was larger in children with larger preexisting vocabulary (1126), suggesting that sleep influences the integration of novel words into lexical long-term stores. However, in older children the sleep effect was independent of, or even negatively correlated with, the child's prior knowledge of vocabulary (1127, 1128).

More thorough examinations indeed show that sleep supports the integration of novel words into preexisting lexical networks (e.g., Refs. 1123, 1129–1131). Lexical integration in some of these studies was measured by probing "lexical competition": When, for example, the participant had learned to associate the novel word "biscal" with a certain object, in the later test session this object was then presented together with another known object with a phonologically similar name, e.g., "biscuit." Participants were then asked to "click on the biscuit" as fast as possible. It is assumed that once a fully fledged representation of the novel words, integrating phonological and semantic features, has been developed in the lexical store, competition and interference with responses to well-integrated known words arises, which in turn slows the response to these known words. In 7- to 8-yr-olds, lexical competition effects emerged already after the learning session, but the effect was distinctly increased on the next day after a period of overnight sleep and even superior to that seen in a group of adult participants (1123). Very similar results with signs of sleep-dependent lexical integration being stronger than in adults were obtained in several foregoing studies (1129–1132). The enhancing effect of sleep on lexical integration, emerging with some delay after encoding, has been taken to propose that word learning in children follows the same active systems consolidation process as described for episodic memory formation (1132, 1133), where the encoding of a new word rapidly leads to the formation of a hippocampal memory trace and, over time and particularly during sleep, a longer-term representation is strengthened and formed within the neocortical lexical network. However, there are also findings pointing to specificities in the processing of word materials during sleep in children (632) as well as studies that failed to show an improving influence of sleep, in comparison with postencoding periods of wakefulness, on memory for verbal materials (e.g., Refs. 567, 1134).

5.1.5. Emotional memory and procedural skills.

Emotional memory has often been examined in clinically oriented studies comparing typically developing (school) children and children with various pediatric diseases, like attention deficit hyperactivity disorder (ADHD) and autism spectrum disorder (ASD). For typically developing children, these studies revealed enhancing effects of postencoding sleep in quite different tasks, such as the recognition of affective pictures, rewarded memories in an object-location learning task, and the recognition of emotion-expressing faces (1099, 1105, 1135). However, there are also a considerable number of studies that failed to reveal sleep-dependent improvements in memory for emotional materials (e.g., Refs. 567, 1102, 1134). For example, opposing findings in adults, in 8- to 12-yr-olds recognition memories for more or less pleasant odor stimuli appeared to weaken across a nocturnal sleep period compared with a wake control condition (1102, 1136). Additionally, sleep in 8- to 12-yr-olds did not affect the emotional enhancement in memory on an affective picture recognition task (567, 864).

As to the arousal response to emotional stimuli, findings point to a deceasing effect of sleep, although with some inconsistency across studies (864, 1137). Typically developing adolescents between 10 and 18 yr showed a decrease in ratings of arousal to negative imagery after a period of nocturnal sleep, which was not seen in age-matched control subjects with PTSD (1138). In 8- to 11-yr-

olds, arousal ratings and signs of emotional processing in the evoked brain response to aversive pictures were decreased after a period of postencoding nocturnal sleep in comparison with a daytime wake period (864). However, in this study heart rate deceleration responses to the aversive stimuli were increased after sleep. As memory for the pictures was generally enhanced after sleep, the increased "automatic" emotional heart rate deceleration response might be considered a consequence of the strengthened "cognitive" content memory for the respective pictures.

Sleep-dependent offline gains on motor skills observed in schoolchildren are rather similar to those in adults (615, 677, 680, 692, 754, 1139, 1140). Benefits, e.g., in finger sequence tapping, were independent of the circadian phase and greater for younger children (677, 692). However, there were also aspects that appeared to be specific to children: Unlike in adults, in 10-yr-olds only accuracy, and not speed, in the finger sequence tapping depended on posttraining sleep (680). Compared with adults, 9-yr-olds showed a more rapid stabilization of finger tapping skills during the wake period immediately following the training, making the acquired skill less sensitive to interference learning (1139, 1140). In 8- to 12-yr-old children long-term training benefits after 1 wk were unrelated to improvements after the night following the first training (615). Also, the benefit of sleep after observational learning on a motor task appeared to be less pronounced in 9- to 12-yr-olds than in adults (684). Overall, sleep-wake comparisons of finger sequence tapping skills indeed point to differences in skill consolidation between children and adults. However, these differences appear to be more related to differences in wake consolidation processes, e.g., a more rapid stabilization of skill memory during the posttraining wake period in children, than to the consolidation during sleep.

Also on other skill tasks, the pattern of sleep effects in children resembled that in adults. For example, as in adults (e.g., Ref. 731), sleep did not induce behavioral gains on tasks requiring simple or complex motor adaptation in 10- to 14-yr-old children (746, 750). Nevertheless, in 10- to 12-yr-olds, a motor adaptation task (motor rotation), trained before sleep, induced greater proactive interference on learning of a new task (performed immediately after testing the old task), indicating a strengthening effect of sleep on these memories (750). Sleep in children likewise enhanced cognitive skills (1141, 1142). On an *n*-back working memory task, sleep after training in 10- to 12-yr-old children induced the same performance gain as in adults when measured in absolute terms (i.e., the difference in performance at test minus performance at the end of training) (1142). However, because of the lower baseline working memory performance in children, gains in children were greater than those in adults if expressed as percent changes in performance at the end of the training, which illustrates the general difficulty of directly comparing behavior in children with that in adults.

5.1.6. Mechanisms of sleep-dependent consolidation during early development.

5.1.6.1. STUDIES IN HUMANS. Findings in human participants link memory formation during sleep to the expression of spindles from early on. For example, in 3-mo-olds, signs of memory formation (for a newly acquired female voice) during a nap correlated with parameters of spindle activity over frontocortical regions (1108). Similar positive correlations have been reported for older infants, toddlers, preschoolers, and schoolchildren and in vastly differing memory tasks, with spindle density and amplitude overall representing the spindle parameters most sensitively linked to the memory function (e.g., Refs. 614, 615, 680, 1090, 1104, 1143). Although spindle activity in most of these studies was assessed during the experimental postencoding sleep period, the increased spindle activity accompanying enhanced memory formation partly reflects a more enduring traitlike condition in the children (1104, 1144). In 5- to 9-yr-olds, spindle power during N2 sleep was positively correlated with enhancements in spatial memory not only in the sleep condition but after the postencoding wake interval (1104). Beyond supporting consolidation of specific memories, sleep spindles during early development probably also support the maturation of respective memory systems (614).

Parameters of slow oscillatory activity were not consistently linked to behavioral measures of memory consolidation, but SOs appear to mainly contribute to memory consolidation in children when they occur together with spindles (177, 353, 568, 1143, 1145). The phase-coupling of spindles into the SO up-state becomes increasingly precise throughout childhood and adolescence, along with an increased capability to form memories for word pairs and procedural juggling skills across sleep (353, 1145). Similarly, in schoolchildren across a wide age range (7–15 yr) recall of word lists after a period of postencoding sleep was better when spindles were strongly phase-coupled to the SO up-state (568). Notably, this relationship occurred independent of the children's age, supporting the view that at this age phase-locking of spindles to the SO up-state is firmly established as a mechanism of memory consolidation. In younger 5- to 6-yr-old preschool children, SO-spindle coupling was less precise and not significantly related to episodic memory formation for object-scene associations (1146). Indeed, these studies in humans suggest that the development of precise SO-spindle coupling is closely connected to the maturation of fast spindles and starts to effectively support consolidation processes only around school age.

There is, moreover, indirect evidence from fMRI studies in sleeping toddlers that episodic memory formation during sleep at this age, as in adults, also involves hippocampal activation (1147, 1148). In these studies, 2-yr-olds were familiarized with different rooms in which they played with different toys while listening to specific songs serving as further contextual stimuli. They were later asked where and in the presence of which toy they heard the song. During a fMRI session on a subsequent day, a TMR procedure was applied, i.e., while the child was sleeping they were presented with 20-s blocks of the learned and a novel song. The learned song produced a distinctly greater hippocampal activation than the novel song, and this activation was higher in the toddlers who did remember the episode where they had heard the song (1148). These findings were confirmed in a second study using a different task (tablet games), with the song-induced hippocampal reactivations in the sleeping toddlers correlating in particular with temporal order aspects of the recalled episode (1149).

5.1.6.2. STUDIES IN RODENTS. There are only a handful of studies in developing animals that which relate behavioral indicators of memory consolidation during sleep to underlying neurophysiological mechanisms. The findings corroborate the importance of sleep spindles for the consolidation process. García-Pérez et al. (1150) tested rat pups on PD26, PD28, PD30, and PD32 (i.e., a time roughly corresponding to the range from toddlerhood to later childhood in humans) on a hippocampus-dependent OPR task using a longer than usual 3-h delay between encoding and retrieval testing. On this task, the pups exhibited persistent OPR memory only after PD28. The increased memory with increasing age was paralleled by an increase in spindle density and SO-spindle coupling strength. The data, however, did not allow for separation of the maturational effect of age itself from that of memory-related neuronal processing.

To what extent sleep-dependent memory consolidation in developing rodents involves hippocampal ripples and their coupling with thalamo-cortical spindles and SOs is currently not clear (1046). Hints at hippocampal contributions are provided by findings indicating that the ripple-related activities can be enhanced by discrete prior experience (1151). In these experiments, juvenile rats were exposed for 5-min periods to changes in the spatial configuration of two identical objects on PD25, PD27, and PD29. When tested on an OPR task, with a 3-h delay between encoding and test, on PD31, these rats showed significant memory, whereas rats of a control group without the prior spatial experiences did not form any significant OPR memory. Importantly, analysis of sleep during the 3-h delay on the OPR task indicated that OPR memory formation in rats with prior spatial experience was accompanied by an increased percentage of hippocampal ripples coupled to parietal SO-spindle complexes as well as enhanced ripple-spindle phase-locking during the retention sleep. Overall, these findings support the idea that experience promotes the functional maturation of the hippocampus-dependent episodic memory system during development by enhancing the finely timed processing of memory information in hippocampal and neocortical networks during sleep.

Such synchronized processing in hippocampal and neocortical networks may ultimately serve the transformation of episodic representations into long-term representations residing in neocortical networks, in particular mPFC areas. Rats that were exposed, on four different days during their infancy, to discrete spatial experience (a change in the configuration of 2 objects) showed enhanced capabilities to form spatial representations at a test in adulthood compared to control rats without such infantile experience (Ref. 525; **FIGURE 11C**). The beneficial effect of the infantile experience was abolished when the rats were kept awake during the 2 h after the experience. Further experiments showed that the adult rats' improved spatial capabilities were mainly based on memory for spatial context information that was formed during the infantile experiences in the prelimbic mPFC rather than the hippocampus. Accordingly, inhibiting the prelimbic mPFC at testing during adulthood abolished the enhancing effect of infantile experience. The spatial experiences benefited adult learning capabilities only when they occurred during a sensitive period of infancy but not when occurring later during childhood. Collectively, these findings are in line with the notion that sleep transforms memories of new encoded episodes into more abstract representations that essentially involve the mPFC and can be used as generalized reference facilitating behavioral adaptation in similar contexts during later life. During early development, this transformation appears to occur at a more rapid rate than in adulthood, a conclusion that has been likewise drawn based on findings in humans (1101).

Sleep, indeed, appears to particularly enhance synaptic plasticity in neocortical networks during early development (167, 168, 1152). In juvenile 1-mo-old mice, sleep after motor training promoted the formation of dendritic filopodia and their conversion into new spines in layer 5 pyramidal neurons of the primary motor cortex (1152). Interestingly, sleep after a second motor training promoted formation of new spines more directly, i.e., without prior emergence of dendritic filopodia. Monocular deprivation in mice at the same juvenile age produced rapid spine elimination in the visual cortex, which was distinctly reduced after REM sleep deprivation (167). A similar REM sleep-dependent increase in spine elimination was observed in frontal cortex areas after cued fear

conditioning. The elimination mainly pertained to subsets of synapses newly formed after the experimental experiences and thereby probably helps shape the respective memory representations (168). Overall, these findings in the juvenile brain align with the view proposed for adulthood regarding a fundamental division of labor in synapse regulation: SWS supports the experience-dependent formation of new synapses in the neocortex, whereas REM sleep facilitates the experience-dependent pruning of established synaptic connections.

5.1.7. Song learning in birds.

Song learning in juvenile birds is considered a model of human language learning and has also been found to depend on sleep, although some findings question the contributions of sleep (1153). Birds like zebra finches develop their song in two steps between 30 and 90 days after hatching. First, a template of a tutored song is formed. Second, the bird learns the song by imitation and auditory feedback. Song learning is accompanied by an increased sleep need (31, 1154). A dependency of song learning on sleep was first demonstrated by Derégnaucourt et al. (1155). The juvenile zebra finches of that study improved their song quality during the day because of intense practice, but unlike procedural skills in children (1142), song structure and quality deteriorated across nocturnal sleep. However, the birds with the strongest song deterioration after sleep were the best learners in the long run. An acutely deteriorating effect of sleep on song quality has been confirmed in more recent studies (e.g., Refs. 1156, 1157).

The mechanisms underlying the sleep-dependent dynamics in song learning are presently not clear. Memory consolidation during sleep in birds, as in mammals, appears to originate from neuronal reactivations of newly encoded song representations during sleep. Song processing in birds centrally involves three brain structures, i.e., *1*) the caudomedial nidopallium (NCM), which has been considered the avian equivalent of the Wernicke area, and *2*) the so-called high vocal center (HVC), which is a premotor-association region thought of as an analog to the human Broca area and which projects to motor pathways via the *3*) robust nucleus of the arcopallium (RA) (1158). The NCM is assumed to contain the neural template for the tutored song (1159). After tutor song experience, a small subset of NCM neurons exhibit highly selective auditory responses to the tutor song, which is decreased after sleep or blockade of GABAergic inhibition (1156). Reactivations of song-related firing patterns during sleep have been identified in the RA, probably driven by reactivations in HVC neurons (195, 1160–1162). Such bursting activity in RA neurons during sleep presumably reflects an integration of the tutored song with auditory feedback information from the bird's own singing. Thus, greater mismatch between the tutored song and the feedback from the bird's own singing has been proposed as an explanation of the acutely deteriorating effects of sleep on song quality, which is most pronounced in the beginning of the learning period. Reactivations during sleep may primarily stabilize inhibitory neuron ensembles. This is suggested by studies of HVC neuron ensembles involved in song production in adult zebra finches, where activity in excitatory neuron ensembles displayed particularly strong changes across sleep periods whereas activity in ensembles dominated by inhibition remained unchanged (1163). Beyond that, the sleep-dependent systems consolidation process may promote the formation of a more lateralized representation to the left NCM (1164) and of separate supraordinate song representation downstream from the initial NCM representation (31, 1165). Interestingly, signs of song reactivations during sleep were also found in suboscines, i.e., birds developing their song innately without the need for acoustic models or auditory feedback, suggesting that neuronal reactivations during sleep evolved as a basic mechanism of behavioral maintenance independent of the amount of new learning required (Ref. 1166, but see Ref. 1167).

5.1.8. Conclusion.

Whereas the number of studies on the early development of sleep and memory was rather small up until 10 years ago (5), the interest in this topic rapidly grew in the last years. The bulk of these studies confirmed that sleep promotes the formation of long-term memory and underlying plasticity also during early development. This effect may even be superior to that in adulthood. Findings in rodents and humans suggest that sleep during early development particularly promotes the fast emergence of more abstract representations in the neocortex, mainly mPFC networks. In stark contrast, the underlying hippocampal and neocortical circuitry appears to be functionally immature, specifically with regard to the fine-tuned interaction between these structures. This functional immaturity in conjunction with the, in certain aspects even superior, memory formation during sleep challenges the view that during early development active systems consolidation during sleep is established in basically the same way as in adulthood. Instead, memory processing in the developing brain may be organized more in parallel at hippocampal and neocortical levels. This organization, driven by a generally increased sleep-dependent plasticity, produces stronger transformations at the neocortical level. There are also a notable number of sleep-wake comparisons that failed to reveal superior memory effects of sleep, particularly in older children. Such findings may point to a greater relevance of consolidation processes taking place during wakefulness in children, with

the mechanisms differing from those during sleep. Also, memory processing may differ at different ages during development. Thus, the central question to be solved in future research is to what extent memory formation during sleep (and possibly also during wakefulness) in infants relies on distinct mechanisms, and at what age these mechanisms become comparable with active systems consolidation processes as observed in adults.

5.2. *From Adulthood to Old Age*

Although the memory function of sleep has been most extensively researched in younger healthy adults (18–35 yr), it is middle-aged (35–60 yr) and especially older (usually >60 yr) individuals who suffer most from sleep loss and are most affected by cognitive decline. Sleep disturbances and cognitive impairment are common in older adults (1168–1178), and many studies have documented specific deficits in declarative and procedural memory formation in these individuals (for reviews, see Refs. 1179–1184). In addition, a growing body of research suggests that sleep disturbances in older adults contribute to the effects of age-related long-term memory impairment (903, 904, 1185–1210).

5.2.1. Alterations of sleep in aged individuals.

Compared with younger individuals, sleep in older healthy adults is characterized by macrostructural alterations (1211), including shorter overall sleep durations, longer sleep latencies, more fragmented sleep, more wake after sleep onset (WASO), and, importantly, less time in SWS (1211–1215). These changes often co-occur with excessive daytime sleepiness and increased daytime naps in older adults (1216). The age-related decrease in SWS depends on sex, with men (<55 yr) showing a more than threefold decrease in the amount of SWS compared with women of the same age (1217, 1218).

The reduction in SWS is further associated with an age-related reduction in amplitude, density, and slope of slow waves (1219, 1220), with the largest decreases in slow-wave amplitude and density observed over frontal cortical areas (1219) (**FIGURE 12**). Accordingly, significant reductions in SWA and delta power have also been seen in middle-aged and, especially, older adults (1214, 1221–1224). Also, sleep spindles undergo significant changes during aging. Spectral EEG power in the sleep spindle frequency range (12–15 Hz) is reduced in middle-aged and older adults relative to younger adults (1214, 1223–1226), with the strongest decline also occurring over frontal cortical areas (1225, 1227, 1228). In addition, the number, duration, peak, and mean amplitude of sleep spindles were found to be decreased in older adults (1225, 1227–1229), with spindle duration decreasing more in posterior than anterior EEG (1228) (**FIGURE 12**).

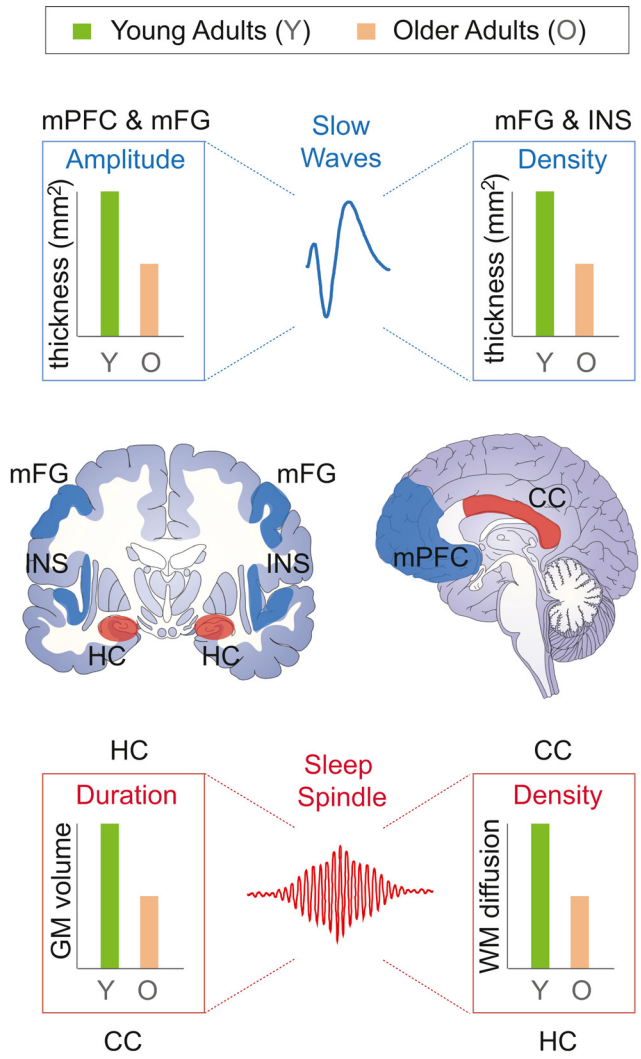

FIGURE 12. Summary of structural brain changes and age-related impairments in non-REM sleep oscillations. *Top* and *middle*: age-related deficits in non-REM slow-wave amplitude and density are significantly associated with the degree of reduced gray matter (GM) volume and thickness (*middle*; blue regions) in the medial prefrontal cortex (mPFC), middle frontal gyrus (mFG), and insula (INS) in older (orange) relative to younger (green) adults. Impairments in non-REM sleep spindle duration and density (*bottom right* bar graph) reductions in older (orange) relative to younger (green) adults are associated with the magnitude of decreased hippocampal (HC) GM volume and white matter (WM) integrity within the body and splenium of the corpus callosum (CC) (*middle*; red regions, lower image). See GLOSSARY for additional abbreviations. Figure from Mander et al. (Ref. 1211). Copyright 2017 by Elsevier. Reprinted with permission.

REM sleep parameters are altered as well in aged people, although these changes appear to be more subtle and mostly occur at very old age (>80 yr) (1215, 1223, 1230). A meta-analysis identified the percentage of REM sleep time and REM sleep latency to slightly, but significantly, decrease during aging (1215). EEG theta power as well as coherence, as a measure of functional

connectivity between distant brain areas, during REM sleep appeared to be increased with age (1226). In another study, the EEG during REM sleep in older compared with younger participants displayed lower proportions of rhythmic theta (as well as alpha) activity, and this decrease was associated in both age groups with diminished dream recall (1231). Increased EEG theta power during REM sleep was linked to better subjective sleep quality and a diminished (wake) LC activity in older but not in younger adults, suggesting that the increase in theta activity in older people marks a more consolidated form of REM sleep (1202).

The diminished expression of SWS hallmarking sleep in healthy older adults is partly a consequence of a diminished homeostatic sleep regulation in these individuals (1211, 1232, 1233). Typically, longer periods of wakefulness produce a rebound in SWA during subsequent sleep, which declines across the night in young adults, reflecting a homeostatic dissipation of the sleep pressure (1234). In older adults, this homeostatic increase in SWA subsequent to longer periods of wakefulness (or SWS disruption) is distinctly weaker (1221, 1235, 1236), and also the slope of the subsequent decline in SWA across the night is more shallow (1214, 1221).

Signs of impaired sleep and a diminished homeostatic sleep regulation in the aged brain are likewise observed in animal models such as *Drosophila* (e.g., Ref. 1237), with older flies (35 days old) showing more fragmented sleep and reduced total sleep time than younger (8 days) flies. In conditions of chronic sleep restriction (3 h per night for multiple nights), older flies recovered much less sleep than younger flies. Similarly, older mice (18–24 mo) showed a slower decline in SWA rebound following sleep deprivation in comparison with younger mice (6 mo) (1238). However, as to the homeostatic regulation of sleep, studies in mice also revealed noticeable differences from humans (1232, 1239, 1240). For example, aging in mice was associated with an increased rather than decreased sleep duration, as well as with higher EEG SWA during non-REM sleep (1238–1241), suggesting that in mice, unlike in humans, aging is associated with an increased need to sleep (1238, 1239).

Beyond a reduced homeostatic sleep regulation, several other mechanisms have been linked to the decline of sleep quality during aging. The number of neurons in the hypothalamic preoptic area expressing the inhibitory neuropeptide galanin, known to play a critical role in maintaining sustained sleep (1242, 1243), was found to decline with age in humans (1244). The severity of the decline predicted the severity of sleep fragmentation. Hypocretin/orexin-expressing neurons in the lateral hypothalamus may also play a role. These neurons contribute to maintaining wake states (1242) and appear to undergo a comparable age-dependent deterioration in rodents as well as humans (1245–1247). Several studies in humans have linked the reduced sleep quality in older individuals to a thinning of cortical gray matter (Ref. 1248; see also Refs. 1220, 1222, 1249–1251).

5.2.2. Sleep-dependent episodic memory consolidation in older adults.

Given the marked alterations in sleep, it does not come as a surprise that the consolidation of memory is overall diminished in older age. In fact, a growing body of research suggests a connection between poor sleep and memory formation in the aging population, with most studies focusing on the hippocampus-dependent episodic memory system. But, noteworthy, there are also a few reports of stronger sleep effects in older compared with younger adults. For example, sleep in comparison with a postencoding wake period enhanced memory for stories and personal events in both young (19–29 yr) and older (69–80 yr) adults, with total sleep time being predictive of the sleep benefit only in the older adults (1252). Similarly, sleep produced a benefit for the consolidation of episodic memory in a what-where-when task in both young (~22 yr) and older (~69 yr) adults, with the benefit in older participants being even superior to that in younger ones (1253). Older adults showed a significant enhancement in the recall not only of factual elements of the to-be-remembered episodes but also of associated details and contextual information as well as in the amount of feature binding in the task.

The majority of findings, however, indicate a less effective memory consolidation during sleep in older in comparison to younger adults (1254–1256). For example, in older adults (~69 yr) postencoding sleep, in comparison with wakefulness, had a weaker enhancing effect on the retention of visuospatial object-location associations than in young adults (1254). In another study (1255), recall of word-picture associations 1 wk after encoding was lower in older (65–75 yr) than young (18–30 yr) adults, and only in the older participants did recall performance correlate negatively with the number of self-reported awakenings during nighttime sleep. Studies of daytime naps likewise indicated a less effective memory consolidation in older adults. Scullin et al. (1256), for example, report an enhancing effect of a 90-min daytime nap over an equivalent period of quiet wakefulness on the retention of words only in young (18–29 yr) and not in community-dwelling older (58–83 yr) adults. The difference was independent of whether the words were instructed to be remembered or to be forgotten (see sect. 4.4). Although these behavioral findings appear to be overall rather consistent, conclusions nevertheless need to be drawn with caution because older adults differ from younger adults also in regard to encoding and retrieval functions. These confounds hamper the straightforward dissociation of age-dependent changes in the consolidation process.

5.2.2.1. THE ROLE OF SWS. As SWS is mostly affected by aging, many studies have focused on the link between memory consolidation and SWS-related measures. However, the findings overall provide a rather mixed picture. Some studies, indeed, found significant associations of signs of diminished SWS with impaired sleep-dependent memory consolidation in the elderly (e.g., Refs. 1257, 1258). For example, in one study (1257) the percentage of SWS was positively correlated with enhanced memory for word lists only in older adults (mean age 70 yr) who actually displayed SWS. In participants who did not show SWS, overnight memory consolidation was associated with slow oscillatory power during non-REM sleep, but only in the first sleep cycle. In middle-aged (48–55 yr) adults, reduced time spent in SWS during the first half of the night following learning of word pairs was linked to a worse retrieval of word pairs compared with young adults (1258). A 90-min nap (mainly containing non-REM sleep) following training on the Tower of Hanoi problem-solving task enhanced subsequent performance in young (20–35 yr) but not older (60–85 yr) participants (662). fMRI indicated that the nap led to a transformation of the task representation in hippocampal and neocortical networks only in younger study participants.

However, other studies failed to find the link to SWS parameters in older adults (e.g., Refs. 1222, 1259–1262). For instance, one study (1259) reported a positive correlation between the percentage of SWS and the retention of word pair memories for young study participants, but this relationship did not emerge in the older participants (mean age 71 yr). Very comparable results were obtained in a study examining postencoding daytime naps in older adults (60–75 yr) (1260). In the older participants of this study, memory recall after the nap was associated with a stronger functional connectivity between hippocampus and PFC. Yet there are also opposite findings pointing to a reduced hippocampal-PFC functional connectivity in connection with impaired word pair retention across sleep in older adults (mean age 72 yr) (1222). In this study, the memory impairment in the older participants was additionally associated with the extent of gray matter atrophy in the mPFC (for related results, see Ref. 1261). In the DRM paradigm, longer time spent in SWS in older adults (~67 yr) was not positively but negatively correlated with the recognition of critical lures, i.e., gist memory (538). This negative association, however, is not specific to older people but was likewise observed in younger participants in DRM-like tasks, and possibly reflects specificities related to the abstraction of gist memory required in such tasks (Refs. 175, 177, 538, 551, see sect. 4.2.1).

As to the microarchitecture of non-REM sleep, findings were more consistent. Decreases in SWA, especially over anterior cortex regions, during nighttime sleep in healthy older adults were robustly correlated with impaired overnight consolidation of word pair and three-dimensional (3-D) spatial memories (1222, 1249), and such correlations were likewise observed in older adults with mild cognitive impairment (1263). Also, changes in spindle dynamics appear to be relevant: Sleep spindles are temporally clustered after an infraslow ~0.02 Hz rhythm, which likely reflects fluctuations in noradrenergic activity of the brain stem LC (376, 377, 1264). In healthy adults between 35 and 69 yr the amplitude of this rhythm, i.e., the proportion of clustered spindles, decreased with increasing age. Although this decrease with age was unrelated to non-REM sleep fragmentation or microarousals, the diminished size of the spindle clusters in the older participants appeared to be linked to a diminished consolidation of visuo-spatial memory (1265). Also, in older adults spindles are less closely coupled to the SO up-state, and this uncoupling of spindles, in several studies, was robustly linked to a diminished consolidation across sleep for word pair memories (352, 1266, 1267). Note that, although less precise, the strength of the SO-spindle coupling itself is still a predictor of memory consolidation during sleep in older age (1267). Beyond predicting a decline in memory consolidation, the age-associated uncoupling of spindles to SOs was also linked to signs of mPFC atrophy and a diminished thalamus volume (352, 1267).

Factors at encoding might modulate the effect of age on the consolidation process. For example, the difference between young (19–28 yr) and older (63–74 yr) adults in maintaining scene-word pair memory was greatest for associations that were encoded with a medium strength (as determined by an immediate recall test), whereas there was no difference between the age groups for poorly encoded memories (1268). In addition, this study found an association between the impaired memory maintenance across sleep and reduced SWA, SOs, fast and slow spindles in older adults, as well as reductions in gray matter in the mPFC, thalamus, entorhinal cortex, and hippocampus. In this context, traits are also to be considered like generally high or low cognitive capabilities that are associated with higher or lower spindle activity. Such traits can interact with memory processing at encoding and consolidation and thereby modulate the effect of age on the consolidation process (e.g., Refs. 1269, 1270). For example, in high-performing older adults (50–79 yr) showing higher initial recall performance at a test before the experimental sleep and wake retention periods, sleep stabilized newly encoded visuo-spatial memories against interference to a similar extent as in young participants. Notably, this stabilizing effect was not obtained in the low-performing older adults.

5.2.2.2. THE ROLE OF REM SLEEP. Of the studies in older adults considering the role of REM sleep in episodic

memory consolidation (905, 1254, 1256, 1258, 1259, 1271–1273), many failed to find any link between REM sleep and memory consolidation (1254, 1256, 1258, 1259). The few hints at a contribution of REM sleep to age-related deficits in memory consolidation during sleep were mostly of an indirect nature. An early study found a positive correlation between overnight memory retention in a word pair learning task and the duration of non-REM-REM sleep cycles in older adults (61–75 yr) (1273), suggesting that rather than non-REM sleep alone, the sequence of non-REM and REM sleep contributes to the consolidation process in older adults (see sect. 3.3). In line with this view, strengthening by sleep of memory for visuo-spatial associations in high-performing older adults (50–79 yr) was specifically related to REM sleep occurring during the early SWS-rich part of the night, whereas in the young participants memory gains were linked to non-REM sleep (1270). There are also findings pointing to a role of REM sleep in an age-dependent decline of the consolidation of prospective memories during sleep (872). In participants aged between 18 and 84 yr, the age-related decline in sleep-associated prospective memory performance was most strongly associated with age-related decreases in REM sleep duration (with no additional contributions of delta power, SOs, or spindle density). However, such a role of REM sleep in prospective memory consolidation is not well supported by other studies, although in these studies the age-related decline in prospective memory consolidation during sleep was a rather robust finding (904, 906–908).

Increases in REM sleep after administration of the acetylcholinesterase inhibitor donepezil in 58- to 78-yr olds were positively correlated with retention of word lists (1271). However, these findings could not be confirmed when REM sleep periods in older adults (60–82 yr) were augmented either by administration of donepezil or by inducing a REM sleep rebound after temporarily depriving the participants from REM sleep (1272). Overall, the picture argues against a substantial role of REM sleep per se in mediating age-dependent declines in memory consolidation during sleep.

5.2.3. Sleep and emotional and procedural memory formation in older adults.

5.2.3.1. EMOTIONAL MEMORY. A preferential sleep-dependent consolidation of emotionally salient (negative) memories as seen in young participants (sect. 4.3) was found to be preserved in middle-aged participants (46–65 yr), with positive correlations between emotionally salient memory and spindle activity being present across the whole age range (491). Others (786), however, report an enhancing effect of sleep on consolidation of negative picture memories only in young (18–30 yr) and not middle-aged (35–50 yr) adults. Studies comparing effects on positive versus negative information point to a stronger sleep-dependent enhancement of positive memory in aged individuals (830, 831, 1274, 1275). For example, in a group of older adults (50–80 yr) sleep after encoding preserved memory for positive but not negative pictures, whereas in younger adults sleep, conversely, preserved memory for negative rather than positive pictures (1275). The memory for positive pictures was positively correlated with percentage of early-night SWS in older adults only. Similarly, another study revealed a facilitating effect of sleep on the consolidation of positive pictures in older adults (58–78 yr), whereas in young adults the enhancing effect of sleep was specific to neutral pictures (830). Interestingly, in a recent study (1276) the preferential consolidation of positive over negative memory was systematically related to SO-spindle coupling during sleep: Whereas in young adults the SO-spindle coupling strength was predictive of negative but not positive emotional memory performance, in older adults (~62 yr) the coupling strength predicted recall of positive but not negative memories after sleep. On a related note, older participants (60–79 yr) upon sleep disruption (by periodical telephone calls) showed a stronger impairment in the consolidation of picture memories than younger control subjects (18–29 yr), but mood rating indicated that they were much less negatively affected by the sleep disruptions (855). Taken together, these findings suggest a consolidation bias in sleep among older adults, leading to a relatively stronger enhancement of positive memories compared to negative ones.

5.2.3.2. PROCEDURAL MEMORY. The few studies in the elderly addressing procedural memories rather consistently report a decline in sleep-dependent consolidation of skills with increasing age, which in some studies appeared to be even stronger than for declarative tasks (e.g., Ref. 1277). For example, sleep-dependent gains in skills on both explicit and implicit versions of motor sequence learning tasks are typically lacking or less pronounced in older in comparison with young participants (Refs. 483, 1277, 1278, for a review see, e.g., Ref. 1279). Age-dependent decline in sleep-dependent motor skill consolidation, independent of the initial training level (1278), was also observed in a motor adaptation task (1280). Additionally, this decline was consistently found to be related to changes in spindle activity. For example, on a motor sequence learning task, reduced sleep-dependent gains observed in older (55–75 yr) in comparison with younger (20–35 yr) adults were accompanied by a reduction of sleep spindle duration and frequency in the older participants (483). fMRI during the participants' task performance moreover revealed an association between sleep spindle density and increased striatal activity from training to retest after sleep, with this activity being increased in young but

reduced in older adults. Others, however, found sleep-dependent improvements in finger sequence tapping in older adults (>55 yr) to be likewise linked to increased (rather than decreased) activity in motor networks, including the putamen, but also hippocampal regions (1281). In these participants, activations in the putamen, cerebellum, and parietal cortex during initial motor sequence learning were moreover predictive of the gains in sleep-dependent consolidation. The age-dependent decline in sleep-dependent motor memory consolidation has also been linked to a thinning of gray matter in the relevant structures. Whereas in young participants sleep-dependent gains in motor sequence skills were, beyond correlations with spindle activity, positively correlated with gray matter volume in the hippocampus and cerebellum, in older adults (55–69 yr) gray matter volume in these structures was generally smaller and did not correlate with offline performance changes (1250). This altogether suggests that structural changes in motor networks including thalamo-cortical, striatal, and also hippocampal networks and associated differences in sleep spindle activity may explain the age-related decline in procedural memory consolidation during sleep (1282, 1283).

A few studies have provided hints that the decline with age in sleep-dependent motor skill consolidation depends on specific task characteristics (1272, 1284). For example, a group of 50-to 85-yr-old healthy adults showed sleep-dependent gains in a motor sequence task version that involved whole hand movements but not in the classical finger sequence tapping task, whereas the young participants of this study showed a converse pattern (682), suggesting a dependency of age-related changes on the kinematic demands. Nevertheless, the findings collectively support the view that sleep in older adults predominantly weakens the efficacy of motor skill consolidation during sleep, with this change involving functional changes in spindle activity that possibly originate from structural changes in the contributing motor networks.

5.2.4. Animal models.

Very few studies have examined sleep effects in aged animals (1285–1288). Sleep deprivation after context fear conditioning impaired memory in young adult (2 mo old) as well as aged (22–23 mo old) mice at a test 1 day after conditioning. Sleep deprivation induced comparable changes in the hippocampal expression of a number of genes related to sleep, circadian regulation, and synaptic plasticity in both ages (1285). However, at a test 1 mo after conditioning, the impairing effect of sleep deprivation on the conditioned fear response was only maintained in young but not aged mice, reflecting the generally faster decay of remote memory in aged mice. In another study (1286), a 5-h post-encoding period of sleep deprivation, followed by recovery sleep, impaired consolidation of spatial memory on an OPR task in young mice (10–24 wk). Surprisingly, old mice (60–76 wk) showed significant OPR memory only in the sleep deprivation condition and not in the sleep condition. Significant OPR memory at the test was, independent of the animals' age, associated with increased spindle counts during pre-REM sleep epochs. Analyses of hippocampal place cell activity, moreover, revealed that the expression of significant OPR memory was linked to place-field remapping at the test session, and older mice showed a greater number of cells with instable place fields than young animals. Noteworthy is a study in gray mouse lemurs (i.e., non-human primates) suggesting that the impairing effects of sleep deprivation on the consolidation of spatial memory can be alleviated, in both young (2–3 yr) and aged (6–7 yr) animals, by the administration of the acetylcholinesterase inhibitor donepezil or of the NMDA receptor agonist memantine (1287, 1288), i.e., drugs approved for the symptomatic treatment of Alzheimer's disease.

5.2.5. Enhancing sleep-dependent memory formation in aged individuals.

There are a rapidly growing number of studies that aim to relieve memory decline in aging by manipulating sleep, using different stimulation techniques like tDCS, CLAS, and targeted memory reactivation (TMR) (for reviews, see Refs. 1289–1290; sect. 7). For example, compared with a sham control condition, tDCS at a slow frequency (0.75 Hz) during an afternoon nap increased SWA during the nap and, at a test 1 wk later, improved recall of word pairs learned before the nap in older (65–85 yr) adults (1291). tDCS over fronto-central cortical areas during a post-encoding nap likewise enhanced picture-location associations in 50- to 80-yr-olds (1292). The enhancing effect was accompanied by increased amplitude of frontal SO and fast spindle activity. However, in this study not all memories benefited from tDCS, with word pair memories, for example, remaining unchanged after tDCS in the aged individuals (see Ref. 359 for related findings in patients with mild cognitive impairment). Positive effects were likewise observed with CLAS. Applied to the SO up-state, CLAS typically increased SO amplitudes and spindle numbers not only in the young but also in the older participants with and without mild cognitive impairment, and these increases were found to be paralleled by enhancing effects on the consolidation of various types of declarative memory (pictures, word pairs, etc.) (1293–1296).

Noteworthy are animal experiments in the common degu (*Octodon degus*) showing a beneficial effect of transcranial magnetic stimulation (TMS) in different memory tasks, i.e., the radial arm maze, Barnes maze, and NOR (1297). TMS was applied for 2 h at a frequency of 60 Hz (dorsally and ventrally to the skull) to sleep-deprived

young (18 mo) and older (40–60 mo) female degus, which slept most of the time during administration. Whereas in the young degus memory was improved already after a single 2-h TMS session, old degus showed distinct improvements in recall only after multiple days of treatment, suggesting that the reduced responsivity of the aged brain to acute stimulation may be compensated by a prolonged administration of the stimulation (for related results, see Ref. 1298).

There are also, however, an increasing number of studies that failed to find beneficial effects of stimulation in older (human) adults (1299–1302). Bifrontal anodal tDCS during early non-REM sleep did not affect consolidation of word pair or finger tapping skill memories in older adults (~69 yr) (1299). Instead, the participants spent more time awake and less in stage 3 non-REM sleep during stimulation-free intervals. tDCS over the frontal cortex likewise failed to induce any beneficial effect on the consolidation of word pair or finger tapping memories in a group of healthy older (50–80 yr) adults (1300). In fact, stimulation even impaired the consolidation of visuo-spatial picture-location memories in the older participants. Negative results have also been reported with CLAS. For example, CLAS during SWS over several nights in older adults (mean age 69 yr) remained without any beneficial effect on their performance on a face-occupation associative memory task (1302). Despite the absence of behavioral memory effects, CLAS in these studies reliably produced increases in spindle- and SWA-related parameters, although these were of overall lower magnitude in the older participants (1301, 1302).

Findings after TMR in older adults are likewise mixed. In 50- to 80-yr-olds, TMR applied during a daytime nap after training improved performance on a sensorimotor task, i.e., throwing balls with the nondominant hand at a target (1303). However, TMR did not support the generalization of the skill to a similar task (dart throwing). In 62- to 83-yr-olds, TMR benefited consolidation of paired word associates (1304). But, in a group of 50- to 74-yr-olds, TMR during sleep failed to improve performance on a motor sequence learning task (1305), Together, these mixed findings suggest that tDCS, CLAS, and TMR may in certain conditions lead to improvements in memory consolidation in older adults as well, although overall these seem to be smaller and less robust than in young participants, possibly reflecting the generally reduced physiological responsiveness to stimulation of the older brain.

5.2.6. Conclusion.

Whereas early research in older humans, partly because of the limited number of studies, remained inconclusive (5), the body of more recent studies now rather consistently documents a decline in the sleep-dependent memory consolidation with increasing age, for both episodic and procedural types of memories. Notably, as to emotionally valenced memory, sleep in older adults appears to induce a bias toward a preferential enhancement of positive over negative memory. The changes in sleep-dependent memory consolidation appear to be linked to age-related changes in non-REM sleep, rather than REM sleep, fitting with the fact that declines in REM sleep with age are much less pronounced than those in SWS sleep. Among the SWS-related parameters, decreases in spindle activity as well as the precise coupling of spindles with SOs appear to be the markers most closely linked to declines in the sleep-dependent memory consolidation in aged individuals. Inconsistencies in the findings are likely related to the rather broad age spectrum covered by the different studies and associated differences in overall memory performance (i.e., low- vs. high-performing older adults). Stimulation techniques like tDCS and CLAS can increase spindle- and SO-related activity in older adults as well, although with reduced responsivity. Parallel effects of stimulation on behavioral measures of memory consolidation in the older adults are rather mixed, challenging the view that decreases in oscillatory signatures of memory processing, like spindles, represent the primary cause of the age-related decline in sleep-dependent consolidation. Nevertheless, more robust behavioral improvements in memory may be achieved with refined methods of brain stimulation or targeted reactivation techniques in future research.

6. SLEEP-DEPENDENT MEMORY FORMATION IN PATIENTS WITH INSOMNIA

Sleep is crucial for memory formation in healthy individuals. Conversely, impairments in sleep-dependent memory formation have been found in many diseases that are accompanied by distinct disturbances of sleep, for example in neurodegenerative diseases such as Alzheimer's disease (1306–1308), neuropsychiatric diseases such as posttraumatic stress disorder (PTSD) (1309), and neurodevelopmental diseases such as attention deficit hyperactivity disorder (ADHD) (1310, 1311) and autism spectrum disorder (ASD) (1312). However, it is difficult to disentangle whether the observed impairments in sleep-dependent memory formation are a result of specific sleep disturbances or of more general cognitive impairments accompanying these pathologies. Therefore, here we restrict our review to studies in patients with primary insomnia disorder, representing a disorder of the sleep process itself (1313).

Insomnia, also known as sleeplessness, is a highly prevalent sleep disorder occurring in up to one-third of

the adult population worldwide and up to 50% of primary care patients. It is characterized by a "sleep continuity disturbance," including increased sleep onset latency, increased number of awakenings and WASO, decreased total sleep time (affecting both non-REM and REM sleep), and decreased sleep efficiency. These sleep disturbances are associated with daytime complaints related to, e.g., cognition, sleepiness, and fatigue (1314–1317). Notably, subjective sleep complaints are often reported in the absence of clear changes in the sleep macroarchitecture (1318, 1319). Some more fine-grained analyses have revealed an increase in power in the EEG beta frequency range during sleep in insomnia patients and a decrease in spindle density, commonly interpreted in terms of a "hyperarousal" due to enhanced activity of the noradrenergic LC, as a key factor in the pathophysiology of the disease (853, 1225, 1264, 1320–1330). Insomnia is typically diagnosed when sleep is disrupted for 30 min or more or if sleep efficiency is below 85% (1331). According to the International Classification of Sleep Disorders (ICSD-3), chronic insomnia is diagnosed when sleep continuity disturbance occurs at least three times per week for >3 mo. Indeed, studies of memory functions have been almost exclusively performed in patients with chronic insomnia, often with a history of taking sleep medications.

6.1. Memory Impairments in Insomnia Patients

6.1.1. Altered cognitive and emotional processing in insomnia patients.

Patients with insomnia suffer from multiple cognitive impairments that can affect perception, working memory, and executive functions (1329, 1332), all of which alter the encoding of new stimuli as well as their retrieval. However, insomnia does not uniformly impair the performance in all memory tasks. For instance, insomnia patients showed enhanced use-dependent plasticity, assessed by TMS, likely due to chronic noradrenergic hyperarousal (1328). Additionally, there are also hints that over shorter wake intervals insomnia patients retain memories better than control subjects with good sleep (556, 557, 913, 914). Compared with good sleepers, insomnia patients showed superior performance on a prospective memory task (913) and increased free recall of gist word memory on a DRM task when memory was tested immediately after task encoding (556, 557).

In contrast to these findings, the processing of emotional stimuli seems to be impaired in insomnia patients, which likely also relates to their increased risk for anxiety disorders. For example, insomnia patients are more likely to misinterpret angry faces as fearful (778), retain positive and neutral stimuli less well over 30 min than negative stimuli (1333), and show an increased anterior cingulate response to shameful stimuli (1334). In addition, dream activity during REM sleep has been characterized to be more negative in individuals with insomnia (1335, 1336). It has been mainly suggested that impairments such as these are a consequence of chronic fragmentation of REM sleep and associated dysfunctional activity in limbic regions (1326). However, alterations of cognitive processing during wakefulness in insomnia patients are also expected to distinctly change the way in which patients encode and retrieve stimuli from memory, thereby confounding the effect of sleep on memory consolidation.

6.1.2. Sleep-dependent consolidation of episodic and procedural memory in insomnia patients.

The few studies that have investigated the role of sleep in episodic memory formation rather consistently showed an impaired consolidation in insomnia patients compared with healthy control subjects (1313, 1337, 1338). For example, insomnia patients are worse in retaining verbal materials (texts, word pairs) overnight than healthy control subjects (1339–1342). Patients who were tested in these studies also reported lower sleep quality and exhibited lower total sleep time, less time in SWS, more awakenings, as well as a reduced number of non-REM sleep spindles, compared to healthy control subjects. Notably, an early study (1339) found that in insomnia patients word pair retention was linked to REM sleep duration (unlike in healthy control subjects, where it was linked to SWS duration) and that impaired memory retention overnight was associated with elevated blood cortisol levels during early nighttime sleep (see Ref. 1342 for similar results). Other studies attempted to model the effects of transient insomnia in healthy humans based on the so-called "first-night effect," i.e., sleeping the first time in an unfamiliar environment, which produces sleep disturbances similar to those in insomnia patients (1342). There was no sleep-dependent benefit for word pair memories in healthy participants showing a strong first-night effect on the experimental night with a >10% decrease in total sleep time. Moreover, overnight memory retention in these participants was associated with REM sleep parameters (percentage of REM sleep, total number of REMs) rather than non-REM parameters, mirroring the findings in insomnia patients.

Studies of sleep-dependent procedural memory consolidation in insomnia patients overall remain inconclusive. Testing mirror tracing skills, Nissen et al. (1343) found a weaker overnight improvement in insomnia patients than in healthy control subjects, although the groups did not differ in their sleep architecture (for related findings, see Ref.

1340). In Backhaus et al. (1339), on the other hand, overnight gains in the skill did not differ between groups, although the insomnia patients spent less time in sleep and in SWS than the healthy control subjects during the experimental night. Similarly, testing sequential finger tapping skills revealed sleep-dependent gains only in healthy control subjects and not in insomnia patients (1344). This difference was accompanied by a shorter total sleep time and increased WASO in the patients. However, the groups of this study already differed at training before sleep, and in another study overnight gains in finger tapping skills were revealed to be comparable between insomnia patients and control subjects (1341). Together, these studies confirm reduced episodic memory formation during sleep in insomnia patients that is likely due to disturbed non-REM sleep-related memory processing. Furthermore, some findings suggest a compensatory role of REM sleep in episodic memory consolidation in insomnia patients. There is no solid evidence for an impaired procedural memory consolidation due to insomnia.

6.1.3. Emotional and gist memory.

Emotional memory processing during sleep in insomnia patients has been studied with a focus on fear extinction memory. Patients with chronic insomnia typically show stronger responses (e.g., SCRs) during the conditioning of fear, consistent with a persistent hyperarousal and plasticity during wakefulness in these patients (798, 853, 1328, 1345). On top of this, in chronic insomnia patients postextinction sleep led to a weaker, less effective extinction memory compared to healthy control subjects when fear extinction was performed right after the conditioning session (798). The impaired extinction memory recall on the day after the experimental night in the patients was associated with increased time in REM sleep and longer REM sleep epochs. In the good sleepers, the average length of continuous REM sleep epochs as well as frontal EEG theta power were associated with improved extinction memory recall. As fear conditioning and extinction procedures in this study were performed in the same session before the experimental sleep period, it is unclear whether the associations with REM sleep parameters reflected enhancing effects on the original conditioned fear memory or on the extinction memory. However, in similar experiments that performed fear conditioning and extinction training on the same day, individuals with insomnia displayed ongoing activation of fear-related brain areas (such as insula, dorsal anterior cingulate cortex, and amygdala) during extinction training as well as during extinction memory recall on the day after nocturnal sleep compared to good sleepers (1345). This suggests that the diminished extinction memory recall observed in insomnia patients is, at least partly, a consequence of diminished efficacy of the extinction training in these patients, rather than a consequence of impaired sleep-dependent consolidation.

Differences in the efficiency of stimuli encoding may likewise contribute to the changes in the sleep-associated formation of gist memory observed in insomnia patients. For example, when tested in the DRM task insomnia patients showed a global increase of gist memory recall compared to good sleepers, which may be a result of lower source monitoring capabilities (557). Notably, when DRM task learning was followed by either 8 h of sleep or wakefulness, insomnia patients also showed a pattern opposite to good sleepers, i.e., increased gist memory recall after wakefulness compared to sleep (558). In combination, the available findings do not provide convincing evidence for a direct impact of the sleep disturbances in insomnia patients on the sleep-associated formation of emotional and gist memory. The respective memory changes observed in insomnia patients more likely reflect changes in wake processing, i.e., in encoding and retrieval of the respective task materials.

6.1.4. Animal models of insomnia.

A few animal models of insomnia have been used to study mechanisms underlying insomnia-associated memory impairments. In *Drosophila melanogaster*, manipulation of genes inducing insomnia-like symptoms (prolonged sleep onset, increased sleep fragmentation and awakenings, reduced total sleep time) produced decreases in short-term memory for a conditioned avoidance response (aversive phototaxic suppressor assay) and underlying neuronal plasticity (1346). Specifically, increasing *faf* and decreasing *hiw* genes in wake-promoting large ventral clock neurons of the flies induced sleep loss, with decreasing *hiw* also impairing short-term memory performance. Knocking down another gene, *Rdl,* protected the flies from sleep loss-induced short-term memory impairments in the absence of changes in synaptic growth. Knocking down both *hiw* and *Rdl* in mushroom bodies also protected against negative effects of sleep deprivation. It is presently unclear, however, to what extent these findings translate to sleep-dependent consolidation processes.

Like the human first-night effect, in rats "sleep in an unfamiliar environment" has been used to model insomnia symptoms. Rats spent less time in sleep and in SWS and REM sleep in an experimental cage when they had less familiarization with the cage during prior habituation sessions (178, 424). Accordingly, sleep-dependent consolidation of spatial memories (in an object place recognition task and in a Morris water maze) was found to be diminished when the rats were less habituated to the experimental cage and sleeping conditions. The sleep changes

in unfamiliar conditions were particularly pronounced during the first hour after encoding in these experiments (see Refs. 423, 1347 for related findings on rodent models of PTSD that included insomnia as a diagnostic criterion).

6.2. Improving Sleep-Dependent Memory Consolidation in Insomnia Patients

Pharmacological treatment with GABA agonists like benzodiazepines and the so-called Z drugs (e.g., zolpidem) is the most common treatment of insomnia. Studies examining sleep-dependent memory formation after administration of these substances in insomnia patients overall remain inconclusive (see Ref. 1348 for a review). In fact, although in healthy participants the nonbenzodiazepine zolpidem in particular showed improving effects on sleep-dependent memory consolidation (e.g., Refs. 314, 1349–1352; see sect. 7.3), no sleep-dependent consolidation-specific effects have been investigated in insomnia patients, and early studies investigating effects on overall memory performance found mixed results (1353–1355). Notably, however, in a rodent insomnia model a more recent study (1356) found a beneficial effect of the novel hypnotic drug DORA-22 (a dual orexin receptor antagonist) on sleep-dependent memory consolidation in a Morris water maze task that was accompanied by attenuated wakefulness and increased times spent in non-REM and REM sleep during the retention interval following learning compared with vehicle treatment.

A few studies have tested experimental treatments (e.g., noninvasive brain stimulation) with regard to their effects on sleep-dependent memory consolidation in patients with insomnia symptoms (1357–1359). Schabus et al. (1357) trained patients with primary insomnia to increase 12- to 15-Hz EEG activity over the sensorimotor cortex using a visual online feedback procedure. Compared with sham training, the sensorimotor rhythm training increased EEG activity in the target frequencies and improved sleep, indicated by a reduction of awakenings, increased SWS, and enhanced subjective sleep quality in the patients. Importantly, in patients responding to the training, the training-induced enhancement in EEG sensory motor rhythms was positively correlated with the overnight consolidation of word pair memories. Another study employed CLAS to acutely enhance SOs during non-REM sleep in patients with chronic insomnia (1358). Whereas SO activity was indeed enhanced by the stimulation, EEG spindle and delta activity were reduced and, importantly, sleep-dependent word pair memory consolidation did not differ between the CLAS and sham stimulation control conditions (for related findings with TMR in patients with nightmare disorder or PTSD, see also Refs. 1360, 1361).

6.3. Conclusion

Altogether, the findings in insomnia patients and models of the disease support the view that specific sleep disturbances characterizing insomnia acutely hamper the consolidation of episodic types of memories. However, as to the formation of emotional, gist, and procedural memory, the available studies remain inconclusive, which appears to be mainly due to the fact that chronic insomnia is associated with distinct alterations of stimulus processing during wakefulness. The patients are in a traitlike state of hyperarousability that also changes the way they encode and retrieve task stimuli, and it is presently unknown how these changes at encoding during wakefulness interact with consolidation processes during sleep.

7. TECHNIQUES FOR ENHANCING MEMORY FORMATION DURING SLEEP IN HUMANS

Growing understanding of the mechanisms behind memory formation during sleep has inspired research into ways to manipulate these processes, aiming to amplify sleep's impact on memory in both healthy individuals and those with pathological conditions. Indeed, a very rapidly growing number of studies have tested the potentially improving effects on memory of different techniques in recent years, specifically, brain stimulation, TMR, and pharmacological treatments, in healthy young (discussed in this section) and old (sect. 5.2.5) people and patients with impaired sleep and memory functions (sect. 6.2). Most of these studies aimed at altering memory processing during non-REM sleep.

7.1. Enhancing Sleep by Noninvasive Brain Stimulation

Several brain stimulation techniques have been tested to improve sleep-dependent memory functions, including electrical, electromagnetic, auditory, vestibular, and somatosensory stimuli, which were administered in either an open- or closed-loop manner. Closed-loop stimulation refers to a presentation of the stimuli time-locked to the occurrence of a specific physiological target event, e.g., the occurrence of an SO in the real time-analyzed EEG signal.

7.1.1. Electrical and electromagnetic stimulation.

Electrical stimuli have been administered as tDCS or transcranial alternating current stimulation (tACS). The stimulation is assumed to induce broad electrical field potential changes in the underlying brain tissue, with the

efficacy of the stimulation depending on multiple factors such as the applied current strength, the size of the stimulation electrodes, their location over the cortex, the polarity of the applied current, the stimulus shape, frequency, etc. (1362, 1363). A major issue in the field concerns the accurate prediction of the local field potential that is induced in the brain by an electrical stimulus (1364–1369).

In one of the first studies (329) in young, healthy humans, tDCS applied at 0.75 Hz (~SO frequency) in 30-s intervals during non-REM sleep effectively induced SO-like potentials, enhancing overnight retention of declarative word pair memories (**FIGURE 13*A***; see Refs. 1370, 1371 for similar results in rats). Subsequent studies reported improving effects of tDCS on the retention of different kinds of memories, in conjunction with increased SO activity and SO-spindle coupling, in healthy young adults (1372, 1373), older adults with and without mild cognitive and memory decline (359, 1291, 1292), patients with temporal lobe epilepsy (1374), as well as children with ADHD (1375). Noteworthy, in healthy participants tDCS also facilitated insight into temporal rules, with the likelihood of detecting such regularities increasing with the number of stimulations a participant received during the night (588) (see also sect. 4.2).

Beneficial effects on sleep-dependent memory consolidation (1376, 1377) and generalization (1378, 1379) were likewise found with tACS. For example, a spindle-like tACS waveform applied with electrodes over the frontal and central cortex enhanced motor memory consolidation in conjunction with increased spindle activity (1380). Conversely, tACS applied bilaterally over the frontal cortex at a SO-like frequency of 0.75 Hz reduced, rather than enhanced, SO activity in the 0.7–4 Hz range, and this disruption was associated with an impaired overnight consolidation of declarative word pair memories (1381). However, there are also a number of studies that failed to reproduce effects of tDCS on memory consolidation (e.g., Refs. 732, 1299, 1300, 1382–1385), despite some of them showing effects on associated EEG oscillatory signatures (1300, 1383, 1384). Likewise, tACS in the theta range, applied in combination with TMR (sect. 7.2) during non-REM sleep, did not affect oscillatory activity or consolidation of word pair memories (1386). On the contrary, this tACS protocol even blocked the TMR-induced memory benefits during sleep. Such inconsistencies may partly reflect interindividual differences in the sensitivity to electrical stimulation. In line with this, tDCS improved memory retention specifically in participants with high baseline performance on the memory task (1387) and those with strong SO-spindle coupling (368) (for reviews, see also Refs. 1388, 1389).

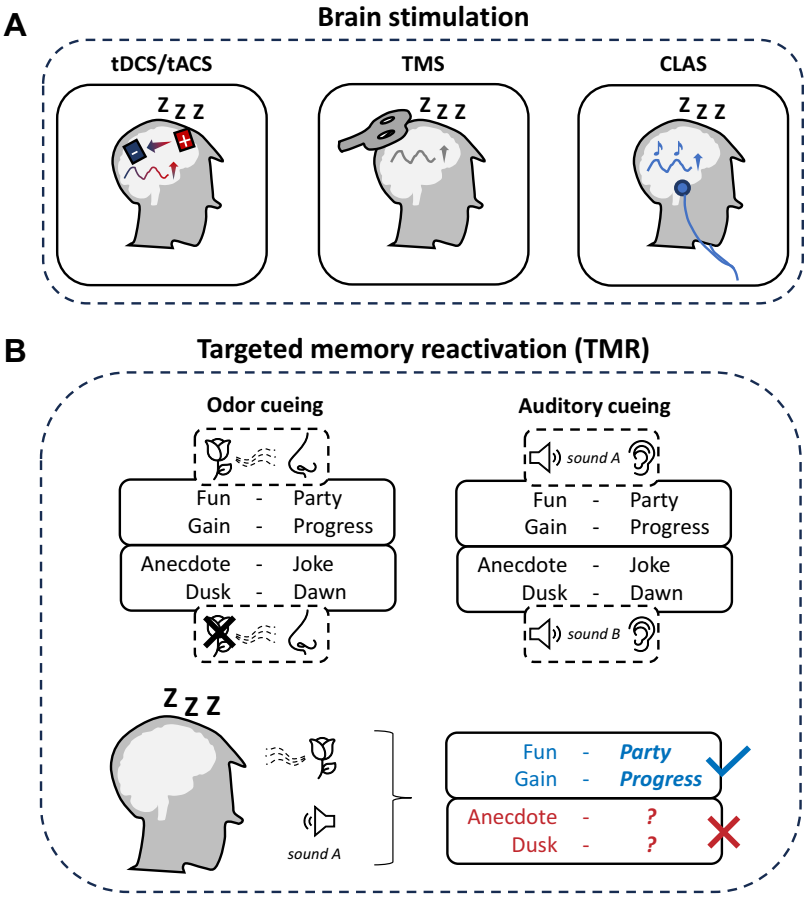

FIGURE 13. Techniques for enhancing memory consolidation during sleep in humans. *A*: noninvasive brain stimulation: For transcranial direct current stimulation (tDCS) and transcranial alternating current stimulation (tACS) 2 scalp electrodes are used to apply currents to the brain, for transcranial magnetic stimulation (TMS) a coil is used to induce electromagnetic fields, and sensory stimulation techniques like closed-loop auditory stimulation (CLAS) refer to presentation of (e.g., auditory) stimuli mostly in a closed-loop manner, i.e., time-locked to specific events, like SOs. *B*: targeted memory reactivation (TMR). During encoding (*top*), some materials are associated with a particular odor (odor cuing; e.g., the smell of a rose) or sounds (auditory cuing; e.g., "meow" or the sound of a "whistle"), whereas other materials are presented with an odorless vehicle or a different sound, respectively. Re-presentation of the odor or sound cues during sleep reactivates and thereby enhances consolidation of the cued in comparison with the uncued materials (*bottom*). See GLOSSARY for additional abbreviations.

7.1.1.1. TRANSCRANIAL MAGNETIC STIMULATION. Transcranial magnetic stimulation (TMS) has been used as another noninvasive technique to induce electrical fields in the sleeping brain. Compared with the direct application of electrical stimuli, the electromagnetic method allows for a much more focused stimulation and the manipulation of excitability within restricted cortical areas (**FIGURE 13*A***) (158, 1390–1392). However, the application of TMS during sleep is practically difficult, given the bulky stimulation coil and the efforts to be made to prevent changes in head position during the stimulation, as well as confounding effects of acoustic clicks accompanying the stimulation. This explains that TMS in sleeping subjects has only been rarely used so far. An early study by Massimini et al. (1393) used TMS to trigger slow waves and sleep spindles during sleep. Repeated TMS pulses administered at a $<$1 Hz rate induced local high-amplitude slow waves spreading over the cortex, thereby overall increasing SWA, i.e., effects likely contributing to synaptic plasticity underlying sleep-dependent memory effects (1394, 1395). Notably, TMS applied during wakefulness alleviated the adverse effects of sleep deprivation on memory in humans (1396–1398) as well as in different animal species (1297, 1298). In waking humans, TMS was also used as a tool to locally disrupt ongoing memory processing, thereby allowing dissection of the contribution of specific regions to sleep-dependent memory formation. For example, posttraining disruption of dorsolateral prefrontal cortex activity by TMS in waking participants induced improvements in SRTT performance, mimicking those after a night of sleep (1399). Similarly, TMS was used to disrupt activity in either the primary motor cortex (M1) or the inferior parietal lobule (IPL) immediately after training, thereby demonstrating that sleep-dependent offline improvements on an SRTT rely on IPL, but not M1, circuits (1400).

Although promising, the diverse and inconsistent findings highlight that the use of electrical and electromagnetic stimulation to enhance memory formation during sleep remains in its early stages of development. Generally, more robust memory enhancements might be achieved by individually adjusting the stimulation parameters, including the exact location and frequency of the stimulation. Additionally, trait factors may generally reduce a person's sensitivity to stimulation. Moreover, both electrical and electromagnetic stimulation do not allow for a targeted stimulation of relevant deeper brain structures, like the thalamus and hippocampus, a disadvantage that may be overcome by a more recently developed technique, i.e., transcranial focused ultrasound stimulation (TUS; Refs. 1401, 1402). TUS can alter neuronal activity in subcortical structures with high precision and also activity during non-REM sleep in humans (1403, 1404), but so far it has not been used to study memory processing during sleep.

7.1.2. Auditory, vestibular, and somatosensory stimulation.

Different from electrical (and ultrasound) stimulation, these stimulation techniques take advantage of the natural existing receptor systems of the different sensory modalities, making these techniques physiologically more "normal," but less flexible, for experimental purposes. The broader application of these techniques is fostered by the recent development of devices allowing for a home-based ambulatory administration, particularly of auditory stimulation, during sleep (e.g., Refs. 1405, 1406).

7.1.2.1. AUDITORY STIMULATION. Auditory stimulation has been mainly administered in a closed-loop manner (i.e., CLAS; **FIGURE 13*A***). In a first study by Ngo et al. (330) two auditory stimuli (short bursts of pink noise) were timed to the respective up-phases of a first, online-detected SO and a second, succeeding SO while participants were in non-REM sleep. The stimulation enhanced SOs as well as phase-coupled spindle activity and, moreover, improved consolidation of declarative word memories. Similar effects were obtained with CLAS that was based on slightly different SO (or K-complex) detection criteria and applied during a daytime nap (1407–1410). A closed loop-based randomized presentation of stimuli or presentation of the stimuli in a fixed sequence, by contrast, tends to suppress SWS and lacks the improving effects on memory, indicating that synchronizing of the stimulation to the natural dynamics of the brain oscillations is of importance for the efficacy of the stimulation (1411, 1412). Attempts to increase efficacy of CLAS by increasing the stimulus rate (i.e., presenting $>$2 stimuli in a row) failed, probably because of the refractoriness of thalamic spindle generators (370). Also, the direct CLAS of spindles (by several clicks in a row) failed to produce enhancements of spindle activity or memory (1413).

Although CLAS in the majority of studies robustly increased slow oscillatory and phase-coupled spindle activity, a parallel improvement in memory consolidation was not always observed (e.g., Refs. 1414–1417), suggesting that the memory effect of CLAS depends on further modulatory factors, like the kind of memory task (1289, 1418–1422) and individual traits. For example, sensitivity to CLAS is decreased in old people (1294, 1301), especially in those showing low SWA responses to the stimulation (1423) (sect. 5.2.5). In children, CLAS improved the retention of reward memory only in typically developing children and not in children with ADHD, although both groups exhibited increased SO activity with CLAS (886). To be effective, the CLAS protocols developed in young healthy participants might need to be better fine-tuned to the specific conditions in older people or in disordered conditions (1122, 1289, 1295, 1358, 1418, 1420,

1424–1426), e.g., with regard to the exact phase of stimulus presentation during the SO cycle (1122, 1427–1429). However, there might also be yet-to-be-identified conditions in which CLAS does not work.

7.1.2.2. GENTLE ROCKING AND SOMATOSENSORY STIMULATION. Gentle rocking has been known to promote sleep in babies for centuries. Experiments in adults showed that gentle rocking (in an ~0.25-Hz rhythm) facilitates the transition from wakefulness to sleep and boosts endogenous SOs and spindles during naps as well as nighttime sleep (331, 1430, 1431). The procedure also strengthened sleep maintenance and, crucially, enhanced overnight memory consolidation. Although rocking stimulation did not affect SO-spindle coupling, both SOs and spindles showed a temporal clustering relative to the rocking cycle (331), suggesting that rocking entrains spontaneous neural oscillations. Similar effects of rocking on sleep (at a faster 1.0-Hz rhythm) were observed in mice (1432), with the procedure accelerating sleep onset, increasing time spent in non-REM sleep, and shortening intermittent wake episodes. However, in mice, unlike in humans, SO and spindle activity remained unchanged. The effects of rocking are mediated by the vestibular system, as rocking did not affect sleep in transgenic B6.Cg-*Otop1*tlt/J *tilted* mice, which cannot encode linear acceleration because of the lack of functional otoliths (1432). Enhancing effects on SWS, SWA, and declarative memory comparable with those after gentle rocking were also observed with closed-loop somatosensory stimulation, i.e., weak vibrations on the wrists that were synchronized with the heartbeat (1433).

7.2. Targeted Memory Reactivation

The neuronal replay of newly encoded memory representations mainly occurring during SWS is considered a key feature mediating the consolidation of representations into long-term memories (Refs. 79, 80; sects. 2.1 and 3.1.1). Based on this concept, numerous studies in humans have aimed at experimentally inducing reactivations of newly encoded memories by presenting reminder cues to the participant during sleep after memory encoding, i.e., a technique termed targeted memory reactivation (TMR; **FIGURE 13*B***; Refs. 1434, 1435). Typically, reminder cues, such as odors or auditory stimuli, are paired with the to-be-memorized materials during the encoding session and then repeatedly presented during subsequent sleep, at a low intensity to avoid sleep disruptions. As spontaneous neuronal memory replay in the hippocampus almost exclusively occurs during SWS, TMR is typically applied during SWS with the aim to enhance hippocampus-dependent episodic memories. However, TMR has also been used to modify emotional and procedural memory and occasionally applied during REM sleep.

7.2.1. Hippocampus-dependent episodic memory.

The first TMR study in humans (26) used odors for cuing (the smell of rose) because odors do not arouse the sleeper. The odor was presented as a contextual cue during the participants' learning of object locations and was then repeatedly reintroduced during SWS following the learning phase. At a later test, object location memories were significantly enhanced in comparison with control conditions where odor cues were applied while the participant was waking or in REM sleep. A subsequent study (203) showed the efficacy of TMR with sounds to enhance object location memories that were cued during non-REM sleep (see also Ref. 1436). TMR was likewise effective in enhancing spatial memories in rats and honeybees (1437, 1438).

Studies using TMR to foster integration and abstraction processes during the systems consolidation of episodic-like memory revealed mostly negative outcomes (505, 573, 729, 1439–1443). Cuing of newly learned words during non-REM sleep did not improve the integration of the words into their phonological neighborhood (505) and also failed to enhance memory for gist words in a DRM paradigm (Ref. 1439; sect. 4.2.1). TMR during SWS even abolished beneficial effects of sleep in a statistical learning paradigm requiring the explicit recognition of tone sequences (729). However, auditory TMR improved the abstraction of rules in visual problem-solving tasks when applied during REM sleep, with the effect emerging with a delay of 1 wk (630). However, others failed to find such improvements in problem-solving with TMR during REM sleep (661). Some findings suggest that TMR facilitates pattern separation during sleep-dependent memory processing (1444): When participants learned object-location associations before sleep periods rich in SWS and during subsequent SWS were cued with similar previously learned associations (same objects but at different locations) instead of the newly encoded ones, this did not lead to interference or impair the consolidation of the newly encoded memories (1444). However, cuing of the interfering associations seemed to enhance the separation of the memories in that it led to fewer intrusions of the interfering materials at a later test. By associating the reminder cue with an instruction to "forget," TMR has also been used to diminish strength of a memory (1009).

7.2.2. Emotional and procedural memories.

Non-REM sleep appears to mainly support the contextual episodic content of an emotional memory, whereas

the effect of REM sleep is more closely linked to the emotional response (see sect. 4). Consistent with this view, TMR during SWS facilitated memory consolidation for spatial locations associated with emotional pictures (493) but did not affect the recognition of emotional pictures themselves (1445) (see also Ref. 1446). Similarly, TMR during non-REM sleep, but not during REM sleep, enhanced memory for associations between words and emotional pictures (1447). Conversely, TMR during REM sleep, but not SWS, reduced the emotional response in terms of subjective arousal to negative stimuli encoded before sleep (464). Furthermore, the effect of TMR during SWS on the amygdalar response to emotional stimuli at a recall was stronger when the participants had spent more time in REM sleep (1448).

TMR-like procedures have also been used to modify fear responses in classical fear conditioning paradigms, with an overall inconsistent outcome (235, 816, 817, 820, 821). In mice, repeatedly re-presenting the auditory tone stimulus, used for conditioning before the experimental sleep interval, weakened the fear memory at a later test when the cue was administered during non-REM sleep but not during REM sleep (964). By contrast, in two other studies in mice and rats, respectively, cuing with the conditioned stimuli (odor or olfactory bulb stimulation) during postconditioning SWS led to an enhanced freezing response to the conditioned stimulus at the later test (235, 821). In two human studies, cuing with the conditioned tone stimulus and a contextual odor stimulus, respectively, produced a diminished fear response to the conditioned stimulus (816, 817). The reasons for these discrepant results are not clear (820). Noteworthy, in humans, cuing with a contextual tone stimulus during SWS also did not enhance but diminished the effect of prior fear-extinction learning (236). However, two clinical studies in patients with spider phobia (818) and social anxiety disorder (819) were unable to find augmenting effects of olfactory or auditory cuing during sleep on therapy-induced extinction of fears.

TMR has been similarly employed to update the emotional response to aversive memories (854, 1449). When cues to older aversive memories were paired (before sleep) with positive words and then re-presented during subsequent non-REM sleep, this counterconditioning procedure triggered an updating process that effectively reduced negative affective judgments of the older memories. TMR during non-REM sleep has been similarly combined with counterconditioning procedures to persistently modify implicit racial and gender biases in social judgments (1450, 1451).

Procedural types of memory overall consistently profited from TMR (465, 472, 706, 714, 723, 1452, 1453). For example, the repeated re-presentation of auditory cues associated with the key presses on a finger sequence tapping task during sleep after the training strengthened the tapping skill, with the effects restricted to those finger transitions that were actually cued during sleep (1452). Comparable improvements in motor sequence skills, which were linked to increases in spindle activity, were obtained with TMR selectively administered during non-REM sleep (706, 714, 764). Comparable enhancements were observed also for more complex skills, like the control of myoelectric activity in specific arm muscles to move a computer cursor (722, 1453), with potential relevance for the use in rehabilitation training. Benefits emerged also after TMR during REM sleep (465) and, in one study, only slowly evolved over the course of several weeks (723).

7.2.3. Factors modulating efficacy of TMR: cue specificity, timing, and memory strength.

TMR effectively enhanced memories only when the same cue (e.g., odor) as during learning was presented during non-REM sleep and not with presentations of a highly distinct control odor (1454). Presentation of odor cues during non-REM sleep to one of the two nostrils produced a greater memory enhancement for visual stimuli that were presented to the same (ipsilateral) hemisphere at encoding (1455). TMR with verbal cues was not effective when the sex of the voice was changed for presentations during non-REM sleep (1456). Indeed, TMR studies using verbal materials suggest that the brain is capable of discriminating rather complex stimuli during non-REM sleep. Cuing newly encoded Dutch-German vocabulary by presenting the Dutch words as cues enhanced the vocabulary in native German speakers (1457), although this effect was not reproduced in adolescents (1458). Noteworthy, in a comparison between cuing with complete versus incomplete word reminders (first syllable of a word), the complete reminders appeared to be less effective than the incomplete word reminders in enhancing sleep-dependent consolidation of sound-word associations (1459). The authors argued that incomplete reminders induced a mismatch, potentially enhancing the processing of the reactivated memories. Memory-enhancing effects of TMR were also observed in field studies with less controlled cuing conditions, such as vocabulary learning in school (1460, 1461).

The timing of TMR is another factor that might determine its efficacy. Enhancing effects of TMR on episodic types of memory have been observed mainly with application of the cues during non-REM sleep (26, 203, 493, 573, 1436, 1447, 1454–1456, 1462–1466), although occasionally effects were revealed with TMR during REM sleep (465, 467, 628, 630). With TMR applied during non-REM sleep, the exact timing of cuing during the SO cycle

is of additional relevance. As spontaneous replay occurs during the SO up-state (Refs. 125, 128, 130, 357; sect. 3.1), it is reasonable to assume that cuing during the depolarizing SO up-states is more effective in enhancing memory than cuing during SO down-states, which was indeed confirmed by analyses of the timing of TMR cues used for enhancing object-location, word-image, and social memories (1451, 1467, 1468). Similarly, cues presented during down-to-up-state transitions of SOs were more likely to elicit classifiable memory reactivation response in the EEG signal (1469). However, others failed to find differential effects on memory after cuing during SO up- or down-states (1470). Also, enhancing low acetylcholine levels (by physostigmine) with the aim to suppress efficacy of hippocampal replay (see BOX 2, sect. 7.3.2) did not abolish the enhancing effect of odor cuing on the consolidation of spatial object-location memories (1462).

Whether the effect of TMR depends on the strength of the encoded association is presently unclear, with some studies pointing to a stronger cuing benefit for less well-encoded associations (1463) and others for more strongly encoded associations (1464, 1471, 1472).

7.2.4. Does TMR induce memory reactivation?

Bendor and Wilson (1438) were the first to show that memory cuing during SWS increases neuronal replay of the cued memory in rats. The experiments used a spatial operant conditioning procedure where the rats learned to discriminate between two sounds indicating whether going into the left or right of two tracks would be reinforced. Cuing with one of the sounds during postlearning SWS biased neuronal replay events in hippocampal place cell ensembles toward enhancing the spatial memory associated with that cue, whereas overall replay of both tracks and associated hippocampal ripples remained unchanged. In humans, evidence for TMR-induced memory reactivations is more indirect. fMRI revealed odor cuing of spatial (object-location) memories during SWS to evoke signs of reactivations in hippocampal as well as posterior cortical areas (26, 1473), and TMR effects were absent in patients with selective bilateral hippocampal sclerosis (1465). Several studies used decoding procedures to successfully identify signs of reactivation from EEG and fMRI responses to the cues presented during non-REM sleep (199, 315, 1474, 1475). In a study by Cairney et al. (315), participants learned two types of associations, adjective-object and adjective-scene associations, and these memories were cued during a subsequent 90-min nap by presenting the adjectives during periods of non-REM sleep. Based on EEG activity during cuing-induced spindle activity, the type of associative memory reactivated by the respective adjective could be reliably decoded. Moreover, the fidelity of this decoding was predictive of the behavioral memory benefit produced by the TMR procedure. Memory categories reactivated by TMR could be likewise discriminated by decoding fMRI responses from ventromedial PFC to odor cuing during non-REM sleep (1474).

Beyond memory reactivations upon TMR, cuing during SWS has been consistently found to evoke increases in SWA and spindle activity in response to the cue presentation (e.g., Refs. 315, 723, 818, 1447, 1454, 1455, 1457, 1476–1478), in line with a bottom-up influence of hippocampal memory reactivations on oscillations originating from the neocortex and thalamus. Thus, odor cuing of spatial memories evoked widespread temporal and spatially coordinated enhancements of spindles, SOs, and coupled SO-spindle events (1478) and an increase in connectivity between the mnemonically relevant cortical and hippocampal regions (1479). Successful cuing during non-REM sleep was moreover accompanied by increases in parietal theta power (1457). The effect of TMR on memory (for sound-word associations), however, did not depend on whether the cues were applied during SWS or N2 sleep, although oscillatory cue responses distinctly differed between the two sleep stages (1476), suggesting that these cortical EEG responses to the cues are only of secondary relevance to the cuing-dependent enhancement of the consolidation process (for similar results, see Ref. 1480).

7.3. Pharmacological and Hypnotic Treatment

Pharmacological studies on sleep-dependent memory consolidation in healthy humans have been performed to probe mechanisms supporting memory formation but also to enhance memory retention. For instance, drugs like benzodiazepines, which improve sleep in clinical conditions, might be expected to improve memory consolidation in healthy subjects as well. Additionally, substances have been tested to assess the contribution to memory consolidation of, e.g., specific neuromodulators and neurohormones like NE and cortisol that are known to be involved in the regulation of brain states at the network level, with presumable primary effects on systems consolidation processes. Finally, pharmacological substances have also been used to probe memory processing during sleep at the synaptic level, thus focusing on synaptic consolidation processes during sleep. Although such pharmacological approaches have undoubtedly deepened our understanding of the mechanisms underlying sleep-dependent memory formation, many of the tested substances show multiple side effects and have not been studied enough to establish dose-response relationships, which often complicates drawing straightforward conclusions from the findings (882, 1481, 1482).

7.3.1. Drugs improving sleep.

Benzodiazepines, together with the so-called Z drugs, i.e., nonbenzodiazepines like zolpidem, zopiclone, zaleplon, and eszopiclone, represent the class of drugs most widely used to treat insomnia (sect. 6). All of these substances increase GABAergic transmission via binding GABA type A receptors, which ultimately facilitates falling asleep and the emergence of consolidated non-REM sleep, with enhanced sleep spindle activity (1481). Effects on memory consolidation were less consistent, with benzodiazepines like zaleplon (1483) and triazolam (1484) yielding no or even impairing effects on memory (1481). Most robust effects on memory were observed with the nonbenzodiazepine zolpidem (1349, 1485). Zolpidem improved nonemotional and emotional types of episodic memory, in conjunction with signs of enhanced non-REM sleep and SWS, including enhancements in spindle activity and SO-spindle coupling (314, 1349–1351). The effects of zolpidem are possibly mediated by increased hippocampal ripple occurrence driving memory reactivations during sleep. In a rat study comparing effects of zolpidem and eszopiclone, both drugs increased spindle activity (1486). However, only zolpidem increased density of hippocampal ripples and memory formation during sleep (see Refs. 1487, 1488 for related findings in schizophrenic patients). Fitting with the enhancing effects on signs of hippocampal reactivations in rats, zolpidem enhanced the effects of memory reactivations that were induced by TMR during non-REM in healthy humans (1352). The combined zolpidem-TMR administration was moreover accompanied by an increased coupling of fast spindles and theta activity to SOs. Noteworthy are findings with the GABA reuptake inhibitor tiagabine, which, unlike zolpidem (and benzodiazepines), leads to a general nonselective activation of synaptic GABA receptors. In healthy humans, tiagabine profoundly increased slow oscillatory activity, with this effect, however, occurring in the absence of any improvements in memory consolidation or SO-spindle coupling (1489). In combination with the distinct effects observed after zolpidem, these findings point to a particular importance of GABA type A in mediating the memory effects through a specific action on spindles. However, the precise profile of GABAergic actions that produce the strongest memory effects during sleep is still unclear (1490).

Based on evidence in rodents that suggests that microbial products like muramyl dipeptide can induce sleep by triggering an immune response, proinflammatory cytokines, like interleukin-1 (IL-1) and tumor necrosis factor-α (TNF-α) have been studied as immune signals that globally induce non-REM sleep and are disturbed by sleep deprivation (1491–1496). Within the brain, these cytokines are mainly released from microglia exerting diverse effects on synaptic plasticity. Contrary to expectations derived from rodent studies, in healthy men the suppression of IL-1 activity by administration of the IL-1 receptor antagonist anakinra increased SWA during non-REM sleep (1497). The increase, however, was not associated with an improved consolidation on different verbal memory tasks. Increases in SWA and non-REM sleep were also observed in healthy men following administration of the anti-inflammatory antibiotic minocycline, and in this study the increase was paralleled by an improved episodic memory consolidation (1498). In rats, similarly, minocycline alleviated the impairing effects of sleep deprivation on spatial memory performance (1499), and comparable effects were observed in mice when neuroinflammatory activity was attenuated by activating dopamine D2 receptors (1500). The few findings so far suggest that, indeed, reducing proinflammatory signaling deepens non-REM sleep in healthy humans, although it remains to be substantiated whether this effect also improves memory formation.

7.3.2. Neuromodulators and neurohormones involved in sleep stage regulation.

Sleep stages are characterized by specific neuromodulatory milieus (BOX 2). Non-REM and SWS are characterized by particularly low levels of acetylcholine in the presence of intermediate levels of NE, whereas during REM sleep cholinergic activity is at a minimum while NE activity in the brain reaches high, wakelike levels.

7.3.2.1. ACETYLCHOLINE. The main sources of acetylcholine are the basal forebrain and the mesopontine tegmentum. High acetylcholinergic activity, as present during wakefulness, reduces output from the hippocampus toward the neocortex via presynaptic inhibition of CA1 principal cells (242). Accordingly, low levels of acetylcholine during non-REM sleep lead to a release of this inhibition, thereby facilitating the hippocampal-to-neocortical transmission of reactivated memory information. Additionally, the low acetylcholinergic tone during sleep appears to favor the emergence of ripples and memory replay in hippocampal networks (968, 1501) and to contribute to the emergence of functional slow waves that enable plastic changes in cortical networks during non-REM sleep (1502, 1503). Concurring with this view, in an early study in healthy humans increasing acetylcholinergic activity during SWS-rich early nocturnal sleep, by administration of the cholinesterase inhibitor physostigmine, impaired the consolidation of declarative (word pair) memories (470). Conversely, suppressing cholinergic transmission during wakefulness in humans, by combined administration of muscarinergic (scopolamine) and nicotinergic (mecamylamine) receptor antagonists, shifted memory processing toward a non-REM-sleep-

like mode with distinctly improved consolidation of declarative memory but impaired capabilities to encode new information (243). Low cholinergic tone during sleep was likewise revealed to be important for the consolidation of motor memories (rotarod walking, single-pellet reaching task) in mice (Ref. 1504; see also Ref. 1505 for related results in humans). However, stimulating or blocking muscarinic or nicotinic acetylcholine receptors did not affect performance of the mice in this study. Also, physostigmine administered during SWS-rich sleep in humans remained without effects on TMR-induced reactivations of spatial (object-location) memories (Ref. 1462; sect. 7.2).

Targeting the high cholinergic tone during REM sleep, administration of the anticholinergic antidepressant amitriptyline in healthy humans profoundly suppressed REM sleep and specifically impaired perceptual skill learning but not motor skill or declarative learning (1506).

7.3.2.2. NOREPINEPHRINE. NE activity plays a crucial role in shaping the sleep microarchitecture underlying memory formation, with its short-term dynamics essentially contributing to regulating the generation of microarousals (and associated awakenings), spindle activity, and the maintenance of non-REM sleep (1264, 1507). In healthy humans, the intravenous infusion of clonidine, an α_2-adrenoceptor agonist that blocks NE release from LC neurons, abolished the sleep-dependent benefit of emotional over neutral memory (Ref. 1508; sect. 4.3). Similarly in rats, clonidine administration impaired the consolidation of food-location memories, and this impairment was likewise seen after administration of the β-adrenoceptor blocker propranolol (1509). The effect of clonidine was associated with a reduction in SOs, spindles, as well as SO-spindle coupling, and both clonidine and propranolol significantly reduced the number of hippocampal ripples. Findings related to clonidine, however, need to be taken with caution, given the clear dose dependency of effects of α_2-adrenoceptor agonists (e.g., Ref. 1510). Diverging from these findings, increasing NE activity by optogenetic LC stimulation during sleep in rats interfered with the consolidation of food-location memories (293), with the decrease in memory being correlated with decreases in sleep spindles, the coupling of spindles with hippocampal ripples, SWA during non-REM, as well as theta activity during REM sleep. Taken together, these findings indicate that both enhancing as well as suppressing LC NE activity can disrupt consolidation and its associated electrophysiological signatures during non-REM sleep, which supports the view that the precise timing of NE bursts and transient silent peaks, rather than the NE levels themselves, is the crucial factor influencing the consolidation process.

7.3.2.3. DOPAMINE. Dopamine signaling is implicated in the emergence of REM sleep (e.g., Refs. 1511–1514) and, in addition, key to the so-called reward system, which integrates the VTA, striatal regions, and several other areas to mediate reinforcement learning. Moreover, findings in rodents support the view that dopaminergic activity during wake reward learning promotes neuronal ensemble replay during subsequent non-REM sleep periods that also captures reward-processing regions like the VTA (see sect. 4.3.7). In humans, activation of dopamine D2-like receptors by pramipexole eliminated the preferential consolidation of high- versus low-rewarded memories during sleep (882), which is consonant with this view that dopaminergic activity during sleep mediates the preferential consolidation of reward memory. However, in a follow-up study, reward memories remained unchanged after administration of the dopamine receptor antagonist sulpiride (890).

7.3.2.4. GLUCOCORTICOIDS. The adrenal stress hormone cortisol (corticosterone in rats) is also released in a sleep-specific manner, reaching minimum level during early SWS-rich sleep and maximum levels during late REM-rich sleep, with this temporal dynamic controlled by an interaction of circadian and sleep-related factors (e.g., Refs. 101, 1515). Cortisol is known to act back on the brain to impact sleep-dependent consolidation through mineralocorticoid and glucocorticoid receptors that are expressed at highest density in limbic and hippocampus regions (866, 1516–1520). Elevating cortisol levels during postencoding sleep consistently impaired consolidation of hippocampus-dependent episodic types of memory in humans (i.e., the temporal sequence of events in a story), and a similar impairment (of spatial memory) was observed in rats after intrahippocampal injection of glucocorticoids (825, 827). These findings are in line with the view that the natural inhibition of cortisol release during early nocturnal SWS serves the efficient consolidation of these memories in hippocampal networks (866, 868, 1520). Notably, administration of corticosteroids during a postencoding wake interval, conversely, enhanced consolidation in both species (see also Ref. 1521). The disrupting effect of cortisol is mediated via an enhanced activation of glucocorticoid receptors during sleep (867) and seems to spare emotional memory. For example, blocking the natural increase in cortisol during late REM sleep by metyrapone (an inhibitor of cortisol production) increased the emotional enhancement in memory, i.e., the difference in recall of emotional versus neutral texts (1519). In a more recent study, however, a similar emotional enhancement in (picture recognition) memory likewise emerged after persistent elevation of cortisol levels (by administration of hydrocortisone) before

postencoding sleep (869). Notably, at the same time, the emotional response, i.e., amygdalar activation to the recalled emotional pictures, was reduced after hydrocortisone. Overall, the findings so far indicate a robust impairing effect of cortisol on hippocampus-mediated episodic memory consolidation that is mediated through the preferential activation of glucocorticoid receptors during non-REM sleep. The effects on emotional memory are more complex, depending probably not only on the acute balance between mineralocorticoid and glucocorticoid receptor activation during postencoding REM sleep but also on that during encoding (865, 1342).

7.3.2.5. INSULIN. Among the many other hormones potentially impacting sleep-dependent memory consolidation, insulin is the only one that has been more systematically tested. The pancreas serves as the primary source of insulin, and significant levels of insulin are found in human cerebrospinal fluid. Additionally, insulin receptors are widely expressed across various brain regions, with particularly high densities in the hippocampus (1522–1524). In experiments in humans, insulin is typically administered intranasally to enable the direct access of the large peptide to the brain compartment (1525) and to avoid side effects like hypoglycemia. Initial findings from an 8-wk subchronic intranasal insulin administration suggest a beneficial effect on the overnight retention of declarative memories, such as word lists (1524, 1526). This aligns with evidence linking increased insulin resistance during sleep to memory impairment and neurodegeneration (1527). Signs of enhanced declarative memory (for word pairs) and procedural finger tapping skills were observed following acute intranasal insulin administration before a single night of sleep (1528), although the effect size was only moderate.

7.3.3. Probing synaptic consolidation.

LTP of glutamatergic synapses is considered the key mechanism underlying synaptic consolidation (1529), which is mainly mediated via activation of postsynaptic NMDA and AMPA receptors (882, 1530). Put in simplified terms, in this concept the AMPA receptor transmits neuronal activation from one neuron to the other, and the NMDA receptor enables plastic changes at the synapse, i.e., the strengthening of the connection between the neurons. In initial studies involving healthy individuals, blocking NMDA receptors (by administration of ketamine) nullified sleep-dependent gains in perceptual skill learning (on a texture discrimination task; Ref. 1531). Such impairments were not observed in later experiments testing declarative memory (1532). In these experiments, neither ketamine nor administration of the AMPA receptor blocker caroverine induced any change in the consolidation of word pair memories, suggesting a minor role of glutamatergic transmission for hippocampal memory processing during sleep. However, substances like ketamine and caroverine that can be used in humans are, by far, less specific blockers of the respective glutamate receptors than those typically used in animal models and have numerous side effects. Indeed, the NMDA coagonist D-cycloserine, which has fewer side effects, enhanced the consolidation of word pairs when given before a postencoding sleep period, and this effect was not found when D-cycloserine was administered before a postencoding wake control interval (1532). At a test after consolidation sleep, D-cycloserine also enhanced the learning of new, more or less interfering word pairs (1533). Besides the ionotropic (NMDA, AMPA) receptors, mGluRs have also been probed, among which mGluR5 appears to be most essentially involved in regulating synaptic plasticity. However, the mGluR5 blocker fenobam did not affect the sleep-dependent consolidation of declarative or procedural types of memory (1534), although it produced massive changes in sleep architecture, including a suppression of spindles, augmented non-REM delta waves, and suppressed theta activity in REM sleep. Despite the overall strong side effects of the substances used to probe glutamatergic transmission in humans, the findings to date, especially the memory-enhancing effects of the NMDA coagonist D-cycloserine, highlight the importance of glutamatergic transmission in sleep-dependent consolidation processes.

7.3.4. Hypnotic treatment.

Although so far no systematic attempts have been made to assess the suggestive effects of placebo on sleep-dependent memory consolidation, a related approach uses hypnotic suggestion as a method aiming to generally deepen sleep, thereby enhancing memory consolidation (1535–1542). However, although hypnotic suggestions ("to sleep deeper" embedded in a metaphor of a fish swimming deeper and deeper, spoken in a calming voice) proved effective in distinctly increasing SWS and SWA during a nap (1535) and nocturnal sleep (1542), they did not enhance sleep-dependent consolidation of declarative (word pairs) or procedural (sequence finger tapping) memories. Notably, clear hypnosis-induced increases in SWS were only observed in the more suggestible participants (low-hypnotizable participants even showed a decrease in SWS; Ref. 1543), and the treatment did not increase spindles or SO-spindle coupling, potentially explaining the lack of effects on memory (1537).

7.4. Conclusion

Techniques for enhancing memory formation during sleep have rapidly advanced over the past decade. In addition to established methods like tDCS/tACS and TMS, CLAS stands out as a widely applicable, easy-to-implement technique that robustly increases SO and spindle activity, capable of improving postsleep memory performance. Overall, evidence also supports benefits of TMR for memory consolidation, with first findings suggesting that TMR might be effective also during REM sleep, particularly for emotional and procedural memory. However, outcomes across studies for all of these techniques appear to be rather variable. This may be owing to the sensitivity to respective stimulations that likely differs depending on factors such as the individual's age, memory capabilities, and specific sleep characteristics and highlights the need for further investigation into the underlying mechanisms and individually tailored protocols. The efficacy of TMR protocols might particularly depend on an optimized timing of stimulus presentations. Pharmacological treatments can likewise produce enhancements in memory formation during sleep, which may be mediated via enhancing effects on oscillatory signatures of memory processing, decreased acetylcholine levels, or increased levels of NE or dopamine. However, the exact mechanisms as well as dose-response relationships remain to be established in further studies.

8. CONCLUDING REMARKS AND FUTURE DIRECTIONS

This review aims to provide a comprehensive update on research into memory formation during sleep since 2013 (5). In this time, the field has faced an impressive growth of research, particularly in humans. Whereas the foregoing research focused on establishing an active role of sleep in memory formation, this role is now widely acknowledged. The work since 2013 overall confirms the basic notion that sleep is a brain state optimally suited for forming long-term memory. Also, the majority of findings are well in line with the two major concepts describing the underlying mechanisms of the consolidation process, i.e., the active systems consolidation concept and the synaptic homeostasis hypothesis (sect. 2). Both concepts highlight the particular importance of non-REM sleep-related oscillatory events in promoting memory consolidation, specifically of slow oscillations and spindles generated in the thalamocortical system and of ripples primarily originating from hippocampal networks. Findings supporting that processes of active systems consolidation and synaptic homeostasis can coexist and complement each other represent a major development in the field.

The review, however, has also identified gaps and areas with highly heterogeneous and partly opposing findings, pointing to unsolved issues in the field. A deep and detailed understanding has emerged from this research about the function of non-REM sleep-related processes for long-term memory consolidation, but the functions of REM sleep are presently much less clear. Similarly, behavioral assessments have provided overall highly consistent evidence that episodic kinds of memories are strengthened by sleep, in particular profiting from neuronal replay occurring during non-REM sleep. Conversely, it is currently not clear how sleep, particularly REM sleep-related processes, contributes to emotional memory formation and the regulation of the emotional response associated with these memories (sect. 4.3).

Episodic memory consolidation implicates a hippocampal-to-neocortical redistribution of the involved neuronal representations, enabling the transformation of the originally encoded memory into more abstract schema-like representations. In the last decade, findings have provided convergent evidence that sleep can support this transformation. However, behavioral assessments are overall inconsistent as to the question of what kind of information is abstracted in this process (sect. 4.2). It remains to be clarified to what extent effects on memory abstraction are domain specific, e.g., stronger for spatial compared to verbal tasks with related task-specific temporal dynamics. On one hand, there is no behavioral evidence for an active forgetting induced by sleep (sect. 4.4). On the other hand, this research has clearly identified neuronal replay and the temporally linked occurrence of ripples, spindles, and slow oscillations as main physiological drivers of the transformation process. There are, moreover, first hints as to how the memories are consolidated into neocortical long-term stores at the synaptic level. Evidence that REM sleep promotes the selective pruning of subsets of synapses that were newly formed during training is intriguing in that it points to a basic function of REM sleep in synaptically shaping the neocortical representations (sects. 2.2 and 3.3.2). Yet, future experiments need to substantiate this view and, importantly, show how such synaptic shaping translates into behavioral changes at memory retrieval.

Notably, over the past decade, there has been a disproportional increase in studies that failed to reveal beneficial effects of sleep on memory consolidation compared with the effects of a postencoding wake period. Rather than challenging the memory effect of sleep, these findings show that sleep is not the only brain state that forms long-term memory and that, depending on the assessment, memories may be as persistent after sleep as after a wake-associated consolidation process. Importantly,

there is also first confirmation of the notion that consolidation during sleep and during wakefulness differ in quality, i.e., rely on different mechanisms (sect. 4). These differences remain to be studied in more detail, as well as the question of which of the two kinds of consolidation processes eventually produces the more persisting representations.

A comparable issue has emerged from investigations of sleep-dependent memory formation during early life (sect. 5.1). Originally motivated by the hypothesis that the deeper sleep in children produces quantitatively stronger effects on memory, the research of the last years also has revealed a number of findings that contradict the active systems consolidation concept as derived from research on mature brains. Considering the immaturity of the hippocampo-prefrontal system during infancy, a central question to be addressed in future is whether memory consolidation during sleep in infancy relies on the same mechanisms of active systems consolidation as those in adults. Conversely, research in older people (sect. 5.2), like that in insomnia patients (sect. 6), has been largely clinically oriented, i.e., motivated by the wish to compensate for age-related deficits in sleep and associated memory functions. Although the findings during the last decade confirm such deficits, attempts to alleviate deficits by sleep-related interventions have yielded only modest success so far.

The growing knowledge about the mechanisms of memory consolidation during sleep has sparked extended research in humans on the development of techniques (sect. 7) like closed-loop auditory stimulation and targeted memory reactivation that may help to enhance memory consolidation during sleep in healthy as well as disordered conditions. The overall mixed outcome of these studies should not discourage but calls for a more thorough examination of the mechanisms mediating the stimulating effect of such procedures. Although firm evidence that stimulation procedures, like targeted memory reactivation, enhance memory consolidation during sleep via enhancing the spontaneous neuronal replay of memories is indeed lacking, future research in this regard may take advantage, to a much greater extent, from the study of rodent models.

GLOSSARY

ACC	Anterior cingulate cortex
ADHD	Attention deficit hyperactivity disorder
AMPA	α-Amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid
ASC	Active systems consolidation
ASD	Autism spectrum disorder
ATN	Anterior thalamic nucleus
BMI	Brain-machine interface
CLAS	Auditory closed-loop stimulation
DRM	Deese–Roediger–McDermott (paradigm)
ERP	Event-related response
fMRI	Functional magnetic resonance imaging
HRD	Heart rate deceleration
IPL	Inferior parietal lobule
LC	Locus coeruleus
LFP	Local field potential
LPP	Late positive potential
LTD	Long-term depression
LTP	Long-term potentiation
M1	Primary motor cortex
MCH	Melanin concentrating hormone (neurons)
MEG	Magnetoencephalography
mEPSC	Miniature excitatory postsynaptic current
MFB	Medial forebrain bundle
mGluR	Metabotropic glutamate receptor
(m)PFC	(Medial) prefrontal cortex
NE	Norepinephrine
NMDA	*N*-methyl-D-aspartate
NOR	Novel object recognition (task)
OPR	Object-place recognition (task)
OSA	Obstructive sleep apnea
PD	Postnatal day
PGO	Ponto-geniculo-occipital (wave)
PTSD	Posttraumatic stress disorder
REM	Rapid eye movement
SCR	Skin conductance response
SHY	Synaptic homeostasis hypothesis
SO	Slow oscillation
SRTT	Serial reaction time task
SWA	Slow-wave activity
SW-R	Sharp-wave ripple
SWS	Slow-wave sleep
tACS	Transcranial alternating current stimulation
tDCS	Transcranial direct current stimulation
TMR	Targeted memory reactivation
TMS	Transcranial magnetic stimulation
TRN	Thalamic reticular nucleus
V1	Primary visual cortex
VTA	Ventral tegmental area
WASO	Wake after sleep onset

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AUTHOR CONTRIBUTIONS

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REFERENCES

1. Brown RE, Basheer R, McKenna JT, Strecker RE, McCarley RW. Control of sleep and wakefulness. **Physiol Rev** 92: 1087–1187, 2012. doi:10.1152/physrev.00032.2011.
2. Scammell TE, Arrigoni E, Lipton JO. Neural circuitry of wakefulness and sleep. **Neuron** 93: 747–765, 2017. doi:10.1016/j.neuron.2017.01.014.
3. Datta S, MacLean RR. Neurobiological mechanisms for the regulation of mammalian sleep-wake behavior: reinterpretation of historical evidence and inclusion of contemporary cellular and molecular evidence. **Neurosci Biobehav Rev** 31: 775–824, 2007. doi:10.1016/j.neubiorev.2007.02.004.
4. Yang Z, Williams SD, Beldzik E, Anakwe S, Schimmelpfennig E, Lewis LD. Attentional failures after sleep deprivation represent moments of cerebrospinal fluid flow (Preprint). **bioRxiv** 2024.11.15.623271, 2024. doi:10.1101/2024.11.15.623271.
5. Rasch B, Born J. About sleep's role in memory. **Physiol Rev** 93: 681–766, 2013. doi:10.1152/physrev.00032.2012.
6. Heine R. *Über Wiedererkennen und rückwirkende Hemmung*. Johann Ambrosius Barth, 1914.
7. Jenkins JG, Dallenbach KM. Obliviscence during sleep and waking. **Am J Psychol** 35: 605, 1924. doi:10.2307/1414040.
8. Müller GE, Pilzecker A. *Experimentelle Beiträge zur Lehre vom Gedächtniss*. J.A. Barth, 1900.
9. Mednick SC, Cai DJ, Shuman T, Anagnostaras S, Wixted JT. An opportunistic theory of cellular and systems consolidation. **Trends Neurosci** 34: 504–514, 2011. doi:10.1016/j.tins.2011.06.003.
10. Abel M, Nickl AT, Reßle A, Unger C, Bäuml KH. The role of sleep for memory consolidation: does sleep protect memories from retroactive interference? **Psychon Bull Rev** 30: 2296–2304, 2023. doi:10.3758/s13423-023-02264-8.
11. Ellenbogen JM, Payne JD, Stickgold R. The role of sleep in declarative memory consolidation: passive, permissive, active or none? **Curr Opin Neurobiol** 16: 716–722, 2006. doi:10.1016/J.CONB.2006.10.006.
12. Ellenbogen JM, Hulbert JC, Stickgold R, Dinges DF, Thompson-Schill SL. Interfering with theories of sleep and memory: sleep, declarative memory, and associative interference. **Curr Biol** 16: 1290–1294, 2006. doi:10.1016/j.cub.2006.05.024.
13. Bailes C, Caldwell M, Wamsley EJ, Tucker MA. Does sleep protect memories against interference? A failure to replicate. **PLoS One** 15: e0220419, 2020. doi:10.1371/journal.pone.0220419.
14. Aserinsky E, Kleitman N. Regularly occurring periods of eye motility, and concomitant phenomena, during sleep. **Science** 118: 273–274, 1953. doi:10.1126/science.118.3062.273.
15. Fowler MJ, Sullivan MJ, Ekstrand BR. Sleep and memory. **Science** 179: 302–304, 1973. doi:10.1126/science.179.4070.302.
16. Barrett TR, Ekstrand BR. Effect of sleep on memory. 3. Controlling for time-of-day effects. **J Exp Psychol** 96: 321–327, 1972. doi:10.1037/h0033625.
17. Yaroush R, Sullivan MJ, Ekstrand BR. Effect of sleep on memory. II. Differential effect of the first and second half of the night. **J Exp Psychol** 88: 361–366, 1971. doi:10.1037/h0030914.
18. Squire LR, Zola SM. Episodic memory, semantic memory, and amnesia. **Hippocampus** 8: 205–211, 1998. doi:10.1002/(SICI)1098-1063(1998)8:3<205::AID-HIPO3>3.0.CO;2-I.
19. Squire LR. The organization and neural substrates of human memory. **Int J Neurol** 21-22: 218–222, 1987.
20. Karni A, Tanne D, Rubenstein BS, Askenasy JJ, Sagi D. Dependence on REM sleep of overnight improvement of a perceptual skill. **Science** 265: 679–682, 1994. doi:10.1126/science.8036518.
21. Plihal W, Born J. Effects of early and late nocturnal sleep on declarative and procedural memory. **J Cogn Neurosci** 9: 534–547, 1997. doi:10.1162/jocn.1997.9.4.534.
22. Plihal W, Born J. Effects of early and late nocturnal sleep on priming and spatial memory. **Psychophysiology** 36: 571–582, 1999.
23. Wilson MA, McNaughton BL. Reactivation of hippocampal ensemble memories during sleep. **Science** 265: 676–679, 1994. doi:10.1126/science.8036517.
24. Skaggs WE, McNaughton BL. Replay of neuronal firing sequences in rat hippocampus during sleep following spatial experience. **Science** 271: 1870–1873, 1996. doi:10.1126/science.271.5257.1870.
25. Girardeau G, Benchenane K, Wiener SI, Buzsáki G, Zugaro MB. Selective suppression of hippocampal ripples impairs spatial memory. **Nat Neurosci** 12: 1222–1223, 2009. doi:10.1038/nn.2384.
26. Rasch B, Büchel C, Gais S, Born J. Odor cues during slow-wave sleep prompt declarative memory consolidation. **Science** 315: 1426–1429, 2007. doi:10.1126/science.1138581.
27. Ego-Stengel V, Wilson MA. Disruption of ripple-associated hippocampal activity during rest impairs spatial learning in the rat. **Hippocampus** 20: 1–10, 2010. doi:10.1002/hipo.20707.

28. Diekelmann S, Born J. The memory function of sleep. **Nat Rev Neurosci** 11: 114–126, 2010. doi:10.1038/nrn2762.

29. Hobson JA, Pace-Schott EF. The cognitive neuroscience of sleep: neuronal systems, consciousness and learning. **Nat Rev Neurosci** 3: 679–693, 2002. doi:10.1038/nrn915.

30. Kryger MH, Roth T, Dement WC. *Principles and Practice of Sleep Medicine* (Expert Consult Premium Edition). Saunders, 2010.

31. Vorster AP, Born J. Sleep and memory in mammals, birds and invertebrates. **Neurosci Biobehav Rev** 50: 103–119, 2015. doi:10.1016/j.neubiorev.2014.09.020.

32. Shein-Idelson M, Ondracek JM, Liaw HP, Reiter S, Laurent G. Slow waves, sharp waves, ripples, and REM in sleeping dragons. **Science** 352: 590–595, 2016. doi:10.1126/science.aaf3621.

33. Siegel JM. Do all animals sleep? **Trends Neurosci** 31: 208–213, 2008. doi:10.1016/j.tins.2008.02.001.

34. Rechtschaffen A. Current perspectives on the function of sleep. **Perspect Biol Med** 41: 359–390, 1998. doi:10.1353/pbm.1998.0051.

35. Sejnowski TJ, Destexhe A. Why do we sleep? **Brain Res** 886: 208–223, 2000. doi:10.1016/s0006-8993(00)03007-9.

36. Siegel JM. Clues to the functions of mammalian sleep. **Nature** 437: 1264–1271, 2005. doi:10.1038/nature04285.

37. Frank MG. The mystery of sleep function: current perspectives and future directions. **Rev Neurosci** 17: 375–392, 2006. doi:10.1515/revneuro.2006.17.4.375.

38. Siegel JM. Why we sleep. **Sci Am** 289: 92–97, 2003. doi:10.1038/scientificamerican1103-92.

39. Adam K. Sleep as a restorative process and a theory to explain why. **Prog Brain Res** 53: 289–305, 1980. doi:10.1016/S0079-6123(08)60070-9.

40. Schmidt MH. The energy allocation function of sleep: a unifying theory of sleep, torpor, and continuous wakefulness. **Neurosci Biobehav Rev** 47: 122–153, 2014. doi:10.1016/j.neubiorev.2014.08.001.

41. Xie L, Kang H, Xu Q, Chen MJ, Liao Y, Thiyagarajan M, O'Donnell J, Christensen DJ, Nicholson C, Iliff JJ, Takano T, Deane R, Nedergaard M. Sleep drives metabolite clearance from the adult brain. **Science** 342: 373–377, 2013. doi:10.1126/science.1241224.

42. Schmid SM, Hallschmid M, Schultes B. The metabolic burden of sleep loss. **Lancet Diabetes Endocrinol** 3: 52–62, 2015. doi:10.1016/S2213-8587(14)70012-9.

43. Aalling NN, Nedergaard M, DiNuzzo M. Cerebral metabolic changes during sleep. **Curr Neurol Neurosci Rep** 18: 57, 2018. doi:10.1007/s11910-018-0868-9.

44. Besedovsky L, Lange T, Born J. Sleep and immune function. **Pflugers Arch** 463: 121–137, 2012. doi:10.1007/s00424-011-1044-0.

45. Besedovsky L, Lange T, Haack M. The sleep-immune crosstalk in health and disease. **Physiol Rev** 99: 1325–1380, 2019. doi:10.1152/physrev.00010.2018.

46. Hobson JA. Sleep is of the brain, by the brain and for the brain. **Nature** 437: 1254–1256, 2005. doi:10.1038/nature04283.

47. Lerner I. Sleep is for the brain. In: *Computational Models of Brain and Behavior*, edited by Moustafa AA. Wiley, 2017, p. 245–256.

48. Stickgold R. Sleep-dependent memory consolidation. **Nature** 437: 1272–1278, 2005. doi:10.1038/nature04286.

49. Squire LR, Dede AJ. Conscious and unconscious memory systems. **Cold Spring Harb Perspect Biol** 7: a021667, 2015. doi:10.1101/CSHPERSPECT.A021667.

50. Scoville WB, Milner B. Loss of recent memory after bilateral hippocampal lesions. **J Neurol Neurosurg Psychiatry** 20: 11–21, 1957. doi:10.1136/jnnp.20.1.11.

51. Squire LR. Declarative and nondeclarative memory: multiple brain systems supporting learning and memory. **J Cogn Neurosci** 4: 232–243, 1992. doi:10.1162/jocn.1992.4.3.232.

52. Graf P, Schacter D. Implicit and explicit memory for new associations in normal and amnesic subjects. **J Exp Psychol Learn Mem Cogn** 11: 501–518, 1985. doi:10.1037//0278-7393.11.3.501.

53. Clark RE, Squire LR. Classical conditioning and brain systems: the role of awareness. **Science** 280: 77–81, 1998. doi:10.1126/science.280.5360.77.

54. Smith CN, Squire LR. Experience-dependent eye movements reflect hippocampus-dependent (aware) memory. **J Neurosci** 28: 12825–12833, 2008. doi:10.1523/JNEUROSCI.4542-08.2008.

55. Squire LR, Genzel L, Wixted JT, Morris RG. Memory consolidation. **Cold Spring Harb Perspect Biol** 7: a021766, 2015. doi:10.1101/cshperspect.a021766.

56. Tulving E. Episodic and semantic memory. In: *Organization of Memory*, edited by Tulving E, Donaldson W. Academic Press, 1972.

57. Reber AS. Implicit learning of artificial grammars. **J Verbal Learning Verbal Behav** 6: 855–863, 1967. doi:10.1016/S0022-5371(67)80149-X.

58. Schacter DL. Implicit memory: history and current status. **J Exp Psychol Learn Mem Cogn** 13: 501–518, 1987. doi:10.1037/0278-7393.13.3.501.

59. Schacter DL. Introduction to "Implicit memory: multiple perspectives". **Bull Psychon Soc** 28: 338–340, 1990. doi:10.3758/BF03334038.

60. Roediger HL. Implicit memory. Retention without remembering. **Am Psychol** 45: 1043–1056, 1990. doi:10.1037//0003-066x.45.9.1043.

61. Roediger HL. Implicit memory: a commentary. **Bull Psychon Soc** 28: 373–380, 1990. doi:10.3758/BF03334044.

62. Dudai Y, Karni A, Born J. The consolidation and transformation of memory. **Neuron** 88: 20–32, 2015. doi:10.1016/j.neuron.2015.09.004.

63. Kandel ER, Dudai Y, Mayford MR. The molecular and systems biology of memory. **Cell** 157: 163–186, 2014. doi:10.1016/j.cell.2014.03.001.

64. Cowan N. The magical number 4 in short-term memory: a reconsideration of mental storage capacity. **Behav Brain Sci** 24: 87–114, 2001. doi:10.1017/S0140525X01003922.

65. Miller GA. The magical number seven, plus or minus two: some limits on our capacity for processing information. **Psychol Rev** 101: 343–352, 1994. doi:10.1037/0033-295x.101.2.343.

66. Moscovitch M, Cabeza R, Winocur G, Nadel L. Episodic memory and beyond: the hippocampus and neocortex in transformation. **Annu Rev Psychol** 67: 105–134, 2016. doi:10.1146/annurev-psych-113011-143733.

67. Clopath C. Synaptic consolidation: an approach to long-term learning. **Cogn Neurodyn** 6: 251–257, 2012. doi:10.1007/s11571-011-9177-6.

68. Dudai Y. The restless engram: consolidations never end. **Annu Rev Neurosci** 35: 227–247, 2012. doi:10.1146/annurev-neuro-062111-150500.

69. Winocur G, Moscovitch M. Memory transformation and systems consolidation. **J Int Neuropsychol Soc** 17: 766–780, 2011. doi:10.1017/S1355617711000683.

70. Robertson EM. Memory instability as a gateway to generalization. **PLoS Biol** 16: e2004633, 2018. doi:10.1371/journal.pbio.2004633.

71. Rechtschaffen A, Kales A. *A Manual of Standardized Terminology, Techniques, and Scoring System for Sleep Stages of Human Subjects*. US Government Printing Office, 1968.

72. Iber C, Ancoli-Israel S, Chesson A, Quan SF. *The AASM Manual for the Scoring of Sleep and Associated Events: Rules, Terminology and Technical Specifications*. American Academy of Sleep Medicine, 2007.

73. Moser D, Anderer P, Gruber G, Parapatics S, Loretz E, Boeck M, Kloesch G, Heller E, Schmidt A, Danker-Hopfe H, Saletu B, Zeitlhofer J, Dorffner G. Sleep classification according to AASM and Rechtschaffen & Kales: effects on sleep scoring parameters. **Sleep** 32: 139–149, 2009. doi:10.1093/sleep/32.2.139.

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

75. Ayoub A, Aumann D, Hörschelmann A, Kouchekmanesch A, Paul P, Born J, Marshall L. Differential effects on fast and slow spindle activity, and the sleep slow oscillation in humans with carbamazepine and flunarizine to antagonize voltage-dependent Na^+ and Ca^{2+} channel activity. **Sleep** 36: 905–911, 2013. doi:10.5665/sleep.2722.

76. Steriade M. Grouping of brain rhythms in corticothalamic systems. **Neuroscience** 137: 1087–1106, 2006. doi:10.1016/j.neuroscience.2005.10.029.

77. Destexhe A, Hughes SW, Rudolph M, Crunelli V. Are corticothalamic 'up' states fragments of wakefulness? **Trends Neurosci** 30: 334–342, 2007. doi:10.1016/j.tins.2007.04.006.

78. Luczak A, Barthó P, Marguet SL, Buzsáki G, Harris KD. Sequential structure of neocortical spontaneous activity in vivo. **Proc Natl Acad Sci USA** 104: 347–352, 2007. doi:10.1073/pnas.0605643104.

79. Klinzing JG, Niethard N, Born J. Mechanisms of systems memory consolidation during sleep. **Nat Neurosci** 22: 1598–1610, 2019. doi:10.1038/s41593-019-0467-3.

80. Schreiner T, Staudigl T. Electrophysiological signatures of memory reactivation in humans. **Philos Trans R Soc Lond B Biol Sci** 375: 20190293, 2020. doi:10.1098/rstb.2019.0293.

81. Menon JM, Nolten C, Achterberg EJ, Joosten R, Dematteis M, Feenstra MG, Drinkenburg WH, Leenaars CH. Brain microdialysate monoamines in relation to circadian rhythms, sleep, and sleep deprivation—a systematic review, network meta-analysis, and new primary data. **J Circadian Rhythms** 17: 1, 2019. doi:10.5334/jcr.174.

82. Jouvet M, Michel F, Courjon J. Sur un stade d'activite electrique cerebrale rapide au cours du sommeil physiologique. **C R Seances Soc Biol Fil** 153: 1024–1028, 1959.

83. Jouvet M, Mournier D. Effects des lesions de la formation reticulee pontique sur le sommeil du chat. **C R Seances Soc Biol Fil** 154: 2301–2305, 1960.

84. Pompeiano O. Mechanisms responsible for spinal inhibition during desynchronized sleep: experimental study. In: *Advances in Sleep Research*, edited by Guilleminault C, Dement WC, Passouant P. Narcolepsy. Spectrum, 1976, 3, p. 411–449.

85. Hodes R, Dement WC. Depression of electrically induced reflexes ("H-reflexes") in man during low voltage EEG "sleep". **Electroencephalogr Clin Neurophysiol** 17: 617–629, 1964. doi:10.1016/0013-4694(64)90229-9.

86. Andrillon T, Nir Y, Cirelli C, Tononi G, Fried I. Single-neuron activity and eye movements during human REM sleep and awake vision. **Nat Commun** 6: 7884, 2015. doi:10.1038/ncomms8884.

87. Hutchison IC, Rathore S. The role of REM sleep theta activity in emotional memory. **Front Psychol** 6: 1439, 2015. doi:10.3389/fpsyg.2015.01439.

88. Fernández-Mendoza J, Lozano B, Seijo F, Santamarta-Liébana E, Ramos-Platón MJ, Vela-Bueno A, Fernández-González F. Evidence of subthalamic PGO-like waves during REM sleep in humans: a deep brain polysomnographic study. **Sleep** 32: 1117–1126, 2009. doi:10.1093/sleep/32.9.1117.

89. Datta S, Li G, Auerbach S. Activation of phasic pontine-wave generator in the rat: a mechanism for expression of plasticity-related genes and proteins in the dorsal hippocampus and amygdala. **Eur J Neurosci** 27: 1876–1892, 2008. doi:10.1111/j.1460-9568.2008.06166.x.

90. Wang Z, Fei X, Liu X, Wang Y, Hu Y, Peng W, Wang YW, Zhang S, Xu M. REM sleep is associated with distinct global cortical dynamics and controlled by occipital cortex. **Nat Commun** 13: 6896, 2022. doi:10.1038/s41467-022-34720-9.

91. Gottesmann C. Detection of seven sleep-waking stages in the rat. **Neurosci Biobehav Rev** 16: 31–38, 1992. doi:10.1016/s0149-7634(05)80048-x.

92. Gottesmann C. The transition from slow-wave sleep to paradoxical sleep: evolving facts and concepts of the neurophysiological processes underlying the intermediate stage of sleep. **Neurosci Biobehav Rev** 20: 367–387, 1996. doi:10.1016/0149-7634(95)00055-0.

93. Carrera-Cañas C, Garzón M, de Andrés I. The transition between slow-wave sleep and REM sleep constitutes an independent sleep stage organized by cholinergic mechanisms in the rostrodorsal pontine tegmentum. **Front Neurosci** 13: 748, 2019. doi:10.3389/fnins.2019.00748.

94. Aserinsky E, Kleitman N. Two types of ocular motility occurring in sleep. **J Appl Physiol** 8: 1–10, 1955. doi:10.1152/jappl.1955.8.1.1.

95. Foulkes D, Schmidt M. Temporal sequence and unit composition in dream reports from different stages of sleep. **Sleep** 6: 265–280, 1983. doi:10.1093/sleep/6.3.265.

96. Stickgold R, Malia A, Fosse R, Propper R, Hobson JA. Brain-mind states: I. Longitudinal field study of sleep/wake factors influencing mentation report length. **Sleep** 24: 171–179, 2001. doi:10.1093/sleep/24.2.171.

97. Helfrich RF, Lendner JD, Knight RT. Aperiodic sleep networks promote memory consolidation. **Trends Cogn Sci** 25: 648–659, 2021. doi:10.1016/j.tics.2021.04.009.

98. Lendner JD, Niethard N, Mander BA, van Schalkwijk FJ, Schuh-Hofer S, Schmidt H, Knight RT, Born J, Walker MP, Lin JJ, Helfrich RF. Human REM sleep recalibrates neural activity in support of memory formation. **Sci Adv** 9: eadj1895, 2023. doi:10.1126/sciadv.adj1895.

99. Dement W, Kleitman N. Cyclic variations in EEG during sleep and their relation to eye movements, body motility, and dreaming.

Electroencephalogr Clin Neurophysiol 9: 673–690, 1957. doi:10.1016/0013-4694(57)90088-3.

100. Feinberg I, Floyd TC**.** Systematic trends across the night in human sleep cycles. **Psychophysiology** 16: 283–291, 1979. doi:10.1111/j.1469-8986.1979.tb02991.x.

101. Bierwolf C, Struve K, Marshall L, Born J, Fehm HL**.** Slow wave sleep drives inhibition of pituitary-adrenal secretion in humans. **J Neuroendocrinol** 9: 479–484, 1997. doi:10.1046/j.1365-2826.1997.00605.x.

102. Born J, Hansen K, Marshall L, Mölle M, Fehm HL**.** Timing the end of nocturnal sleep. **Nature** 397: 29–30, 1999. doi:10.1038/16166.

103. Durán E, Oyanedel CN, Niethard N, Inostroza M, Born J**.** Sleep stage dynamics in neocortex and hippocampus. **Sleep** 41: 2018. doi:10.1093/sleep/zsy060.

104. Emrick JJ, Gross BA, Riley BT, Poe GR**.** Different simultaneous sleep states in the hippocampus and neocortex. **Sleep** 39: 2201–2209, 2016. doi:10.5665/sleep.6326.

105. Bernardi G, Siclari F, Handjaras G, Riedner BA, Tononi G**.** Local and widespread slow waves in stable NREM sleep: evidence for distinct regulation mechanisms. **Front Hum Neurosci** 12: 248, 2018. doi:10.3389/fnhum.2018.00248.

106. Siclari F, Bernardi G, Riedner BA, LaRocque JJ, Benca RM, Tononi G**.** Two distinct synchronization processes in the transition to sleep: a high-density electroencephalographic study. **Sleep** 37: 1621–1637, 2014. doi:10.5665/sleep.4070.

107. Inostroza M, Born J**.** Sleep for preserving and transforming episodic memory. **Annu Rev Neurosci** 36: 79–102, 2013. doi:10.1146/annurev-neuro-062012-170429.

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

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

110. Tononi G, Cirelli C**.** Sleep and synaptic homeostasis: a hypothesis. **Brain Res Bull** 62: 143–150, 2003. doi:10.1016/j.brainresbull.2003.09.004.

111. Tononi G, Cirelli C**.** Sleep function and synaptic homeostasis. **Sleep Med Rev** 10: 49–62, 2006. doi:10.1016/j.smrv.2005.05.002.

112. Tononi G, Cirelli C**.** Sleep and the price of plasticity: from synaptic and cellular homeostasis to memory consolidation and integration. **Neuron** 81: 12–34, 2014. doi:10.1016/j.neuron.2013.12.025.

113. Tononi G, Cirelli C**.** Sleep and synaptic down-selection. **Eur J Neurosci** 51: 413–421, 2020. doi:10.1111/ejn.14335.

114. Cirelli C, Tononi G**.** The why and how of sleep-dependent synaptic down-selection. **Semin Cell Dev Biol** 125: 91–100, 2022. doi:10.1016/j.semcdb.2021.02.007.

115. Wixted JT**.** The psychology and neuroscience of forgetting. **Annu Rev Psychol** 55: 235–269, 2004. doi:10.1146/annurev.psych.55.090902.141555.

116. Frankland PW, Bontempi B**.** The organization of recent and remote memories. **Nat Rev Neurosci** 6: 119–130, 2005. doi:10.1038/nrn1607.

117. Marshall L, Born J**.** The contribution of sleep to hippocampus-dependent memory consolidation. **Trends Cogn Sci** 11: 442–450, 2007. doi:10.1016/j.tics.2007.09.001.

118. Ji D, Wilson MA**.** Coordinated memory replay in the visual cortex and hippocampus during sleep. **Nat Neurosci** 10: 100–107, 2007. doi:10.1038/nn1825.

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

120. Gais S, Albouy G, Boly M, Dang-Vu TT, Darsaud A, Desseilles M, Rauchs G, Schabus M, Sterpenich V, Vandewalle G, Maquet P, Peigneux P**.** Sleep transforms the cerebral trace of declarative memories. **Proc Natl Acad Sci USA** 104: 18778–18783, 2007. doi:10.1073/pnas.0705454104.

121. Orban P, Rauchs G, Balteau E, Degueldre C, Luxen A, Maquet P, Peigneux P**.** Sleep after spatial learning promotes covert reorganization of brain activity. **Proc Natl Acad Sci USA** 103: 7124–7129, 2006. doi:10.1073/pnas.0510198103.

122. Takashima A, Nieuwenhuis IL, Jensen O, Talamini LM, Rijpkema M, Fernández G**.** Shift from hippocampal to neocortical centered retrieval network with consolidation. **J Neurosci** 29: 10087–10093, 2009. doi:10.1523/JNEUROSCI.0799-09.2009.

123. Takashima A, Petersson KM, Rutters F, Tendolkar I, Jensen O, Zwarts MJ, McNaughton BL, Fernández G**.** Declarative memory consolidation in humans: a prospective functional magnetic resonance imaging study. **Proc Natl Acad Sci USA** 103: 756–761, 2006. doi:10.1073/pnas.0507774103.

124. Miyamoto D, Marshall W, Tononi G, Cirelli C**.** Net decrease in spine-surface GluA1-containing AMPA receptors after post-learning sleep in the adult mouse cortex. **Nat Commun** 12: 2881, 2021. doi:10.1038/s41467-021-23156-2.

125. Clemens Z, Mölle M, Eross L, Barsi P, Halász P, Born J**.** Temporal coupling of parahippocampal ripples, sleep spindles and slow oscillations in humans. **Brain** 130: 2868–2878, 2007. doi:10.1093/brain/awm146.

126. Azimi A, Alizadeh Z, Ghorbani M**.** The essential role of hippocampo-cortical connections in temporal coordination of spindles and ripples. **Neuroimage** 243: 118485, 2021. doi:10.1016/j.neuroimage.2021.118485.

127. Mölle M, Eschenko O, Gais S, Sara SJ, Born J**.** The influence of learning on sleep slow oscillations and associated spindles and ripples in humans and rats. **Eur J Neurosci** 29: 1071–1081, 2009. doi:10.1111/j.1460-9568.2009.06654.x.

128. Oyanedel CN, Durán E, Niethard N, Inostroza M, Born J**.** Temporal associations between sleep slow oscillations, spindles and ripples. **Eur J Neurosci** 52: 4762–4778, 2020. doi:10.1111/ejn.14906.

129. Siapas AG, Wilson MA**.** Coordinated interactions between hippocampal ripples and cortical spindles during slow-wave sleep. **Neuron** 21: 1123–1128, 1998. doi:10.1016/s0896-6273(00)80629-7.

130. Staresina BP, Bergmann TO, Bonnefond M, van der Meij R, Jensen O, Deuker L, Elger CE, Axmacher N, Fell J**.** Hierarchical nesting of slow oscillations, spindles and ripples in the human hippocampus during sleep. **Nat Neurosci** 18: 1679–1686, 2015. doi:10.1038/nn.4119.

131. Lutz ND, Martínez-Albert E, Friedrich H, Born J, Besedovsky L**.** Sleep shapes the associative structure underlying pattern completion in multielement event memory. **Proc Natl Acad Sci USA** 121: e2314423121, 2024. doi:10.1073/pnas.2314423121.

132. Lutz ND, Diekelmann S, Hinse-Stern P, Born J, Rauss K**.** Sleep supports the slow abstraction of gist from visual perceptual memories. **Sci Rep** 7: 42950, 2017. doi:10.1038/srep42950.

133. Friedrich M, Wilhelm I, Born J, Friederici AD. Generalization of word meanings during infant sleep. **Nat Commun** 6: 6004, 2015. doi:10.1038/ncomms7004.

134. Lewis PA, Durrant SJ. Overlapping memory replay during sleep builds cognitive schemata. **Trends Cogn Sci** 15: 343–351, 2011. doi:10.1016/j.tics.2011.06.004.

135. Sawangjit A, Oyanedel CN, Niethard N, Salazar C, Born J, Inostroza M. The hippocampus is crucial for forming non-hippocampal long-term memory during sleep. **Nature** 564: 109–113, 2018. doi:10.1038/s41586-018-0716-8.

136. Schapiro AC, Reid AG, Morgan A, Manoach DS, Verfaellie M, Stickgold R. The hippocampus is necessary for the consolidation of a task that does not require the hippocampus for initial learning. **Hippocampus** 29: 1091–1100, 2019. doi:10.1002/hipo.23101.

137. Albouy G, Fogel S, King BR, Laventure S, Benali H, Karni A, Carrier J, Robertson EM, Doyon J. Maintaining vs. enhancing motor sequence memories: respective roles of striatal and hippocampal systems. **Neuroimage** 108: 423–434, 2015. doi:10.1016/J.NEUROIMAGE.2014.12.049.

138. King BR, Hoedlmoser K, Hirschauer F, Dolfen N, Albouy G. Sleeping on the motor engram: the multifaceted nature of sleep-related motor memory consolidation. **Neurosci Biobehav Rev** 80: 1–22, 2017. doi:10.1016/j.neubiorev.2017.04.026.

139. Nere A, Hashmi A, Cirelli C, Tononi G. Sleep-dependent synaptic down-selection (I): modeling the benefits of sleep on memory consolidation and integration. **Front Neurol** 4: 143, 2013. doi:10.3389/fneur.2013.00143.

140. Suppermpool A, Lyons DG, Broom E, Rihel J. Sleep pressure modulates single-neuron synapse number in zebrafish. **Nature** 629: 639–645, 2024. doi:10.1038/s41586-024-07367-3.

141. Puentes-Mestril C, Aton SJ. Linking network activity to synaptic plasticity during sleep: hypotheses and recent data. **Front Neural Circuits** 11: 61, 2017. doi:10.3389/fncir.2017.00061.

142. de Vivo L, Bellesi M, Marshall W, Bushong EA, Ellisman MH, Tononi G, Cirelli C. Ultrastructural evidence for synaptic scaling across the wake/sleep cycle. **Science** 355: 507–510, 2017. doi:10.1126/science.aah5982.

143. Spano GM, Banningh SW, Marshall W, de Vivo L, Bellesi M, Loschky SS, Tononi G, Cirelli C. Sleep deprivation by exposure to novel objects increases synapse density and axon-spine interface in the hippocampal CA1 region of adolescent mice. **J Neurosci** 39: 6613–6625, 2019. doi:10.1523/JNEUROSCI.0380-19.2019.

144. Vyazovskiy VV, Cirelli C, Pfister-Genskow M, Faraguna U, Tononi G. Molecular and electrophysiological evidence for net synaptic potentiation in wake and depression in sleep. **Nat Neurosci** 11: 200–208, 2008. doi:10.1038/nn2035.

145. Diering GH, Nirujogi RS, Roth RH, Worley PF, Pandey A, Huganir RL. Homer1a drives homeostatic scaling-down of excitatory synapses during sleep. **Science** 355: 511–515, 2017. doi:10.1126/science.aai8355.

146. Brüning F, Noya SB, Bange T, Koutsouli S, Rudolph JD, Tyagarajan SK, Cox J, Mann M, Brown SA, Robles MS. Sleep-wake cycles drive daily dynamics of synaptic phosphorylation. **Science** 366: eaav3617, 2019. doi:10.1126/science.aav3617.

147. Vyazovskiy VV, Olcese U, Lazimy YM, Faraguna U, Esser SK, Williams JC, Cirelli C, Tononi G. Cortical firing and sleep homeostasis. **Neuron** 63: 865–878, 2009. doi:10.1016/j.neuron.2009.08.024.

148. Grosmark AD, Mizuseki K, Pastalkova E, Diba K, Buzsáki G. REM sleep reorganizes hippocampal excitability. **Neuron** 75: 1001–1007, 2012. doi:10.1016/j.neuron.2012.08.015.

149. Miyawaki H, Diba K. Regulation of hippocampal firing by network oscillations during sleep. **Curr Biol** 26: 893–902, 2016. doi:10.1016/j.cub.2016.02.024.

150. Hengen KB, Torrado Pacheco A, McGregor JN, van Hooser SD, Turrigiano GG. Neuronal firing rate homeostasis is inhibited by sleep and promoted by wake. **Cell** 165: 180–191, 2016. doi:10.1016/j.cell.2016.01.046.

151. Torrado Pacheco A, Bottorff J, Gao Y, Turrigiano GG. Sleep promotes downward firing rate homeostasis. **Neuron** 109: 530–544.e6, 2021. doi:10.1016/j.neuron.2020.11.001.

152. Liu ZW, Faraguna U, Cirelli C, Tononi G, Gao XB. Direct evidence for wake-related increases and sleep-related decreases in synaptic strength in rodent cortex. **J Neurosci** 30: 8671–8675, 2010. doi:10.1523/JNEUROSCI.1409-10.2010.

153. Bjorness TE, Kulkarni A, Rybalchenko V, Suzuki A, Bridges C, Harrington AJ, Cowan CW, Takahashi JS, Konopka G, Greene RW. An essential role for MEF2C in the cortical response to loss of sleep in mice. **eLife** 9: e58331, 2020. doi:10.7554/eLife.58331.

154. Khlghatyan J, Evstratova A, Bozoyan L, Chamberland S, Chatterjee D, Marakhovskaia A, Soares Silva T, Toth K, Mongrain V, Beaulieu JM. Fxr1 regulates sleep and synaptic homeostasis. **EMBO J** 39: e103864, 2020. doi:10.15252/embj.2019103864.

155. Bridi MC, Zong FJ, Min X, Luo N, Tran T, Qiu J, Severin D, Zhang XT, Wang G, Zhu ZJ, He KW, Kirkwood A. Daily oscillation of the excitation-inhibition balance in visual cortical circuits. **Neuron** 105: 621–629.e4, 2020. doi:10.1016/j.neuron.2019.11.011.

156. Cary BA, Turrigiano GG. Stability of neocortical synapses across sleep and wake states during the critical period in rats. **eLife** 10: e66304, 2021. doi:10.7554/eLife.66304.

157. Huber R, Mäki H, Rosanova M, Casarotto S, Canali P, Casali AG, Tononi G, Massimini M. Human cortical excitability increases with time awake. **Cereb Cortex** 23: 332–338, 2013. doi:10.1093/cercor/bhs014.

158. Kuhn M, Wolf E, Maier JG, Mainberger F, Feige B, Schmid H, Bürklin J, Maywald S, Mall V, Jung NH, Reis J, Spiegelhalder K, Klöppel S, Sterr A, Eckert A, Riemann D, Normann C, Nissen C. Sleep recalibrates homeostatic and associative synaptic plasticity in the human cortex. **Nat Commun** 7: 12455, 2016. doi:10.1038/ncomms12455.

159. Salehinejad MA, Ghanavati E, Reinders J, Hengstler JG, Kuo MF, Nitsche MA. Sleep-dependent upscaled excitability, saturated neuroplasticity, and modulated cognition in the human brain. **eLife** 11: e69308, 2022. doi:10.7554/eLife.69308.

160. Niethard N, Hasegawa M, Itokazu T, Oyanedel CN, Born J, Sato TR. Sleep-stage-specific regulation of cortical excitation and inhibition. **Curr Biol** 26: 2739–2749, 2016. doi:10.1016/j.cub.2016.08.035.

161. Huber R, Ghilardi MF, Massimini M, Ferrarelli F, Riedner BA, Peterson MJ, Tononi G. Arm immobilization causes cortical plastic changes and locally decreases sleep slow wave activity. **Nat Neurosci** 9: 1169–1176, 2006. doi:10.1038/nn1758.

162. Liu J, Niethard N, Lun Y, Dimitrov S, Ehrlich I, Born J, Hallschmid M. Slow-wave sleep drives sleep-dependent renormalization of synaptic AMPA receptor levels in the hypothalamus. **PLoS Biol** 22: e3002768, 2024. doi:10.1371/journal.pbio.3002768.

163. Squarcio F, Tononi G, Cirelli C**.** Effects of non-rapid eye movement sleep on the cortical synaptic expression of GluA1-containing AMPA receptors. **Eur J Neurosci** 60: 3961–3972, 2024. doi:10.1111/ejn.16460.

164. Yang G, Lai CS, Cichon J, Ma L, Li W, Gan WB**.** Sleep promotes branch-specific formation of dendritic spines after learning. **Science** 344: 1173–1178, 2014. doi:10.1126/science.1249098.

165. Chauvette S, Seigneur J, Timofeev I**.** Sleep oscillations in the thalamocortical system induce long-term neuronal plasticity. **Neuron** 75: 1105–1113, 2012. doi:10.1016/j.neuron.2012.08.034.

166. Watson BO, Levenstein D, Greene JP, Gelinas JN, Buzsáki G**.** Network homeostasis and state dynamics of neocortical sleep. **Neuron** 90: 839–852, 2016. doi:10.1016/j.neuron.2016.03.036.

167. Zhou Y, Lai CS, Bai Y, Li W, Zhao R, Yang G, Frank MG, Gan WB**.** REM sleep promotes experience-dependent dendritic spine elimination in the mouse cortex. **Nat Commun** 11: 4819, 2020. doi:10.1038/s41467-020-18592-5.

168. Li W, Ma L, Yang G, Gan WB**.** REM sleep selectively prunes and maintains new synapses in development and learning. **Nat Neurosci** 20: 427–437, 2017. doi:10.1038/nn.4479.

169. Diekelmann S, Born J**.** Slow-wave sleep takes the leading role in memory reorganization. **Nat Rev Neurosci** 11: 218, 2010. doi:10.1038/nrn2762-c2.

170. Born J**.** Slow-wave sleep and the consolidation of long-term memory. **World J Biol Psychiatry** 11, *Suppl* 2: 16–21, 2010. doi:10.3109/15622971003637637.

171. Walker MP**.** The role of slow wave sleep in memory processing. **J Clin Sleep Med** 5: S20–S26, 2009.

172. Cordi MJ, Rasch B**.** No evidence for intra-individual correlations between sleep-mediated declarative memory consolidation and slow-wave sleep. **Sleep** 44: zsab034, 2021. doi:10.1093/sleep/zsab034.

173. Genzel L, Kroes MC, Dresler M, Battaglia FP**.** Light sleep versus slow wave sleep in memory consolidation: a question of global versus local processes? **Trends Neurosci** 37: 10–19, 2014. doi:10.1016/j.tins.2013.10.002.

174. Niknazar H, Malerba P, Mednick SC**.** Slow oscillations promote long-range effective communication: the key for memory consolidation in a broken-down network. **Proc Natl Acad Sci USA** 119: e2122515119, 2022. doi:10.1073/pnas.2122515119.

175. Payne JD, Schacter DL, Propper RE, Huang LW, Wamsley EJ, Tucker MA, Walker MP, Stickgold R**.** The role of sleep in false memory formation. **Neurobiol Learn Mem** 92: 327–334, 2009. doi:10.1016/j.nlm.2009.03.007.

176. Pardilla-Delgado E, Payne JD**.** The impact of sleep on true and false memory across long delays. **Neurobiol Learn Mem** 137: 123–133, 2017. doi:10.1016/j.nlm.2016.11.016.

177. Kurz EM, Conzelmann A, Barth GM, Renner TJ, Zinke K, Born J**.** How do children with autism spectrum disorder form gist memory during sleep? A study of slow oscillation-spindle coupling. **Sleep** 44: zsaa290, 2021. doi:10.1093/sleep/zsaa290.

178. Sawangjit A, Oyanedel CN, Niethard N, Born J, Inostroza M**.** Deepened sleep makes hippocampal spatial memory more persistent. **Neurobiol Learn Mem** 173: 107245, 2020. doi:10.1016/j.nlm.2020.107245.

179. Sterpenich V, van Schie MK, Catsiyannis M, Ramyead A, Perrig S, Yang HD, van de Ville D, Schwartz S**.** Reward biases spontaneous neural reactivation during sleep. **Nat Commun** 12: 4162, 2021. doi:10.1038/s41467-021-24357-5.

180. Giri B, Miyawaki H, Mizuseki K, Cheng S, Diba K**.** Hippocampal reactivation extends for several hours following novel experience. **J Neurosci** 39: 866–875, 2019. doi:10.1523/JNEUROSCI.1950-18.2018.

181. de Lavilléon G, Lacroix MM, Rondi-Reig L, Benchenane K**.** Explicit memory creation during sleep demonstrates a causal role of place cells in navigation. **Nat Neurosci** 18: 493–495, 2015. doi:10.1038/nn.3970.

182. Pavlides C, Winson J**.** Influences of hippocampal place cell firing in the awake state on the activity of these cells during subsequent sleep episodes. **J Neurosci** 9: 2907–2918, 1989. doi:10.1523/JNEUROSCI.09-08-02907.1989.

183. O'Neill J, Pleydell-Bouverie B, Dupret D, Csicsvari J**.** Play it again: reactivation of waking experience and memory. **Trends Neurosci** 33: 220–229, 2010. doi:10.1016/j.tins.2010.01.006.

184. Findlay G, Tononi G, Cirelli C**.** The evolving view of replay and its functions in wake and sleep. **Sleep Adv** 1: zpab002, 2020. doi:10.1093/sleepadvances/zpab002.

185. Meier K, Merseburg A, Isbrandt D, Marguet SL, Morellini F**.** Dentate gyrus sharp waves, a local field potential correlate of learning in the dentate gyrus of mice. **J Neurosci** 40: 7105–7118, 2020. doi:10.1523/JNEUROSCI.2275-19.2020.

186. Buzsáki G**.** Hippocampal sharp wave-ripple: a cognitive biomarker for episodic memory and planning. **Hippocampus** 25: 1073–1188, 2015. doi:10.1002/hipo.22488.

187. Villalobos C, Maldonado PE, Valdés JL**.** Asynchronous ripple oscillations between left and right hippocampi during slow-wave sleep. **PLoS One** 12: e0171304, 2017. doi:10.1371/journal.pone.0171304.

188. Hwaun E, Colgin LL**.** CA3 place cells that represent a novel waking experience are preferentially reactivated during sharp wave-ripples in subsequent sleep. **Hippocampus** 29: 921–938, 2019. doi:10.1002/hipo.23090.

189. Oliva A, Fernández-Ruiz A, Leroy F, Siegelbaum SA**.** Hippocampal CA2 sharp-wave ripples reactivate and promote social memory. **Nature** 587: 264–269, 2020. doi:10.1038/s41586-020-2758-y.

190. van de Ven GM, Trouche S, McNamara CG, Allen K, Dupret D**.** Hippocampal offline reactivation consolidates recently formed cell assembly patterns during sharp wave-ripples. **Neuron** 92: 968–974, 2016. doi:10.1016/j.neuron.2016.10.020.

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

192. Fernández-Ruiz A, Oliva A, Fermino de Oliveira E, Rocha-Almeida F, Tingley D, Buzsáki G**.** Long-duration hippocampal sharp wave ripples improve memory. **Science** 364: 1082–1086, 2019. doi:10.1126/science.aax0758.

193. Quigley LD, Pendry R, Mendoza ML, Pfeiffer BE, Volk LJ**.** Experience alters hippocampal and cortical network communication via a KIBRA-dependent mechanism. **Cell Rep** 42: 112662, 2023. doi:10.1016/j.celrep.2023.112662.

194. Karaba LA, Robinson HL, Harvey RE, Chen W, Fernandez-Ruiz A, Oliva A**.** A hippocampal circuit mechanism to balance memory

reactivation during sleep. **Science** 385: 738–743, 2024. doi:10.1126/science.ado5708.

195. Dave AS, Margoliash D. Song replay during sleep and computational rules for sensorimotor vocal learning. **Science** 290: 812–816, 2000. doi:10.1126/science.290.5492.812.

196. Dag U, Lei Z, Le JQ, Wong A, Bushey D, Keleman K. Neuronal reactivation during post-learning sleep consolidates long-term memory in *Drosophila*. **eLife** 8: e42786, 2019. doi:10.7554/eLife.42786.

197. Piantoni G, van der Werf YD, Jensen O, van Someren EJ. Memory traces of long-range coordinated oscillations in the sleeping human brain. **Hum Brain Mapp** 36: 67–84, 2015. doi:10.1002/hbm.22613.

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

199. Belal S, Cousins J, El-Deredy W, Parkes L, Schneider J, Tsujimura H, Zoumpoulaki A, Perapoch M, Santamaria L, Lewis P. Identification of memory reactivation during sleep by EEG classification. **Neuroimage** 176: 203–214, 2018. doi:10.1016/j.neuroimage.2018.04.029.

200. Jiang X, Shamie I, K Doyle W, Friedman D, Dugan P, Devinsky O, Eskandar E, Cash SS, Thesen T, Halgren E. Replay of large-scale spatio-temporal patterns from waking during subsequent NREM sleep in human cortex. **Sci Rep** 7: 17380, 2017. doi:10.1038/s41598-017-17469-w.

201. Tacikowski P, Kalender G, Ciliberti D, Fried I. Human hippocampal and entorhinal neurons encode the temporal structure of experience. **Nature** 635: 160–167, 2024. doi:10.1038/s41586-024-07973-1.

202. Norimoto H, Makino K, Gao M, Shikano Y, Okamoto K, Ishikawa T, Sasaki T, Hioki H, Fujisawa S, Ikegaya Y. Hippocampal ripples down-regulate synapses. **Science** 359: 1524–1527, 2018. doi:10.1126/science.aao0702.

203. Rudoy JD, Voss JL, Westerberg CE, Paller KA. Strengthening individual memories by reactivating them during sleep. **Science** 326: 1079, 2009. doi:10.1126/science.1179013.

204. Foster DJ, Wilson MA. Reverse replay of behavioural sequences in hippocampal place cells during the awake state. **Nature** 440: 680–683, 2006. doi:10.1038/nature04587.

205. Karlsson MP, Frank LM. Awake replay of remote experiences in the hippocampus. **Nat Neurosci** 12: 913–918, 2009. doi:10.1038/nn.2344.

206. Shin JD, Tang W, Jadhav SP. Dynamics of awake hippocampal-prefrontal replay for spatial learning and memory-guided decision making. **Neuron** 104: 1110–1125.e7, 2019. doi:10.1016/j.neuron.2019.09.012.

207. Diba K, Buzsáki G. Forward and reverse hippocampal place-cell sequences during ripples. **Nat Neurosci** 10: 1241–1242, 2007. doi:10.1038/nn1961.

208. Pfeiffer BE, Foster DJ. Hippocampal place-cell sequences depict future paths to remembered goals. **Nature** 497: 74–79, 2013. doi:10.1038/nature12112.

209. Bush D, Ólafsdóttir HF, Barry C, Burgess N. Ripple band phase precession of place cell firing during replay. **Curr Biol** 32: 64–73.e5, 2022. doi:10.1016/j.cub.2021.10.033.

210. Liu Y, Dolan RJ, Kurth-Nelson Z, Behrens TE. Human replay spontaneously reorganizes experience. **Cell** 178: 640–652.e14, 2019. doi:10.1016/j.cell.2019.06.012.

211. Schuck NW, Niv Y. Sequential replay of nonspatial task states in the human hippocampus. **Science** 364: eaaw5181, 2019. doi:10.1126/science.aaw5181.

212. Wamsley EJ. Memory consolidation during waking rest. **Trends Cogn Sci** 23: 171–173, 2019. doi:10.1016/j.tics.2018.12.007.

213. Wikenheiser AM, Redish AD. The balance of forward and backward hippocampal sequences shifts across behavioral states. **Hippocampus** 23: 22–29, 2013. doi:10.1002/hipo.22049.

214. Dragoi G, Tonegawa S. Preplay of future place cell sequences by hippocampal cellular assemblies. **Nature** 469: 397–401, 2011. doi:10.1038/nature09633.

215. Davidson TJ, Kloosterman F, Wilson MA. Hippocampal replay of extended experience. **Neuron** 63: 497–507, 2009. doi:10.1016/j.neuron.2009.07.027.

216. Ólafsdóttir HF, Barry C, Saleem AB, Hassabis D, Spiers HJ. Hippocampal place cells construct reward related sequences through unexplored space. **eLife** 4: e06063, 2015. doi:10.7554/eLife.06063.

217. Stella F, Baracskay P, O'Neill J, Csicsvari J. Hippocampal reactivation of random trajectories resembling Brownian diffusion. **Neuron** 102: 450–461.e7, 2019. doi:10.1016/j.neuron.2019.01.052.

218. Joo HR, Frank LM. The hippocampal sharp wave-ripple in memory retrieval for immediate use and consolidation. **Nat Rev Neurosci** 19: 744–757, 2018. doi:10.1038/s41583-018-0077-1.

219. Foster DJ. Replay comes of age. **Annu Rev Neurosci** 40: 581–602, 2017. doi:10.1146/annurev-neuro-072116-031538.

220. O'Neill J, Senior TJ, Allen K, Huxter JR, Csicsvari J. Reactivation of experience-dependent cell assembly patterns in the hippocampus. **Nat Neurosci** 11: 209–215, 2008. doi:10.1038/nn2037.

221. Ambrose RE, Pfeiffer BE, Foster DJ. Reverse replay of hippocampal place cells is uniquely modulated by changing reward. **Neuron** 91: 1124–1136, 2016. doi:10.1016/j.neuron.2016.07.047.

222. Michon F, Sun JJ, Kim CY, Ciliberti D, Kloosterman F. Post-learning hippocampal replay selectively reinforces spatial memory for highly rewarded locations. **Curr Biol** 29: 1436–1444.e5, 2019. doi:10.1016/j.cub.2019.03.048.

223. Gruber MJ, Ritchey M, Wang SF, Doss MK, Ranganath C. Post-learning hippocampal dynamics promote preferential retention of rewarding events. **Neuron** 89: 1110–1120, 2016. doi:10.1016/j.neuron.2016.01.017.

224. Carey AA, Tanaka Y, van der Meer MA. Reward revaluation biases hippocampal replay content away from the preferred outcome. **Nat Neurosci** 22: 1450–1459, 2019. doi:10.1038/s41593-019-0464-6.

225. Grosmark AD, Sparks FT, Davis MJ, Losonczy A. Reactivation predicts the consolidation of unbiased long-term cognitive maps. **Nat Neurosci** 24: 1574–1585, 2021. doi:10.1038/s41593-021-00920-7.

226. Dupret D, O'Neill J, Pleydell-Bouverie B, Csicsvari J. The reorganization and reactivation of hippocampal maps predict spatial memory performance. **Nat Neurosci** 13: 995–1002, 2010. doi:10.1038/nn.2599.

227. Carr MF, Jadhav SP, Frank LM. Hippocampal replay in the awake state: a potential substrate for memory consolidation and retrieval. **Nat Neurosci** 14: 147–153, 2011. doi:10.1038/nn.2732.

228. Staresina BP, Alink A, Kriegeskorte N, Henson RN. Awake reactivation predicts memory in humans. **Proc Natl Acad Sci USA** 110: 21159–21164, 2013. doi:10.1073/pnas.1311989110.

229. Tambini A, Davachi L. Persistence of hippocampal multivoxel patterns into postencoding rest is related to memory. **Proc Natl Acad Sci USA** 110: 19591–19596, 2013. doi:10.1073/pnas.1308499110.

230. Roux L, Hu B, Eichler R, Stark E, Buzsáki G. Sharp wave ripples during learning stabilize the hippocampal spatial map. **Nat Neurosci** 20: 845–853, 2017. doi:10.1038/nn.4543.

231. Tang W, Shin JD, Frank LM, Jadhav SP. Hippocampal-prefrontal reactivation during learning is stronger in awake compared with sleep states. **J Neurosci** 37: 11789–11805, 2017. doi:10.1523/JNEUROSCI.2291-17.2017.

232. Grosmark AD, Buzsáki G. Diversity in neural firing dynamics supports both rigid and learned hippocampal sequences. **Science** 351: 1440–1443, 2016. doi:10.1126/science.aad1935.

233. Roumis DK, Frank LM. Hippocampal sharp-wave ripples in waking and sleeping states. **Curr Opin Neurobiol** 35: 6–12, 2015. doi:10.1016/j.conb.2015.05.001.

234. Sawangjit A, Harkotte M, Oyanedel CN, Niethard N, Born J, Inostroza M. Two distinct ways to form long-term object recognition memory during sleep and wakefulness. **Proc Natl Acad Sci USA** 119: e2203165119, 2022. doi:10.1073/pnas.2203165119.

235. Barnes DC, Wilson DA. Slow-wave sleep-imposed replay modulates both strength and precision of memory. **J Neurosci** 34: 5134–5142, 2014. doi:10.1523/JNEUROSCI.5274-13.2014.

236. Ai SZ, Chen J, Liu JF, He J, Xue YX, Bao YP, Han F, Tang XD, Lu L, Shi J. Exposure to extinction-associated contextual tone during slow-wave sleep and wakefulness differentially modulates fear expression. **Neurobiol Learn Mem** 123: 159–167, 2015. doi:10.1016/j.nlm.2015.06.005.

237. Brodt S, Pöhlchen D, Flanagin VL, Glasauer S, Gais S, Schönauer M. Rapid and independent memory formation in the parietal cortex. **Proc Natl Acad Sci USA** 113: 13251–13256, 2016. doi:10.1073/pnas.1605719113.

238. Himmer L, Schönauer M, Heib DP, Schabus M, Gais S. Rehearsal initiates systems memory consolidation, sleep makes it last. **Sci Adv** 5: eaav1695, 2019. doi:10.1126/sciadv.aav1695.

239. Chouhan NS, Griffith LC, Haynes P, Sehgal A. Availability of food determines the need for sleep in memory consolidation. **Nature** 589: 582–585, 2021. doi:10.1038/s41586-020-2997-y.

240. de Sousa AF, Cowansage KK, Zutshi I, Cardozo LM, Yoo EJ, Leutgeb S, Mayford M. Optogenetic reactivation of memory ensembles in the retrosplenial cortex induces systems consolidation. **Proc Natl Acad Sci USA** 116: 8576–8581, 2019. doi:10.1073/pnas.1818432116.

241. Atherton LA, Dupret D, Mellor JR. Memory trace replay: the shaping of memory consolidation by neuromodulation. **Trends Neurosci** 38: 560–570, 2015. doi:10.1016/j.tins.2015.07.004.

242. Hasselmo ME, McGaughy J. High acetylcholine levels set circuit dynamics for attention and encoding and low acetylcholine levels set dynamics for consolidation. **Prog Brain Res** 145: 207–231, 2004. doi:10.1016/S0079-6123(03)45015-2.

243. Rasch BH, Born J, Gais S. Combined blockade of cholinergic receptors shifts the brain from stimulus encoding to memory consolidation. **J Cogn Neurosci** 18: 793–802, 2006. doi:10.1162/jocn.2006.18.5.793.

244. Girardeau G, Inema I, Buzsáki G. Reactivations of emotional memory in the hippocampus-amygdala system during sleep. **Nat Neurosci** 20: 1634–1642, 2017. doi:10.1038/nn.4637.

245. Buzsáki G. The hippocampo-neocortical dialogue. **Cereb Cortex** 6: 81–92, 1996. doi:10.1093/cercor/6.2.81.

246. Olcese U, Bos JJ, Vinck M, Pennartz CM. Functional determinants of enhanced and depressed interareal information flow in nonrapid eye movement sleep between neuronal ensembles in rat cortex and hippocampus. **Sleep** 41: 2018. doi:10.1093/sleep/zsy167.

247. Mitra A, Snyder AZ, Hacker CD, Pahwa M, Tagliazucchi E, Laufs H, Leuthardt EC, Raichle ME. Human cortical-hippocampal dialogue in wake and slow-wave sleep. **Proc Natl Acad Sci USA** 113: E6868–E6876, 2016. doi:10.1073/pnas.1607289113.

248. Qin YL, McNaughton BL, Skaggs WE, Barnes CA. Memory reprocessing in corticocortical and hippocampocortical neuronal ensembles. **Philos Trans R Soc Lond B Biol Sci** 352: 1525–1533, 1997. doi:10.1098/rstb.1997.0139.

249. Aly MH, Abdou K, Okubo-Suzuki R, Nomoto M, Inokuchi K. Selective engram coreactivation in idling brain inspires implicit learning. **Proc Natl Acad Sci USA** 119: e2201578119, 2022. doi:10.1073/pnas.2201578119.

250. Kaefer K, Nardin M, Blahna K, Csicsvari J. Replay of behavioral sequences in the medial prefrontal cortex during rule switching. **Neuron** 106: 154–165.e6, 2020. doi:10.1016/j.neuron.2020.01.015.

251. Wilber AA, Skelin I, Wu W, McNaughton BL. Laminar organization of encoding and memory reactivation in the parietal cortex. **Neuron** 95: 1406–1419.e5, 2017. doi:10.1016/j.neuron.2017.08.033.

252. Gulati T, Ramanathan DS, Wong CC, Ganguly K. Reactivation of emergent task-related ensembles during slow-wave sleep after neuroprosthetic learning. **Nat Neurosci** 17: 1107–1113, 2014. doi:10.1038/nn.3759.

253. Gulati T, Guo L, Ramanathan DS, Bodepudi A, Ganguly K. Neural reactivations during sleep determine network credit assignment. **Nat Neurosci** 20: 1277–1284, 2017. doi:10.1038/nn.4601.

254. Rubin DB, Hosman T, Kelemen JN, Kapitonava A, Willett FR, Coughlin BF, Halgren E, Kimchi EY, Williams ZM, Simeral JD, Hochberg LR, Cash SS. Learned motor patterns are replayed in human motor cortex during sleep. **J Neurosci** 42: 5007–5020, 2022. doi:10.1523/JNEUROSCI.2074-21.2022.

255. Clawson BC, Pickup EJ, Ensing A, Geneseo L, Shaver J, Gonzalez-Amoretti J, Zhao M, York AK, Kuhn FR, Swift K, Martinez JD, Wang L, Jiang S, Aton SJ. Causal role for sleep-dependent reactivation of learning-activated sensory ensembles for fear memory consolidation. **Nat Commun** 12: 1200, 2021. doi:10.1038/s41467-021-21471-2.

256. Miyamoto D, Hirai D, Fung CC, Inutsuka A, Odagawa M, Suzuki T, Boehringer R, Adaikkan C, Matsubara C, Matsuki N, Fukai T, McHugh TJ, Yamanaka A, Murayama M. Top-down cortical input during NREM sleep consolidates perceptual memory. **Science** 352: 1315–1318, 2016. doi:10.1126/science.aaf0902.

257. O'Neill J, Boccara CN, Stella F, Schoenenberger P, Csicsvari J. Superficial layers of the medial entorhinal cortex replay independently of the hippocampus. **Science** 355: 184–188, 2017. doi:10.1126/science.aag2787.

258. Trettel SG, Trimper JB, Hwaun E, Fiete IR, Colgin LL. Grid cell co-activity patterns during sleep reflect spatial overlap of grid fields during active behaviors. **Nat Neurosci** 22: 609–617, 2019. doi:10.1038/s41593-019-0359-6.

259. Peyrache A, Khamassi M, Benchenane K, Wiener SI, Battaglia FP. Replay of rule-learning related neural patterns in the prefrontal cortex during sleep. **Nat Neurosci** 12: 919–926, 2009. doi:10.1038/nn.2337.

260. Lansink CS, Goltstein PM, Lankelma JV, McNaughton BL, Pennartz CM. Hippocampus leads ventral striatum in replay of place-reward information. **PLoS Biol** 7: e1000173, 2009. doi:10.1371/journal.pbio.1000173.

261. Valdés JL, McNaughton BL, Fellous JM. Offline reactivation of experience-dependent neuronal firing patterns in the rat ventral tegmental area. **J Neurophysiol** 114: 1183–1195, 2015. doi:10.1152/jn.00758.2014.

262. Gomperts SN, Kloosterman F, Wilson MA. VTA neurons coordinate with the hippocampal reactivation of spatial experience. **eLife** 4: e05360, 2015. doi:10.7554/eLife.05360.

263. Feliciano-Ramos PA, Galazo M, Penagos H, Wilson M. Hippocampal memory reactivation during sleep is correlated with specific cortical states of the retrosplenial and prefrontal cortices. **Learn Mem** 30: 221–236, 2023. doi:10.1101/lm.053834.123.

264. Dickey CW, Verzhbinsky IA, Jiang X, Rosen BQ, Kajfez S, Eskandar EN, Gonzalez-Martinez J, Cash SS, Halgren E. Cortical ripples during NREM sleep and waking in humans. **J Neurosci** 42: 7931–7946, 2022. doi:10.1523/JNEUROSCI.0742-22.2022.

265. Khodagholy D, Gelinas JN, Buzsáki G. Learning-enhanced coupling between ripple oscillations in association cortices and hippocampus. **Science** 358: 369–372, 2017. doi:10.1126/science.aan6203.

266. Grenier F, Timofeev I, Steriade M. Focal synchronization of ripples (80-200 Hz) in neocortex and their neuronal correlates. **J Neurophysiol** 86: 1884–1898, 2001. doi:10.1152/jn.2001.86.4.1884.

267. von Ellenrieder N, Frauscher B, Dubeau F, Gotman J. Interaction with slow waves during sleep improves discrimination of physiologic and pathologic high-frequency oscillations (80-500 Hz). **Epilepsia** 57: 869–878, 2016. doi:10.1111/epi.13380.

268. Shin JD, Jadhav SP. Prefrontal cortical ripples mediate top-down suppression of hippocampal reactivation during sleep memory consolidation. **Curr Biol** 34: 2801–2811.e9, 2024. doi:10.1016/j.cub.2024.05.018.

269. Hoffman KL, McNaughton BL. Coordinated reactivation of distributed memory traces in primate neocortex. **Science** 297: 2070–2073, 2002. doi:10.1126/science.1073538.

270. Sirota A, Csicsvari J, Buhl D, Buzsáki G. Communication between neocortex and hippocampus during sleep in rodents. **Proc Natl Acad Sci USA** 100: 2065–2069, 2003. doi:10.1073/pnas.0437938100.

271. Ngo HV, Fell J, Staresina B. Sleep spindles mediate hippocampal-neocortical coupling during long-duration ripples. **eLife** 9: e57011, 2020. doi:10.7554/eLife.57011.

272. Varela C, Kumar S, Yang JY, Wilson MA. Anatomical substrates for direct interactions between hippocampus, medial prefrontal cortex, and the thalamic nucleus reuniens. **Brain Struct Funct** 219: 911–929, 2014. doi:10.1007/s00429-013-0543-5.

273. Schönauer M, Pöhlchen D. Sleep spindles. **Curr Biol** 28: R1129–R1130, 2018. doi:10.1016/j.cub.2018.07.035.

274. Lüthi A. Sleep spindles: where they come from, what they do. **Neuroscientist** 20: 243–256, 2014. doi:10.1177/1073858413500854.

275. Antony JW, Schönauer M, Staresina BP, Cairney SA. Sleep spindles and memory reprocessing. **Trends Neurosci** 42: 1–3, 2019. doi:10.1016/j.tins.2018.09.012.

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

277. Fernandez LM, Lüthi A. Sleep spindles: mechanisms and functions. **Physiol Rev** 100: 805–868, 2020. doi:10.1152/physrev.00042.2018.

278. Varela C, Wilson MA. mPFC spindle cycles organize sparse thalamic activation and recently active CA1 cells during non-REM sleep. **eLife** 9: e48881, 2020. doi:10.7554/eLife.48881.

279. Vertes RP, Hoover WB, Do Valle AC, Sherman A, Rodriguez JJ. Efferent projections of reuniens and rhomboid nuclei of the thalamus in the rat. **J Comp Neurol** 499: 768–796, 2006. doi:10.1002/cne.21135.

280. Sullivan D, Mizuseki K, Sorgi A, Buzsáki G. Comparison of sleep spindles and theta oscillations in the hippocampus. **J Neurosci** 34: 662–674, 2014. doi:10.1523/JNEUROSCI.0552-13.2014.

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

282. Halassa MM, Chen Z, Wimmer RD, Brunetti PM, Zhao S, Zikopoulos B, Wang F, Brown EN, Wilson MA. State-dependent architecture of thalamic reticular subnetworks. **Cell** 158: 808–821, 2014. doi:10.1016/J.CELL.2014.06.025.

283. Yang M, Logothetis NK, Eschenko O. Occurrence of hippocampal ripples is associated with activity suppression in the mediodorsal thalamic nucleus. **J Neurosci** 39: 434–444, 2019. doi:10.1523/JNEUROSCI.2107-18.2018.

284. Peyrache A, Seibt J. A mechanism for learning with sleep spindles. **Philos Trans R Soc Lond B Biol Sci** 375: 20190230, 2020. doi:10.1098/rstb.2019.0230.

285. Jourde HR, Coffey EB. Auditory processing up to cortex is maintained during sleep spindles. **PNAS Nexus** 3: pgae479, 2024. doi:10.1093/pnasnexus/pgae479.

286. Chen Z, Wimmer RD, Wilson MA, Halassa MM. Thalamic circuit mechanisms link sensory processing in sleep and attention. **Front Neural Circuits** 9: 83, 2015. doi:10.3389/fncir.2015.00083.

287. Wimmer RD, Schmitt LI, Davidson TJ, Nakajima M, Deisseroth K, Halassa MM. Thalamic control of sensory selection in divided attention. **Nature** 526: 705–709, 2015. doi:10.1038/nature15398.

288. Clemente-Perez A, Makinson SR, Higashikubo B, Brovarney S, Cho FS, Urry A, Holden SS, Wimer M, Dávid C, Fenno LE, Acsády L, Deisseroth K, Paz JT. Distinct thalamic reticular cell types differentially modulate normal and pathological cortical rhythms. **Cell Rep** 19: 2130–2142, 2017. doi:10.1016/j.celrep.2017.05.044.

289. Ahissar M, Hochstein S. The reverse hierarchy theory of visual perceptual learning. **Trends Cogn Sci** 8: 457–464, 2004. doi:10.1016/j.tics.2004.08.011.

290. Halassa MM, Kastner S. Thalamic functions in distributed cognitive control. **Nat Neurosci** 20: 1669–1679, 2017. doi:10.1038/s41593-017-0020-1.

291. Aston-Jones G, Bloom FE. Activity of norepinephrine-containing locus coeruleus neurons in behaving rats anticipates fluctuations in the sleep-waking cycle. **J Neurosci** 1: 876–886, 1981. doi:10.1523/JNEUROSCI.01-08-00876.1981.

292. Lee KH, McCormick DA. Abolition of spindle oscillations by serotonin and norepinephrine in the ferret lateral geniculate and

perigeniculate nuclei in vitro. **Neuron** 17: 309–321, 1996. doi:10.1016/s0896-6273(00)80162-2.

293. Swift KM, Gross BA, Frazer MA, Bauer DS, Clark KJ, Vazey EM, Aston-Jones G, Li Y, Pickering AE, Sara SJ, Poe GR**.** Abnormal locus coeruleus sleep activity alters sleep signatures of memory consolidation and impairs place cell stability and spatial memory. **Curr Biol** 28: 3599–3609.e4, 2018. doi:10.1016/j.cub.2018.09.054.

294. Hagler DJ, Ulbert I, Wittner L, Erőss L, Madsen JR, Devinsky O, Doyle W, Fabó D, Cash SS, Halgren E**.** Heterogeneous origins of human sleep spindles in different cortical layers. **J Neurosci** 38: 3013–3025, 2018. doi:10.1523/JNEUROSCI.2241-17.2018.

295. Krishnan GP, Rosen BQ, Chen JY, Muller L, Sejnowski TJ, Cash SS, Halgren E, Bazhenov M**.** Thalamocortical and intracortical laminar connectivity determines sleep spindle properties. **PLoS Comput Biol** 14: e1006171, 2018. doi:10.1371/journal.pcbi.1006171.

296. Bergmann TO, Mölle M, Diedrichs J, Born J, Siebner HR**.** Sleep spindle-related reactivation of category-specific cortical regions after learning face-scene associations. **Neuroimage** 59: 2733–2742, 2012. doi:10.1016/j.neuroimage.2011.10.036.

297. Yordanova J, Kolev V, Bruns E, Kirov R, Verleger R**.** Sleep spindles in the right hemisphere support awareness of regularities and reflect pre-sleep activations. **Sleep** 40: zsx151, 2017. doi:10.1093/sleep/zsx151.

298. Thom JL, Staresina BP**.** Human sleep spindles track experimentally excited brain circuits. **Sleep** 48: zsaf114, 2025. doi:10.1093/sleep/zsaf114.

299. Clemens Z, Fabó D, Halász P**.** Twenty-four hours retention of visuospatial memory correlates with the number of parietal sleep spindles. **Neurosci Lett** 403: 52–56, 2006. doi:10.1016/j.neulet.2006.04.035.

300. Nishida M, Walker MP**.** Daytime naps, motor memory consolidation and regionally specific sleep spindles. **PLoS One** 2: e341, 2007. doi:10.1371/journal.pone.0000341.

301. Tamaki M, Matsuoka T, Nittono H, Hori T**.** Activation of fast sleep spindles at the premotor cortex and parietal areas contributes to motor learning: a study using sLORETA. **Clin Neurophysiol** 120: 878–886, 2009. doi:10.1016/J.CLINPH.2009.03.006.

302. Johnson LA, Blakely T, Hermes D, Hakimian S, Ramsey NF, Ojemann JG**.** Sleep spindles are locally modulated by training on a brain-computer interface. **Proc Natl Acad Sci USA** 109: 18583–18588, 2012. doi:10.1073/pnas.1207532109.

303. Bang JW, Khalilzadeh O, Hämäläinen M, Watanabe T, Sasaki Y**.** Location specific sleep spindle activity in the early visual areas and perceptual learning. **Vision Res** 99: 162–171, 2014. doi:10.1016/J.VISRES.2013.12.014.

304. Cox R, Hofman WF, de Boer M, Talamini LM**.** Local sleep spindle modulations in relation to specific memory cues. **Neuroimage** 99: 103–110, 2014. doi:10.1016/j.neuroimage.2014.05.028.

305. Lutz ND, Admard M, Genzoni E, Born J, Rauss K**.** Occipital sleep spindles predict sequence learning in a visuo-motor task. **Sleep** 44: zsab056, 2021. doi:10.1093/sleep/zsab056.

306. Jegou A, Schabus M, Gosseries O, Dahmen B, Albouy G, Desseilles M, Sterpenich V, Phillips C, Maquet P, Grova C, Dang-Vu TT**.** Cortical reactivations during sleep spindles following declarative learning. **Neuroimage** 195: 104–112, 2019. doi:10.1016/j.neuroimage.2019.03.051.

307. Petzka M, Chatburn A, Charest I, Balanos GM, Staresina BP**.** Sleep spindles track cortical learning patterns for memory consolidation. **Curr Biol** 32: 2349–2356.e4, 2022. doi:10.1016/j.cub.2022.04.045.

308. Weber FD, Supp GG, Klinzing JG, Mölle M, Engel AK, Born J**.** Coupling of gamma band activity to sleep spindle oscillations—a combined EEG/MEG study. **Neuroimage** 224: 117452, 2021. doi:10.1016/j.neuroimage.2020.117452.

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

310. Seibt J, Richard CJ, Sigl-Glöckner J, Takahashi N, Kaplan DI, Doron G, de Limoges D, Bocklisch C, Larkum ME**.** Cortical dendritic activity correlates with spindle-rich oscillations during sleep in rodents. **Nat Commun** 8: 684, 2017. doi:10.1038/s41467-017-00735-w.

311. Niethard N, Burgalossi A, Born J**.** Plasticity during sleep is linked to specific regulation of cortical circuit activity. **Front Neural Circuits** 11: 65, 2017. doi:10.3389/fncir.2017.00065.

312. Niethard N, Ngo HV, Ehrlich I, Born J**.** Cortical circuit activity underlying sleep slow oscillations and spindles. **Proc Natl Acad Sci USA** 115: E9220–E9229, 2018. doi:10.1073/pnas.1805517115.

313. Niethard N, Brodt S, Born J**.** Cell-type-specific dynamics of calcium activity in cortical circuits over the course of slow-wave sleep and rapid eye movement sleep. **J Neurosci** 41: 4212–4222, 2021. doi:10.1523/JNEUROSCI.1957-20.2021.

314. Kaestner EJ, Wixted JT, Mednick SC**.** Pharmacologically increasing sleep spindles enhances recognition for negative and high-arousal memories. **J Cogn Neurosci** 25: 1597–1610, 2013. doi:10.1162/jocn_a_00433.

315. Cairney SA, Guttesen AÁ, El Marj N, Staresina BP**.** Memory consolidation is linked to spindle-mediated information processing during sleep. **Curr Biol** 28: 948–954.e4, 2018. doi:10.1016/j.cub.2018.01.087.

316. Massimini M, Huber R, Ferrarelli F, Hill S, Tononi G**.** The sleep slow oscillation as a traveling wave. **J Neurosci** 24: 6862–6870, 2004. doi:10.1523/JNEUROSCI.1318-04.2004.

317. Nir Y, Staba RJ, Andrillon T, Vyazovskiy VV, Cirelli C, Fried I, Tononi G**.** Regional slow waves and spindles in human sleep. **Neuron** 70: 153–169, 2011. doi:10.1016/j.neuron.2011.02.043.

318. Wierzynski CM, Lubenov EV, Gu M, Siapas AG**.** State-dependent spike-timing relationships between hippocampal and prefrontal circuits during sleep. **Neuron** 61: 587–596, 2009. doi:10.1016/j.neuron.2009.01.011.

319. Dervinis M, Crunelli V**.** Sleep waves in a large-scale corticothalamic model constrained by activities intrinsic to neocortical networks and single thalamic neurons. **CNS Neurosci Ther** 30: e14206, 2024. doi:10.1111/cns.14206.

320. Malerba P, Whitehurst LN, Simons SB, Mednick SC**.** Spatio-temporal structure of sleep slow oscillations on the electrode manifold and its relation to spindles. **Sleep** 42: zsy197, 2019. doi:10.1093/sleep/zsy197.

321. Hauer BE, Pagliardini S, Dickson CT**.** The reuniens nucleus of the thalamus has an essential role in coordinating slow-wave activity between neocortex and hippocampus. **eNeuro** 6: ENEURO.0365-19.2019, 2019. doi:10.1523/ENEURO.0365-19.2019.

322. Cox R, Rüber T, Staresina BP, Fell J**.** Phase-based coordination of hippocampal and neocortical oscillations during human sleep. **Commun Biol** 3: 176, 2020. doi:10.1038/s42003-020-0913-5.

323. Adamantidis AR, Gutierrez Herrera C, Gent TC. Oscillating circuitries in the sleeping brain. **Nat Rev Neurosci** 20: 746–762, 2019. doi:10.1038/s41583-019-0223-4.

324. Funk CM, Peelman K, Bellesi M, Marshall W, Cirelli C, Tononi G. Role of somatostatin-positive cortical interneurons in the generation of sleep slow waves. **J Neurosci** 37: 9132–9148, 2017. doi:10.1523/JNEUROSCI.1303-17.2017.

325. Osorio-Forero A, Foustoukos G, Cardis R, Cherrad N, Devenoges C, Fernandez LM, Lüthi A. Infraslow noradrenergic locus coeruleus activity fluctuations are gatekeepers of the NREM-REM sleep cycle. **Nat Neurosci** 28: 84–96, 2025. doi:10.1038/s41593-024-01822-0.

326. Miyamoto D, Hirai D, Murayama M. The Roles of cortical slow waves in synaptic plasticity and memory consolidation. **Front Neural Circuits** 11: 92, 2017. doi:10.3389/fncir.2017.00092.

327. Schreiner T, Doeller CF, Jensen O, Rasch B, Staudigl T. Theta phase-coordinated memory reactivation reoccurs in a slow-oscillatory rhythm during NREM Sleep. **Cell Rep** 25: 296–301, 2018. doi:10.1016/j.celrep.2018.09.037.

328. Ferraris M, Ghestem A, Vicente AF, Nallet-Khosrofian L, Bernard C, Quilichini PP. The nucleus reuniens controls long-range hippocampo-prefrontal gamma synchronization during slow oscillations. **J Neurosci** 38: 3026–3038, 2018. doi:10.1523/JNEUROSCI.3058-17.2018.

329. Marshall L, Helgadóttir H, Mölle M, Born J. Boosting slow oscillations during sleep potentiates memory. **Nature** 444: 610–613, 2006. doi:10.1038/nature05278.

330. Ngo HV, Martinetz T, Born J, Mölle M. Auditory closed-loop stimulation of the sleep slow oscillation enhances memory. **Neuron** 78: 545–553, 2013. doi:10.1016/j.neuron.2013.03.006.

331. Perrault AA, Khani A, Quairiaux C, Kompotis K, Franken P, Muhlethaler M, Schwartz S, Bayer L. Whole-night continuous rocking entrains spontaneous neural oscillations with benefits for sleep and memory. **Curr Biol** 29: 402–411.e3, 2019. doi:10.1016/j.cub.2018.12.028.

332. Tatsuno M, Malek S, Kalvi L, Ponce-Alvarez A, Ali K, Euston DR, Gruen S, McNaughton BL. Memory reactivation in rat medial prefrontal cortex occurs in a subtype of cortical UP state during slow-wave sleep. **Philos Trans R Soc Lond B Biol Sci** 375: 20190227, 2020. doi:10.1098/rstb.2019.0227.

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

334. Todorova R, Zugaro M. Isolated cortical computations during delta waves support memory consolidation. **Science** 366: 377–381, 2019. doi:10.1126/science.aay0616.

335. Steriade M, Nuñez A, Amzica F. Intracellular analysis of relations between the slow (<1 Hz) neocortical oscillation and other sleep rhythms of the electroencephalogram. **J Neurosci** 13: 3266–3283, 1993. doi:10.1523/JNEUROSCI.13-08-03266.1993.

336. Battaglia FP, Sutherland GR, McNaughton BL. Hippocampal sharp wave bursts coincide with neocortical "up-state" transitions. **Learn Mem** 11: 697–704, 2004. doi:10.1101/lm.73504.

337. Mölle M, Yeshenko O, Marshall L, Sara SJ, Born J. Hippocampal sharp wave-ripples linked to slow oscillations in rat slow-wave sleep. **J Neurophysiol** 96: 62–70, 2006. doi:10.1152/jn.00014.2006.

338. El-Kanbi K, de Levalléon G, Bagur S, Lacroix M, Benchenane K. Distinction between slow waves and delta waves sheds light to sleep homeostasis and their association to hippocampal sharp waves ripples (Preprint). **bioRxiv** 2022.12.27.522034, 2022. doi:10.1101/2022.12.27.522034.

339. Sirota A, Buzsáki G. Interaction between neocortical and hippocampal networks via slow oscillations. **Thalamus Relat Syst** 3: 245–259, 2005. doi:10.1017/S1472928807000258.

340. Mölle M, Born J. Slow oscillations orchestrating fast oscillations and memory consolidation. **Prog Brain Res** 193: 93–110, 2011. doi:10.1016/B978-0-444-53839-0.00007-7.

341. González-Rueda A, Pedrosa V, Feord RC, Clopath C, Paulsen O. Activity-dependent downscaling of subthreshold synaptic inputs during slow-wave-sleep-like activity in vivo. **Neuron** 97: 1244–1252.e5, 2018. doi:10.1016/j.neuron.2018.01.047.

342. Klinzing JG, Mölle M, Weber F, Supp G, Hipp JF, Engel AK, Born J. Spindle activity phase-locked to sleep slow oscillations. **Neuroimage** 134: 607–616, 2016. doi:10.1016/j.neuroimage.2016.04.031.

343. Skelin I, Kilianski S, McNaughton BL. Hippocampal coupling with cortical and subcortical structures in the context of memory consolidation. **Neurobiol Learn Mem** 160: 21–31, 2019. doi:10.1016/j.nlm.2018.04.004.

344. Girardeau G, Lopes-Dos-Santos V. Brain neural patterns and the memory function of sleep. **Science** 374: 560–564, 2021. doi:10.1126/science.abi8370.

345. Mizuseki K, Miyawaki H. Fast network oscillations during non-REM sleep support memory consolidation. **Neurosci Res** 189: 3–12, 2023. doi:10.1016/j.neures.2022.12.019.

346. Mak-McCully RA, Rolland M, Sargsyan A, Gonzalez C, Magnin M, Chauvel P, Rey M, Bastuji H, Halgren E. Coordination of cortical and thalamic activity during non-REM sleep in humans. **Nat Commun** 8: 15499, 2017. doi:10.1038/ncomms15499.

347. Schreiner T, Kaufmann E, Noachtar S, Mehrkens JH, Staudigl T. The human thalamus orchestrates neocortical oscillations during NREM sleep. **Nat Commun** 13: 5231, 2022. doi:10.1038/s41467-022-32840-w.

348. Alizadeh Z, Azimi A, Ghorbani M. Enhancement of hippocampal-thalamocortical temporal coordination during slow-frequency long-duration anterior thalamic spindles. **J Neurosci** 42: 7222–7243, 2022. doi:10.1523/JNEUROSCI.2515-21.2022.

349. Ramanathan DS, Gulati T, Ganguly K. Sleep-dependent reactivation of ensembles in motor cortex promotes skill consolidation. **PLoS Biol** 13: e1002263, 2015. doi:10.1371/journal.pbio.1002263.

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

351. Gelinas JN, Khodagholy D, Thesen T, Devinsky O, Buzsáki G. Interictal epileptiform discharges induce hippocampal-cortical coupling in temporal lobe epilepsy. **Nat Med** 22: 641–648, 2016. doi:10.1038/nm.4084.

352. Helfrich RF, Mander BA, Jagust WJ, Knight RT, Walker MP. Old brains come uncoupled in sleep: slow wave-spindle synchrony, brain atrophy, and forgetting. **Neuron** 97: 221–230.e4, 2018. doi:10.1016/j.neuron.2017.11.020.

353. Hahn MA, Heib D, Schabus M, Hoedlmoser K, Helfrich RF. Slow oscillation-spindle coupling predicts enhanced memory formation from childhood to adolescence. **eLife** 9: e53730, 2020. doi:10.7554/eLife.53730.

354. Helfrich RF, Lendner JD, Mander BA, Guillen H, Paff M, Mnatsakanyan L, Vadera S, Walker MP, Lin JJ, Knight RT. Bidirectional prefrontal-hippocampal dynamics organize information transfer during sleep in humans. **Nat Commun** 10: 3572, 2019. doi:10.1038/s41467-019-11444-x.

355. Binder S, Mölle M, Lippert M, Bruder R, Aksamaz S, Ohl F, Wiegert JS, Marshall L. Monosynaptic hippocampal-prefrontal projections contribute to spatial memory consolidation in mice. **J Neurosci** 39: 6978–6991, 2019. doi:10.1523/JNEUROSCI.2158-18.2019.

356. Bastian L, Samanta A, Ribeiro de Paula D, Weber FD, Schoenfeld R, Dresler M, Genzel L. Spindle-slow oscillation coupling correlates with memory performance and connectivity changes in a hippocampal network after sleep. **Hum Brain Mapp** 43: 3923–3943, 2022. doi:10.1002/hbm.25893.

357. Schreiner T, Petzka M, Staudigl T, Staresina BP. Endogenous memory reactivation during sleep in humans is clocked by slow oscillation-spindle complexes. **Nat Commun** 12: 3112, 2021. doi:10.1038/s41467-021-23520-2.

358. Ng T, Noh E, Spencer RM. Does slow oscillation-spindle coupling contribute to sleep-dependent memory consolidation? A Bayesian meta-analysis. **eLife** 13: RP101992, 2024. doi:10.7554/eLife.101992.1.

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

360. Latchoumane CF, Ngo HV, Born J, Shin HS. Thalamic spindles promote memory formation during sleep through triple phase-locking of cortical, thalamic, and hippocampal rhythms. **Neuron** 95: 424–435.e6, 2017. doi:10.1016/j.neuron.2017.06.025.

361. Murayama M, Pérez-Garci E, Nevian T, Bock T, Senn W, Larkum ME. Dendritic encoding of sensory stimuli controlled by deep cortical interneurons. **Nature** 457: 1137–1141, 2009. doi:10.1038/nature07663.

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

363. Sanda P, Malerba P, Jiang X, Krishnan GP, Gonzalez-Martinez J, Halgren E, Bazhenov M. Bidirectional interaction of hippocampal ripples and cortical slow waves leads to coordinated spiking activity during NREM sleep. **Cereb Cortex** 31: 324–340, 2021. doi:10.1093/cercor/bhaa228.

364. Logothetis NK, Eschenko O, Murayama Y, Augath M, Steudel T, Evrard HC, Besserve M, Oeltermann A. Hippocampal-cortical interaction during periods of subcortical silence. **Nature** 491: 547–553, 2012. doi:10.1038/nature11618.

365. Maingret N, Girardeau G, Todorova R, Goutierre M, Zugaro M. Hippocampo-cortical coupling mediates memory consolidation during sleep. **Nat Neurosci** 19: 959–964, 2016. doi:10.1038/nn.4304.

366. Xia F, Richards BA, Tran MM, Josselyn SA, Takehara-Nishiuchi K, Frankland PW. Parvalbumin-positive interneurons mediate neocortical-hippocampal interactions that are necessary for memory consolidation. **eLife** 6: e27868, 2017. doi:10.7554/eLife.27868.

367. Lewis LD, Voigts J, Flores FJ, Schmitt LI, Wilson MA, Halassa MM, Brown EN. Thalamic reticular nucleus induces fast and local modulation of arousal state. **eLife** 4: e08760, 2015. doi:10.7554/eLife.08760.

368. Dehnavi F, Koo-Poeggel PC, Ghorbani M, Marshall L. Spontaneous slow oscillation-slow spindle features predict induced overnight memory retention. **Sleep** 44: zsab127, 2021. doi:10.1093/sleep/zsab127.

369. Antony JW, Piloto L, Wang M, Pacheco P, Norman KA, Paller KA. Sleep spindle refractoriness segregates periods of memory reactivation. **Curr Biol** 28: 1736–1743.e4, 2018. doi:10.1016/j.cub.2018.04.020.

370. Ngo HV, Miedema A, Faude I, Martinetz T, Mölle M, Born J. Driving sleep slow oscillations by auditory closed-loop stimulation—a self-limiting process. **J Neurosci** 35: 6630–6638, 2015. doi:10.1523/JNEUROSCI.3133-14.2015.

371. Rothschild G, Eban E, Frank LM. A cortical-hippocampal-cortical loop of information processing during memory consolidation. **Nat Neurosci** 20: 251–259, 2017. doi:10.1038/nn.4457.

372. Ólafsdóttir HF, Carpenter F, Barry C. Coordinated grid and place cell replay during rest. **Nat Neurosci** 19: 792–794, 2016. doi:10.1038/nn.4291.

373. Kim J, Joshi A, Frank L, Ganguly K. Cortical-hippocampal coupling during manifold exploration in motor cortex. **Nature** 613: 103–110, 2023. doi:10.1038/s41586-022-05533-z.

374. Baena D, Gabitov E, Ray LB, Doyon J, Fogel SM. Motor learning promotes regionally-specific spindle-slow wave coupled cerebral memory reactivation. **Commun Biol** 7: 1492, 2024. doi:10.1038/s42003-024-07197-z.

375. Marshall L, Mölle M, Born J. Spindle and slow wave rhythms at slow wave sleep transitions are linked to strong shifts in the cortical direct current potential. **Neuroscience** 121: 1047–1053, 2003. doi:10.1016/s0306-4522(03)00458-5.

376. Lecci S, Fernandez LM, Weber FD, Cardis R, Chatton JY, Born J, Lüthi A. Coordinated infraslow neural and cardiac oscillations mark fragility and offline periods in mammalian sleep. **Sci Adv** 3: e1602026, 2017. doi:10.1126/sciadv.1602026.

377. Osorio-Forero A, Cardis R, Vantomme G, Guillaume-Gentil A, Katsioudi G, Devenoges C, Fernandez LM, Lüthi A. Noradrenergic circuit control of non-REM sleep substates. **Curr Biol** 31: 5009–5023.e7, 2021. doi:10.1016/j.cub.2021.09.041.

378. Stucynski JA, Schott AL, Baik J, Chung S, Weber F. Regulation of REM sleep by inhibitory neurons in the dorsomedial medulla. **Curr Biol** 32: 37–50.e6, 2022. doi:10.1016/j.cub.2021.10.030.

379. Lahlou S, Kaminska M, Doyon J, Carrier J, Sharp M. Sleep spindle density and temporal clustering are associated with sleep-dependent memory consolidation in Parkinson's disease. **J Clin Sleep Med** 20: 1153–1162, 2024. doi:10.5664/jcsm.11080.

380. Doppler CE, Smit JA, Hommelsen M, Seger A, Horsager J, Kinnerup MB, Hansen AK, Fedorova TD, Knudsen K, Otto M, Nahimi A, Borghammer P, Sommerauer M. Microsleep disturbances are associated with noradrenergic dysfunction in Parkinson's disease. **Sleep** 44: zsab040, 2021. doi:10.1093/sleep/zsab040.

381. Naji M, Krishnan GP, McDevitt EA, Bazhenov M, Mednick SC. Coupling of autonomic and central events during sleep benefits declarative memory consolidation. **Neurobiol Learn Mem** 157: 139–150, 2019. doi:10.1016/j.nlm.2018.12.008.

382. Chang H, Tang W, Wulf AM, Nyasulu T, Wolf ME, Fernandez-Ruiz A, Oliva A. Sleep microstructure organizes memory replay. **Nature** 637: 1161–1169, 2025. doi:10.1038/s41586-024-08340-w.

383. McCormick DA, Nestvogel DB, He BJ. Neuromodulation of brain state and behavior. **Annu Rev Neurosci** 43: 391–415, 2020. doi:10.1146/annurev-neuro-100219-105424.

384. Schreiner T, Petzka M, Staudigl T, Staresina BP. Respiration modulates sleep oscillations and memory reactivation in humans. **Nat Commun** 14: 8351, 2023. doi:10.1038/s41467-023-43450-5.

385. Karalis N, Sirota A. Breathing coordinates cortico-hippocampal dynamics in mice during offline states. **Nat Commun** 13: 467, 2022. doi:10.1038/s41467-022-28090-5.

386. Poe GR, Walsh CM, Bjorness TE. Cognitive neuroscience of sleep. **Prog Brain Res** 185: 1–19, 2010. doi:10.1016/B978-0-444-53702-7.00001-4.

387. Vertes RP, Eastman KE. The case against memory consolidation in REM sleep. **Behav Brain Sci** 23: 867–876, 2000. doi:10.1017/S0140525X00004003.

388. Magidov E, Hayat H, Sharon O, Andelman F, Katzav S, Lavie P, Tauman R, Nir Y. Near-total absence of REM sleep co-occurring with normal cognition: an update of the 1984 paper. **Sleep Med** 52: 134–137, 2018. doi:10.1016/j.sleep.2018.09.003.

389. Datta S, O'Malley MW. Fear extinction memory consolidation requires potentiation of pontine-wave activity during REM sleep. **J Neurosci** 33: 4561–4569, 2013. doi:10.1523/JNEUROSCI.5525-12.2013.

390. Almeida-Filho DG, Queiroz CM, Ribeiro S. Memory corticalization triggered by REM sleep: mechanisms of cellular and systems consolidation. **Cell Mol Life Sci** 75: 3715–3740, 2018. doi:10.1007/s00018-018-2886-9.

391. Clemens Z, Borbély C, Weiss B, Erőss L, Szűcs A, Kelemen A, Fabó D, Rásonyi G, Janszky J, Halász P. Increased mesiotemporal delta activity characterizes virtual navigation in humans. **Neurosci Res** 76: 67–75, 2013. doi:10.1016/j.neures.2013.03.004.

392. Cantero JL, Atienza M, Stickgold R, Kahana MJ, Madsen JR, Kocsis B. Sleep-dependent theta oscillations in the human hippocampus and neocortex. **J Neurosci** 23: 10897–10903, 2003. doi:10.1523/JNEUROSCI.23-34-10897.2003.

393. Nishida M, Hirai N, Miwakeichi F, Maehara T, Kawai K, Shimizu H, Uchida S. Theta oscillation in the human anterior cingulate cortex during all-night sleep: an electrocorticographic study. **Neurosci Res** 50: 331–341, 2004. doi:10.1016/j.neures.2004.08.004.

394. Uchida S, Maehara T, Hirai N, Okubo Y, Shimizu H. Cortical oscillations in human medial temporal lobe during wakefulness and all-night sleep. **Brain Res** 891: 7–19, 2001. doi:10.1016/s0006-8993(00)03154-1.

395. Uchida S, Maehara T, Hirai N, Kawai K, Shimizu H. Theta oscillation in the anterior cingulate and beta-1 oscillation in the medial temporal cortices: a human case report. **J Clin Neurosci** 10: 371–374, 2003. doi:10.1016/s0967-5868(03)00025-0.

396. Cohen N, Pell L, Edelson MG, Ben-Yakov A, Pine A, Dudai Y. Peri-encoding predictors of memory encoding and consolidation. **Neurosci Biobehav Rev** 50: 128–142, 2015. doi:10.1016/j.neubiorev.2014.11.002.

397. Hölscher C, Anwyl R, Rowan MJ. Stimulation on the positive phase of hippocampal theta rhythm induces long-term potentiation that can be depotentiated by stimulation on the negative phase in area CA1 in vivo. **J Neurosci** 17: 6470–6477, 1997. doi:10.1523/JNEUROSCI.17-16-06470.1997.

398. Pavlides C, Greenstein YJ, Grudman M, Winson J. Long-term potentiation in the dentate gyrus is induced preferentially on the positive phase of theta-rhythm. **Brain Res** 439: 383–387, 1988. doi:10.1016/0006-8993(88)91499-0.

399. Goutagny R, Jackson J, Williams S. Self-generated theta oscillations in the hippocampus. **Nat Neurosci** 12: 1491–1493, 2009. doi:10.1038/nn.2440.

400. Patel J, Fujisawa S, Berényi A, Royer S, Buzsáki G. Traveling theta waves along the entire septotemporal axis of the hippocampus. **Neuron** 75: 410–417, 2012. doi:10.1016/j.neuron.2012.07.015.

401. Kowalczyk T, Caban B, Bocian R. Rytm theta rejestrowany w formacji hipokampa w warunkach pozaustrojowych. **Postepy Hig Med Dosw (Online)** 67: 617–630, 2013. doi:10.5604/17322693.1058537.

402. Mizuseki K, Miyawaki H. Hippocampal information processing across sleep/wake cycles. **Neurosci Res** 118: 30–47, 2017. doi:10.1016/j.neures.2017.04.018.

403. Fujisawa S, Buzsáki G. A 4 Hz oscillation adaptively synchronizes prefrontal, VTA, and hippocampal activities. **Neuron** 72: 153–165, 2011. doi:10.1016/j.neuron.2011.08.018.

404. Sirota A, Montgomery S, Fujisawa S, Isomura Y, Zugaro M, Buzsáki G. Entrainment of neocortical neurons and gamma oscillations by the hippocampal theta rhythm. **Neuron** 60: 683–697, 2008. doi:10.1016/j.neuron.2008.09.014.

405. Tort AB, Ponsel S, Jessberger J, Yanovsky Y, Brankačk J, Draguhn A. Parallel detection of theta and respiration-coupled oscillations throughout the mouse brain. **Sci Rep** 8: 6432, 2018. doi:10.1038/s41598-018-24629-z.

406. Jung F, Witte V, Yanovsky Y, Klumpp M, Brankačk J, Tort AB, Draguhn A. Differential modulation of parietal cortex activity by respiration and θ oscillations. **J Neurophysiol** 127: 801–817, 2022. doi:10.1152/jn.00376.2021.

407. Montgomery SM, Sirota A, Buzsáki G. Theta and gamma coordination of hippocampal networks during waking and rapid eye movement sleep. **J Neurosci** 28: 6731–6741, 2008. doi:10.1523/JNEUROSCI.1227-08.2008.

408. Poe GR, Nitz DA, McNaughton BL, Barnes CA. Experience-dependent phase-reversal of hippocampal neuron firing during REM sleep. **Brain Res** 855: 176–180, 2000. doi:10.1016/s0006-8993(99)02310-0.

409. Harris KD, Henze DA, Hirase H, Leinekugel X, Dragoi G, Czurkó A, Buzsáki G. Spike train dynamics predicts theta-related phase precession in hippocampal pyramidal cells. **Nature** 417: 738–741, 2002. doi:10.1038/nature00808.

410. Booth V, Poe GR. Input source and strength influences overall firing phase of model hippocampal CA1 pyramidal cells during theta: relevance to REM sleep reactivation and memory consolidation. **Hippocampus** 16: 161–173, 2006. doi:10.1002/hipo.20143.

411. Fogel SM, Smith CT, Beninger RJ. Evidence for 2-stage models of sleep and memory: learning-dependent changes in spindles and theta in rats. **Brain Res Bull** 79: 445–451, 2009. doi:10.1016/j.brainresbull.2009.03.002.

412. Hellman K, Abel T. Fear conditioning increases NREM sleep. **Behav Neurosci** 121: 310–323, 2007. doi:10.1037/0735-7044.121.2.310.

413. Louie K, Wilson MA. Temporally structured replay of awake hippocampal ensemble activity during rapid eye movement sleep. **Neuron** 29: 145–156, 2001. doi:10.1016/S0896-6273(01)00186-6.

414. Nishida M, Pearsall J, Buckner RL, Walker MP. REM sleep, prefrontal theta, and the consolidation of human emotional memory. **Cereb Cortex** 19: 1158–1166, 2009. doi:10.1093/cercor/bhn155.

415. Born J, Feld GB. Sleep to upscale, sleep to downscale: balancing homeostasis and plasticity. **Neuron** 75: 933–935, 2012. doi:10.1016/j.neuron.2012.09.007.

416. van der Helm E, Yao J, Dutt S, Rao V, Saletin JM, Walker MP. REM sleep depotentiates amygdala activity to previous emotional experiences. **Curr Biol** 21: 2029–2032, 2011. doi:10.1016/j.cub.2011.10.052.

417. Tort AB, Scheffer-Teixeira R, Souza BC, Draguhn A, Brankačk J. Theta-associated high-frequency oscillations (110-160Hz) in the hippocampus and neocortex. **Prog Neurobiol** 100: 1–14, 2013. doi:10.1016/j.pneurobio.2012.09.002.

418. Tort AB, Komorowski RW, Manns JR, Kopell NJ, Eichenbaum H. Theta-gamma coupling increases during the learning of item-context associations. **Proc Natl Acad Sci USA** 106: 20942–20947, 2009. doi:10.1073/pnas.0911331106.

419. Bandarabadi M, Boyce R, Gutierrez Herrera C, Bassetti CL, Williams S, Schindler K, Adamantidis A. Dynamic modulation of theta-gamma coupling during rapid eye movement sleep. **Sleep** 42: zsz182, 2019. doi:10.1093/sleep/zsz182.

420. Boyce R, Glasgow SD, Williams S, Adamantidis A. Causal evidence for the role of REM sleep theta rhythm in contextual memory consolidation. **Science** 352: 812–816, 2016. doi:10.1126/science.aad5252.

421. de Almeida-Filho DG, Koike BD, Billwiller F, Farias KS, de Sales IR, Luppi PH, Ribeiro S, Queiroz CM. Hippocampus-retrosplenial cortex interaction is increased during phasic REM and contributes to memory consolidation. **Sci Rep** 11: 13078, 2021. doi:10.1038/s41598-021-91659-5.

422. Sampath D, Sabitha KR, Hegde P, Jayakrishnan HR, Kutty BM, Chattarji S, Rangarajan G, Laxmi TR. A study on fear memory retrieval and REM sleep in maternal separation and isolation stressed rats. **Behav Brain Res** 273: 144–154, 2014. doi:10.1016/j.bbr.2014.07.034.

423. Vanderheyden WM, George SA, Urpa L, Kehoe M, Liberzon I, Poe GR. Sleep alterations following exposure to stress predict fear-associated memory impairments in a rodent model of PTSD. **Exp Brain Res** 233: 2335–2346, 2015. doi:10.1007/s00221-015-4302-0.

424. McKenna JT, Gamble MC, Anderson-Chernishof MB, Shah SR, McCoy JG, Strecker RE. A rodent cage change insomnia model disrupts memory consolidation. **J Sleep Res** 28: e12792, 2019. doi:10.1111/jsr.12792.

425. Totty MS, Chesney LA, Geist PA, Datta S. Sleep-dependent oscillatory synchronization: a role in fear memory consolidation. **Front Neural Circuits** 11: 49, 2017. doi:10.3389/fncir.2017.00049.

426. Ognjanovski N, Broussard C, Zochowski M, Aton SJ. Hippocampal network oscillations rescue memory consolidation deficits caused by sleep loss. **Cereb Cortex** 28: 3711–3723, 2018. doi:10.1093/cercor/bhy174.

427. Sopp MR, Michael T, Weeß HG, Mecklinger A. Remembering specific features of emotional events across time: the role of REM sleep and prefrontal theta oscillations. **Cogn Affect Behav Neurosci** 17: 1186–1209, 2017. doi:10.3758/s13415-017-0542-8.

428. McMenamin BW, Marsolek CJ. Can theories of visual representation help to explain asymmetries in amygdala function? **Cogn Affect Behav Neurosci** 13: 211–224, 2013. doi:10.3758/s13415-012-0139-1.

429. Bolduc C, Daoust AM, Limoges E, Braun CM, Godbout R. Hemispheric lateralization of the EEG during wakefulness and REM sleep in young healthy adults. **Brain Cogn** 53: 193–196, 2003. doi:10.1016/s0278-2626(03)00108-8.

430. Vyazovskiy VV, Borbély AA, Tobler I. Interhemispheric sleep EEG asymmetry in the rat is enhanced by sleep deprivation. **J Neurophysiol** 88: 2280–2286, 2002. doi:10.1152/jn.00304.2002.

431. Tessier S, Lambert A, Scherzer P, Jemel B, Godbout R. REM sleep and emotional face memory in typically-developing children and children with autism. **Biol Psychol** 110: 107–114, 2015. doi:10.1016/j.biopsycho.2015.07.012.

432. Kim SY, Kark SM, Daley RT, Alger SE, Rebouças D, Kensinger EA, Payne JD. Interactive effects of stress reactivity and rapid eye movement sleep theta activity on emotional memory formation. **Hippocampus** 30: 829–841, 2020. doi:10.1002/hipo.23138.

433. Cross ZR, Santamaria A, Corcoran AW, Chatburn A, Alday PM, Coussens S, Kohler MJ. Individual alpha frequency modulates sleep-related emotional memory consolidation. **Neuropsychologia** 148: 107660, 2020. doi:10.1016/j.neuropsychologia.2020.107660.

434. Klimesch W. EEG alpha and theta oscillations reflect cognitive and memory performance: a review and analysis. **Brain Res Brain Res Rev** 29: 169–195, 1999. doi:10.1016/s0165-0173(98)00056-3.

435. Sopp MR, Brueckner AH, Schäfer SK, Lass-Hennemann J, Michael T. REM theta activity predicts re-experiencing symptoms after exposure to a traumatic film. **Sleep Med** 54: 142–152, 2019. doi:10.1016/j.sleep.2018.10.030.

436. Cabrera Y, Holloway J, Poe GR. Sleep changes across the female hormonal cycle affecting memory: implications for resilient adaptation to traumatic experiences. **J Womens Health (Larchmt)** 29: 446–451, 2020. doi:10.1089/jwh.2020.8332.

437. Durrant SJ, Cairney SA, McDermott C, Lewis PA. Schema-conformant memories are preferentially consolidated during REM sleep. **Neurobiol Learn Mem** 122: 41–50, 2015. doi:10.1016/j.nlm.2015.02.011.

438. Karashima A, Nakao M, Honda K, Iwasaki N, Katayama N, Yamamoto M. Theta wave amplitude and frequency are differentially correlated with pontine waves and rapid eye movements during REM sleep in rats. **Neurosci Res** 50: 283–289, 2004. doi:10.1016/j.neures.2004.07.007.

439. Karashima A, Katayama N, Nakao M. Phase-locking of spontaneous and tone-elicited pontine waves to hippocampal theta waves during REM sleep in rats. **Brain Res** 1182: 73–81, 2007. doi:10.1016/j.brainres.2007.08.060.

440. Karashima A, Katayama N, Nakao M. Enhancement of synchronization between hippocampal and amygdala theta waves associated with pontine wave density. **J Neurophysiol** 103: 2318–2325, 2010. doi:10.1152/jn.00551.2009.

441. Gott JA, Liley DT, Hobson JA. Towards a functional understanding of PGO waves. **Front Hum Neurosci** 11: 89, 2017. doi:10.3389/fnhum.2017.00089.

442. Frauscher B, Joshi S, von Ellenrieder N, Nguyen DK, Dubeau F, Gotman J. Sharply contoured theta waves are the human correlate of ponto-geniculo-occipital waves in the primary visual cortex. **Clin Neurophysiol** 129: 1526–1533, 2018. doi:10.1016/j.clinph.2018.04.605.

443. Bernardi G, Betta M, Ricciardi E, Pietrini P, Tononi G, Siclari F. Regional delta waves in human rapid eye movement sleep. **J Neurosci** 39: 2686–2697, 2019. doi:10.1523/JNEUROSCI.2298-18.2019.

444. Hobson JA. Sleeping, waking, and dreaming. In: *Encyclopedia of Behavioral Neuroscience*. Elsevier Inc., 2010.

445. Koroma M, Lacaux C, Andrillon T, Legendre G, Léger D, Kouider S. Sleepers selectively suppress informative inputs during rapid eye movements. **Curr Biol** 30: 2411–2417.e3, 2020. doi:10.1016/j.cub.2020.04.047.

446. Ramirez-Villegas JF, Besserve M, Murayama Y, Evrard HC, Oeltermann A, Logothetis NK. Coupling of hippocampal theta and ripples with pontogeniculooccipital waves. **Nature** 589: 96–102, 2021. doi:10.1038/s41586-020-2914-4.

447. Fan FF, Vetrivelan R, Yang Y, Guo ZN, Lu J. Role of pontine sub-laterodorsal tegmental nucleus (SLD) in rapid eye movement (REM) sleep, cataplexy, and emotion. **CNS Neurosci Ther** 29: 1192–1196, 2023. doi:10.1111/cns.14074.

448. Wen YJ, Yang WJ, Guo CN, Qiu MH, Kroeger D, Niu JG, Zhan SQ, Yang XF, Gisabella B, Vetrivelan R, Lu J. Pontine control of rapid eye movement sleep and fear memory. **CNS Neurosci Ther** 29: 1602–1614, 2023. doi:10.1111/cns.14123.

449. Datta S. Avoidance task training potentiates phasic pontine-wave density in the rat: a mechanism for sleep-dependent plasticity. **J Neurosci** 20: 8607–8613, 2000. doi:10.1523/JNEUROSCI.20-22-08607.2000.

450. Mavanji V, Datta S. Activation of the phasic pontine-wave generator enhances improvement of learning performance: a mechanism for sleep-dependent plasticity. **Eur J Neurosci** 17: 359–370, 2003. doi:10.1046/j.1460-9568.2003.02460.x.

451. Datta S, Mavanji V, Ulloor J, Patterson EH. Activation of phasic pontine-wave generator prevents rapid eye movement sleep deprivation-induced learning impairment in the rat: a mechanism for sleep-dependent plasticity. **J Neurosci** 24: 1416–1427, 2004. doi:10.1523/JNEUROSCI.4111-03.2004.

452. Mavanji V, Ulloor J, Saha S, Datta S. Neurotoxic lesions of phasic pontine-wave generator cells impair retention of 2-way active avoidance memory. **Sleep** 27: 1282–1292, 2004. doi:10.1093/sleep/27.7.1282.

453. Siwek DF, Knapp CM, Kaur G, Datta S. Dorsal subcoeruleus nucleus (SubCD) involvement in context-associated fear memory consolidation. **Exp Brain Res** 232: 1535–1545, 2014. doi:10.1007/s00221-014-3858-4.

454. Santos PD, Targa AD, Noseda AC, Rodrigues LS, Fagotti J, Lima MM. Cholinergic oculomotor nucleus activity is induced by REM sleep deprivation negatively impacting on cognition. **Mol Neurobiol** 54: 5721–5729, 2017. doi:10.1007/s12035-016-0112-z.

455. Datta S, Saha S, Prutzman SL, Mullins OJ, Mavanji V. Pontine-wave generator activation-dependent memory processing of avoidance learning involves the dorsal hippocampus in the rat. **J Neurosci Res** 80: 727–737, 2005. doi:10.1002/jnr.20501.

456. Saha S, Datta S. Two-way active avoidance training-specific increases in phosphorylated cAMP response element-binding protein in the dorsal hippocampus, amygdala, and hypothalamus. **Eur J Neurosci** 21: 3403–3414, 2005. doi:10.1111/j.1460-9568.2005.04166.x.

457. Hennevin E, Hars B, Maho C, Bloch V. Processing of learned information in paradoxical sleep: relevance for memory. **Behav Brain Res** 69: 125–135, 1995. doi:10.1016/0166-4328(95)00013-j.

458. Hasselmo ME. Temporally structured replay of neural activity in a model of entorhinal cortex, hippocampus and postsubiculum. **Eur J Neurosci** 28: 1301–1315, 2008. doi:10.1111/j.1460-9568.2008.06437.x.

459. Brandon MP, Bogaard AR, Andrews CM, Hasselmo ME. Head direction cells in the postsubiculum do not show replay of prior waking sequences during sleep. **Hippocampus** 22: 604–618, 2012. doi:10.1002/hipo.20924.

460. Kudrimoti HS, Barnes CA, McNaughton BL. Reactivation of hippocampal cell assemblies: effects of behavioral state, experience, and EEG dynamics. **J Neurosci** 19: 4090–4101, 1999. doi:10.1523/JNEUROSCI.19-10-04090.1999.

461. Eckert MJ, McNaughton BL, Tatsuno M. Neural ensemble reactivation in rapid eye movement and slow-wave sleep coordinate with muscle activity to promote rapid motor skill learning. **Philos Trans R Soc Lond B Biol Sci** 375: 20190655, 2020. doi:10.1098/rstb.2019.0655.

462. Maquet P, Laureys S, Peigneux P, Fuchs S, Petiau C, Phillips C, Aerts J, Del Fiore G, Degueldre C, Meulemans T, Luxen A, Franck G, van der Linden M, Smith C, Cleeremans A. Experience-dependent changes in cerebral activation during human REM sleep. **Nat Neurosci** 3: 831–836, 2000. doi:10.1038/77744.

463. Rihm JS, Rasch B. Replay of conditioned stimuli during late REM and stage N2 sleep influences affective tone rather than emotional memory strength. **Neurobiol Learn Mem** 122: 142–151, 2015. doi:10.1016/j.nlm.2015.04.008.

464. Hutchison IC, Pezzoli S, Tsimpanouli ME, Abdellahi ME, Pobric G, Hulleman J, Lewis PA. Targeted memory reactivation in REM but not SWS selectively reduces arousal responses. **Commun Biol** 4: 636, 2021. doi:10.1038/s42003-021-02196-w.

465. Picard-Deland C, Aumont T, Samson-Richer A, Paquette T, Nielsen T. Whole-body procedural learning benefits from targeted memory reactivation in REM sleep and task-related dreaming. **Neurobiol Learn Mem** 183: 107460, 2021. doi:10.1016/j.nlm.2021.107460.

466. Picard-Deland C, Nielsen T. Targeted memory reactivation has a sleep stage-specific delayed effect on dream content. **J Sleep Res** 31: e13391, 2022. doi:10.1111/jsr.13391.

467. Abdellahi ME, Koopman AC, Treder MS, Lewis PA. Targeted memory reactivation in human REM sleep elicits detectable reactivation. **eLife** 12: e84324, 2023. doi:10.7554/eLife.84324.

468. Giuditta A, Ambrosini MV, Montagnese P, Mandile P, Cotugno M, Grassi Zucconi G, Vescia S. The sequential hypothesis of the function of sleep. **Behav Brain Res** 69: 157–166, 1995. doi:10.1016/0166-4328(95)00012-l.

469. Giuditta A. Sleep memory processing: the sequential hypothesis. **Front Syst Neurosci** 8: 219, 2014. doi:10.3389/fnsys.2014.00219.

470. Gais S, Born J. Low acetylcholine during slow-wave sleep is critical for declarative memory consolidation. **Proc Natl Acad Sci USA** 101: 2140–2144, 2004. doi:10.1073/pnas.0305404101.

471. Lokhandwala S, Spencer RM. Slow wave sleep in naps supports episodic memories in early childhood. **Dev Sci** 24: e13035, 2021. doi:10.1111/desc.13035.

472. Cousins JN, El-Deredy W, Parkes LM, Hennies N, Lewis PA. Cued reactivation of motor learning during sleep leads to overnight changes in functional brain activity and connectivity. **PLoS Biol** 14: e1002451, 2016. doi:10.1371/journal.pbio.1002451.

473. Nitsche MA, Jakoubkova M, Thirugnanasambandam N, Schmalfuss L, Hullemann S, Sonka K, Paulus W, Trenkwalder C, Happe S. Contribution of the premotor cortex to consolidation of motor

sequence learning in humans during sleep. **J Neurophysiol** 104: 2603–2614, 2010. doi:10.1152/jn.00611.2010.

474. Laureys S, Peigneux P, Phillips C, Fuchs S, Degueldre C, Aerts J, Del Fiore G, Petiau C, Luxen A, van der Linden M, Cleeremans A, Smith C, Maquet P**.** Experience-dependent changes in cerebral functional connectivity during human rapid eye movement sleep. **Neuroscience** 105: 521–525, 2001. doi:10.1016/s0306-4522(01)00269-x.

475. Weber FD, Wang JY, Born J, Inostroza M**.** Sleep benefits in parallel implicit and explicit measures of episodic memory. **Learn Mem** 21: 190–198, 2014. doi:10.1101/lm.033530.113.

476. Rauchs G, Bertran F, Guillery-Girard B, Desgranges B, Kerrouche N, Denise P, Foret J, Eustache F**.** Consolidation of strictly episodic memories mainly requires rapid eye movement sleep. **Sleep** 27: 395–401, 2004. doi:10.1093/sleep/27.3.395.

477. Ackermann S, Rasch B**.** Differential effects of non-REM and REM sleep on memory consolidation? **Curr Neurol Neurosci Rep** 14: 430, 2014. doi:10.1007/s11910-013-0430-8.

478. Albouy G, King BR, Schmidt C, Desseilles M, Dang-Vu TT, Balteau E, Phillips C, Degueldre C, Orban P, Benali H, Peigneux P, Luxen A, Karni A, Doyon J, Maquet P, Korman M**.** Cerebral activity associated with transient sleep-facilitated reduction in motor memory vulnerability to interference. **Sci Rep** 6: 34948, 2016. doi:10.1038/srep34948.

479. Backhaus W, Braaß H, Renné T, Krüger C, Gerloff C, Hummel FC**.** Daytime sleep has no effect on the time course of motor sequence and visuomotor adaptation learning. **Neurobiol Learn Mem** 131: 147–154, 2016. doi:10.1016/j.nlm.2016.03.017.

480. Nettersheim A, Hallschmid M, Born J, Diekelmann S**.** The role of sleep in motor sequence consolidation: stabilization rather than enhancement. **J Neurosci** 35: 6696–6702, 2015. doi:10.1523/JNEUROSCI.1236-14.2015.

481. Albouy G, Fogel S, Pottiez H, Nguyen VA, Ray L, Lungu O, Carrier J, Robertson E, Doyon J**.** Daytime sleep enhances consolidation of the spatial but not motoric representation of motor sequence memory. **PLoS One** 8: e52805, 2013. doi:10.1371/journal.pone.0052805.

482. Barakat M, Carrier J, Debas K, Lungu O, Fogel S, Vandewalle G, Hoge RD, Bellec P, Karni A, Ungerleider LG, Benali H, Doyon J**.** Sleep spindles predict neural and behavioral changes in motor sequence consolidation. **Hum Brain Mapp** 34: 2918–2928, 2013. doi:10.1002/hbm.22116.

483. Fogel SM, Albouy G, Vien C, Popovicci R, King BR, Hoge R, Jbabdi S, Benali H, Karni A, Maquet P, Carrier J, Doyon J**.** fMRI and sleep correlates of the age-related impairment in motor memory consolidation. **Hum Brain Mapp** 35: 3625–3645, 2014. doi:10.1002/hbm.22426.

484. Tamaki M, Huang TR, Yotsumoto Y, Hämäläinen M, Lin FH, Náñez JE, Watanabe T, Sasaki Y**.** Enhanced spontaneous oscillations in the supplementary motor area are associated with sleep-dependent offline learning of finger-tapping motor-sequence task. **J Neurosci** 33: 13894–13902, 2013. doi:10.1523/JNEUROSCI.1198-13.2013.

485. Qian L, Ru T, He M, Li S, Zhou G**.** Effects of a brief afternoon nap on declarative and procedural memory. **Neurobiol Learn Mem** 194: 107662, 2022. doi:10.1016/j.nlm.2022.107662.

486. Genzel L, Dresler M, Wehrle R, Grözinger M, Steiger A**.** Slow wave sleep and REM sleep awakenings do not affect sleep dependent memory consolidation. **Sleep** 32: 302–310, 2009. doi:10.1093/sleep/32.3.302.

487. Rasch B, Pommer J, Diekelmann S, Born J**.** Pharmacological REM sleep suppression paradoxically improves rather than impairs skill memory. **Nat Neurosci** 12: 396–397, 2009. doi:10.1038/nn.2206.

488. Korman M, Doyon J, Doljansky J, Carrier J, Dagan Y, Karni A**.** Daytime sleep condenses the time course of motor memory consolidation. **Nat Neurosci** 10: 1206–1213, 2007. doi:10.1038/nn1959.

489. Tucker MA, Fishbein W**.** The impact of sleep duration and subject intelligence on declarative and motor memory performance: how much is enough? **J Sleep Res** 18: 304–312, 2009. doi:10.1111/j.1365-2869.2009.00740.x.

490. Schmid D, Erlacher D, Klostermann A, Kredel R, Hossner EJ**.** Sleep-dependent motor memory consolidation in healthy adults: a meta-analysis. **Neurosci Biobehav Rev** 118: 270–281, 2020. doi:10.1016/j.neubiorev.2020.07.028.

491. Alger SE, Kensinger EA, Payne JD**.** Preferential consolidation of emotionally salient information during a nap is preserved in middle age. **Neurobiol Aging** 68: 34–47, 2018. doi:10.1016/j.neurobiolaging.2018.03.030.

492. Alger SE, Chen S, Payne JD**.** Do different salience cues compete for dominance in memory over a daytime nap? **Neurobiol Learn Mem** 160: 48–57, 2019. doi:10.1016/j.nlm.2018.06.005.

493. Cairney SA, Durrant SJ, Hulleman J, Lewis PA**.** Targeted memory reactivation during slow wave sleep facilitates emotional memory consolidation. **Sleep** 37: 701–707, 2014. doi:10.5665/sleep.3572.

494. Cunningham TJ, Stickgold R, Kensinger EA**.** Investigating the effects of sleep and sleep loss on the different stages of episodic emotional memory: a narrative review and guide to the future. **Front Behav Neurosci** 16: 910317, 2022. doi:10.3389/fnbeh.2022.910317.

495. Qin H, Fu L, Jian T, Jin W, Liang M, Li J, Chen Q, Yang X, Du H, Liao X, Zhang K, Wang R, Liang S, Yao J, Hu B, Ren S, Zhang C, Wang Y, Hu Z, Jia H, Konnerth A, Chen X**.** REM sleep-active hypothalamic neurons may contribute to hippocampal social-memory consolidation. **Neuron** 110: 4000–4014.e6, 2022. doi:10.1016/j.neuron.2022.09.004.

496. Groch S, Zinke K, Wilhelm I, Born J**.** Dissociating the contributions of slow-wave sleep and rapid eye movement sleep to emotional item and source memory. **Neurobiol Learn Mem** 122: 122–130, 2015. doi:10.1016/j.nlm.2014.08.013.

497. Wiesner CD, Pulst J, Krause F, Elsner M, Baving L, Pedersen A, Prehn-Kristensen A, Göder R**.** The effect of selective REM-sleep deprivation on the consolidation and affective evaluation of emotional memories. **Neurobiol Learn Mem** 122: 131–141, 2015. doi:10.1016/j.nlm.2015.02.008.

498. Genzel L, Spoormaker VI, Konrad BN, Dresler M**.** The role of rapid eye movement sleep for amygdala-related memory processing. **Neurobiol Learn Mem** 122: 110–121, 2015. doi:10.1016/j.nlm.2015.01.008.

499. Popa D, Duvarci S, Popescu AT, Léna C, Paré D**.** Coherent amygdalocortical theta promotes fear memory consolidation during paradoxical sleep. **Proc Natl Acad Sci USA** 107: 6516–6519, 2010. doi:10.1073/pnas.0913016107.

500. Menz MM, Rihm JS, Salari N, Born J, Kalisch R, Pape HC, Marshall L, Büchel C**.** The role of sleep and sleep deprivation in consolidating fear memories. **Neuroimage** 75: 87–96, 2013. doi:10.1016/j.neuroimage.2013.03.001.

501. Machida M, Sweeten BL, Adkins AM, Wellman LL, Sanford LD**.** The basolateral amygdala mediates the role of rapid eye movement

sleep in integrating fear memory responses. **Life (Basel)** 12: 17, 2021. doi:10.3390/life12010017.

502. Strauss M, Griffon L, van Beers P, Elbaz M, Bouziotis J, Sauvet F, Chennaoui M, Léger D, Peigneux P**.** Order matters: sleep spindles contribute to memory consolidation only when followed by rapid-eye-movement sleep. **Sleep** 45: zsac022, 2022. doi:10.1093/sleep/zsac022.

503. Cheng S, Werning M**.** Composition and replay of mnemonic sequences: the contributions of REM and slow-wave sleep to episodic memory. **Behav Brain Sci** 36: 610–611, 2013. doi:10.1017/S0140525X13001234.

504. Walker MP, Stickgold R**.** Overnight alchemy: sleep-dependent memory evolution. **Nat Rev Neurosci** 11: 218, 2010. doi:10.1038/nrn2762-c1.

505. Tamminen J, Lambon Ralph MA, Lewis PA**.** Targeted memory reactivation of newly learned words during sleep triggers REM-mediated integration of new memories and existing knowledge. **Neurobiol Learn Mem** 137: 77–82, 2017. doi:10.1016/j.nlm.2016.11.012.

506. Kaida K, Mori I, Kihara K, Kaida N**.** The function of REM and NREM sleep on memory distortion and consolidation. **Neurobiol Learn Mem** 204: 107811, 2023. doi:10.1016/j.nlm.2023.107811.

507. Batterink LJ, Westerberg CE, Paller KA**.** Vocabulary learning benefits from REM after slow-wave sleep. **Neurobiol Learn Mem** 144: 102–113, 2017. doi:10.1016/j.nlm.2017.07.001.

508. Lewis PA, Knoblich G, Poe G**.** How memory replay in sleep boosts creative problem-solving. **Trends Cogn Sci** 22: 491–503, 2018. doi:10.1016/j.tics.2018.03.009.

509. McClelland JL, McNaughton BL, O'Reilly RC**.** 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, 1995. doi:10.1037/0033-295X.102.3.419.

510. Squire LR, Cohen NJ, Nadel L**.** The medial temporal region and memory consolidation: a new hypothesis. In: *Memory Consolidation. Psychobiology of Cognition*, edited by Weingartner H, Parker ES. Psychology Press, 1984.

511. Feld GB, Born J**.** Sculpting memory during sleep: concurrent consolidation and forgetting. **Curr Opin Neurobiol** 44: 20–27, 2017. doi:10.1016/j.conb.2017.02.012.

512. Gilboa A, Marlatte H**.** Neurobiology of schemas and schema-mediated memory. **Trends Cogn Sci** 21: 618–631, 2017. doi:10.1016/j.tics.2017.04.013.

513. Moscovitch M, Gilboa A**.** Has the concept of systems consolidation outlived its usefulness? Identification and evaluation of premises underlying systems consolidation. **Fac Rev** 11: 33, 2022. doi:10.12703/r/11-33.

514. Feld GB, Weis PP, Born J**.** The limited capacity of sleep-dependent memory consolidation. **Front Psychol** 7: 1368, 2016. doi:10.3389/fpsyg.2016.01368.

515. Kolibius LD, Born J, Feld GB**.** Vast amounts of encoded items nullify but do not reverse the effect of sleep on declarative memory. **Front Psychol** 11: 607070, 2020. doi:10.3389/fpsyg.2020.607070.

516. Cellini N, Mercurio M, Vanzetti V, Bergamo D, Sarlo M**.** Comparing the effect of daytime sleep and wakefulness on mnemonic discrimination. **Physiol Behav** 224: 113078, 2020. doi:10.1016/j.physbeh.2020.113078.

517. Winocur G, Moscovitch M, Sekeres M**.** Memory consolidation or transformation: context manipulation and hippocampal representations of memory. **Nat Neurosci** 10: 555–557, 2007. doi:10.1038/nn1880.

518. Nadel L, Moscovitch M**.** Memory consolidation, retrograde amnesia and the hippocampal complex. **Curr Opin Neurobiol** 7: 217–227, 1997. doi:10.1016/S0959-4388(97)80010-4.

519. Nadel L, Hupbach A, Gomez R, Newman-Smith K**.** Memory formation, consolidation and transformation. **Neurosci Biobehav Rev** 36: 1640–1645, 2012. doi:10.1016/J.NEUBIOREV.2012.03.001.

520. Glickman SE**.** Perseverative neural processes and consolidation of the memory trace. **Psychol Bull** 58: 218–233, 1961. doi:10.1037/h0044212.

521. McGaugh JL, Herz MJ**.** *Memory Consolidation*. Albion Pub. Co., 1972.

522. Squire LR, Alvarez P**.** Retrograde amnesia and memory consolidation: a neurobiological perspective. **Curr Opin Neurobiol** 5: 169–177, 1995. doi:10.1016/0959-4388(95)80023-9.

523. Marr D**.** Simple memory: a theory for archicortex. **Philos Trans R Soc Lond B Biol Sci** 262: 23–81, 1971. doi:10.1098/rstb.1971.0078.

524. Genzel L, Rossato JI, Jacobse J, Grieves RM, Spooner PA, Battaglia FP, Fernández G, Morris RG**.** The yin and yang of memory consolidation: hippocampal and neocortical. **PLoS Biol** 15: e2000531, 2017. doi:10.1371/journal.pbio.2000531.

525. Contreras MP, Mendez M, Shan X, Fechner J, Sawangjit A, Born J, Inostroza M**.** Context memory formed in medial prefrontal cortex during infancy enhances learning in adulthood. **Nat Commun** 15: 2475, 2024. doi:10.1038/s41467-024-46734-6.

526. Samanta A, van Rongen LS, Rossato JI, Jacobse J, Schoenfeld R, Genzel L**.** Sleep leads to brain-wide neural changes independent of allocentric and egocentric spatial training in humans and rats. **Cereb Cortex** 31: 4970–4985, 2021. doi:10.1093/cercor/bhab135.

527. Sterpenich V, Albouy G, Boly M, Vandewalle G, Darsaud A, Balteau E, Dang-Vu TT, Desseilles M, D'Argembeau A, Gais S, Rauchs G, Schabus M, Degueldre C, Luxen A, Collette F, Maquet P**.** Sleep-related hippocampo-cortical interplay during emotional memory recollection. **PLoS Biol** 5: e282, 2007. doi:10.1371/journal.pbio.0050282.

528. Albouy G, Sterpenich V, Vandewalle G, Darsaud A, Gais S, Rauchs G, Desseilles M, Boly M, Dang-Vu T, Balteau E, Degueldre C, Phillips C, Luxen A, Maquet P**.** Interaction between hippocampal and striatal systems predicts subsequent consolidation of motor sequence memory. **PLoS One** 8: e59490, 2013. doi:10.1371/journal.pone.0059490.

529. Rosier M, Le Barillier L, Meunier D, El Yacoubi M, Malleret G, Salin PA**.** Post-learning paradoxical sleep deprivation impairs reorganization of limbic and cortical networks associated with consolidation of remote contextual fear memory in mice. **Sleep** 41: 2018. doi:10.1093/sleep/zsy188.

530. Sterpenich V, Albouy G, Darsaud A, Schmidt C, Vandewalle G, Dang Vu TT, Desseilles M, Phillips C, Degueldre C, Balteau E, Collette F, Luxen A, Maquet P**.** Sleep promotes the neural reorganization of remote emotional memory. **J Neurosci** 29: 5143–5152, 2009. doi:10.1523/JNEUROSCI.0561-09.2009.

531. Ghosh VE, Gilboa A**.** What is a memory schema? A historical perspective on current neuroscience literature. **Neuropsychologia** 53: 104–114, 2014. doi:10.1016/J.NEUROPSYCHOLOGIA.2013.11.010.

532. Gilboa A, Moscovitch M. No consolidation without representation: correspondence between neural and psychological representations in recent and remote memory. **Neuron** 109: 2239–2255, 2021. doi:10.1016/j.neuron.2021.04.025.

533. Sekeres MJ, Winocur G, Moscovitch M. The hippocampus and related neocortical structures in memory transformation. **Neurosci Lett** 680: 39–53, 2018. doi:10.1016/j.neulet.2018.05.006.

534. Matorina N, Poppenk J. Memory decay distinguishes subtypes of gist. **Neurobiol Learn Mem** 185: 107519, 2021. doi:10.1016/j.nlm.2021.107519.

535. Deese J. On the prediction of occurrence of particular verbal intrusions in immediate recall. **J Exp Psychol** 58: 17–22, 1959. doi:10.1037/h0046671.

536. Roediger HL, McDermott KB. Creating false memories: remembering words not presented in lists. **J Exp Psychol Learn Mem Cogn** 21: 803–814, 1995. doi:10.1037/0278-7393.21.4.803.

537. Diekelmann S, Born J, Wagner U. Sleep enhances false memories depending on general memory performance. **Behav Brain Res** 208: 425–429, 2010. doi:10.1016/j.bbr.2009.12.021.

538. Lo JC, Sim SK, Chee MW. Sleep reduces false memory in healthy older adults. **Sleep** 37: 665–671, 2014. doi:10.5665/sleep.3564.

539. Fenn KM, Gallo DA, Margoliash D, Roediger HL, Nusbaum HC. Reduced false memory after sleep. **Learn Mem** 16: 509–513, 2009. doi:10.1101/lm.1500808.

540. Darsaud A, Dehon H, Lahl O, Sterpenich V, Boly M, Dang-Vu T, Desseilles M, Gais S, Matarazzo L, Peters F, Schabus M, Schmidt C, Tinguely G, Vandewalle G, Luxen A, Maquet P, Collette F. Does sleep promote false memories? **J Cogn Neurosci** 23: 26–40, 2011. doi:10.1162/jocn.2010.21448.

541. Newbury CR, Monaghan P. When does sleep affect veridical and false memory consolidation? A meta-analysis. **Psychon Bull Rev** 26: 387–400, 2019. doi:10.3758/s13423-018-1528-4.

542. Stickgold R. How do I remember? Let me count the ways. **Sleep Med Rev** 13: 305–308, 2009. doi:10.1016/j.smrv.2009.05.004.

543. Drosopoulos S, Schulze C, Fischer S, Born J. Sleep's function in the spontaneous recovery and consolidation of memories. **J Exp Psychol Gen** 136: 169–183, 2007. doi:10.1037/0096-3445.136.2.169.

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

545. Schapiro AC, McDevitt EA, Rogers TT, Mednick SC, Norman KA. Human hippocampal replay during rest prioritizes weakly learned information and predicts memory performance. **Nat Commun** 9: 3920, 2018. doi:10.1038/s41467-018-06213-1.

546. Petzka M, Charest I, Balanos GM, Staresina BP. Does sleep-dependent consolidation favour weak memories? **Cortex** 134: 65–75, 2021. doi:10.1016/j.cortex.2020.10.005.

547. Macera J, Daurat A. Increased phantom recollection after sleep. **Conscious Cogn** 66: 101–114, 2018. doi:10.1016/j.concog.2018.11.003.

548. Wernette EM, Fenn KM. Consolidation without intention: sleep strengthens veridical and gist representations of information after incidental encoding. **Psychon Bull Rev** 30: 1475–1483, 2023. doi:10.3758/s13423-023-02247-9.

549. Mak MH, O'Hagan A, Horner AJ, Gaskell MG. A registered report testing the effect of sleep on Deese-Roediger-McDermott false memory: greater lure and veridical recall but fewer intrusions after sleep. **R Soc Open Sci** 10: 220595, 2023. doi:10.1098/rsos.220595.

550. Shaw JJ, Monaghan P. Lateralised sleep spindles relate to false memory generation. **Neuropsychologia** 107: 60–67, 2017. doi:10.1016/j.neuropsychologia.2017.11.002.

551. Huan SY, Xu HZ, Wang R, Yu J. The different roles of sleep on false memory formation between young and older adults. **Psychol Res** 86: 443–451, 2022. doi:10.1007/s00426-021-01516-3.

552. Diekelmann S, Landolt HP, Lahl O, Born J, Wagner U. Sleep loss produces false memories. **PLoS One** 3: e3512, 2008. doi:10.1371/journal.pone.0003512.

553. Sarhane M, Daurat A. False memories in obstructive sleep apnoea syndrome: evidence from the divided attention paradigm at encoding or retrieval. **Memory** 27: 328–339, 2019. doi:10.1080/09658211.2018.1508592.

554. Berndt C, Diekelmann S, Alexander N, Pustal A, Kirschbaum C. Sleep fragmentation and false memories during pregnancy and motherhood. **Behav Brain Res** 266: 52–57, 2014. doi:10.1016/j.bbr.2014.02.030.

555. Zinke K, Lehnert V, Fritsche A, Preissl H, Hallschmid M. Pregnant women do not display impaired memory formation across one night of sleep. **J Sleep Res** 30: e13204, 2021. doi:10.1111/jsr.13204.

556. Malloggi S, Conte F, Rosa O D, Cellini N, Di Iorio I, Ficca G, Giganti F. False recalls, but not false recognitions, at the DRM paradigm are increased in subjects reporting insomnia symptoms: an online study. **Sleep Med** 100: 347–353, 2022. doi:10.1016/j.sleep.2022.09.005.

557. Malloggi S, Conte F, Ode R, Righi S, Gronchi G, Ficca G, Giganti F. False memories formation is increased in individuals with insomnia. **J Sleep Res** 31: e13527, 2022. doi:10.1111/jsr.13527.

558. Malloggi S, Conte F, De Rosa O, Cellini N, Gavazzi G, Di Iorio I, Ficca G, Giganti F. False memories formation after a retention period spent asleep or awake in individuals with insomnia and good sleepers: a polysomnographic study. **J Sleep Res** 32: e13896, 2023. doi:10.1111/jsr.13896.

559. Zander T, Volz KG, Born J, Diekelmann S. Sleep increases explicit solutions and reduces intuitive judgments of semantic coherence. **Learn Mem** 24: 641–645, 2017. doi:10.1101/lm.044511.116.

560. Landmann N, Kuhn M, Maier JG, Feige B, Spiegelhalder K, Riemann D, Nissen C. Sleep strengthens but does not reorganize memory traces in a verbal creativity task. **Sleep** 39: 705–713, 2016. doi:10.5665/sleep.5556.

561. van Rijn E, Carter N, McMurtrie H, Willner P, Blagrove MT. Sleep does not cause false memories on a story-based test of suggestibility. **Conscious Cogn** 52: 39–46, 2017. doi:10.1016/j.concog.2017.04.010.

562. Ashton JE, Staresina BP, Cairney SA. Sleep bolsters schematically incongruent memories. **PLoS One** 17: e0269439, 2022. doi:10.1371/journal.pone.0269439.

563. Stickgold R, Walker MP. Sleep-dependent memory triage: evolving generalization through selective processing. **Nat Neurosci** 16: 139–145, 2013. doi:10.1038/nn.3303.

564. Reverberi S, Dolfen N, van Roy A, Albouy G, King BR. Sleep does not influence schema-facilitated motor memory consolidation. **PLoS One** 18: e0280591, 2023. doi:10.1371/journal.pone.0280591.

565. Jano S, Romeo J, Hendrickx MD, Schlesewsky M, Chatburn A. Sleep influences neural representations of true and false memories:

an event-related potential study. **Neurobiol Learn Mem** 186: 107553, 2021. doi:10.1016/j.nlm.2021.107553.

566. Kuula L, Tamminen J, Makkonen T, Merikanto I, Räikkönen K, Pesonen AK**.** Higher sleep spindle activity is associated with fewer false memories in adolescent girls. **Neurobiol Learn Mem** 157: 96–105, 2019. doi:10.1016/j.nlm.2018.12.005.

567. Kurz EM, Conzelmann A, Barth GM, Hepp L, Schenk D, Renner TJ, Born J, Zinke K**.** Signs of enhanced formation of gist memory in children with autism spectrum disorder—a study of memory functions of sleep. **J Child Psychol Psychiatry** 60: 907–916, 2019. doi:10.1111/jcpp.13048.

568. Kurz EM, Zinke K, Born J**.** Sleep electroencephalogram (EEG) oscillations and associated memory processing during childhood and early adolescence. **Dev Psychol** 59: 297–311, 2023. doi:10.1037/dev0001487.

569. Werchan DM, Gómez RL**.** Generalizing memories over time: sleep and reinforcement facilitate transitive inference. **Neurobiol Learn Mem** 100: 70–76, 2013. doi:10.1016/j.nlm.2012.12.006.

570. Ellenbogen JM, Hu PT, Payne JD, Titone D, Walker MP**.** Human relational memory requires time and sleep. **Proc Natl Acad Sci USA** 104: 7723–7728, 2007. doi:10.1073/pnas.0700094104.

571. Tadros T, Bazhenov M**.** Role of sleep in formation of relational associative memory. **J Neurosci** 42: 5330–5345, 2022. doi:10.1523/JNEUROSCI.2044-21.2022.

572. Foldes T, Santamaria L, Lewis P**.** Sleep-related benefits to transitive inference are modulated by encoding strength and joint rank. **Learn Mem** 30: 201–211, 2023. doi:10.1101/lm.053787.123.

573. Santamaria L, Kashif I, McGinley N, Lewis PA**.** Memory reactivation in slow wave sleep enhances relational learning in humans. **Commun Biol** 7: 288, 2024. doi:10.1038/s42003-024-05947-7.

574. Joensen BH, Gaskell MG, Horner AJ**.** United we fall: all-or-none forgetting of complex episodic events. **J Exp Psychol Gen** 149: 230–248, 2020. doi:10.1037/xge0000648.

575. Golkashani HA, Ghorbani S, Leong RL, Ong JL, Chee MW**.** Advantage conferred by overnight sleep on schema-related memory may last only a day. **Sleep Adv** 4: zpad019, 2023. doi:10.1093/sleepadvances/zpad019.

576. Golkashani HA, Leong RL, Ghorbani S, Ong JL, Fernández G, Chee MW**.** A sleep schedule incorporating naps benefits the transformation of hierarchical knowledge. **Sleep** 45: zsac025, 2022. doi:10.1093/sleep/zsac025.

577. Lau H, Tucker MA, Fishbein W**.** Daytime napping: effects on human direct associative and relational memory. **Neurobiol Learn Mem** 93: 554–560, 2010. doi:10.1016/j.nlm.2010.02.003.

578. Preston AR, Eichenbaum H**.** Interplay of hippocampus and prefrontal cortex in memory. **Curr Biol** 23: R764–R773, 2013. doi:10.1016/j.cub.2013.05.041.

579. Seger CA, Miller EK**.** Category learning in the brain. **Annu Rev Neurosci** 33: 203–219, 2010. doi:10.1146/annurev.neuro.051508.135546.

580. O'Reilly RC, McClelland JL**.** Hippocampal conjunctive encoding, storage, and recall: avoiding a trade-off. **Hippocampus** 4: 661–682, 1994. doi:10.1002/hipo.450040605.

581. Treves A, Rolls ET**.** Computational analysis of the role of the hippocampus in memory. **Hippocampus** 4: 374–391, 1994. doi:10.1002/hipo.450040319.

582. Rolls ET**.** Pattern completion and pattern separation mechanisms in the hippocampus. In: *The Neurobiological Basis of Memory*, edited by Jackson PA, Chiba AA, Berman RF, Ragozzino ME. Springer International Publishing, 2016, p. 77–113.

583. Ngo CT, Michelmann S, Olson IR, Newcombe NS**.** Pattern separation and pattern completion: behaviorally separable processes? **Mem Cognit** 49: 193–205, 2021. doi:10.3758/s13421-020-01072-y.

584. Lerner I, Gluck MA**.** Sleep and the extraction of hidden regularities: a systematic review and the importance of temporal rules. **Sleep Med Rev** 47: 39–50, 2019. doi:10.1016/j.smrv.2019.05.004.

585. Lutz ND, Born J**.** Sleep to make more of your memories: decoding hidden rules from encoded information. **Sleep Med Rev** 47: 122–124, 2019. doi:10.1016/j.smrv.2019.07.009.

586. Friedrich M, Mölle M, Friederici AD, Born J**.** The reciprocal relation between sleep and memory in infancy: memory-dependent adjustment of sleep spindles and spindle-dependent improvement of memories. **Dev Sci** 22: e12743, 2019. doi:10.1111/desc.12743.

587. Wagner U, Gais S, Haider H, Verleger R, Born J**.** Sleep inspires insight. **Nature** 427: 352–355, 2004. doi:10.1038/nature02223.

588. Yordanova J, Kolev V, Wagner U, Verleger R**.** Differential associations of early- and late-night sleep with functional brain states promoting insight to abstract task regularity. **PLoS One** 5: e9442, 2010. doi:10.1371/journal.pone.0009442.

589. Lerner I, Ketz NA, Jones AP, Bryant NB, Robert B, Skorheim SW, Hartholt A, Rizzo AS, Gluck MA, Clark VP, Pilly PK**.** Transcranial current stimulation during sleep facilitates insight into temporal rules, but does not consolidate memories of individual sequential experiences. **Sci Rep** 9: 1516, 2019. doi:10.1038/s41598-018-36107-7.

590. Yordanova J, Kolev V, Wagner U, Born J, Verleger R**.** Increased alpha (8-12 Hz) activity during slow wave sleep as a marker for the transition from implicit knowledge to explicit insight. **J Cogn Neurosci** 24: 119–132, 2012. doi:10.1162/jocn_a_00097.

591. Yordanova J, Kolev V, Verleger R, Bataghva Z, Born J, Wagner U**.** Shifting from implicit to explicit knowledge: different roles of early- and late-night sleep. **Learn Mem** 15: 508–515, 2008. doi:10.1101/lm.897908.

592. Yordanova J, Kolev V, Verleger R**.** Awareness of knowledge or awareness of processing? Implications for sleep-related memory consolidation. **Front Hum Neurosci** 3: 40, 2009. doi:10.3389/neuro.09.040.2009.

593. Yordanova J, Kolev V, Wagner U, Verleger R**.** Covert reorganization of implicit task representations by slow wave sleep. **PLoS One** 4: e5675, 2009. doi:10.1371/journal.pone.0005675.

594. Debarnot U, Maley L, De Rossi D, Guillot A**.** Motor interference does not impair the memory consolidation of imagined movements. **Brain Cogn** 74: 52–57, 2010. doi:10.1016/j.bandc.2010.06.004.

595. Lerner I, Gluck MA**.** Individual differences in slow-wave-sleep predict acquisition of full cognitive maps. **Front Hum Neurosci** 12: 404, 2018. doi:10.3389/fnhum.2018.00404.

596. Lerner I, Gluck MA**.** Sleep facilitates extraction of temporal regularities with varying timescales. **Front Behav Neurosci** 16: 847083, 2022. doi:10.3389/fnbeh.2022.847083.

597. Vickrey B, Lerner I**.** Overnight exposure to pink noise could jeopardize sleep-dependent insight and pattern detection. **Front Hum Neurosci** 17: 1302836, 2023. doi:10.3389/fnhum.2023.1302836.

598. Barsky MM, Tucker MA, Stickgold R. REM sleep enhancement of probabilistic classification learning is sensitive to subsequent interference. **Neurobiol Learn Mem** 122: 63–68, 2015. doi:10.1016/j.nlm.2015.02.015.

599. Lerner I, Lupkin SM, Corter JE, Peters SE, Cannella LA, Gluck MA. The influence of sleep on emotional and cognitive processing is primarily trait- (but not state-) dependent. **Neurobiol Learn Mem** 134: 275–286, 2016. doi:10.1016/j.nlm.2016.07.032.

600. Freitas E, Saimpont A, Blache Y, Debarnot U. Acquisition and consolidation of sequential footstep movements with physical and motor imagery practice. **Scand J Med Sci Sports** 30: 2477–2484, 2020. doi:10.1111/sms.13799.

601. Blischke K, Malangré A. Task complexity modulates sleep-related offline learning in sequential motor skills. **Front Hum Neurosci** 11: 374, 2017. doi:10.3389/fnhum.2017.00374.

602. Deliens G, Schmitz R, Peigneux P. Interocular transfer of perceptual skills after sleep. **J Vis** 14: 23, 2014. doi:10.1167/14.1.23.

603. Durrant SJ, Cairney SA, Lewis PA. Cross-modal transfer of statistical information benefits from sleep. **Cortex** 78: 85–99, 2016. doi:10.1016/j.cortex.2016.02.011.

604. Lutz ND, Wolf I, Hübner S, Born J, Rauss K. Sleep strengthens predictive sequence coding. **J Neurosci** 38: 8989–9000, 2018. doi:10.1523/JNEUROSCI.1352-18.2018.

605. Lacaux C, Andrillon T, Bastoul C, Idir Y, Fonteix-Galet A, Arnulf I, Oudiette D. Sleep onset is a creative sweet spot. **Sci Adv** 7: eabj5866, 2021. doi:10.1126/sciadv.abj5866.

606. Fischer S, Drosopoulos S, Tsen J, Born J. Implicit learning–explicit knowing: a role for sleep in memory system interaction. **J Cogn Neurosci** 18: 311–319, 2006. doi:10.1162/jocn.2006.18.3.311.

607. Sánchez-Mora J, Tamayo RM. From incidental learning to explicit memory: the role of sleep after exposure to a serial reaction time task. **Acta Psychol (Amst)** 217: 103325, 2021. doi:10.1016/j.actpsy.2021.103325.

608. Wilhelm I, Rose M, Imhof KI, Rasch B, Büchel C, Born J. The sleeping child outplays the adult's capacity to convert implicit into explicit knowledge. **Nat Neurosci** 16: 391–393, 2013. doi:10.1038/nn.3343.

609. Drosopoulos S, Harrer D, Born J. Sleep and awareness about presence of regularity speed the transition from implicit to explicit knowledge. **Biol Psychol** 86: 168–173, 2011. doi:10.1016/j.biopsycho.2010.11.005.

610. Kirov R, Kolev V, Verleger R, Yordanova J. Labile sleep promotes awareness of abstract knowledge in a serial reaction time task. **Front Psychol** 6: 1354, 2015. doi:10.3389/fpsyg.2015.01354.

611. Graveline YM, Wamsley EJ. The impact of sleep on novel concept learning. **Neurobiol Learn Mem** 141: 19–26, 2017. doi:10.1016/j.nlm.2017.03.008.

612. Schapiro AC, McDevitt EA, Chen L, Norman KA, Mednick SC, Rogers TT. Sleep benefits memory for semantic category structure while preserving exemplar-specific information. **Sci Rep** 7: 14869, 2017. doi:10.1038/s41598-017-12884-5.

613. Sandoval M, Leclerc JA, Gómez RL. Words to sleep on: naps facilitate verb generalization in habitually and nonhabitually napping preschoolers. **Child Dev** 88: 1615–1628, 2017. doi:10.1111/cdev.12723.

614. Friedrich M, Wilhelm I, Mölle M, Born J, Friederici AD. The sleeping infant brain anticipates development. **Curr Biol** 27: 2374–2380.e3, 2017. doi:10.1016/j.cub.2017.06.070.

615. Zinke K, Wilhelm I, Bayramoglu M, Klein S, Born J. Children's initial sleep-associated changes in motor skill are unrelated to long-term skill levels. **Dev Sci** 20: 2017. doi:10.1111/desc.12463.

616. Chatburn A, Lushington K, Kohler MJ. Consolidation and generalisation across sleep depend on individual EEG factors and sleep spindle density. **Neurobiol Learn Mem** 179: 107384, 2021. doi:10.1016/j.nlm.2021.107384.

617. Debarnot U, Rossi M, Faraguna U, Schwartz S, Sebastiani L. Sleep does not facilitate insight in older adults. **Neurobiol Learn Mem** 140: 106–113, 2017. doi:10.1016/j.nlm.2017.02.005.

618. Viczko J, Sergeeva V, Ray LB, Owen AM, Fogel SM. Does sleep facilitate the consolidation of allocentric or egocentric representations of implicitly learned visual-motor sequence learning? **Learn Mem** 25: 67–77, 2018. doi:10.1101/lm.044719.116.

619. Sweegers CC, Talamini LM. Generalization from episodic memories across time: a route for semantic knowledge acquisition. **Cortex** 59: 49–61, 2014. doi:10.1016/j.cortex.2014.07.006.

620. Tandoc MC, Bayda M, Poskanzer C, Cho E, Cox R, Stickgold R, Schapiro AC. Examining the effects of time of day and sleep on generalization. **PLoS One** 16: e0255423, 2021. doi:10.1371/journal.pone.0255423.

621. Hennies N, Lewis PA, Durrant SJ, Cousins JN, Ralph MA. Time- but not sleep-dependent consolidation promotes the emergence of cross-modal conceptual representations. **Neuropsychologia** 63: 116–123, 2014. doi:10.1016/j.neuropsychologia.2014.08.021.

622. Maddox WT, Glass BD, Zeithamova D, Savarie ZR, Bowen C, Matthews MD, Schnyer DM. The effects of sleep deprivation on dissociable prototype learning systems. **Sleep** 34: 253–260, 2011. doi:10.1093/sleep/34.3.253.

623. Werchan DM, Gómez RL. Wakefulness (not sleep) promotes generalization of word learning in 2.5-year-old children. **Child Dev** 85: 429–436, 2014. doi:10.1111/cdev.12149.

624. Hanert A, Weber FD, Pedersen A, Born J, Bartsch T. Sleep in humans stabilizes pattern separation performance. **J Neurosci** 37: 12238–12246, 2017. doi:10.1523/JNEUROSCI.1189-17.2017.

625. Doxey CR, Hodges CB, Bodily TA, Muncy NM, Kirwan CB. The effects of sleep on the neural correlates of pattern separation. **Hippocampus** 28: 108–120, 2018. doi:10.1002/hipo.22814.

626. Schechtman E. When memories get complex, sleep comes to their rescue. **Proc Natl Acad Sci USA** 121: e2402178121, 2024. doi:10.1073/pnas.2402178121.

627. Poh JH, Cousins JN. Is there a role for pattern separation during sleep? **J Neurosci** 38: 4062–4064, 2018. doi:10.1523/JNEUROSCI.0167-18.2018.

628. Sterpenich V, Schmidt C, Albouy G, Matarazzo L, Vanhaudenhuyse A, Boveroux P, Degueldre C, Leclercq Y, Balteau E, Collette F, Luxen A, Phillips C, Maquet P. Memory reactivation during rapid eye movement sleep promotes its generalization and integration in cortical stores. **Sleep** 37: 1061–1075, 2014. doi:10.5665/sleep.3762.

629. Barry DN, Love BC. A neural network account of memory replay and knowledge consolidation. **Cereb Cortex** 33: 83–95, 2022. doi:10.1093/cercor/bhac054.

630. Pereira SI, Santamaria L, Andrews R, Schmidt E, van Rossum MCW, Lewis P. Rule abstraction is facilitated by auditory cuing in REM sleep. **J Neurosci** 43: 3838–3848, 2023. doi:10.1523/JNEUROSCI.1966-21.2022.

631. van der Helm E, Gujar N, Nishida M, Walker MP. Sleep-dependent facilitation of episodic memory details. **PLoS One** 6: e27421, 2011. doi:10.1371/journal.pone.0027421.

632. Wang JY, Weber FD, Zinke K, Noack H, Born J. Effects of sleep on word pair memory in children—separating item and source memory aspects. **Front Psychol** 8: 1533, 2017. doi:10.3389/fpsyg.2017.01533.

633. Johnson JM, Durrant SJ. Commentary: Effects of sleep on word pair memory in children-separating item and source memory aspects. **Front Psychol** 9: 1022, 2018. doi:10.3389/fpsyg.2018.01022.

634. Konrad C, Herbert JS, Schneider S, Seehagen S. Gist extraction and sleep in 12-month-old infants. **Neurobiol Learn Mem** 134: 216–220, 2016. doi:10.1016/j.nlm.2016.08.021.

635. Deliens G, Gilson M, Schmitz R, Peigneux P. Sleep unbinds memories from their emotional context. **Cortex** 49: 2221–2228, 2013. doi:10.1016/j.cortex.2012.11.014.

636. Debarnot U, Abichou K, Kalenzaga S, Sperduti M, Piolino P. Variable motor imagery training induces sleep memory consolidation and transfer improvements. **Neurobiol Learn Mem** 119: 85–92, 2015. doi:10.1016/j.nlm.2014.12.010.

637. Cairney SA, Durrant SJ, Musgrove H, Lewis PA. Sleep and environmental context: interactive effects for memory. **Exp Brain Res** 214: 83–92, 2011. doi:10.1007/s00221-011-2808-7.

638. Lewis PA, Cairney S, Manning L, Critchley HD. The impact of overnight consolidation upon memory for emotional and neutral encoding contexts. **Neuropsychologia** 49: 2619–2629, 2011. doi:10.1016/j.neuropsychologia.2011.05.009.

639. Borquez M, Born J, Navarro V, Betancourt R, Inostroza M. Sleep enhances inhibitory behavioral control in discrimination learning in rats. **Exp Brain Res** 232: 1469–1477, 2014. doi:10.1007/s00221-013-3797-5.

640. Miao X, Müller C, Lutz ND, Yang Q, Waszak F, Born J, Rauss K. Sleep consolidates stimulus-response learning. **Learn Mem** 30: 175–184, 2023. doi:10.1101/lm.053753.123.

641. Wang B, Fu XL. Gender difference in the effect of daytime sleep on declarative memory for pictures. **J Zhejiang Univ Sci B** 10: 536–546, 2009. doi:10.1631/jzus.B0820384.

642. Cox R, van Bronkhorst ML, Bayda M, Gomillion H, Cho E, Parr ME, Manickas-Hill OP, Schapiro AC, Stickgold R. Sleep selectively stabilizes contextual aspects of negative memories. **Sci Rep** 8: 17861, 2018. doi:10.1038/s41598-018-35999-9.

643. Jurewicz K, Cordi MJ, Staudigl T, Rasch B. No evidence for memory decontextualization across one night of sleep. **Front Hum Neurosci** 10: 7, 2016. doi:10.3389/fnhum.2016.00007.

644. Cox R, Tijdens RR, Meeter MM, Sweegers CC, Talamini LM. Time, not sleep, unbinds contexts from item memory. **PLoS One** 9: e88307, 2014. doi:10.1371/journal.pone.0088307.

645. Deliens G, Peigneux P. One night of sleep is insufficient to achieve sleep-to-forget emotional decontextualisation processes. **Cogn Emot** 28: 698–706, 2014. doi:10.1080/02699931.2013.844105.

646. Deliens G, Neu D, Peigneux P. Rapid eye movement sleep does not seem to unbind memories from their emotional context. **J Sleep Res** 22: 656–662, 2013. doi:10.1111/jsr.12065.

647. Besedovsky L, Benischke M, Fischer J, Yazdi AS, Born J. Human sleep consolidates allergic responses conditioned to the environmental context of an allergen exposure. **Proc Natl Acad Sci USA** 117: 10983–10988, 2020. doi:10.1073/PNAS.1920564117.

648. Schechtman E, Heilberg J, Paller KA. Memory consolidation during sleep involves context reinstatement in humans. **Cell Rep** 42: 112331, 2023. doi:10.1016/j.celrep.2023.112331.

649. Schechtman E, Heilberg J, Paller KA. Context matters: changes in memory over a period of sleep are driven by encoding context. **Learn Mem** 30: 36–42, 2023. doi:10.1101/lm.053634.122.

650. Kurinec CA, Whitney P, Hinson JM, Hansen DA, van Dongen HP. Sleep deprivation impairs binding of information with its context. **Sleep** 44: zsab113, 2021. doi:10.1093/sleep/zsab113.

651. Tempesta D, Socci V, Coppo M, Dello Ioio G, Nepa V, De Gennaro L, Ferrara M. The effect of sleep deprivation on the encoding of contextual and non-contextual aspects of emotional memory. **Neurobiol Learn Mem** 131: 9–17, 2016. doi:10.1016/j.nlm.2016.03.007.

652. Javadi AH, Tolat A, Spiers HJ. Sleep enhances a spatially mediated generalization of learned values. **Learn Mem** 22: 532–536, 2015. doi:10.1101/lm.038828.115.

653. Cairney SA, Durrant SJ, Jackson R, Lewis PA. Sleep spindles provide indirect support to the consolidation of emotional encoding contexts. **Neuropsychologia** 63: 285–292, 2014. doi:10.1016/j.neuropsychologia.2014.09.016.

654. Oyanedel CN, Binder S, Kelemen E, Petersen K, Born J, Inostroza M. Role of slow oscillatory activity and slow wave sleep in consolidation of episodic-like memory in rats. **Behav Brain Res** 275: 126–130, 2014. doi:10.1016/j.bbr.2014.09.008.

655. Inostroza M, Binder S, Born J. Sleep-dependency of episodic-like memory consolidation in rats. **Behav Brain Res** 237: 15–22, 2013. doi:10.1016/j.bbr.2012.09.011.

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

657. Berres S, Erdfelder E, Kuhlmann BG. Does sleep benefit source memory? Investigating 12-h retention intervals with a multinomial modeling approach. **Mem Cognit** 53: 467–493, 2025. doi:10.3758/s13421-024-01579-8.

658. Mawdsley M, Grasby K, Talk A. The effect of sleep on item recognition and source memory recollection among shift-workers and permanent day-workers. **J Sleep Res** 23: 538–544, 2014. doi:10.1111/jsr.12149.

659. Monaghan P, Sio UN, Lau SW, Woo HK, Linkenauger SA, Ormerod TC. Sleep promotes analogical transfer in problem solving. **Cognition** 143: 25–30, 2015. doi:10.1016/j.cognition.2015.06.005.

660. Beijamini F, Pereira SI, Cini FA, Louzada FM. After being challenged by a video game problem, sleep increases the chance to solve it. **PLoS One** 9: e84342, 2014. doi:10.1371/journal.pone.0084342.

661. Beijamini F, Valentin A, Jäger R, Born J, Diekelmann S. Sleep facilitates problem solving with no additional gain through targeted memory reactivation. **Front Behav Neurosci** 15: 645110, 2021. doi:10.3389/fnbeh.2021.645110.

662. Toor B, van den Berg N, Fang Z, Pozzobon A, Ray LB, Fogel SM. Age-related differences in problem-solving skills: reduced benefit of sleep for memory trace consolidation. **Neurobiol Aging** 116: 55–66, 2022. doi:10.1016/j.neurobiolaging.2022.04.011.

663. Toor B, van den Berg N, Ray LB, Fogel SM. Sleep spindles and slow waves are physiological markers for age-related changes in gray matter in brain regions supporting problem-solving skills. **Learn Mem** 30: 12–24, 2023. doi:10.1101/lm.053649.122.

664. van den Berg NH, Pozzobon A, Fang Z, Al-Kuwatli J, Toor B, Ray LB, Fogel SM. Sleep enhances consolidation of memory traces for complex problem-solving skills. **Cereb Cortex** 32: 653–667, 2022. doi:10.1093/cercor/bhab216.

665. Sanders KE, Beeman M. Sleep and incubation: using problem reactivation during sleep to study forgetting fixation and unconscious processing during sleep incubation. **J Cogn Psychol (Hove)** 33: 738–756, 2021. doi:10.1080/20445911.2021.1912050.

666. Sanders KE, Osburn S, Paller KA, Beeman M. Targeted memory reactivation during sleep improves next-day problem solving. **Psychol Sci** 30: 1616–1624, 2019. doi:10.1177/0956797619873344.

667. van den Berg NH, Gibbings A, Baena D, Pozzobon A, Al-Kuwatli J, Ray LB, Fogel SM. Eye movements during phasic versus tonic rapid eye movement sleep are biomarkers of dissociable electroencephalogram processes for the consolidation of novel problem-solving skills. **Sleep** 46: zsad151, 2023. doi:10.1093/sleep/zsad151.

668. van den Berg NH, Smith D, Fang Z, Pozzobon A, Toor B, Al-Kuwatli J, Ray L, Fogel SM. Sleep strengthens resting-state functional communication between brain areas involved in the consolidation of problem-solving skills. **Learn Mem** 30: 25–35, 2023. doi:10.1101/lm.053638.122.

669. Brodt S, Pöhlchen D, Täumer E, Gais S, Schönauer M. Incubation, not sleep, aids problem-solving. **Sleep** 41: 2018. doi:10.1093/sleep/zsy155.

670. Schönauer M, Brodt S, Pöhlchen D, Breßmer A, Danek AH, Gais S. Sleep does not promote solving classical insight problems and magic tricks. **Front Hum Neurosci** 12: 72, 2018. doi:10.3389/fnhum.2018.00072.

671. Stark SM, Reagh ZM, Yassa MA, Stark CEL. What's in a context? Cautions, limitations, and potential paths forward. **Neurosci Lett** 680: 77–87, 2018. doi:10.1016/j.neulet.2017.05.022.

672. Gais S, Plihal W, Wagner U, Born J. Early sleep triggers memory for early visual discrimination skills. **Nat Neurosci** 3: 1335–1339, 2000. doi:10.1038/81881.

673. Stickgold R, James L, Hobson JA. Visual discrimination learning requires sleep after training. **Nat Neurosci** 3: 1237–1238, 2000. doi:10.1038/81756.

674. Walker MP, Brakefield T, Seidman J, Morgan A, Hobson JA, Stickgold R. Sleep and the time course of motor skill learning. **Learn Mem** 10: 275–284, 2003. doi:10.1101/lm.58503.

675. Walker MP, Brakefield T, Hobson JA, Stickgold R. Dissociable stages of human memory consolidation and reconsolidation. **Nature** 425: 616–620, 2003. doi:10.1038/nature01930.

676. Pace-Schott EF, Spencer RM. Age-related changes in consolidation of perceptual and muscle-based learning of motor skills. **Front Aging Neurosci** 5: 83, 2013. doi:10.3389/fnagi.2013.00083.

677. Ren J, Guo W, Yan JH, Liu G, Jia F. Practice and nap schedules modulate children's motor learning. **Dev Psychobiol** 58: 107–119, 2016. doi:10.1002/dev.21380.

678. Al-Sharman A, Siengsukon CF. Sleep enhances learning of a functional motor task in young adults. **Phys Ther** 93: 1625–1635, 2013. doi:10.2522/ptj.20120502.

679. Al-Sharman A, Siengsukon CF. Performance on a functional motor task is enhanced by sleep in middle-aged and older adults. **J Neurol Phys Ther** 38: 161–169, 2014. doi:10.1097/NPT.0000000000000048.

680. Astill RG, Piantoni G, Raymann RJ, Vis JC, Coppens JE, Walker MP, Stickgold R, van der Werf YD, van Someren EJ. Sleep spindle and slow wave frequency reflect motor skill performance in primary school-age children. **Front Hum Neurosci** 8: 910, 2014. doi:10.3389/fnhum.2014.00910.

681. Schönauer M, Grätsch M, Gais S. Evidence for two distinct sleep-related long-term memory consolidation processes. **Cortex** 63: 68–78, 2015. doi:10.1016/j.cortex.2014.08.005.

682. Gudberg C, Wulff K, Johansen-Berg H. Sleep-dependent motor memory consolidation in older adults depends on task demands. **Neurobiol Aging** 36: 1409–1416, 2015. doi:10.1016/j.neurobiolaging.2014.12.014.

683. Borragán G, Urbain C, Schmitz R, Mary A, Peigneux P. Sleep and memory consolidation: motor performance and proactive interference effects in sequence learning. **Brain Cogn** 95: 54–61, 2015. doi:10.1016/j.bandc.2015.01.011.

684. van Schalkwijk FJ, Benjamins JS, Migliorati F, de Nooijer JA, van Someren EJ, van Gog T, van der Werf YD. The role of sleep timing in children's observational learning. **Neurobiol Learn Mem** 125: 98–105, 2015. doi:10.1016/j.nlm.2015.08.003.

685. Mantua J, Baran B, Spencer RM. Sleep benefits consolidation of visuo-motor adaptation learning in older adults. **Exp Brain Res** 234: 587–595, 2016. doi:10.1007/s00221-015-4490-7.

686. Malangré A, Blischke K. Sleep-related offline improvements in gross motor task performance occur under free recall requirements. **Front Hum Neurosci** 10: 134, 2016. doi:10.3389/fnhum.2016.00134.

687. Verweij IM, Onuki Y, van Someren EJ, van der Werf YD. Sleep to the beat: a nap favours consolidation of timing. **Behav Neurosci** 130: 298–304, 2016. doi:10.1037/bne0000146.

688. Blischke K, Malangré A. Chunk concatenation evolves with practice and sleep-related enhancement consolidation in a complex arm movement sequence. **J Hum Kinet** 51: 5–17, 2016. doi:10.1515/hukin-2015-0163.

689. Tucker MA, Nguyen N, Stickgold R. Experience playing a musical instrument and overnight sleep enhance performance on a sequential typing task. **PLoS One** 11: e0159608, 2016. doi:10.1371/journal.pone.0159608.

690. Bottary R, Sonni A, Wright D, Spencer RM. Insufficient chunk concatenation may underlie changes in sleep-dependent consolidation of motor sequence learning in older adults. **Learn Mem** 23: 455–459, 2016. doi:10.1101/lm.043042.116.

691. Tucker MA, Morris CJ, Morgan A, Yang J, Myers S, Pierce JG, Stickgold R, Scheer FA. The relative impact of sleep and circadian drive on motor skill acquisition and memory consolidation. **Sleep** 40: zsx036, 2017. doi:10.1093/sleep/zsx036.

692. Yan JH. Children benefit differently from night- and day-time sleep in motor learning. **Hum Mov Sci** 54: 297–307, 2017. doi:10.1016/j.humov.2017.05.015.

693. Johnson BP, Scharf SM, Westlake KP. Targeted memory reactivation during sleep, but not wake, enhances sensorimotor skill performance: a pilot study. **J Mot Behav** 50: 202–209, 2018. doi:10.1080/00222895.2017.1327411.

694. Picchioni D, Schmidt KC, McWhirter KK, Loutaev I, Pavletic AJ, Speer AM, Zametkin AJ, Miao N, Bishu S, Turetsky KM, Morrow AS,

Nadel JL, Evans BC, Vesselinovitch DM, Sheeler CA, Balkin TJ, Smith CB. Rates of cerebral protein synthesis in primary visual cortex during sleep-dependent memory consolidation, a study in human subjects. **Sleep** 41: zsy088, 2018. doi:10.1093/sleep/zsy088.

695. Tamaki M, Wang Z, Watanabe T, Sasaki Y. Trained-feature-specific offline learning by sleep in an orientation detection task. **J Vis** 19: 12, 2019. doi:10.1167/19.12.12.

696. Nissen C, Piosczyk H, Holz J, Maier JG, Frase L, Sterr A, Riemann D, Feige B. Sleep is more than rest for plasticity in the human cortex. **Sleep** 44: zsaa216, 2021. doi:10.1093/sleep/zsaa216.

697. Ameen MS, Petzka M, Peigneux P, Hoedlmoser K. Post-training sleep modulates motor adaptation and task-related beta oscillations. **J Sleep Res** 33: e14082, 2024. doi:10.1111/jsr.14082.

698. Di Rienzo F, Debarnot U, Daligault S, Delpuech C, Doyon J, Guillot A. Brain plasticity underlying sleep-dependent motor consolidation after motor imagery. **Cereb Cortex** 33: 11431–11445, 2023. doi:10.1093/cercor/bhad379.

699. McDevitt EA, Rowe KM, Brady M, Duggan KA, Mednick SC. The benefit of offline sleep and wake for novel object recognition. **Exp Brain Res** 232: 1487–1496, 2014. doi:10.1007/s00221-014-3830-3.

700. Cedernaes J, Sand F, Liethof L, Lampola L, Hassanzadeh S, Axelsson EK, Yeganeh A, Ros O, Broman JE, Schiöth HB, Benedict C. Learning and sleep-dependent consolidation of spatial and procedural memories are unaltered in young men under a fixed short sleep schedule. **Neurobiol Learn Mem** 131: 87–94, 2016. doi:10.1016/j.nlm.2016.03.012.

701. Gregory MD, Agam Y, Selvadurai C, Nagy A, Vangel M, Tucker M, Robertson EM, Stickgold R, Manoach DS. Resting state connectivity immediately following learning correlates with subsequent sleep-dependent enhancement of motor task performance. **Neuroimage** 102: 666–673, 2014. doi:10.1016/j.neuroimage.2014.08.044.

702. Vien C, Boré A, Lungu O, Benali H, Carrier J, Fogel S, Doyon J. Age-related white-matter correlates of motor sequence learning and consolidation. **Neurobiol Aging** 48: 13–22, 2016. doi:10.1016/j.neurobiolaging.2016.08.006.

703. Iranmanesh H, Kakhki AS, Taheri H, Shea CH. Motor memory consolidation in children: the role of awareness and sleep on offline general and sequence-specific learning. **Biomed Hum Kinet** 14: 83–94, 2022. doi:10.2478/bhk-2022-0011.

704. Rångtell FH, Karamchedu S, Andersson P, van Egmond L, Hultgren T, Broman JE, Cedernaes J, Benedict C. Learning performance is linked to procedural memory consolidation across both sleep and wakefulness. **Sci Rep** 7: 10234, 2017. doi:10.1038/s41598-017-09263-5.

705. Durrant SJ, Cairney SA, Lewis PA. Overnight consolidation aids the transfer of statistical knowledge from the medial temporal lobe to the striatum. **Cereb Cortex** 23: 2467–2478, 2013. doi:10.1093/cercor/bhs244.

706. Cousins JN, El-Deredy W, Parkes LM, Hennies N, Lewis PA. Cued memory reactivation during slow-wave sleep promotes explicit knowledge of a motor sequence. **J Neurosci** 34: 15870–15876, 2014. doi:10.1523/JNEUROSCI.1011-14.2014.

707. Djonlagic I, Guo M, Matteis P, Carusona A, Stickgold R, Malhotra A. Untreated sleep-disordered breathing: links to aging-related decline in sleep-dependent memory consolidation. **PLoS One** 9: e85918, 2014. doi:10.1371/journal.pone.0085918.

708. Malangré A, Leinen P, Blischke K. Sleep-related offline learning in a complex arm movement sequence. **J Hum Kinet** 40: 7–20, 2014. doi:10.2478/hukin-2014-0002.

709. Landry S, Anderson C, Andrewartha P, Sasse A, Conduit R. The impact of obstructive sleep apnea on motor skill acquisition and consolidation. **J Clin Sleep Med** 10: 491–496, 2014. doi:10.5664/jcsm.3692.

710. Csabi E, Varszegi-Schulz M, Janacsek K, Malecek N, Nemeth D. The consolidation of implicit sequence memory in obstructive sleep apnea. **PLoS One** 9: e109010, 2014. doi:10.1371/journal.pone.0109010.

711. Sprenger A, Weber FD, Machner B, Talamo S, Scheffelmeier S, Bethke J, Helmchen C, Gais S, Kimmig H, Born J. Deprivation and recovery of sleep in succession enhances reflexive motor behavior. **Cereb Cortex** 25: 4610–4618, 2015. doi:10.1093/cercor/bhv115.

712. Csábi E, Benedek P, Janacsek K, Zavecz Z, Katona G, Nemeth D. Declarative and non-declarative memory consolidation in children with sleep disorder. **Front Hum Neurosci** 9: 709, 2015. doi:10.3389/fnhum.2015.00709.

713. Nishida M, Nakashima Y, Nishikawa T. Slow sleep spindle and procedural memory consolidation in patients with major depressive disorder. **Nat Sci Sleep** 8: 63–72, 2016. doi:10.2147/NSS.S100337.

714. Laventure S, Fogel S, Lungu O, Albouy G, Sévigny-Dupont P, Vien C, Sayour C, Carrier J, Benali H, Doyon J. NREM2 and sleep spindles are instrumental to the consolidation of motor sequence memories. **PLoS Biol** 14: e1002429, 2016. doi:10.1371/journal.pbio.1002429.

715. Landry S, O'Driscoll DM, Hamilton GS, Conduit R. Overnight motor skill learning outcomes in obstructive sleep apnea: effect of continuous positive airway pressure. **J Clin Sleep Med** 12: 681–688, 2016. doi:10.5664/jcsm.5794.

716. Fogel S, Albouy G, King BR, Lungu O, Vien C, Bore A, Pinsard B, Benali H, Carrier J, Doyon J. Reactivation or transformation? Motor memory consolidation associated with cerebral activation time-locked to sleep spindles. **PLoS One** 12: e0174755, 2017. doi:10.1371/journal.pone.0174755.

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

718. Sugawara SK, Koike T, Kawamichi H, Makita K, Hamano YH, Takahashi HK, Nakagawa E, Sadato N. Qualitative differences in offline improvement of procedural memory by daytime napping and overnight sleep: an fMRI study. **Neurosci Res** 132: 37–45, 2018. doi:10.1016/j.neures.2017.09.006.

719. Laventure S, Pinsard B, Lungu O, Carrier J, Fogel S, Benali H, Lina JM, Boutin A, Doyon J. Beyond spindles: interactions between sleep spindles and boundary frequencies during cued reactivation of motor memory representations. **Sleep** 41: zsy142, 2018. doi:10.1093/sleep/zsy142.

720. van Schalkwijk FJ, Hauser T, Hoedlmoser K, Ameen MS, Wilhelm FH, Sauter C, Klösch G, Moser D, Gruber G, Anderer P, Saletu B, Parapatics S, Zeitlhofer J, Schabus M. Procedural memory consolidation is associated with heart rate variability and sleep spindles. **J Sleep Res** 29: e12910, 2020. doi:10.1111/jsr.12910.

721. Purple RJ, Cosgrave J, Vyazovskiy V, Foster RG, Porcheret K, Wulff K. Sleep-related memory consolidation in the psychosis spectrum phenotype. **Neurobiol Learn Mem** 174: 107273, 2020. doi:10.1016/j.nlm.2020.107273.

722. Cheng LY, Che T, Tomic G, Slutzky MW, Paller KA. Memory reactivation during sleep improves execution of a challenging motor skill. **J Neurosci** 41: 9608–9616, 2021. doi:10.1523/JNEUROSCI.0265-21.2021.

723. Rakowska M, Abdellahi ME, Bagrowska P, Navarrete M, Lewis PA. Long term effects of cueing procedural memory reactivation during NREM sleep. **Neuroimage** 244: 118573, 2021. doi:10.1016/j.neuroimage.2021.118573.

724. Stee W, Peigneux P. Does motor memory reactivation through practice and post-learning sleep modulate consolidation? **Clocks Sleep** 5: 72–84, 2023. doi:10.3390/clockssleep5010008.

725. Wamsley EJ, Hamilton K, Graveline Y, Manceor S, Parr E. Test expectation enhances memory consolidation across both sleep and wake. **PLoS One** 11: e0165141, 2016. doi:10.1371/journal.pone.0165141.

726. Friedman J, Korman M. Offline optimization of the relative timing of movements in a sequence is blocked by retroactive behavioral interference. **Front Hum Neurosci** 10: 623, 2016. doi:10.3389/fnhum.2016.00623.

727. Song S, Cohen LG. Practice and sleep form different aspects of skill. **Nat Commun** 5: 3407, 2014. doi:10.1038/ncomms4407.

728. Hallgató E, Győri-Dani D, Pekár J, Janacsek K, Nemeth D. The differential consolidation of perceptual and motor learning in skill acquisition. **Cortex** 49: 1073–1081, 2013. doi:10.1016/j.cortex.2012.01.002.

729. Hennies N, Lambon Ralph MA, Durrant SJ, Cousins JN, Lewis PA. Cued memory reactivation during SWS abolishes the beneficial effect of sleep on abstraction. **Sleep** 40: 2017. doi:10.1093/sleep/zsx102.

730. Urbain C, Schmitz R, Schmidt C, Cleeremans A, van Bogaert P, Maquet P, Peigneux P. Sleep-dependent neurophysiological processes in implicit sequence learning. **J Cogn Neurosci** 25: 2003–2014, 2013. doi:10.1162/jocn_a_00439.

731. Thürer B, Weber FD, Born J, Stein T. Variable training but not sleep improves consolidation of motor adaptation. **Sci Rep** 8: 15977, 2018. doi:10.1038/s41598-018-34225-w.

732. Reis J, Fischer JT, Prichard G, Weiller C, Cohen LG, Fritsch B. Time- but not sleep-dependent consolidation of tDCS-enhanced visuomotor skills. **Cereb Cortex** 25: 109–117, 2015. doi:10.1093/cercor/bht208.

733. Honma M, Yoshiike T, Ikeda H, Kuriyama K. Sleep-independent offline consolidation of response inhibition during the daytime post-training period. **Sci Rep** 5: 10362, 2015. doi:10.1038/srep10362.

734. Landry S, Anderson C, Conduit R. The effects of sleep, wake activity and time-on-task on offline motor sequence learning. **Neurobiol Learn Mem** 127: 56–63, 2016. doi:10.1016/j.nlm.2015.11.009.

735. Kemény F, Lukács Á. Sleep-independent off-line enhancement and time of the day effects in three forms of skill learning. **Cogn Process** 17: 163–174, 2016. doi:10.1007/s10339-016-0750-0.

736. Rickard TC, Pan SC. Time for considering the possibility that sleep plays no unique role in motor memory consolidation: reply to Adi-Japha and Karni (2016). **Psychol Bull** 143: 454–458, 2017. doi:10.1037/bul0000094.

737. van den Berg NH, Al-Kuwatli J, Paulin J, Ray LB, Owen AM, Fogel SM. Sleep preferentially enhances memory for a cognitive strategy but not the implicit motor skills used to acquire it. **Neurobiol Learn Mem** 161: 135–142, 2019. doi:10.1016/j.nlm.2019.04.005.

738. Klinzing JG, Nienborg H, Rauss K. Sleep does not aid the generalisation of binocular disparity-based learning to the other visual hemifield. **J Sleep Res** 30: e13335, 2021. doi:10.1111/jsr.13335.

739. Ben-Zion D, Gabitov E, Prior A, Bitan T. Effects of sleep on language and motor consolidation: evidence of domain general and specific mechanisms. **Neurobiol Lang (Camb)** 3: 180–213, 2022. doi:10.1162/nol_a_00060.

740. Rickard TC, Pan SC, Gupta MW. Severe publication bias contributes to illusory sleep consolidation in the motor sequence learning literature. **J Exp Psychol Learn Mem Cogn** 48: 1787–1796, 2022. doi:10.1037/xlm0001090.

741. Pan SC, Rickard TC. Sleep and motor learning: is there room for consolidation? **Psychol Bull** 141: 812–834, 2015. doi:10.1037/bul0000009.

742. Conessa A, Debarnot U, Siegler I, Boutin A. Sleep-related motor skill consolidation and generalizability after physical practice, motor imagery, and action observation. **iScience** 26: 107314, 2023. doi:10.1016/j.isci.2023.107314.

743. McDevitt EA, Zhang J, MacKenzie KJ, Fiser J, Mednick SC. The effect of interference, offline sleep, and wake on spatial statistical learning. **Neurobiol Learn Mem** 193: 107650, 2022. doi:10.1016/j.nlm.2022.107650.

744. Maier JG, Piosczyk H, Holz J, Landmann N, Deschler C, Frase L, Kuhn M, Klöppel S, Spiegelhalder K, Sterr A, Riemann D, Feige B, Voderholzer U, Nissen C. Brief periods of NREM sleep do not promote early offline gains but subsequent on-task performance in motor skill learning. **Neurobiol Learn Mem** 145: 18–27, 2017. doi:10.1016/j.nlm.2017.08.006.

745. Nemeth D, Janacsek K, Londe Z, Ullman MT, Howard DV, Howard JH. Sleep has no critical role in implicit motor sequence learning in young and old adults. **Exp Brain Res** 201: 351–358, 2010. doi:10.1007/s00221-009-2024-x.

746. Bothe K, Hirschauer F, Wiesinger HP, Edfelder J, Gruber G, Birklbauer J, Hoedlmoser K. The impact of sleep on complex gross-motor adaptation in adolescents. **J Sleep Res** 28: e12797, 2019. doi:10.1111/jsr.12797.

747. Bothe K, Hirschauer F, Wiesinger HP, Edfelder JM, Gruber G, Hoedlmoser K, Birklbauer J. Gross motor adaptation benefits from sleep after training. **J Sleep Res** 29: e12961, 2020. doi:10.1111/jsr.12961.

748. Hoedlmoser K, Birklbauer J, Schabus M, Eibenberger P, Rigler S, Mueller E. The impact of diurnal sleep on the consolidation of a complex gross motor adaptation task. **J Sleep Res** 24: 100–109, 2015. doi:10.1111/jsr.12207.

749. Albouy G, Vandewalle G, Sterpenich V, Rauchs G, Desseilles M, Balteau E, Degueldre C, Phillips C, Luxen A, Maquet P. Sleep stabilizes visuomotor adaptation memory: a functional magnetic resonance imaging study. **J Sleep Res** 22: 144–154, 2013. doi:10.1111/j.1365-2869.2012.01059.x.

750. Urbain C, Houyoux E, Albouy G, Peigneux P. Consolidation through the looking-glass: sleep-dependent proactive interference on visuomotor adaptation in children. **J Sleep Res** 23: 44–52, 2014. doi:10.1111/jsr.12082.

751. Hotermans C, Peigneux P, Maertens de Noordhout A, Moonen G, Maquet P. Early boost and slow consolidation in motor skill learning. **Learn Mem** 13: 580–583, 2006. doi:10.1101/lm.239406.

752. Hotermans C, Peigneux P, de Noordhout AM, Moonen G, Maquet P. Repetitive transcranial magnetic stimulation over the primary

motor cortex disrupts early boost but not delayed gains in performance in motor sequence learning. **Eur J Neurosci** 28: 1216–1221, 2008. doi:10.1111/j.1460-9568.2008.06421.x.

753. Rickard TC, Cai DJ, Rieth CA, Jones J, Ard MC**.** Sleep does not enhance motor sequence learning. **J Exp Psychol Learn Mem Cogn** 34: 834–842, 2008. doi:10.1037/0278-7393.34.4.834.

754. Adi-Japha E, Karni A**.** Time for considering constraints on procedural memory consolidation processes: comment on Pan and Rickard (2015) with specific reference to developmental changes. **Psychol Bull** 142: 568–571, 2016. doi:10.1037/bul0000048.

755. Gupta MW, Rickard TC**.** Comparison of online, offline, and hybrid hypotheses of motor sequence learning using a quantitative model that incorporate reactive inhibition. **Sci Rep** 14: 4661, 2024. doi:10.1038/s41598-024-52726-9.

756. Gupta MW, Rickard TC**.** Dissipation of reactive inhibition is sufficient to explain post-rest improvements in motor sequence learning. **NPJ Sci Learn** 7: 25, 2022. doi:10.1038/s41539-022-00140-z.

757. Albouy G, Ruby P, Phillips C, Luxen A, Peigneux P, Maquet P**.** Implicit oculomotor sequence learning in humans: time course of offline processing. **Brain Res** 1090: 163–171, 2006. doi:10.1016/j.brainres.2006.03.076.

758. Albouy G, Sterpenich V, Balteau E, Vandewalle G, Desseilles M, Dang-Vu T, Darsaud A, Ruby P, Luppi PH, Degueldre C, Peigneux P, Luxen A, Maquet P**.** Both the hippocampus and striatum are involved in consolidation of motor sequence memory. **Neuron** 58: 261–272, 2008. doi:10.1016/j.neuron.2008.02.008.

759. Brawn TP, Fenn KM, Nusbaum HC, Margoliash D**.** Consolidating the effects of waking and sleep on motor-sequence learning. **J Neurosci** 30: 13977–13982, 2010. doi:10.1523/JNEUROSCI.3295-10.2010.

760. Schmitz R, Schabus M, Perrin F, Luxen A, Maquet P, Peigneux P**.** Recurrent boosting effects of short inactivity delays on performance: an ERPs study. **BMC Res Notes** 2: 170, 2009. doi:10.1186/1756-0500-2-170.

761. Debarnot U, Clerget E, Olivier E**.** Role of the primary motor cortex in the early boost in performance following mental imagery training. **PLoS One** 6: e26717, 2011. doi:10.1371/journal.pone.0026717.

762. Simor P, Zavecz Z, Horváth K, Éltető N, Török C, Pesthy O, Gombos F, Janacsek K, Nemeth D**.** Deconstructing procedural memory: different learning trajectories and consolidation of sequence and statistical learning. **Front Psychol** 9: 2708, 2018. doi:10.3389/fpsyg.2018.02708.

763. Ballesio A, Cellini N**.** Updating internal cognitive models during sleep. **J Neurosci** 39: 1966–1968, 2019. doi:10.1523/JNEUROSCI.2926-18.2019.

764. Diekelmann S, Born J, Rasch B**.** Increasing explicit sequence knowledge by odor cueing during sleep in men but not women. **Front Behav Neurosci** 10: 74, 2016. doi:10.3389/fnbeh.2016.00074.

765. Albouy G, King BR, Maquet P, Doyon J**.** Hippocampus and striatum: dynamics and interaction during acquisition and sleep-related motor sequence memory consolidation. **Hippocampus** 23: 985–1004, 2013. doi:10.1002/hipo.22183.

766. Fang Z, Smith DM, Albouy G, King BR, Vien C, Benali H, Carrier J, Doyon J, Fogel S**.** Differential effects of a nap on motor sequence learning-related functional connectivity between young and older adults. **Front Aging Neurosci** 13: 747358, 2021. doi:10.3389/fnagi.2021.747358.

767. Mylonas D, Schapiro AC, Verfaellie M, Baxter B, Vangel M, Stickgold R, Manoach DS**.** Maintenance of procedural motor memory across brief rest periods requires the hippocampus. **J Neurosci** 44: e1839232024, 2024. doi:10.1523/JNEUROSCI.1839-23.2024.

768. Genzel L, Schut E, Schröder T, Eichler R, Khamassi M, Gomez A, Navarro Lobato I, Battaglia F**.** The object space task shows cumulative memory expression in both mice and rats. **PLoS Biol** 17: e3000322, 2019. doi:10.1371/journal.pbio.3000322.

769. Harkotte M, Contreras MP, Inostroza M, Born J**.** Effects of information load on schema and episodic memory formation. **Front Behav Neurosci** 16: 923713, 2022. doi:10.3389/fnbeh.2022.923713.

770. Tse D, Langston RF, Kakeyama M, Bethus I, Spooner PA, Wood ER, Witter MP, Morris RG**.** Schemas and memory consolidation. **Science** 316: 76–82, 2007. doi:10.1126/science.1135935.

771. Benchenane K, Peyrache A, Khamassi M, Tierney PL, Gioanni Y, Battaglia FP, Wiener SI**.** Coherent theta oscillations and reorganization of spike timing in the hippocampal- prefrontal network upon learning. **Neuron** 66: 921–936, 2010. doi:10.1016/j.neuron.2010.05.013.

772. Abdou K, Nomoto M, Aly MH, Ibrahim AZ, Choko K, Okubo-Suzuki R, Muramatsu SI, Inokuchi K**.** Prefrontal coding of learned and inferred knowledge during REM and NREM sleep. **Nat Commun** 15: 4566, 2024. doi:10.1038/s41467-024-48816-x.

773. Brukhnová A, Szczurowska E, Vejmola Č, Horsley RR, Kelemen E**.** Effects of intra-hippocampal corticosterone and sleep on consolidation of memories of aversive experience in rats. **Neurobiol Learn Mem** 198: 107721, 2023. doi:10.1016/j.nlm.2023.107721.

774. Wilhelm I, Diekelmann S, Molzow I, Ayoub A, Mölle M, Born J**.** Sleep selectively enhances memory expected to be of future relevance. **J Neurosci** 31: 1563–1569, 2011. doi:10.1523/JNEUROSCI.3575-10.2011.

775. van Dongen EV, Thielen JW, Takashima A, Barth M, Fernández G**.** Sleep supports selective retention of associative memories based on relevance for future utilization. **PLoS One** 7: e43426, 2012. doi:10.1371/journal.pone.0043426.

776. Carollo G, Degasperi G, Cellini N**.** The role of sleep and wakefulness in the recognition of emotional pictures. **J Sleep Res** 31: e13695, 2022. doi:10.1111/jsr.13695.

777. Gobin CM, Banks JB, Fins AI, Tartar JL**.** Poor sleep quality is associated with a negative cognitive bias and decreased sustained attention. **J Sleep Res** 24: 535–542, 2015. doi:10.1111/jsr.12302.

778. Zhang J, Chan AB, Lau EY, Hsiao JH**.** Individuals with insomnia misrecognize angry faces as fearful faces while missing the eyes: an eye-tracking study. **Sleep** 42: 2019. doi:10.1093/sleep/zsy220.

779. Kaida K, Niki K, Born J**.** Role of sleep for encoding of emotional memory. **Neurobiol Learn Mem** 121: 72–79, 2015. doi:10.1016/j.nlm.2015.04.002.

780. Sack B, Broer K, Anders S**.** Sleep deprivation selectively enhances interpersonal emotion recognition from dynamic facial expressions at long viewing times: an observational study. **Neurosci Lett** 694: 225–230, 2019. doi:10.1016/j.neulet.2018.10.035.

781. Seehagen S, Herbert JS, Zmyj N**.** Prior sleep timing and visual recognition of emotional faces in 6-month-old infants. **Infant Behav Dev** 65: 101655, 2021. doi:10.1016/j.infbeh.2021.101655.

782. Wagner U, Gais S, Born J**.** Emotional memory formation is enhanced across sleep intervals with high amounts of rapid eye movement sleep. **Learn Mem** 8: 112–119, 2001. doi:10.1101/lm.36801.

783. Wagner U, Hallschmid M, Rasch B, Born J. Brief sleep after learning keeps emotional memories alive for years. **Biol Psychiatry** 60: 788–790, 2006. doi:10.1016/j.biopsych.2006.03.061.

784. Siegel JM. Memory consolidation is similar in waking and sleep. **Curr Sleep Med Rep** 7: 15–18, 2021. doi:10.1007/s40675-020-00199-3.

785. Denis D, Sanders KE, Kensinger EA, Payne JD. Sleep preferentially consolidates negative aspects of human memory: well-powered evidence from two large online experiments. **Proc Natl Acad Sci USA** 119: e2202657119, 2022. doi:10.1073/pnas.2202657119.

786. Jones BJ, Mackay A, Mantua J, Schultz KS, Spencer RM. The role of sleep in emotional memory processing in middle age. **Neurobiol Learn Mem** 155: 208–215, 2018. doi:10.1016/j.nlm.2018.08.002.

787. Schoch SF, Cordi MJ, Rasch B. Modulating influences of memory strength and sensitivity of the retrieval test on the detectability of the sleep consolidation effect. **Neurobiol Learn Mem** 145: 181–189, 2017. doi:10.1016/j.nlm.2017.10.009.

788. Payne JD, Chambers AM, Kensinger EA. Sleep promotes lasting changes in selective memory for emotional scenes. **Front Integr Neurosci** 6: 108, 2012. doi:10.3389/fnint.2012.00108.

789. Payne JD, Kensinger EA, Wamsley EJ, Spreng RN, Alger SE, Gibler K, Schacter DL, Stickgold R. Napping and the selective consolidation of negative aspects of scenes. **Emotion** 15: 176–186, 2015. doi:10.1037/a0038683.

790. Martinez BS, Denis D, Kim SY, DiPietro CH, Stare C, Kensinger EA, Payne JD. The effects of cognitive reappraisal and sleep on emotional memory formation. **Cogn Emot** 37: 942–958, 2023. doi:10.1080/02699931.2023.2221843.

791. Kuriyama K, Honma M, Yoshiike T, Kim Y. Valproic acid but not D-cycloserine facilitates sleep-dependent offline learning of extinction and habituation of conditioned fear in humans. **Neuropharmacology** 64: 424–431, 2013. doi:10.1016/j.neuropharm.2012.07.045.

792. Pace-Schott EF, Tracy LE, Rubin Z, Mollica AG, Ellenbogen JM, Bianchi MT, Milad MR, Pitman RK, Orr SP. Interactions of time of day and sleep with between-session habituation and extinction memory in young adult males. **Exp Brain Res** 232: 1443–1458, 2014. doi:10.1007/s00221-014-3829-9.

793. Menz MM, Rihm JS, Büchel C. REM sleep is causal to successful consolidation of dangerous and safety stimuli and reduces return of fear after extinction. **J Neurosci** 36: 2148–2160, 2016. doi:10.1523/JNEUROSCI.3083-15.2016.

794. Straus LD, Acheson DT, Risbrough VB, Drummond SP. Sleep deprivation disrupts recall of conditioned fear extinction. **Biol Psychiatry Cogn Neurosci Neuroimaging** 2: 123–129, 2017. doi:10.1016/j.bpsc.2016.05.004.

795. Straus LD, Drummond SP, Risbrough VB, Norman SB. Sleep disruption, safety learning, and fear extinction in humans: implications for posttraumatic stress disorder. **Curr Top Behav Neurosci** 38: 193–205, 2018. doi:10.1007/7854_2017_31.

796. Straus LD, Richards A, Inslicht SS, Dolsen EA, Neylan TC. Examining the effect of sleep disruption on the neural correlates of fear extinction. **Biol Psychiatry Cogn Neurosci Neuroimaging** 6: 251–252, 2021. doi:10.1016/j.bpsc.2020.12.009.

797. Zenses AK, Lenaert B, Peigneux P, Beckers T, Boddez Y. Sleep deprivation increases threat beliefs in human fear conditioning. **J Sleep Res** 29: e12873, 2020. doi:10.1111/jsr.12873.

798. Bottary R, Seo J, Daffre C, Gazecki S, Moore KN, Kopotiyenko K, Dominguez JP, Gannon K, Lasko NB, Roth B, Milad MR, Pace-Schott EF. Fear extinction memory is negatively associated with REM sleep in insomnia disorder. **Sleep** 43: zsaa007, 2020. doi:10.1093/sleep/zsaa007.

799. Spoormaker VI, Gvozdanovic GA, Sämann PG, Czisch M. Ventromedial prefrontal cortex activity and rapid eye movement sleep are associated with subsequent fear expression in human subjects. **Exp Brain Res** 232: 1547–1554, 2014. doi:10.1007/s00221-014-3831-2.

800. Sterpenich V, Piguet C, Desseilles M, Ceravolo L, Gschwind M, van de Ville D, Vuilleumier P, Schwartz S. Sleep sharpens sensory stimulus coding in human visual cortex after fear conditioning. **Neuroimage** 100: 608–618, 2014. doi:10.1016/j.neuroimage.2014.06.003.

801. Lerner I, Lupkin SM, Sinha N, Tsai A, Gluck MA. Baseline levels of rapid eye movement sleep may protect against excessive activity in fear-related neural circuitry. **J Neurosci** 37: 11233–11244, 2017. doi:10.1523/JNEUROSCI.0578-17.2017.

802. Feng P, Becker B, Zheng Y, Feng T. Sleep deprivation affects fear memory consolidation: bi-stable amygdala connectivity with insula and ventromedial prefrontal cortex. **Soc Cogn Affect Neurosci** 13: 145–155, 2018. doi:10.1093/scan/nsx148.

803. Wallace ML, Banihashemi L, O'Donnell C, Nimgaonkar VL, Kodavali C, McNamee R, Germain A. Using optimal combined moderators to define heterogeneity in neural responses to randomized conditions: application to the effect of sleep loss on fear learning. **Neuroimage** 181: 718–727, 2018. doi:10.1016/j.neuroimage.2018.07.051.

804. Seo J, Pace-Schott EF, Milad MR, Song H, Germain A. Partial and total sleep deprivation interferes with neural correlates of consolidation of fear extinction memory. **Biol Psychiatry Cogn Neurosci Neuroimaging** 6: 299–309, 2021. doi:10.1016/j.bpsc.2020.09.013.

805. Denis D, Bottary R, Cunningham TJ, Drummond SPA, Straus LD. Beta spectral power during sleep is associated with impaired recall of extinguished fear. **Sleep** 46: zsad209, 2023. doi:10.1093/sleep/zsad209.

806. Bottary R, Straus LD, Pace-Schott EF. The impact of sleep on fear extinction. **Curr Top Behav Neurosci** 64: 133–156, 2023. doi:10.1007/7854_2023_431.

807. Pace-Schott EF, Seo J, Bottary R. The influence of sleep on fear extinction in trauma-related disorders. **Neurobiol Stress** 22: 100500, 2023. doi:10.1016/j.ynstr.2022.100500.

808. Ai SZ, Dai XJ. Causal role of rapid-eye-movement sleep on successful memory consolidation of fear extinction. **J Thorac Dis** 10: 1214–1216, 2018. doi:10.21037/jtd.2018.01.163.

809. Seo J, Oliver KI, Daffre C, Moore KN, Gazecki S, Lasko NB, Milad MR, Pace-Schott EF. Associations of sleep measures with neural activations accompanying fear conditioning and extinction learning and memory in trauma-exposed individuals. **Sleep** 45: zsab261, 2022. doi:10.1093/sleep/zsab261.

810. Feng P, Becker B, Feng T, Zheng Y. Alter spontaneous activity in amygdala and vmPFC during fear consolidation following 24 h sleep deprivation. **Neuroimage** 172: 461–469, 2018. doi:10.1016/j.neuroimage.2018.01.057.

811. Peters AC, Blechert J, Sämann PG, Eidner I, Czisch M, Spoormaker VI. One night of partial sleep deprivation affects habituation of hypothalamus and skin conductance responses. **J Neurophysiol** 112: 1267–1276, 2014. doi:10.1152/jn.00657.2013.

812. Sturm A, Czisch M, Spoormaker VI. Effects of unconditioned stimulus intensity and fear extinction on subsequent sleep architecture in an afternoon nap. **J Sleep Res** 22: 648–655, 2013. doi:10.1111/jsr.12074.

813. Straus LD, Norman SB, Risbrough VB, Acheson DT, Drummond SP. REM sleep and safety signal learning in posttraumatic stress disorder: a preliminary study in military veterans. **Neurobiol Stress** 9: 22–28, 2018. doi:10.1016/j.ynstr.2018.07.001.

814. Stickgold R, Manoach DS. The importance of sleep in fear conditioning and posttraumatic stress disorder. **Biol Psychiatry Cogn Neurosci Neuroimaging** 2: 109–110, 2017. doi:10.1016/j.bpsc.2017.01.006.

815. Pavlov YG, Pavlova NV, Diekelmann S, Kotchoubey B. Fear memory in humans is consolidated over time independently of sleep. **Cogn Affect Behav Neurosci** 23: 100–113, 2023. doi:10.3758/s13415-022-01037-5.

816. Hauner KK, Howard JD, Zelano C, Gottfried JA. Stimulus-specific enhancement of fear extinction during slow-wave sleep. **Nat Neurosci** 16: 1553–1555, 2013. doi:10.1038/nn.3527.

817. He J, Sun HQ, Li SX, Zhang WH, Shi J, Ai SZ, Li Y, Li XJ, Tang X-D, Lu L. Effect of conditioned stimulus exposure during slow wave sleep on fear memory extinction in humans. **Sleep** 38: 423–431, 2015. doi:10.5665/sleep.4502.

818. Rihm JS, Sollberger SB, Soravia LM, Rasch B. Re-presentation of olfactory exposure therapy success cues during non-rapid eye movement sleep did not increase therapy outcome but increased sleep spindles. **Front Hum Neurosci** 10: 340, 2016. doi:10.3389/fnhum.2016.00340.

819. Borghese F, Henckaerts P, Guy F, Perez Mayo C, Delplanque S, Schwartz S, Perogamvros L. Targeted memory reactivation during REM sleep in patients with social anxiety disorder. **Front Psychiatry** 13: 904704, 2022. doi:10.3389/fpsyt.2022.904704.

820. Diekelmann S, Born J. Cueing fear memory during sleep—to extinguish or to enhance fear? **Sleep** 38: 337–339, 2015. doi:10.5665/sleep.4484.

821. Rolls A, Makam M, Kroeger D, Colas D, de Lecea L, Heller HC. Sleep to forget: interference of fear memories during sleep. **Mol Psychiatry** 18: 1166–1170, 2013. doi:10.1038/mp.2013.121.

822. Bennion KA, Payne JD, Kensinger EA. Residual effects of emotion are reflected in enhanced visual activity after sleep. **Cogn Affect Behav Neurosci** 17: 290–304, 2017. doi:10.3758/s13415-016-0479-3.

823. Tempesta D, Socci V, Dello Ioio G, De Gennaro L, Ferrara M. The effect of sleep deprivation on retrieval of emotional memory: a behavioural study using film stimuli. **Exp Brain Res** 235: 3059–3067, 2017. doi:10.1007/s00221-017-5043-z.

824. Cellini N, Torre J, Stegagno L, Sarlo M. Sleep before and after learning promotes the consolidation of both neutral and emotional information regardless of REM presence. **Neurobiol Learn Mem** 133: 136–144, 2016. doi:10.1016/j.nlm.2016.06.015.

825. Carr M, Nielsen T. Morning rapid eye movement sleep naps facilitate broad access to emotional semantic networks. **Sleep** 38: 433–443, 2015. doi:10.5665/sleep.4504.

826. van Rijn E, Eichenlaub JB, Lewis PA, Walker MP, Gaskell MG, Malinowski JE, Blagrove M. The dream-lag effect: selective processing of personally significant events during rapid eye movement sleep, but not during slow wave sleep. **Neurobiol Learn Mem** 122: 98–109, 2015. doi:10.1016/j.nlm.2015.01.009.

827. Scarpelli S, Bartolacci C, D'Atri A, Gorgoni M, De Gennaro L. The functional role of dreaming in emotional processes. **Front Psychol** 10: 459, 2019. doi:10.3389/fpsyg.2019.00459.

828. Tsunematsu T. What are the neural mechanisms and physiological functions of dreams? **Neurosci Res** 189: 54–59, 2023. doi:10.1016/j.neures.2022.12.017.

829. Goldschmied JR, Cheng P, Kim HS, Casement M, Armitage R, Deldin PJ. Slow-wave disruption enhances the accessibility of positive memory traces. **Neurobiol Learn Mem** 125: 168–175, 2015. doi:10.1016/j.nlm.2015.09.006.

830. Gui WJ, Wang PY, Lei X, Lin T, Horta M, Liu XY, Yu J. Sleep facilitates consolidation of positive emotional memory in healthy older adults. **Memory** 27: 387–396, 2019. doi:10.1080/09658211.2018.1513038.

831. Huan SY, Liu KP, Lei X, Yu J. Age-related emotional bias in associative memory consolidation: the role of sleep. **Neurobiol Learn Mem** 171: 107204, 2020. doi:10.1016/j.nlm.2020.107204.

832. Tempesta D, Socci V, De Gennaro L, Ferrara M. Sleep and emotional processing. **Sleep Med Rev** 40: 183–195, 2018. doi:10.1016/j.smrv.2017.12.005.

833. Murkar AL, De Koninck J. Consolidative mechanisms of emotional processing in REM sleep and PTSD. **Sleep Med Rev** 41: 173–184, 2018. doi:10.1016/j.smrv.2018.03.001.

834. Schäfer SK, Wirth BE, Staginnus M, Becker N, Michael T, Sopp MR. Sleep's impact on emotional recognition memory: a meta-analysis of whole-night, nap, and REM sleep effects. **Sleep Med Rev** 51: 101280, 2020. doi:10.1016/j.smrv.2020.101280.

835. Gilson M, Deliens G, Leproult R, Bodart A, Nonclercq A, Ercek R, Peigneux P. REM-enriched naps are associated with memory consolidation for sad stories and enhance mood-related reactivity. **Brain Sci** 6: 1, 2015. doi:10.3390/brainsci6010001.

836. Rho YA, Sherfey J, Vijayan S. Emotional memory processing during REM sleep with implications for post-traumatic stress disorder. **J Neurosci** 43: 433–446, 2023. doi:10.1523/JNEUROSCI.1020-22.2022.

837. Laventure S, Benchenane K. Validating the theoretical bases of sleep reactivation during sharp-wave ripples and their association with emotional valence. **Hippocampus** 30: 19–27, 2020. doi:10.1002/hipo.23143.

838. Morgenthaler J, Wiesner CD, Hinze K, Abels LC, Prehn-Kristensen A, Göder R. Selective REM-sleep deprivation does not diminish emotional memory consolidation in young healthy subjects. **PLoS One** 9: e89849, 2014. doi:10.1371/journal.pone.0089849.

839. Reid A, Bloxham A, Carr M, van Rijn E, Basoudan N, Tulip C, Blagrove M. Effects of sleep on positive, negative and neutral valenced story and image memory. **Br J Psychol** 113: 777–797, 2022. doi:10.1111/bjop.12559.

840. Kurdziel LB, Kent J, Spencer RM. Sleep-dependent enhancement of emotional memory in early childhood. **Sci Rep** 8: 12609, 2018. doi:10.1038/s41598-018-30980-y.

841. Ward MP, Peters KR, Smith CT. Effect of emotional and neutral declarative memory consolidation on sleep architecture. **Exp Brain Res** 232: 1525–1534, 2014. doi:10.1007/s00221-013-3781-0.

842. Sopp MR, Michael T, Mecklinger A. Effects of early morning nap sleep on associative memory for neutral and emotional stimuli. **Brain Res** 1698: 29–42, 2018. doi:10.1016/j.brainres.2018.06.020.

843. Halonen R, Luokkala S, Kuula L, Antila M, Pesonen AK. Right-lateralized sleep spindles are associated with neutral over emotional bias in picture recognition: an overnight study. **Cogn Affect Behav Neurosci** 23: 1445–1459, 2023. doi:10.3758/s13415-023-01113-4.

844. Groch S, Wilhelm I, Diekelmann S, Born J. The role of REM sleep in the processing of emotional memories: evidence from behavior and event-related potentials. **Neurobiol Learn Mem** 99: 1–9, 2013. doi:10.1016/j.nlm.2012.10.006.

845. Harrington MO, Johnson JM, Croom HE, Pennington K, Durrant SJ. The influence of REM sleep and SWS on emotional memory consolidation in participants reporting depressive symptoms. **Cortex** 99: 281–295, 2018. doi:10.1016/j.cortex.2017.12.004.

846. Harrington MO, Nedberge KM, Durrant SJ. The effect of sleep deprivation on emotional memory consolidation in participants reporting depressive symptoms. **Neurobiol Learn Mem** 152: 10–19, 2018. doi:10.1016/j.nlm.2018.04.013.

847. Kleim B, Wysokowsky J, Schmid N, Seifritz E, Rasch B. Effects of sleep after experimental trauma on intrusive emotional memories. **Sleep** 39: 2125–2132, 2016. doi:10.5665/sleep.6310.

848. Cairney SA, Durrant SJ, Power R, Lewis PA. Complementary roles of slow-wave sleep and rapid eye movement sleep in emotional memory consolidation. **Cereb Cortex** 25: 1565–1575, 2015. doi:10.1093/cercor/bht349.

849. Corsi-Cabrera M, Velasco F, Del Río-Portilla Y, Armony JL, Trejo-Martínez D, Guevara MA, Velasco AL. Human amygdala activation during rapid eye movements of rapid eye movement sleep: an intracranial study. **J Sleep Res** 25: 576–582, 2016. doi:10.1111/jsr.12415.

850. Wofford N, Ceballos N, Elkins G, Westerberg CE. A brief nap during an acute stressor improves negative affect. **J Sleep Res** 31: e13701, 2022. doi:10.1111/jsr.13701.

851. Ashton JE, Harrington MO, Guttesen AÁ, Smith AK, Cairney SA. Sleep preserves physiological arousal in emotional memory. **Sci Rep** 9: 5966, 2019. doi:10.1038/s41598-019-42478-2.

852. Wassing R, Lakbila-Kamal O, Ramautar JR, Stoffers D, Schalkwijk F, Van Someren EJ. Restless REM sleep impedes overnight amygdala adaptation. **Curr Biol** 29: 2351–2358.e4, 2019. doi:10.1016/j.cub.2019.06.034.

853. Cabrera Y, Koymans KJ, Poe GR, Kessels HW, van Someren EJ, Wassing R. Overnight neuronal plasticity and adaptation to emotional distress. **Nat Rev Neurosci** 25: 253–271, 2024. doi:10.1038/s41583-024-00799-w.

854. Xia T, Yao Z, Guo X, Liu J, Chen D, Liu Q, Paller KA, Hu X. Updating memories of unwanted emotions during human sleep. **Curr Biol** 33: 309–320.e5, 2023. doi:10.1016/j.cub.2022.12.004.

855. Liu X, Peng X, Peng P, Li L, Lei X, Yu J. The age differences of sleep disruption on mood states and memory performance. **Aging Ment Health** 24: 1444–1451, 2020. doi:10.1080/13607863.2019.1603286.

856. Tempesta D, De Gennaro L, Natale V, Ferrara M. Emotional memory processing is influenced by sleep quality. **Sleep Med** 16: 862–870, 2015. doi:10.1016/j.sleep.2015.01.024.

857. Cunningham TJ, Crowell CR, Alger SE, Kensinger EA, Villano MA, Mattingly SM, Payne JD. Psychophysiological arousal at encoding leads to reduced reactivity but enhanced emotional memory following sleep. **Neurobiol Learn Mem** 114: 155–164, 2014. doi:10.1016/j.nlm.2014.06.002.

858. Bolinger E, Cunningham TJ, Payne JD, Bowman MA, Bulca E, Born J, Zinke K. Sleep's benefits to emotional processing emerge in the long term. **Cortex** 120: 457–470, 2019. doi:10.1016/j.cortex.2019.07.008.

859. Zeng S, Lin X, Wang J, Hu X. Sleep's short-term memory preservation and long-term affect depotentiation effect in emotional memory consolidation: behavioral and EEG evidence. **Sleep** 44: zsab155, 2021. doi:10.1093/sleep/zsab155.

860. Azza Y, Wilhelm FH, Seifritz E, Junghanns K, Kleim B, Wilhelm I. Sleep's role in updating aversive autobiographical memories. **Transl Psychiatry** 12: 117, 2022. doi:10.1038/s41398-022-01878-1.

861. Kuriyama K, Honma M, Yoshiike T, Kim Y. Memory suppression trades prolonged fear and sleep-dependent fear plasticity for the avoidance of current fear. **Sci Rep** 3: 2227, 2013. doi:10.1038/srep02227.

862. Marshall AJ, Acheson DT, Risbrough VB, Straus LD, Drummond SP. Fear conditioning, safety learning, and sleep in humans. **J Neurosci** 34: 11754–11760, 2014. doi:10.1523/JNEUROSCI.0478-14.2014.

863. Wang J, Chen B, Sha M, Gu Y, Wu H, Forcato C, Qin S. Positive and neutral updating reconsolidate aversive episodic memories via different routes. **Neurobiol Learn Mem** 184: 107500, 2021. doi:10.1016/j.nlm.2021.107500.

864. Bolinger E, Born J, Zinke K. Sleep divergently affects cognitive and automatic emotional response in children. **Neuropsychologia** 117: 84–91, 2018. doi:10.1016/j.neuropsychologia.2018.05.015.

865. Bennion KA, Mickley Steinmetz KR, Kensinger EA, Payne JD. Sleep and cortisol interact to support memory consolidation. **Cereb Cortex** 25: 646–657, 2015. doi:10.1093/cercor/bht255.

866. Wilhelm I, Wagner U, Born J. Opposite effects of cortisol on consolidation of temporal sequence memory during waking and sleep. **J Cogn Neurosci** 23: 3703–3712, 2011. doi:10.1162/jocn_a_00093.

867. Groch S, Wilhelm I, Lange T, Born J. Differential contribution of mineralocorticoid and glucocorticoid receptors to memory formation during sleep. **Psychoneuroendocrinology** 38: 2962–2972, 2013. doi:10.1016/j.psyneuen.2013.08.006.

868. Kelemen E, Bahrendt M, Born J, Inostroza M. Hippocampal corticosterone impairs memory consolidation during sleep but improves consolidation in the wake state. **Hippocampus** 24: 510–515, 2014. doi:10.1002/hipo.22266.

869. van Marle HJ, Hermans EJ, Qin S, Overeem S, Fernández G. The effect of exogenous cortisol during sleep on the behavioral and neural correlates of emotional memory consolidation in humans. **Psychoneuroendocrinology** 38: 1639–1649, 2013. doi:10.1016/j.psyneuen.2013.01.009.

870. Landmann N, Kuhn M, Piosczyk H, Feige B, Baglioni C, Spiegelhalder K, Frase L, Riemann D, Sterr A, Nissen C. The reorganisation of memory during sleep. **Sleep Med Rev** 18: 531–541, 2014. doi:10.1016/j.smrv.2014.03.005.

871. Alger SE, Payne JD. The differential effects of emotional salience on direct associative and relational memory during a nap. **Cogn Affect Behav Neurosci** 16: 1150–1163, 2016. doi:10.3758/s13415-016-0460-1.

872. Huguet M, Payne JD, Kim SY, Alger SE. Overnight sleep benefits both neutral and negative direct associative and relational memory. **Cogn Affect Behav Neurosci** 19: 1391–1403, 2019. doi:10.3758/s13415-019-00746-8.

873. Pace-Schott EF, Milad MR, Orr SP, Rauch SL, Stickgold R, Pitman RK. Sleep promotes generalization of extinction of conditioned fear. **Sleep** 32: 19–26, 2009.

874. Pace-Schott EF, Germain A, Milad MR. Effects of sleep on memory for conditioned fear and fear extinction. **Psychol Bull** 141: 835–857, 2015. doi:10.1037/bul0000014.

875. Davidson P, Carlsson I, Jönsson P, Johansson M. Sleep and the generalization of fear learning. **J Sleep Res** 25: 88–95, 2016. doi:10.1111/jsr.12339.

876. Davidson P, Carlsson I, Jönsson P, Johansson M. A more generalized fear response after a daytime nap. **Neurobiol Learn Mem** 151: 18–27, 2018. doi:10.1016/j.nlm.2018.03.005.

877. Lerner I, Lupkin SM, Tsai A, Khawaja A, Gluck MA. Sleep to remember, sleep to forget: rapid eye movement sleep can have inverse effects on recall and generalization of fear memories. **Neurobiol Learn Mem** 180: 107413, 2021. doi:10.1016/j.nlm.2021.107413.

878. Pace-Schott EF, Spencer RM, Vijayakumar S, Ahmed NA, Verga PW, Orr SP, Pitman RK, Milad MR. Extinction of conditioned fear is better learned and recalled in the morning than in the evening. **J Psychiatr Res** 47: 1776–1784, 2013. doi:10.1016/j.jpsychires.2013.07.027.

879. Lisman JE, Grace AA. The hippocampal-VTA loop: controlling the entry of information into long-term memory. **Neuron** 46: 703–713, 2005. doi:10.1016/j.neuron.2005.05.002.

880. Adcock RA, Thangavel A, Whitfield-Gabrieli S, Knutson B, Gabrieli JD. Reward-motivated learning: mesolimbic activation precedes memory formation. **Neuron** 50: 507–517, 2006. doi:10.1016/j.neuron.2006.03.036.

881. McNamara CG, Tejero-Cantero Á, Trouche S, Campo-Urriza N, Dupret D. Dopaminergic neurons promote hippocampal reactivation and spatial memory persistence. **Nat Neurosci** 17: 1658–1660, 2014. doi:10.1038/nn.3843.

882. Feld GB, Born J. Neurochemical mechanisms for memory processing during sleep: basic findings in humans and neuropsychiatric implications. **Neuropsychopharmacology** 45: 31–44, 2020. doi:10.1038/s41386-019-0490-9.

883. Duszkiewicz AJ, McNamara CG, Takeuchi T, Genzel L. Novelty and dopaminergic modulation of memory persistence: a tale of two systems. **Trends Neurosci** 42: 102–114, 2019. doi:10.1016/j.tins.2018.10.002.

884. Knowlton BJ, Castel AD. Memory and reward-based learning: a value-directed remembering perspective. **Annu Rev Psychol** 73: 25–52, 2022. doi:10.1146/annurev-psych-032921-050951.

885. Studte S, Bridger E, Mecklinger A. Sleep spindles during a nap correlate with post sleep memory performance for highly rewarded word-pairs. **Brain Lang** 167: 28–35, 2017. doi:10.1016/j.bandl.2016.03.003.

886. Prehn-Kristensen A, Ngo HV, Lentfer L, Berghäuser J, Brandes L, Schulze L, Göder R, Mölle M, Baving L. Acoustic closed-loop stimulation during sleep improves consolidation of reward-related memory information in healthy children but not in children with attention-deficit hyperactivity disorder. **Sleep** 43: zsaa017, 2020. doi:10.1093/sleep/zsaa017.

887. Feld GB, Besedovsky L, Kaida K, Münte TF, Born J. Dopamine D2-like receptor activation wipes out preferential consolidation of high over low reward memories during human sleep. **J Cogn Neurosci** 26: 2310–2320, 2014. doi:10.1162/jocn_a_00629.

888. Ai S, Yin Y, Chen Y, Wang C, Sun Y, Tang X, Lu L, Zhu L, Shi J. Promoting subjective preferences in simple economic choices during nap. **eLife** 7: e40583, 2018. doi:10.7554/eLife.40583.

889. Stamm AW, Nguyen ND, Seicol BJ, Fagan A, Oh A, Drumm M, Lundt M, Stickgold R, Wamsley EJ. Negative reinforcement impairs overnight memory consolidation. **Learn Mem** 21: 591–596, 2014. doi:10.1101/lm.035196.114.

890. Asfestani MA, Brechtmann V, Santiago J, Peter A, Born J, Feld GB. Consolidation of reward memory during sleep does not require dopaminergic activation. **J Cogn Neurosci** 32: 1688–1703, 2020. doi:10.1162/jocn_a_01585.

891. Fischer S, Born J. Anticipated reward enhances offline learning during sleep. **J Exp Psychol Learn Mem Cogn** 35: 1586–1593, 2009. doi:10.1037/a0017256.

892. Reverberi S, Kohn N, Fernández G. No evidence for an effect of explicit relevance instruction on consolidation of associative memories. **Neuropsychologia** 143: 107491, 2020. doi:10.1016/j.neuropsychologia.2020.107491.

893. Diekelmann S, Wilhelm I, Wagner U, Born J. Sleep improves prospective remembering by facilitating spontaneous-associative retrieval processes. **PLoS One** 8: e77621, 2013. doi:10.1371/journal.pone.0077621.

894. Diekelmann S, Wilhelm I, Wagner U, Born J. Sleep to implement an intention. **Sleep** 36: 149–153, 2013. doi:10.5665/sleep.2322.

895. Barner C, Seibold M, Born J, Diekelmann S. Consolidation of prospective memory: effects of sleep on completed and reinstated intentions. **Front Psychol** 7: 2025, 2016. doi:10.3389/fpsyg.2016.02025.

896. Barner C, Altgassen M, Born J, Diekelmann S. Effects of sleep on the realization of complex plans. **J Sleep Res** 28: e12655, 2019. doi:10.1111/jsr.12655.

897. Leong RL, Koh SY, Chee MW, Lo JC. Slow wave sleep facilitates spontaneous retrieval in prospective memory. **Sleep** 42: zsz003, 2019. doi:10.1093/sleep/zsz003.

898. Cunningham TJ, Bottary R, Denis D, Payne JD. Sleep spectral power correlates of prospective memory maintenance. **Learn Mem** 28: 291–299, 2021. doi:10.1101/lm.053412.121.

899. Böhm MF, Bayen UJ, Pietrowsky R. Nighttime sleep benefits the prospective component of prospective memory. **Mem Cognit** 49: 1690–1704, 2021. doi:10.3758/s13421-021-01187-w.

900. Esposito MJ, Occhionero M, Cicogna P. Sleep deprivation and time-based prospective memory. **Sleep** 38: 1823–1826, 2015. doi:10.5665/sleep.5172.

901. Grundgeiger T, Bayen UJ, Horn SS. Effects of sleep deprivation on prospective memory. **Memory** 22: 679–686, 2014. doi:10.1080/09658211.2013.812220.

902. Occhionero M, Cicogna P, Esposito MJ. The effect of sleep loss on dual time-based prospective memory tasks. **Am J Psychol** 130: 93–103, 2017. doi:10.5406/amerjpsyc.130.1.0093.

903. Cavuoto MG, Ong B, Pike KE, Nicholas CL, Bei B, Kinsella GJ. Objective but not subjective sleep predicts memory in community-dwelling older adults. **J Sleep Res** 25: 475–485, 2016. doi:10.1111/jsr.12391.

904. Fine L, Weinborn M, Ng A, Loft S, Li YR, Hodgson E, Parker D, Rainey Smith S, Sohrabi HR, Brown B, Martins R, Bucks RS. Sleep disruption explains age-related prospective memory deficits:

implications for cognitive aging and intervention. **Neuropsychol Dev Cogn B Aging Neuropsychol Cogn** 26: 621–636, 2019. doi:10.1080/13825585.2018.1513449.

905. Scullin MK, Gao C, Fillmore P, Roberts RL, Pruett N, Bliwise DL**.** Rapid eye movement sleep mediates age-related decline in prospective memory consolidation. **Sleep** 42: zsz055, 2019. doi:10.1093/sleep/zsz055.

906. Rehel S, Legrand N, Lecouvey G, Laniepce A, Bertran F, Fleury P, Madeleine S, Eustache F, Desgranges B, Rauchs G**.** Effects of sleep and age on prospective memory consolidation: a walk in a virtual museum. **Clocks Sleep** 1: 332–351, 2019. doi:10.3390/clockssleep1030028.

907. Occhionero M, Tonetti L, Fabbri M, Boreggiani M, Martoni M, Giovagnoli S, Natale V**.** Prospective memory, sleep, and age. **Brain Sci** 10: 422, 2020. doi:10.3390/brainsci10070422.

908. Leong RL, Lo JC, Chee MWL**.** Sleep-dependent prospective memory consolidation is impaired with aging. **Sleep** 44: zsab069, 2021. doi:10.1093/sleep/zsab069.

909. Zhang B, Zhu DM, Zhao W, Zhang Y, Yang Y, Zhang C, Zhu J, Yu Y**.** Selective microstructural integrity impairments of the anterior corpus callosum are associated with cognitive deficits in obstructive sleep apnea. **Brain Behav** 9: e01482, 2019. doi:10.1002/brb3.1482.

910. Fabbri M, Tonetti L, Martoni M, Natale V**.** Sleep and prospective memory. **Biol Rhythm Res** 45: 115–120, 2014. doi:10.1080/09291016.2013.830510.

911. Tonetti L, Occhionero M, Boreggiani M, Conca A, Dondi P, Elbaz M, Fabbri M, Gauriau C, Giupponi G, Leger D, Martoni M, Rafanelli C, Roncuzzi R, Zoppello M, Natale V**.** Sleep and prospective memory: a retrospective study in different clinical populations. **Int J Environ Res Public Health** 17: 6113, 2020. doi:10.3390/ijerph17176113.

912. Occhionero M, Tonetti L, Giudetti F, Natale V**.** Activity-based prospective memory in insomniacs. **Sensors (Basel)** 24: 3612, 2024. doi:10.3390/s24113612.

913. Fabbri M, Tonetti L, Martoni M, Natale V**.** Remember to do: insomnia versus control groups in a prospective memory task. **Behav Sleep Med** 13: 231–240, 2015. doi:10.1080/15402002.2013.860896.

914. Kyle SD, Sexton CE, Feige B, Luik AI, Lane J, Saxena R, Anderson SG, Bechtold DA, Dixon W, Little MA, Ray D, Riemann D, Espie CA, Rutter MK, Spiegelhalder K**.** Sleep and cognitive performance: cross-sectional associations in the UK Biobank. **Sleep Med** 38: 85–91, 2017. doi:10.1016/j.sleep.2017.07.001.

915. Bezdicek O, Nikolai T, Nepožitek J, Peřinová P, Kemlink D, Dušek P, Příhodová I, Dostálová S, Ibarburu V, Trnka J, Kupka K, Mecková Z, Keller J, Vymazal J, Růžička E, Šonka K, Dušek P**.** Prospective memory impairment in idiopathic REM sleep behavior disorder. **Clin Neuropsychol** 32: 1019–1037, 2018. doi:10.1080/13854046.2017.1394493.

916. Li X, Wang K, Jia S, Zhou Z, Jin Y, Zhang X, Hou C, Zheng W, Rong P, Jiao J**.** The prospective memory of patients with idiopathic REM sleep behavior disorder. **Sleep Med** 47: 19–24, 2018. doi:10.1016/j.sleep.2018.03.019.

917. Marcone S, Gagnon JF, Desjardins C, David AC, Postuma RB, Montplaisir J, Joubert S, Rouleau I**.** Prospective memory in idiopathic REM sleep behavior disorder with or without mild cognitive impairment: a preliminary study. **Clin Neuropsychol** 33: 571–593, 2019. doi:10.1080/13854046.2018.1435825.

918. McBean AL, Schlosnagle L**.** Sleep, health and memory: comparing parents of typically developing children and parents of children with special health-care needs. **J Sleep Res** 25: 78–87, 2016. doi:10.1111/jsr.12329.

919. Böhm MF, Bayen UJ, Schaper ML**.** Are subjective sleepiness and sleep quality related to prospective memory? **Cogn Res Princ Implic** 5: 5, 2020. doi:10.1186/s41235-019-0199-7.

920. Goldberg ZL, Thomas KG, Lipinska G**.** Bedtime stress increases sleep latency and impairs next-day prospective memory performance. **Front Neurosci** 14: 756, 2020. doi:10.3389/fnins.2020.00756.

921. Leong RL, Cheng GH, Chee MW, Lo JC**.** The effects of sleep on prospective memory: a systematic review and meta-analysis. **Sleep Med Rev** 47: 18–27, 2019. doi:10.1016/j.smrv.2019.05.006.

922. Bennion KA, Payne JD, Kensinger EA**.** The impact of napping on memory for future-relevant stimuli: prioritization among multiple salience cues. **Behav Neurosci** 130: 281–289, 2016. doi:10.1037/bne0000142.

923. Ognjanovski N, Maruyama D, Lashner N, Zochowski M, Aton SJ**.** CA1 hippocampal network activity changes during sleep-dependent memory consolidation. **Front Syst Neurosci** 8: 61, 2014. doi:10.3389/fnsys.2014.00061.

924. Rossi VC, Tiba PA, Di Moreira KM, Ferreira TL, Oliveira MG, Suchecki D**.** Effects of sleep deprivation on different phases of memory in the rat: dissociation between contextual and tone fear conditioning tasks. **Front Behav Neurosci** 8: 389, 2014. doi:10.3389/fnbeh.2014.00389.

925. Melo I, Ehrlich I**.** Sleep supports cued fear extinction memory consolidation independent of circadian phase. **Neurobiol Learn Mem** 132: 9–17, 2016. doi:10.1016/j.nlm.2016.04.007.

926. Qureshi MF, Jha SK**.** Short-term total sleep-deprivation impairs contextual fear memory, and contextual fear-conditioning reduces REM sleep in moderately anxious Swiss mice. **Front Behav Neurosci** 11: 239, 2017. doi:10.3389/fnbeh.2017.00239.

927. Cho J, Sypniewski KA, Arai S, Yamada K, Ogawa S, Pavlides C**.** Fear memory consolidation in sleep requires protein kinase A. **Learn Mem** 25: 241–246, 2018. doi:10.1101/lm.046458.117.

928. Sharma R, Sahota P, Thakkar MM**.** Sleep loss immediately after fear memory reactivation attenuates fear memory reconsolidation. **Neuroscience** 428: 70–75, 2020. doi:10.1016/j.neuroscience.2019.12.024.

929. Jung T, Noh J**.** Alteration of fear behaviors in sleep-deprived adolescent rats: increased fear expression and delayed fear extinction. **Anim Cells Syst (Seoul)** 25: 83–92, 2021. doi:10.1080/19768354.2021.1902854.

930. Montes-Rodríguez CJ, Rueda-Orozco PE, Prospéro-García O**.** Total sleep deprivation impairs fear memory retrieval by decreasing the basolateral amygdala activity. **Brain Res** 1719: 17–23, 2019. doi:10.1016/j.brainres.2019.05.030.

931. Subramaniyan M, Manivannan S, Chelur V, Tsetsenis T, Jiang E, Dani JA**.** Fear conditioning potentiates the hippocampal CA1 commissural pathway in vivo and increases awake phase sleep. **Hippocampus** 31: 1154–1175, 2021. doi:10.1002/hipo.23381.

932. Hashizume M, Ito R, Suge R, Hojo Y, Murakami G, Murakoshi T**.** Correlation between cued fear memory retrieval and oscillatory network inhibition in the amygdala is disrupted by acute REM sleep deprivation. **Neuroscience** 536: 12–20, 2024. doi:10.1016/j.neuroscience.2023.08.037.

933. Wen Y, Jiang J, Zhai F, Fan F, Lu J. Sleep-wake dependent hippocampal regulation of fear memory. **Sleep Med** 115: 162–173, 2024. doi:10.1016/j.sleep.2024.02.022.

934. Pinho N, Moreira KM, Hipolide DC, Sinigaglia-Coimbra R, Ferreira TL, Nobrega JN, Tufik S, Oliveira MG. Sleep deprivation alters phosphorylated CREB levels in the amygdala: relationship with performance in a fear conditioning task. **Behav Brain Res** 236: 221–224, 2013. doi:10.1016/j.bbr.2012.08.043.

935. Lee ML, Katsuyama ÂM, Duge LS, Sriram C, Krushelnytskyy M, Kim JJ, Iglesia L, de HO. Fragmentation of rapid eye movement and nonrapid eye movement sleep without total sleep loss impairs hippocampus-dependent fear memory consolidation. **Sleep** 39: 2021–2031, 2016. doi:10.5665/sleep.6236.

936. Chang HF, Su CL, Chang CH, Chen YW, Gean PW. The beneficial effects of leptin on REM sleep deprivation-induced cognitive deficits in mice. **Learn Mem** 20: 328–335, 2013. doi:10.1101/lm.030775.113.

937. Polta SA, Fenzl T, Jakubcakova V, Kimura M, Yassouridis A, Wotjak CT. Prognostic and symptomatic aspects of rapid eye movement sleep in a mouse model of posttraumatic stress disorder. **Front Behav Neurosci** 7: 60, 2013. doi:10.3389/fnbeh.2013.00060.

938. Machida M, Yang L, Wellman LL, Sanford LD. Effects of stressor predictability on escape learning and sleep in mice. **Sleep** 36: 421–430, 2013. doi:10.5665/sleep.2464.

939. Wellman LL, Yang L, Ambrozewicz MA, Machida M, Sanford LD. Basolateral amygdala and the regulation of fear-conditioned changes in sleep: role of corticotropin-releasing factor. **Sleep** 36: 471–480, 2013. doi:10.5665/sleep.2526.

940. Hunter AS. The effects of social housing on extinction of fear conditioning in rapid eye movement sleep-deprived rats. **Exp Brain Res** 232: 1459–1467, 2014. doi:10.1007/s00221-014-3828-x.

941. Wellman LL, Fitzpatrick ME, Machida M, Sanford LD. The basolateral amygdala determines the effects of fear memory on sleep in an animal model of PTSD. **Exp Brain Res** 232: 1555–1565, 2014. doi:10.1007/s00221-014-3850-z.

942. Wellman LL, Fitzpatrick ME, Hallum OY, Sutton AM, Williams BL, Sanford LD. Individual differences in animal stress models: considering resilience, vulnerability, and the amygdala in mediating the effects of stress and conditioned fear on sleep. **Sleep** 39: 1293–1303, 2016. doi:10.5665/sleep.5856.

943. Wellman LL, Fitzpatrick ME, Hallum OY, Sutton AM, Williams BL, Sanford LD. The basolateral amygdala can mediate the effects of fear memory on sleep independently of fear behavior and the peripheral stress response. **Neurobiol Learn Mem** 137: 27–35, 2017. doi:10.1016/j.nlm.2016.11.004.

944. Wellman LL, Fitzpatrick ME, Sutton AM, Williams BL, Machida M, Sanford LD. Antagonism of corticotropin releasing factor in the basolateral amygdala of resilient and vulnerable rats: effects on fear-conditioned sleep, temperature and freezing. **Horm Behav** 100: 20–28, 2018. doi:10.1016/j.yhbeh.2018.02.013.

945. Hunter AS. REM deprivation but not sleep fragmentation produces a sex-specific impairment in extinction. **Physiol Behav** 196: 84–94, 2018. doi:10.1016/j.physbeh.2018.08.008.

946. Balakathiresan NS, Bhomia M, Zhai M, Sweeten BL, Wellman LL, Sanford LD, Knollmann-Ritschel B. MicroRNAs in basolateral amygdala associated with stress and fear memories regulate rapid eye movement sleep in rats. **Brain Sci** 11: 489, 2021. doi:10.3390/brainsci11040489.

947. Kim SM, Zhang S, Park J, Sung HJ, Tran TD, Chung C, Han IO. REM sleep deprivation impairs learning and memory by decreasing brain O-GlcNAc cycling in mouse. **Neurotherapeutics** 18: 2504–2517, 2021. doi:10.1007/s13311-021-01094-7.

948. Hong J, Choi K, Fuccillo MV, Chung S, Weber F. Infralimbic activity during REM sleep facilitates fear extinction memory. **Curr Biol** 34: 2247–2255.e5, 2024. doi:10.1016/j.cub.2024.04.018.

949. Aime M, Calcini N, Borsa M, Campelo T, Rusterholz T, Sattin A, Fellin T, Adamantidis A. Paradoxical somatodendritic decoupling supports cortical plasticity during REM sleep. **Science** 376: 724–730, 2022. doi:10.1126/science.abk2734.

950. Kordestani-Moghadam P, Nasehi M, Khodagholi F, Vaseghi S, Zarrindast MR, Khani M. The fluctuations of metabotropic glutamate receptor subtype 5 (mGluR5) in the amygdala in fear conditioning model of male Wistar rats following sleep deprivation, reverse circadian and napping. **Brain Res** 1734: 146739, 2020. doi:10.1016/j.brainres.2020.146739.

951. Ravassard P, Hamieh AM, Joseph MA, Fraize N, Libourel PA, Lebarillier L, Arthaud S, Meissirel C, Touret M, Malleret G, Salin PA. REM sleep-dependent bidirectional regulation of hippocampal-based emotional memory and LTP. **Cereb Cortex** 26: 1488–1500, 2016. doi:10.1093/cercor/bhu310.

952. Laitman BM, Gajewski ND, Mann GL, Kubin L, Morrison AR, Ross RJ. The α1 adrenoceptor antagonist prazosin enhances sleep continuity in fear-conditioned Wistar-Kyoto rats. **Prog Neuropsychopharmacol Biol Psychiatry** 49: 7–15, 2014. doi:10.1016/j.pnpbp.2013.11.004.

953. Kumar T, Jha SK. Influence of cued-fear conditioning and its impairment on NREM sleep. **Neurobiol Learn Mem** 144: 155–165, 2017. doi:10.1016/j.nlm.2017.07.008.

954. DaSilva JK, Husain E, Lei Y, Mann GL, Morrison AR, Tejani-Butt S. Social partnering alters sleep in fear-conditioned Wistar rats. **PLoS One** 12: e0186017, 2017. doi:10.1371/journal.pone.0186017.

955. Kant D, Jha SK. The formation of compensatory contextual fear memory in the absence of dorsal hippocampus does not change sleep architecture. **Behav Brain Res** 370: 111944, 2019. doi:10.1016/j.bbr.2019.111944.

956. Machida M, Sutton AM, Williams BL, Wellman LL, Sanford LD. Differential behavioral, stress, and sleep responses in mice with different delays of fear extinction. **Sleep** 42: zsz147, 2019. doi:10.1093/sleep/zsz147.

957. Pawlyk AC, Jha SK, Brennan FX, Morrison AR, Ross RJ. A rodent model of sleep disturbances in posttraumatic stress disorder: the role of context after fear conditioning. **Biol Psychiatry** 57: 268–277, 2005. doi:10.1016/j.biopsych.2004.11.008.

958. Sanford LD, Fang J, Tang X. Sleep after differing amounts of conditioned fear training in BALB/cJ mice. **Behav Brain Res** 147: 193–202, 2003. doi:10.1016/s0166-4328(03)00180-3.

959. Sanford LD, Tang X, Ross RJ, Morrison AR. Influence of shock training and explicit fear-conditioned cues on sleep architecture in mice: strain comparison. **Behav Genet** 33: 43–58, 2003. doi:10.1023/a:1021051516829.

960. Sanford LD, Yang L, Tang X. Influence of contextual fear on sleep in mice: a strain comparison. **Sleep** 26: 527–540, 2003. doi:10.1093/sleep/26.5.527.

961. Kumar D, Koyanagi I, Carrier-Ruiz A, Vergara P, Srinivasan S, Sugaya Y, Kasuya M, Yu TS, Vogt KE, Muratani M, Ohnishi T, Singh S, Teixeira CM, Chérasse Y, Naoi T, Wang SH, Nondhalee P, Osman BA, Kaneko N, Sawamoto K, Kernie SG, Sakurai T, McHugh

TJ, Kano M, Yanagisawa M, Sakaguchi M. Sparse activity of hippocampal adult-born neurons during REM sleep is necessary for memory consolidation. **Neuron** 107: 552–565.e10, 2020. doi:10.1016/j.neuron.2020.05.008.

962. Bozic I, Rusterholz T, Mikutta C, Del Rio-Bermudez C, Nissen C, Adamantidis A. Coupling between the prelimbic cortex, nucleus reuniens, and hippocampus during NREM sleep remains stable under cognitive and homeostatic demands. **Eur J Neurosci** 57: 106–128, 2023. doi:10.1111/ejn.15853.

963. Machida M, Sweeten BL, Adkins AM, Wellman LL, Sanford LD. Basolateral amygdala regulates EEG theta-activity during rapid eye movement sleep. **Neuroscience** 468: 176–185, 2021. doi:10.1016/j.neuroscience.2021.06.018.

964. Purple RJ, Sakurai T, Sakaguchi M. Auditory conditioned stimulus presentation during NREM sleep impairs fear memory in mice. **Sci Rep** 7: 46247, 2017. doi:10.1038/srep46247.

965. McDowell AL, Filippone AB, Balbir A, Germain A, O'Donnell CP. Mild transient hypercapnia as a novel fear conditioning stimulus allowing re-exposure during sleep. **PLoS One** 8: e67435, 2013. doi:10.1371/journal.pone.0067435.

966. Dugan BJ, Fraigne JJ, Peever J. REM sleep: out-dreaming fear. **Curr Biol** 34: R510–R512, 2024. doi:10.1016/j.cub.2024.04.033.

967. Yang W, Sun C, Huszár R, Hainmueller T, Kiselev K, Buzsáki G. Selection of experience for memory by hippocampal sharp wave ripples. **Science** 383: 1478–1483, 2024. doi:10.1126/science.adk8261.

968. Jarzebowski P, Tang CS, Paulsen O, Hay YA. Impaired spatial learning and suppression of sharp wave ripples by cholinergic activation at the goal location. **eLife** 10: e65998, 2021. doi:10.7554/eLife.65998.

969. Pinheiro-da-Silva J, Tran S, Silva PF, Luchiari AC. Good night, sleep tight: the effects of sleep deprivation on spatial associative learning in zebrafish. **Pharmacol Biochem Behav** 159: 36–47, 2017. doi:10.1016/j.pbb.2017.06.011.

970. Sosa M, Joo HR, Frank LM. Dorsal and ventral hippocampal sharp-wave ripples activate distinct nucleus accumbens networks. **Neuron** 105: 725–741.e8, 2020. doi:10.1016/j.neuron.2019.11.022.

971. Chouhan NS, Sehgal A. Consolidation of sleep-dependent appetitive memory is mediated by a sweet-sensing circuit. **J Neurosci** 42: 3856–3867, 2022. doi:10.1523/JNEUROSCI.0106-22.2022.

972. Reicher V, Kovács T, Csibra B, Gácsi M. Potential interactive effect of positive expectancy violation and sleep on memory consolidation in dogs. **Sci Rep** 14: 9487, 2024. doi:10.1038/s41598-024-60166-8.

973. Mu P, Huang YH. Cholinergic system in sleep regulation of emotion and motivation. **Pharmacol Res** 143: 113–118, 2019. doi:10.1016/j.phrs.2019.03.013.

974. Lansink CS, Goltstein PM, Lankelma JV, Joosten R, McNaughton BL, Pennartz CM. Preferential reactivation of motivationally relevant information in the ventral striatum. **J Neurosci** 28: 6372–6382, 2008. doi:10.1523/JNEUROSCI.1054-08.2008.

975. Livneh U, Paz R. Aversive-bias and stage-selectivity in neurons of the primate amygdala during acquisition, extinction, and overnight retention. **J Neurosci** 32: 8598–8610, 2012. doi:10.1523/JNEUROSCI.0323-12.2012.

976. Carlezon WA, Chartoff EH. Intracranial self-stimulation (ICSS) in rodents to study the neurobiology of motivation. **Nat Protoc** 2: 2987–2995, 2007. doi:10.1038/nprot.2007.441.

977. Kobayashi T, Nishijo H, Fukuda M, Bures J, Ono T. Task-dependent representations in rat hippocampal place neurons. **J Neurophysiol** 78: 597–613, 1997. doi:10.1152/jn.1997.78.2.597.

978. Gundersen B. Forming artificial memories during sleep. **Nat Neurosci** 18: 483, 2015. doi:10.1038/nn1504-483.

979. Leenaars CH, Girardi CE, Joosten R, Lako IM, Ruimschotel E, Hanegraaf MA, Dematteis M, Feenstra MG, van Someren EJ. Instrumental learning: an animal model for sleep dependent memory enhancement. **J Neurosci Methods** 217: 44–53, 2013. doi:10.1016/j.jneumeth.2013.04.003.

980. Shahveisi K, Abdoli N, Farnia V, Khazaie H, Hosseini M, Ghazvini H, Khodamoradi M. REM sleep deprivation before extinction or reinstatement alters methamphetamine reward memory via D1-like dopamine receptors. **Pharmacol Biochem Behav** 213: 173319, 2022. doi:10.1016/j.pbb.2021.173319.

981. Shahveisi K, Abdoli N, Khazaie H, Farnia V, Khodamoradi M. Maternal sleep deprivation affects extinction and reinstatement of methamphetamine reward memory in male offspring: role of the D1-like and D2-like dopamine receptors. **Brain Res** 1792: 148033, 2022. doi:10.1016/j.brainres.2022.148033.

982. Shahveisi K, Zarei SA, Naderi S, Khodamoradi M. Role of sex hormones in the effects of sleep deprivation on methamphetamine reward memory. **Neurosci Lett** 814: 137440, 2023. doi:10.1016/j.neulet.2023.137440.

983. Yonelinas AP, Ranganath C, Ekstrom AD, Wiltgen BJ. A contextual binding theory of episodic memory: systems consolidation reconsidered. **Nat Rev Neurosci** 20: 364–375, 2019. doi:10.1038/s41583-019-0150-4.

984. González OC, Sokolov Y, Krishnan GP, Delanois JE, Bazhenov M. Can sleep protect memories from catastrophic forgetting? **eLife** 9: e51005, 2020. doi:10.7554/eLife.51005.

985. Antony JW, Paller KA. Retrieval and sleep both counteract the forgetting of spatial information. **Learn Mem** 25: 258–263, 2018. doi:10.1101/lm.046268.117.

986. Dumay N. Sleep not just protects memories against forgetting, it also makes them more accessible. **Cortex** 74: 289–296, 2016. doi:10.1016/j.cortex.2015.06.007.

987. McDevitt EA, Duggan KA, Mednick SC. REM sleep rescues learning from interference. **Neurobiol Learn Mem** 122: 51–62, 2015. doi:10.1016/j.nlm.2014.11.015.

988. Berry JA, Cervantes-Sandoval I, Chakraborty M, Davis RL. Sleep facilitates memory by blocking dopamine neuron-mediated forgetting. **Cell** 161: 1656–1667, 2015. doi:10.1016/j.cell.2015.05.027.

989. Denis D, Bottary R, Cunningham TJ, Tcheukado MC, Payne JD. The influence of encoding strategy on associative memory consolidation across wake and sleep. **Learn Mem** 30: 185–191, 2023. doi:10.1101/lm.053765.123.

990. Ashton JE, Harrington MO, Langthorne D, Ngo HV, Cairney SA. Sleep deprivation induces fragmented memory loss. **Learn Mem** 27: 130–135, 2020. doi:10.1101/lm.050757.119.

991. Cousins JN, Wong KF, Chee MW. Multi-night sleep restriction impairs long-term retention of factual knowledge in adolescents. **J Adolesc Health** 65: 549–557, 2019. doi:10.1016/j.jadohealth.2019.04.030.

992. Huang S, Deshpande A, Yeo SC, Lo JC, Chee MW, Gooley JJ. Sleep restriction impairs vocabulary learning when adolescents cram for exams: the need for sleep study. **Sleep** 39: 1681–1690, 2016. doi:10.5665/sleep.6092.

993. Pacozzi L, Knüsel L, Ruch S, Henke K. Inverse forgetting in unconscious episodic memory. **Sci Rep** 12: 20595, 2022. doi:10.1038/s41598-022-25100-w.

994. Whalley K. Sleep: don't forget. **Nat Rev Neurosci** 16: 442–443, 2015. doi:10.1038/nrn3990.

995. Whalley K. Sleep to forget. **Nat Rev Neurosci** 20: 716–717, 2019. doi:10.1038/s41583-019-0232-3.

996. Poe GR. Sleep is for forgetting. **J Neurosci** 37: 464–473, 2017. doi:10.1523/JNEUROSCI.0820-16.2017.

997. Ryan TJ, Frankland PW. Forgetting as a form of adaptive engram cell plasticity. **Nat Rev Neurosci** 23: 173–186, 2022. doi:10.1038/s41583-021-00548-3.

998. van der Helm E, Walker MP. Sleep and emotional memory processing. **Sleep Med Clin** 6: 31–43, 2011. doi:10.1016/j.jsmc.2010.12.010.

999. Reinhold FL, Gerlicher AM, van Someren EJ, Kindt M. Do your troubles today seem further away than yesterday? On sleep's role in mitigating the blushing response to a reactivated embarrassing episode. **Sleep** 45: zsac220, 2022. doi:10.1093/sleep/zsac220.

1000. Deliens G, Gilson M, Peigneux P. Sleep and the processing of emotions. **Exp Brain Res** 232: 1403–1414, 2014. doi:10.1007/s00221-014-3832-1.

1001. Lipinska G, Austin H, Moonsamy JR, Henry M, Lewis R, Baldwin DS, Thomas KG, Stuart B. Preferential consolidation of emotional reactivity during sleep: a systematic review and meta-analysis. **Front Behav Neurosci** 16: 976047, 2022. doi:10.3389/fnbeh.2022.976047.

1002. Sahakyan L. Current perspectives on directed forgetting. In: *The Oxford Handbook of Human Memory*, edited by Kahana MJ. Oxford University Press, 2024, p. 1257–1277.

1003. Anderson MC, Hanslmayr S. Neural mechanisms of motivated forgetting. **Trends Cogn Sci** 18: 279–292, 2014. doi:10.1016/j.tics.2014.03.002.

1004. Anderson MC, Hulbert JC. Active forgetting: adaptation of memory by prefrontal control. **Annu Rev Psychol** 72: 1–36, 2021. doi:10.1146/annurev-psych-072720-094140.

1005. Fischer S, Diekelmann S, Born J. Sleep's role in the processing of unwanted memories. **J Sleep Res** 20: 267–274, 2011. doi:10.1111/j.1365-2869.2010.00881.x.

1006. Dehnavi F, Moghimi S, Sadrabadi Haghighi S, Safaie M, Ghorbani M. Opposite effect of motivated forgetting on sleep spindles during stage 2 and slow wave sleep. **Sleep** 42: zsz085, 2019. doi:10.1093/sleep/zsz085.

1007. Blaskovich B, Szollosi Á, Gombos F, Racsmány M, Simor P. The benefit of directed forgetting persists after a daytime nap: the role of spindles and rapid eye movement sleep in the consolidation of relevant memories. **Sleep** 40: 2017. doi:10.1093/sleep/zsw076.

1008. Abel M, Bäuml KH. Sleep can eliminate list-method directed forgetting. **J Exp Psychol Learn Mem Cogn** 39: 946–952, 2013. doi:10.1037/a0030529.

1009. Simon KC, Gómez RL, Nadel L. Losing memories during sleep after targeted memory reactivation. **Neurobiol Learn Mem** 151: 10–17, 2018. doi:10.1016/j.nlm.2018.03.003.

1010. Schechtman E, Witkowski S, Lampe A, Wilson BJ, Paller KA. Targeted memory reactivation during sleep boosts intentional forgetting of spatial locations. **Sci Rep** 10: 2327, 2020. doi:10.1038/s41598-020-59019-x.

1011. Schechtman E, Lampe A, Wilson BJ, Kwon E, Anderson MC, Paller KA. Sleep reactivation did not boost suppression-induced forgetting. **Sci Rep** 11: 1383, 2021. doi:10.1038/s41598-020-80671-w.

1012. Atherton KE, Nobre AC, Lazar AS, Wulff K, Whittaker RG, Dhawan V, Lazar ZI, Zeman AZ, Butler CR. Slow wave sleep and accelerated forgetting. **Cortex** 84: 80–89, 2016. doi:10.1016/j.cortex.2016.08.013.

1013. Fraize N, Carponcy J, Joseph MA, Comte JC, Luppi PH, Libourel PA, Salin PA, Malleret G, Parmentier R. Levels of interference in long and short-term memory differentially modulate non-REM and REM sleep. **Sleep** 39: 2173–2188, 2016. doi:10.5665/sleep.6322.

1014. Martin SC, Monroe SK, Diering GH. Homer1a and mGluR1/5 signaling in homeostatic sleep drive and output. **Yale J Biol Med** 92: 93–101, 2019.

1015. Diering GH, Huganir RL. The AMPA receptor code of synaptic plasticity. **Neuron** 100: 314–329, 2018. doi:10.1016/j.neuron.2018.10.018.

1016. Diering GH. Remembering and forgetting in sleep: selective synaptic plasticity during sleep driven by scaling factors Homer1a and Arc. **Neurobiol Stress** 22: 100512, 2023. doi:10.1016/j.ynstr.2022.100512.

1017. Reyes-Resina I, Samer S, Kreutz MR, Oelschlegel AM. Molecular mechanisms of memory consolidation that operate during sleep. **Front Mol Neurosci** 14: 767384, 2021. doi:10.3389/fnmol.2021.767384.

1018. Crunelli V, Hughes SW. The slow (<1 Hz) rhythm of non-REM sleep: a dialogue between three cardinal oscillators. **Nat Neurosci** 13: 9–17, 2010. doi:10.1038/nn.2445.

1019. Ngo HV, Born J. Sleep and the balance between memory and forgetting. **Cell** 179: 289–291, 2019. doi:10.1016/j.cell.2019.09.007.

1020. Maboudi K, Giri B, Miyawaki H, Kemere C, Diba K. Retuning of hippocampal representations during sleep. **Nature** 629: 630–638, 2024. doi:10.1038/s41586-024-07397-x.

1021. Valdivia G, Espinosa N, Lara-Vasquez A, Caneo M, Inostroza M, Born J, Fuentealba P. Sleep-dependent decorrelation of hippocampal spatial representations. **iScience** 27: 110076, 2024. doi:10.1016/j.isci.2024.110076.

1022. Huerta PT, Lisman JE. Bidirectional synaptic plasticity induced by a single burst during cholinergic theta oscillation in CA1 in vitro. **Neuron** 15: 1053–1063, 1995. doi:10.1016/0896-6273(95)90094-2.

1023. Izawa S, Chowdhury S, Miyazaki T, Mukai Y, Ono D, Inoue R, Ohmura Y, Mizoguchi H, Kimura K, Yoshioka M, Terao A, Kilduff TS, Yamanaka A. REM sleep-active MCH neurons are involved in forgetting hippocampus-dependent memories. **Science** 365: 1308–1313, 2019. doi:10.1126/science.aax9238.

1024. Thomas MJ, Moody TD, Makhinson M, O'Dell TJ. Activity-dependent beta-adrenergic modulation of low frequency stimulation induced LTP in the hippocampal CA1 region. **Neuron** 17: 475–482, 1996. doi:10.1016/s0896-6273(00)80179-8.

1025. O'Dell TJ, Connor SA, Guglietta R, Nguyen PV. β-Adrenergic receptor signaling and modulation of long-term potentiation in the mammalian hippocampus. **Learn Mem** 22: 461–471, 2015. doi:10.1101/lm.031088.113.

1026. Sara SJ. Sleep to remember. **J Neurosci** 37: 457–463, 2017. doi:10.1523/JNEUROSCI.0297-16.2017.

1027. Sara SJ, Hars B. In memory of consolidation. **Learn Mem** 13: 515–521, 2006. doi:10.1101/lm.338406.

1028. Khazipov R, Luhmann HJ. Early patterns of electrical activity in the developing cerebral cortex of humans and rodents. **Trends Neurosci** 29: 414–418, 2006. doi:10.1016/j.tins.2006.05.007.

1029. Grigg-Damberger MM. The visual scoring of sleep in infants 0 to 2 months of age. **J Clin Sleep Med** 12: 429–445, 2016. doi:10.5664/jcsm.5600.

1030. Campbell IG, Feinberg I. Maturational patterns of sigma frequency power across childhood and adolescence: a longitudinal study. **Sleep** 39: 193–201, 2016. doi:10.5665/sleep.5346.

1031. Spencer RM, Riggins T. Contributions of memory and brain development to the bioregulation of naps and nap transitions in early childhood. **Proc Natl Acad Sci USA** 119: e2123415119, 2022. doi:10.1073/pnas.2123415119.

1032. Zhang Z, Adamo KB, Ogden N, Goldfield GS, Okely AD, Kuzik N, Crozier M, Hunter S, Predy M, Carson V. Longitudinal correlates of sleep duration in young children. **Sleep Med** 78: 128–134, 2021. doi:10.1016/j.sleep.2020.12.023.

1033. Dumoulin Bridi MC, Aton SJ, Seibt J, Renouard L, Coleman T, Frank MG. Rapid eye movement sleep promotes cortical plasticity in the developing brain. **Sci Adv** 1: e1500105, 2015. doi:10.1126/sciadv.1500105.

1034. Gramsbergen A. The development of the EEG in the rat. **Dev Psychobiol** 9: 501–515, 1976. doi:10.1002/dev.420090604.

1035. Cirelli C, Tononi G. Cortical development, electroencephalogram rhythms, and the sleep/wake cycle. **Biol Psychiatry** 77: 1071–1078, 2015. doi:10.1016/j.biopsych.2014.12.017.

1036. Lindemann C, Ahlbeck J, Bitzenhofer SH, Hanganu-Opatz IL. Spindle activity orchestrates plasticity during development and sleep. **Neural Plast** 2016: 5787423, 2016. doi:10.1155/2016/5787423.

1037. Scholle S, Zwacka G, Scholle HC. Sleep spindle evolution from infancy to adolescence. **Clin Neurophysiol** 118: 1525–1531, 2007. doi:10.1016/j.clinph.2007.03.007.

1038. Grigg-Damberger MM. Ontogeny of sleep and its functions in infancy, childhood, and adolescence. In: *Sleep Disorders in Children*, edited by Nevšímalová S, Bruni O. Springer International Publishing, 2017, p. 3–29.

1039. Jenni OG, Borbély AA, Achermann P. Development of the nocturnal sleep electroencephalogram in human infants. **Am J Physiol Regul Integr Comp Physiol** 286: R528–R538, 2004. doi:10.1152/ajpregu.00503.2003.

1040. Huber R, Born J. Sleep, synaptic connectivity, and hippocampal memory during early development. **Trends Cogn Sci** 18: 141–152, 2014. doi:10.1016/j.tics.2013.12.005.

1041. Schoch SF, Riedner BA, Deoni SC, Huber R, Lebourgeois MK, Kurth S. Across-night dynamics in traveling sleep slow waves throughout childhood. **Sleep** 41: zsy165, 2018. doi:10.1093/sleep/zsy165.

1042. Campbell IG, Feinberg I. Longitudinal trajectories of non-rapid eye movement delta and theta EEG as indicators of adolescent brain maturation. **Proc Natl Acad Sci USA** 106: 5177–5180, 2009. doi:10.1073/pnas.0812947106.

1043. Lebourgeois MK, Dean DC, Deoni SC, Kohler M, Kurth S. A simple sleep EEG marker in childhood predicts brain myelin 3.5 years later. **Neuroimage** 199: 342–350, 2019. doi:10.1016/j.neuroimage.2019.05.072.

1044. Kwon H, Walsh KG, Berja ED, Manoach DS, Eden UT, Kramer MA, Chu CJ. Sleep spindles in the healthy brain from birth through 18 years. **Sleep** 46: zsad017, 2023. doi:10.1093/sleep/zsad017.

1045. Timofeev I, Schoch SF, Lebourgeois MK, Huber R, Riedner BA, Kurth S. Spatio-temporal properties of sleep slow waves and implications for development. **Curr Opin Physiol** 15: 172–182, 2020. doi:10.1016/j.cophys.2020.01.007.

1046. Fechner J, Contreras MP, Zorzo C, Shan X, Born J, Inostroza M. Sleep-slow oscillation-spindle coupling precedes spindle-ripple coupling during development. **Sleep** 47: zsae061, 2024. doi:10.1093/sleep/zsae061.

1047. Kurth S, Jenni OG, Riedner BA, Tononi G, Carskadon MA, Huber R. Characteristics of sleep slow waves in children and adolescents. **Sleep** 33: 475–480, 2010. doi:10.1093/sleep/33.4.475.

1048. Fattinger S, Jenni OG, Schmitt B, Achermann P, Huber R. Overnight changes in the slope of sleep slow waves during infancy. **Sleep** 37: 245–253, 2014. doi:10.5665/sleep.3390.

1049. Kurz EM, Bastian L, Mölle M, Born J, Friedrich M. Development of slow oscillation-spindle coupling from infancy to toddlerhood. **Sleep Adv** 5: zpae084, 2024. doi:10.1093/sleepadvances/zpae084.

1050. Jaramillo V, Schoch SF, Markovic A, Kohler M, Huber R, Lustenberger C, Kurth S. An infant sleep electroencephalographic marker of thalamocortical connectivity predicts behavioral outcome in late infancy. **Neuroimage** 269: 119924, 2023. doi:10.1016/j.neuroimage.2023.119924.

1051. Muessig L, Lasek M, Varsavsky I, Cacucci F, Wills TJ. Coordinated emergence of hippocampal replay and theta sequences during post-natal development. **Curr Biol** 29: 834–840.e4, 2019. doi:10.1016/j.cub.2019.01.005.

1052. Farooq U, Dragoi G. Emergence of preconfigured and plastic time-compressed sequences in early postnatal development. **Science** 363: 168–173, 2019. doi:10.1126/science.aav0502.

1053. Buhl DL, Buzsáki G. Developmental emergence of hippocampal fast-field "ripple" oscillations in the behaving rat pups. **Neuroscience** 134: 1423–1430, 2005. doi:10.1016/j.neuroscience.2005.05.030.

1054. Dumas TC. Late postnatal maturation of excitatory synaptic transmission permits adult-like expression of hippocampal-dependent behaviors. **Hippocampus** 15: 562–578, 2005. doi:10.1002/hipo.20077.

1055. Mullally SL, Maguire EA. Learning to remember: the early ontogeny of episodic memory. **Dev Cogn Neurosci** 9: 12–29, 2014. doi:10.1016/j.dcn.2013.12.006.

1056. Josselyn SA, Frankland PW. Infantile amnesia: a neurogenic hypothesis. **Learn Mem** 19: 423–433, 2012. doi:10.1101/lm.021311.110.

1057. Travaglia A, Bisaz R, Sweet ES, Blitzer RD, Alberini CM. Infantile amnesia reflects a developmental critical period for hippocampal learning. **Nat Neurosci** 19: 1225–1233, 2016. doi:10.1038/nn.4348.

1058. Guskjolen A, Kenney JW, de la Parra J, Yeung BR, Josselyn SA, Frankland PW. Recovery of "lost" infant memories in mice. **Curr Biol** 28: 2283–2290.e3, 2018. doi:10.1016/j.cub.2018.05.059.

1059. Bessières B, Travaglia A, Mowery TM, Zhang X, Alberini CM. Early life experiences selectively mature learning and memory abilities. **Nat Commun** 11: 628, 2020. doi:10.1038/s41467-020-14461-3.

1060. Jabès A, Nelson CA. 20 years after "The ontogeny of human memory: a cognitive neuroscience perspective," where are we? **Int J Behav Dev** 39: 293–303, 2015. doi:10.1177/0165025415575766.

1061. Richmond J, Nelson CA. Relational memory during infancy: evidence from eye tracking. **Dev Sci** 12: 549–556, 2009. doi:10.1111/j.1467-7687.2009.00795.x.

1062. Koski J, Olson IR, Newcombe NS. Tracking the eyes to see what children remember. **Memory** 21: 396–407, 2013. doi:10.1080/09658211.2012.735241.

1063. Barr R, Dowden A, Hayne H. Developmental changes in deferred imitation by 6- to 24-month-old infants. **Infant Behav Dev** 19: 159–170, 1996. doi:10.1016/S0163-6383(96)90015-6.

1064. Ribordy F, Jabès A, Banta Lavenex P, Lavenex P. Development of allocentric spatial memory abilities in children from 18 months to 5 years of age. **Cogn Psychol** 66: 1–29, 2013. doi:10.1016/j.cogpsych.2012.08.001.

1065. Newcombe N, Huttenlocher J, Drummey AB, Wiley JG. The development of spatial location coding: place learning and dead reckoning in the second and third years. **Cogn Dev** 13: 185–200, 1998. doi:10.1016/S0885-2014(98)90038-7.

1066. Keresztes A, Ngo CT, Lindenberger U, Werkle-Bergner M, Newcombe NS. Hippocampal maturation drives memory from generalization to specificity. **Trends Cogn Sci** 22: 676–686, 2018. doi:10.1016/j.tics.2018.05.004.

1067. Nickel M, Gu C. Regulation of central nervous system myelination in higher brain functions. **Neural Plast** 2018: 6436453, 2018. doi:10.1155/2018/6436453.

1068. Sorrells SF, Paredes MF, Cebrian-Silla A, Sandoval K, Qi D, Kelley KW, James D, Mayer S, Chang J, Auguste KI, Chang EF, Gutierrez AJ, Kriegstein AR, Mathern GW, Oldham MC, Huang EJ, Garcia-Verdugo JM, Yang Z, Alvarez-Buylla A. Human hippocampal neurogenesis drops sharply in children to undetectable levels in adults. **Nature** 555: 377–381, 2018. doi:10.1038/nature25975.

1069. Knoth R, Singec I, Ditter M, Pantazis G, Capetian P, Meyer RP, Horvat V, Volk B, Kempermann G. Murine features of neurogenesis in the human hippocampus across the lifespan from 0 to 100 years. **PLoS One** 5: e8809, 2010. doi:10.1371/journal.pone.0008809.

1070. Kozareva DA, Cryan JF, Nolan YM. Born this way: hippocampal neurogenesis across the lifespan. **Aging Cell** 18: e13007, 2019. doi:10.1111/acel.13007.

1071. Wu C, Sun D. GABA receptors in brain development, function, and injury. **Metab Brain Dis** 30: 367–379, 2015. doi:10.1007/s11011-014-9560-1.

1072. Paoletti P, Bellone C, Zhou Q. NMDA receptor subunit diversity: impact on receptor properties, synaptic plasticity and disease. **Nat Rev Neurosci** 14: 383–400, 2013. doi:10.1038/nrn3504.

1073. Law AJ, Weickert CS, Webster MJ, Herman MM, Kleinman JE, Harrison PJ. Changes in NMDA receptor subunit mRNAs and cyclophilin mRNA during development of the human hippocampus. **Ann NY Acad Sci** 1003: 426–430, 2003. doi:10.1196/annals.1300.043.

1074. Law AJ, Weickert CS, Webster MJ, Herman MM, Kleinman JE, Harrison PJ. Expression of NMDA receptor NR1, NR2A and NR2B subunit mRNAs during development of the human hippocampal formation. **Eur J Neurosci** 18: 1197–1205, 2003. doi:10.1046/j.1460-9568.2003.02850.x.

1075. Knudsen EI. Sensitive periods in the development of the brain and behavior. **J Cogn Neurosci** 16: 1412–1425, 2004. doi:10.1162/0898929042304796.

1076. Hensch TK. Critical period plasticity in local cortical circuits. **Nat Rev Neurosci** 6: 877–888, 2005. doi:10.1038/nrn1787.

1077. Nabel EM, Morishita H. Regulating critical period plasticity: insight from the visual system to fear circuitry for therapeutic interventions. **Front Psychiatry** 4: 146, 2013. doi:10.3389/fpsyt.2013.00146.

1078. Lee JS, Kim HG, Jeon CJ. Identification of synaptic pattern of NMDA receptor subunits upon direction-selective retinal ganglion cells in developing and adult mouse retina. **Acta Histochem** 119: 495–507, 2017. doi:10.1016/j.acthis.2017.05.002.

1079. Travaglia A, Bisaz R, Cruz E, Alberini CM. Developmental changes in plasticity, synaptic, glia and connectivity protein levels in rat dorsal hippocampus. **Neurobiol Learn Mem** 135: 125–138, 2016. doi:10.1016/j.nlm.2016.08.005.

1080. Travaglia A, Steinmetz AB, Miranda JM, Alberini CM. Mechanisms of critical period in the hippocampus underlie object location learning and memory in infant rats. **Learn Mem** 25: 176–182, 2018. doi:10.1101/lm.046946.117.

1081. Seehagen S, Konrad C, Herbert JS, Schneider S. Timely sleep facilitates declarative memory consolidation in infants. **Proc Natl Acad Sci USA** 112: 1625–1629, 2015. doi:10.1073/pnas.1414000112.

1082. Konrad C, Seehagen S, Schneider S, Herbert JS. Naps promote flexible memory retrieval in 12-month-old infants. **Dev Psychobiol** 58: 866–874, 2016. doi:10.1002/dev.21431.

1083. Konrad C, Herbert JS, Schneider S, Seehagen S. The relationship between prior night's sleep and measures of infant imitation. **Dev Psychobiol** 58: 450–461, 2016. doi:10.1002/dev.21387.

1084. Konrad C, Dirks ND, Warmuth A, Herbert JS, Schneider S, Seehagen S. Sleep-dependent selective imitation in infants. **J Sleep Res** 28: e12777, 2019. doi:10.1111/jsr.12777.

1085. Mason GM, Kurdziel LB, Spencer RM. The memory benefits of two naps per day during infancy: a pilot investigation. **Infant Behav Dev** 65: 101647, 2021. doi:10.1016/j.infbeh.2021.101647.

1086. Tham EK, Richmond J, Gooley JJ, Jafar NK, Chong YS, Yap F, Teoh OH, Goh DY, Broekman BF, Rifkin-Graboi A. Variations in habitual sleep and relational memory in 6-month-olds. **Sleep Health** 5: 257–265, 2019. doi:10.1016/j.sleh.2018.12.007.

1087. Pisch M, Wiesemann F, Karmiloff-Smith A. Infant wake after sleep onset serves as a marker for different trajectories in cognitive development. **J Child Psychol Psychiatry** 60: 189–198, 2019. doi:10.1111/jcpp.12948.

1088. Lukowski AF, Milojevich HM. Sleeping like a baby: examining relations between habitual infant sleep, recall memory, and generalization across cues at 10 months. **Infant Behav Dev** 36: 369–376, 2013. doi:10.1016/j.infbeh.2013.02.001.

1089. Lukowski AF, Slonecker EM, Milojevich HM. Sleep problems and recall memory in children with Down syndrome and typically developing controls. **Res Dev Disabil** 96: 103512, 2020. doi:10.1016/j.ridd.2019.103512.

1090. Kurdziel L, Duclos K, Spencer RM. Sleep spindles in midday naps enhance learning in preschool children. **Proc Natl Acad Sci USA** 110: 17267–17272, 2013. doi:10.1073/pnas.1306418110.

1091. Giganti F, Arzilli C, Conte F, Toselli M, Viggiano MP, Ficca G. The effect of a daytime nap on priming and recognition tasks in

preschool children. **Sleep** 37: 1087–1093, 2014. doi:10.5665/sleep.3766.

1092. Riggins T, Spencer RM**.** Habitual sleep is associated with both source memory and hippocampal subfield volume during early childhood. **Sci Rep** 10: 15304, 2020. doi:10.1038/s41598-020-72231-z.

1093. Cabral T, Mota NB, Fraga L, Copelli M, McDaniel MA, Ribeiro S**.** Post-class naps boost declarative learning in a naturalistic school setting. **npj Sci Learn** 3: 14, 2018. doi:10.1038/s41539-018-0031-z.

1094. Lemos N, Weissheimer J, Ribeiro S**.** Naps in school can enhance the duration of declarative memories learned by adolescents. **Front Syst Neurosci** 8: 103, 2014. doi:10.3389/fnsys.2014.00103.

1095. Wang JY, Weber FD, Zinke K, Inostroza M, Born J**.** More effective consolidation of episodic long-term memory in children than adults—unrelated to sleep. **Child Dev** 89: 1720–1734, 2018. doi:10.1111/cdev.12839.

1096. Peiffer A, Brichet M, De Tiège X, Peigneux P, Urbain C**.** The power of children's sleep—improved declarative memory consolidation in children compared with adults. **Sci Rep** 10: 9979, 2020. doi:10.1038/s41598-020-66880-3.

1097. Maski K, Holbrook H, Manoach D, Hanson E, Kapur K, Stickgold R**.** Sleep dependent memory consolidation in children with autism spectrum disorder. **Sleep** 38: 1955–1963, 2015. doi:10.5665/sleep.5248.

1098. Maski KP**.** Sleep-dependent memory consolidation in children. **Semin Pediatr Neurol** 22: 130–134, 2015. doi:10.1016/j.spen.2015.03.008.

1099. Prehn-Kristensen A, Munz M, Molzow I, Wilhelm I, Wiesner CD, Baving L**.** Sleep promotes consolidation of emotional memory in healthy children but not in children with attention-deficit hyperactivity disorder. **PLoS One** 8: e65098, 2013. doi:10.1371/journal.pone.0065098.

1100. van Rijn E, Gouws A, Walker SA, Knowland VC, Cairney SA, Gaskell MG, Henderson LM**.** Do naps benefit novel word learning? Developmental differences and white matter correlates. **Cortex** 158: 37–60, 2023. doi:10.1016/j.cortex.2022.09.016.

1101. Urbain C, De Tiège X, Op De Beeck M, Bourguignon M, Wens V, Verheulpen D, Van Bogaert P, Peigneux P**.** Sleep in children triggers rapid reorganization of memory-related brain processes. **Neuroimage** 134: 213–222, 2016. doi:10.1016/j.neuroimage.2016.03.055.

1102. Prehn-Kristensen A, Lotzkat K, Bauhofer E, Wiesner CD, Baving L**.** Sleep supports memory of odors in adults but not in children. **PLoS One** 10: e0139069, 2015. doi:10.1371/journal.pone.0139069.

1103. Schommartz I, Lembcke PF, Pupillo F, Schuetz H, de Chamorro NW, Bauer M, Kaindl AM, Buss C, Shing YL**.** Distinct multivariate structural brain profiles are related to variations in short- and long-delay memory consolidation across children and young adults. **Dev Cogn Neurosci** 59: 101192, 2023. doi:10.1016/j.dcn.2022.101192.

1104. Maski K, Steinhart E, Holbrook H, Katz ES, Kapur K, Stickgold R**.** Impaired memory consolidation in children with obstructive sleep disordered breathing. **PLoS One** 12: e0186915, 2017. doi:10.1371/journal.pone.0186915.

1105. Prehn-Kristensen A, Böhmig A, Schult J, Pedersen A, Wiesner CD, Baving L**.** Does sleep help prevent forgetting rewarded memory representations in children and adults? **Front Psychol** 9: 924, 2018. doi:10.3389/fpsyg.2018.00924.

1106. Johnson EG, Mooney L, Graf Estes K, Nordahl CW, Ghetti S**.** Activation for newly learned words in left medial-temporal lobe during toddlers' sleep is associated with memory for words. **Curr Biol** 31: 5429–5438.e5, 2021. doi:10.1016/j.cub.2021.09.058.

1107. Himmer L, Müller E, Gais S, Schönauer M**.** Sleep-mediated memory consolidation depends on the level of integration at encoding. **Neurobiol Learn Mem** 137: 101–106, 2017. doi:10.1016/j.nlm.2016.11.019.

1108. Bastian L, Kurz EM, Näher T, Zinke K, Friedrich M, Born J**.** Long-term memory formation for voices during sleep in three-month-old infants. **Neurobiol Learn Mem** 215: 107987, 2024. doi:10.1016/j.nlm.2024.107987.

1109. Axelsson EL, Williams SE, Horst JS**.** The effect of sleep on children's word retention and generalization. **Front Psychol** 7: 1192, 2016. doi:10.3389/fpsyg.2016.01192.

1110. Horváth K, Myers K, Foster R, Plunkett K**.** Napping facilitates word learning in early lexical development. **J Sleep Res** 24: 503–509, 2015. doi:10.1111/jsr.12306.

1111. He AX, Huang S, Waxman S, Arunachalam S**.** Two-year-olds consolidate verb meanings during a nap. **Cognition** 198: 104205, 2020. doi:10.1016/j.cognition.2020.104205.

1112. Gais S, Mölle M, Helms K, Born J**.** Learning-dependent increases in sleep spindle density. **J Neurosci** 22: 6830–6834, 2002. doi:10.1523/JNEUROSCI.22-15-06830.2002.

1113. Werchan DM, Kim JS, Gómez RL**.** A daytime nap combined with nighttime sleep promotes learning in toddlers. **J Exp Child Psychol** 202: 105006, 2021. doi:10.1016/j.jecp.2020.105006.

1114. Vlach HA, Sandhofer CM**.** Developmental differences in children's context-dependent word learning. **J Exp Child Psychol** 108: 394–401, 2011. doi:10.1016/j.jecp.2010.09.011.

1115. Goto A, Bota A, Miya K, Wang J, Tsukamoto S, Jiang X, Hirai D, Murayama M, Matsuda T, McHugh TJ, Nagai T, Hayashi Y**.** Stepwise synaptic plasticity events drive the early phase of memory consolidation. **Science** 374: 857–863, 2021. doi:10.1126/science.abj9195.

1116. Friedrich M, Mölle M, Friederici AD, Born J**.** Sleep-dependent memory consolidation in infants protects new episodic memories from existing semantic memories. **Nat Commun** 11: 1298, 2020. doi:10.1038/s41467-020-14850-8.

1117. Friedrich M, Mölle M, Born J, Friederici AD**.** Memory for nonadjacent dependencies in the first year of life and its relation to sleep. **Nat Commun** 13: 7896, 2022. doi:10.1038/s41467-022-35558-x.

1118. Gómez RL, Bootzin RR, Nadel L**.** Naps promote abstraction in language-learning infants. **Psychol Sci** 17: 670–674, 2006. doi:10.1111/j.1467-9280.2006.01764.x.

1119. Hupbach A, Gomez RL, Bootzin RR, Nadel L**.** Nap-dependent learning in infants. **Dev Sci** 12: 1007–1012, 2009. doi:10.1111/j.1467-7687.2009.00837.x.

1120. Simon KN, Werchan D, Goldstein MR, Sweeney L, Bootzin RR, Nadel L, Gómez RL**.** Sleep confers a benefit for retention of statistical language learning in 6.5 month old infants. **Brain Lang** 167: 3–12, 2017. doi:10.1016/j.bandl.2016.05.002.

1121. Schaadt G, Paul M, Muralikrishnan R, Männel C, Friederici AD**.** Seven-year-olds recall non-adjacent dependencies after overnight retention. **Neurobiol Learn Mem** 171: 107225, 2020. doi:10.1016/j.nlm.2020.107225.

1122. Torres FA, Orio P, Escobar MJ. Selection of stimulus parameters for enhancing slow wave sleep events with a neural-field theory thalamocortical model. **PLoS Comput Biol** 17: e1008758, 2021. doi:10.1371/journal.pcbi.1008758.

1123. Weighall AR, Henderson LM, Barr DJ, Cairney SA, Gaskell MG. Eye-tracking the time-course of novel word learning and lexical competition in adults and children. **Brain Lang** 167: 13–27, 2017. doi:10.1016/j.bandl.2016.07.010.

1124. Spanò G, Gómez RL, Demara BI, Alt M, Cowen SL, Edgin JO. REM sleep in naps differentially relates to memory consolidation in typical preschoolers and children with Down syndrome. **Proc Natl Acad Sci USA** 115: 11844–11849, 2018. doi:10.1073/pnas.1811488115.

1125. Smith FR, Gaskell MG, Weighall AR, Warmington M, Reid AM, Henderson LM. Consolidation of vocabulary is associated with sleep in typically developing children, but not in children with dyslexia. **Dev Sci** 21: e12639, 2018. doi:10.1111/desc.12639.

1126. Henderson LM, van Rijn E, James E, Walker S, Knowland VC, Gareth Gaskell M. Timing storytime to maximize children's ability to retain new vocabulary. **J Exp Child Psychol** 210: 105207, 2021. doi:10.1016/j.jecp.2021.105207.

1127. James E, Gaskell MG, Henderson LM. Sleep-dependent consolidation in children with comprehension and vocabulary weaknesses: it'll be alright on the night? **J Child Psychol Psychiatry** 61: 1104–1115, 2020. doi:10.1111/jcpp.13253.

1128. Walker S, Gaskell MG, Knowland VC, Fletcher FE, Cairney SA, Henderson LM. Growing up with interfering neighbours: the influence of time of learning and vocabulary knowledge on written word learning in children. **R Soc Open Sci** 7: 191597, 2020. doi:10.1098/rsos.191597.

1129. Henderson LM, Weighall AR, Brown H, Gareth Gaskell M. Consolidation of vocabulary is associated with sleep in children. **Dev Sci** 15: 674–687, 2012. doi:10.1111/j.1467-7687.2012.01172.x.

1130. Henderson L, Weighall A, Gaskell G. Learning new vocabulary during childhood: effects of semantic training on lexical consolidation and integration. **J Exp Child Psychol** 116: 572–592, 2013. doi:10.1016/j.jecp.2013.07.004.

1131. Henderson L, Devine K, Weighall A, Gaskell G. When the daffodat flew to the intergalactic zoo: off-line consolidation is critical for word learning from stories. **Dev Psychol** 51: 406–417, 2015. doi:10.1037/a0038786.

1132. James E, Gaskell MG, Weighall A, Henderson L. Consolidation of vocabulary during sleep: the rich get richer? **Neurosci Biobehav Rev** 77: 1–13, 2017. doi:10.1016/j.neubiorev.2017.01.054.

1133. Davis MH, Gaskell MG. A complementary systems account of word learning: neural and behavioural evidence. **Philos Trans R Soc Lond B Biol Sci** 364: 3773–3800, 2009. doi:10.1098/rstb.2009.0111.

1134. Vermeulen MC, van der Heijden KB, Benjamins JS, Swaab H, van Someren EJ. Memory effects of sleep, emotional valence, arousal and novelty in children. **J Sleep Res** 26: 309–317, 2017. doi:10.1111/jsr.12506.

1135. Prehn-Kristensen A, Molzow I, Förster A, Siebenhühner N, Gesch M, Wiesner CD, Baving L. Memory consolidation of socially relevant stimuli during sleep in healthy children and children with attention-deficit/hyperactivity disorder and oppositional defiant disorder: what you can see in their eyes. **Biol Psychol** 123: 196–204, 2017. doi:10.1016/j.biopsycho.2016.12.017.

1136. Munz M, Baving L, Prehn-Kristensen A. Transient destabilization of declarative memory-opposing impact of physical exercise or rest after encoding in typically developing children and children with attention deficit hyperactivity disorder but no difference after subsequent sleep. **Brain Sci** 12: 322, 2022. doi:10.3390/brainsci12030322.

1137. Jones CE, Chau AQ, Olson RJ, Moore C, Wickham PT, Puranik N, Guizzetti M, Cao H, Meshul CK, Lim MM. Early life sleep disruption alters glutamate and dendritic spines in prefrontal cortex and impairs cognitive flexibility in prairie voles. **Curr Res Neurobiol** 2: 100020, 2021. doi:10.1016/j.crneur.2021.100020.

1138. Jones S, Castelnovo A, Riedner B, Flaherty B, Prehn-Kristensen A, Benca R, Tononi G, Herringa R. Sleep and emotion processing in paediatric posttraumatic stress disorder: a pilot investigation. **J Sleep Res** 30: e13261, 2021. doi:10.1111/jsr.13261.

1139. Ashtamker L, Karni A. Motor memory in childhood: early expression of consolidation phase gains. **Neurobiol Learn Mem** 106: 26–30, 2013. doi:10.1016/j.nlm.2013.07.003.

1140. Adi-Japha E, Badir R, Dorfberger S, Karni A. A matter of time: rapid motor memory stabilization in childhood. **Dev Sci** 17: 424–433, 2014. doi:10.1111/desc.12132.

1141. Joyce A, Hill CM, Karmiloff-Smith A, Dimitriou D. A cross-syndrome comparison of sleep-dependent learning on a cognitive procedural task. **Am J Intellect Dev Disabil** 124: 339–353, 2019. doi:10.1352/1944-7558-124.4.339.

1142. Zinke K, Noack H, Born J. Sleep augments training-induced improvement in working memory in children and adults. **Neurobiol Learn Mem** 147: 46–53, 2018. doi:10.1016/j.nlm.2017.11.009.

1143. Mylonas D, Machado S, Larson O, Patel R, Cox R, Vangel M, Maski K, Stickgold R, Manoach DS. Dyscoordination of non-rapid eye movement sleep oscillations in autism spectrum disorder. **Sleep** 45: zsac010, 2022. doi:10.1093/sleep/zsac010.

1144. Reda F, Gorgoni M, D'Atri A, Scarpelli S, Carpi M, Di Cola E, Menghini D, Vicari S, Stella G, De Gennaro L. Sleep-related declarative memory consolidation in children and adolescents with developmental dyslexia. **Brain Sci** 11: 73, 2021. doi:10.3390/brainsci11010073.

1145. Hahn MA, Bothe K, Heib D, Schabus M, Helfrich RF, Hoedlmoser K. Slow oscillation-spindle coupling strength predicts real-life gross-motor learning in adolescents and adults. **eLife** 11: e66761, 2022. doi:10.7554/eLife.66761.

1146. Joechner AK, Wehmeier S, Werkle-Bergner M. Electrophysiological indicators of sleep-associated memory consolidation in 5- to 6-year-old children. **Psychophysiology** 58: e13829, 2021. doi:10.1111/psyp.13829.

1147. Johnson EG, Prabhakar J, Mooney LN, Ghetti S. Neuroimaging the sleeping brain: Insight on memory functioning in infants and toddlers. **Infant Behav Dev** 58: 101427, 2020. doi:10.1016/j.infbeh.2020.101427.

1148. Prabhakar J, Johnson EG, Nordahl CW, Ghetti S. Memory-related hippocampal activation in the sleeping toddler. **Proc Natl Acad Sci USA** 115: 6500–6505, 2018. doi:10.1073/pnas.1805572115.

1149. Mooney LN, Johnson EG, Prabhakar J, Ghetti S. Memory-related hippocampal activation during sleep and temporal memory in toddlers. **Dev Cogn Neurosci** 47: 100908, 2021. doi:10.1016/j.dcn.2020.100908.

1150. García-Pérez MA, Irani M, Tiznado V, Bustamante T, Inostroza M, Maldonado PE, Valdés JL. Cortico-hippocampal oscillations are associated with the developmental onset of hippocampal-dependent memory. **Front Neurosci** 16: 891523, 2022. doi:10.3389/fnins.2022.891523.

1151. Contreras MP, Fechner J, Born J, Inostroza M. Accelerating maturation of spatial memory systems by experience: evidence from sleep oscillation signatures of memory processing. **J Neurosci** 43: 3509–3519, 2023. doi:10.1523/JNEUROSCI.1967-22.2023.

1152. Adler A, Lai CS, Yang G, Geron E, Bai Y, Gan WB. Sleep promotes the formation of dendritic filopodia and spines near learning-inactive existing spines. **Proc Natl Acad Sci USA** 118: e2114856118, 2021. doi:10.1073/pnas.2114856118.

1153. Tachibana RO, Lee D, Kai K, Kojima S. Performance-dependent consolidation of learned vocal changes in adult songbirds. **J Neurosci** 42: 1974–1986, 2022. doi:10.1523/JNEUROSCI.1942-21.2021.

1154. Margoliash D, Brawn TP. Sleep and learning in birds. In: *Sleep and Brain Activity*. Elsevier, 2012, p. 109–146.

1155. Derégnaucourt S, Mitra PP, Fehér O, Pytte C, Tchernichovski O. How sleep affects the developmental learning of bird song. **Nature** 433: 710–716, 2005. doi:10.1038/nature03275.

1156. Yanagihara S, Yazaki-Sugiyama Y. Auditory experience-dependent cortical circuit shaping for memory formation in bird song learning. **Nat Commun** 7: 11946, 2016. doi:10.1038/ncomms11946.

1157. Hayase S, Wada K. Singing activity-driven Arc expression associated with vocal acoustic plasticity in juvenile songbird. **Eur J Neurosci** 48: 1728–1742, 2018. doi:10.1111/ejn.14057.

1158. Moorman S, Gobes SM, Kuijpers M, Kerkhofs A, Zandbergen MA, Bolhuis JJ. Human-like brain hemispheric dominance in birdsong learning. **Proc Natl Acad Sci USA** 109: 12782–12787, 2012. doi:10.1073/pnas.1207207109.

1159. Bolhuis JJ, Gahr M. Neural mechanisms of birdsong memory. **Nat Rev Neurosci** 7: 347–357, 2006. doi:10.1038/nrn1904.

1160. Hahnloser RH, Fee MS. Sleep-related spike bursts in HVC are driven by the nucleus interface of the nidopallium. **J Neurophysiol** 97: 423–435, 2007. doi:10.1152/jn.00547.2006.

1161. Hahnloser RH, Wang CZ, Nager A, Naie K. Spikes and bursts in two types of thalamic projection neurons differentially shape sleep patterns and auditory responses in a songbird. **J Neurosci** 28: 5040–5052, 2008. doi:10.1523/JNEUROSCI.5059-07.2008.

1162. Brawn TP, Margoliash D. A bird's eye view of sleep-dependent memory consolidation. **Curr Top Behav Neurosci** 25: 207–237, 2015. doi:10.1007/7854_2014_349.

1163. Liberti WA, Markowitz JE, Perkins LN, Liberti DC, Leman DP, Guitchounts G, Velho T, Kotton DN, Lois C, Gardner TJ. Unstable neurons underlie a stable learned behavior. **Nat Neurosci** 19: 1665–1671, 2016. doi:10.1038/nn.4405.

1164. Moorman S, Gobes SM, van de Kamp FC, Zandbergen MA, Bolhuis JJ. Learning-related brain hemispheric dominance in sleeping songbirds. **Sci Rep** 5: 9041, 2015. doi:10.1038/srep09041.

1165. Bolhuis JJ, Moorman S. Birdsong memory and the brain: in search of the template. **Neurosci Biobehav Rev** 50: 41–55, 2015. doi:10.1016/j.neubiorev.2014.11.019.

1166. Döppler JF, Peltier M, Amador A, Goller F, Mindlin GB. Replay of innate vocal patterns during night sleep in suboscines. **Proc Biol Sci** 288: 20210610, 2021. doi:10.1098/rspb.2021.0610.

1167. Huelin Gorriz M, Takigawa M, Bendor D. The role of experience in prioritizing hippocampal replay. **Nat Commun** 14: 8157, 2023. doi:10.1038/s41467-023-43939-z.

1168. Yaffe K, Falvey CM, Hoang T. Connections between sleep and cognition in older adults. **Lancet Neurol** 13: 1017–1028, 2014. doi:10.1016/S1474-4422(14)70172-3.

1169. Yeh AY, Pressler SJ, Giordani BJ, Pozehl BJ, Berger AM. Integrative review of the relationship between sleep disturbances and episodic memory in older adults. **Biol Res Nurs** 20: 440–451, 2018. doi:10.1177/1099800418768070.

1170. Scullin MK, Bliwise DL. Sleep, cognition, and normal aging: integrating a half century of multidisciplinary research. **Perspect Psychol Sci** 10: 97–137, 2015. doi:10.1177/1745691614556680.

1171. Tarragon E, Lopez D, Estrada C, Gonzalez-Cuello A, Ros CM, Lamberty Y, Pifferi F, Cella M, Canovi M, Guiso G, Gobbi M, Fernández-Villalba E, Blin O, Bordet R, Richardson JC, Herrero MT. Memantine prevents reference and working memory impairment caused by sleep deprivation in both young and aged *Octodon degus*. **Neuropharmacology** 85: 206–214, 2014. doi:10.1016/j.neuropharm.2014.05.023.

1172. Pasula EY, Brown GG, McKenna BS, Mellor A, Turner T, Anderson C, Drummond SP. Effects of sleep deprivation on component processes of working memory in younger and older adults. **Sleep** 41: 2018. doi:10.1093/sleep/zsx213.

1173. Sattari N, Whitehurst LN, Ahmadi M, Mednick SC. Does working memory improvement benefit from sleep in older adults? **Neurobiol Sleep Circadian Rhythms** 6: 53–61, 2019. doi:10.1016/j.nbscr.2019.01.001.

1174. Gerhardsson A, Fischer H, Lekander M, Kecklund G, Axelsson J, Åkerstedt T, Schwarz J. Positivity effect and working memory performance remains intact in older adults after sleep deprivation. **Front Psychol** 10: 605, 2019. doi:10.3389/fpsyg.2019.00605.

1175. Cabanel N, Speier C, Müller MJ, Kundermann B. Actigraphic, but not subjective, sleep measures are associated with cognitive impairment in memory clinic patients. **Psychogeriatrics** 20: 133–139, 2020. doi:10.1111/psyg.12474.

1176. Lücke AJ, Wrzus C, Gerstorf D, Kunzmann U, Katzorreck M, Schmiedek F, Hoppmann C, Schilling OK. Between-person and within-person associations of sleep and working-memory in the everyday lives of old and very old adults: initial level, learning, and variability. **Sleep** 45: zsab279, 2022. doi:10.1093/sleep/zsab279.

1177. Cao Y, Xu X, Li M, Liu J, Shi Z. Both short and long sleep durations are associated with poor cognition and memory in Chinese adults aged 55+ years—results from China Health and Nutrition Survey. **Life (Basel)** 12: 1798, 2022. doi:10.3390/life12111798.

1178. Gao J, Zhang L, Zhu J, Guo Z, Lin M, Bai L, Zheng P, Liu W, Huang J, Liu Z. Prefrontal cortex hemodynamics and functional connectivity changes during performance working memory tasks in older adults with sleep disorders. **Brain Sci** 13: 497, 2023. doi:10.3390/brainsci13030497.

1179. Gutchess A, Cho I. Memory and aging across cultures. **Curr Opin Psychol** 55: 101728, 2024. doi:10.1016/j.copsyc.2023.101728.

1180. Mammarella N, Di Domenico A, Palumbo R, Fairfield B. Noradrenergic modulation of emotional memory in aging. **Ageing Res Rev** 27: 61–66, 2016. doi:10.1016/j.arr.2016.03.004.

1181. Nyberg L, Pudas S. Successful memory aging. **Annu Rev Psychol** 70: 219–243, 2019. doi:10.1146/annurev-psych-010418-103052.

1182. Tromp D, Dufour A, Lithfous S, Pebayle T, Després O. Episodic memory in normal aging and Alzheimer disease: Insights from imaging and behavioral studies. **Ageing Res Rev** 24: 232–262, 2015. doi:10.1016/j.arr.2015.08.006.

1183. Khan ZU, Martín-Montañez E, Navarro-Lobato I, Muly EC. Memory deficits in aging and neurological diseases. **Prog Mol Biol Transl Sci** 122: 1–29, 2014. doi:10.1016/B978-0-12-420170-5.00001-5.

1184. Grilli MD, Sheldon S. Autobiographical event memory and aging: older adults get the gist. **Trends Cogn Sci** 26: 1079–1089, 2022. doi:10.1016/j.tics.2022.09.007.

1185. Carlson EJ, Wilckens KA, Wheeler ME. The interactive role of sleep and circadian rhythms in episodic memory in older adults. **J Gerontol A Biol Sci Med Sci** 78: 1844–1852, 2023. doi:10.1093/gerona/glad112.

1186. Muehlroth BE, Rasch B, Werkle-Bergner M. Episodic memory consolidation during sleep in healthy aging. **Sleep Med Rev** 52: 101304, 2020. doi:10.1016/j.smrv.2020.101304.

1187. Pace-Schott EF, Spencer RM. Sleep-dependent memory consolidation in healthy aging and mild cognitive impairment. **Curr Top Behav Neurosci** 25: 307–330, 2015. doi:10.1007/7854_2014_300.

1188. Gui WJ, Li HJ, Guo YH, Peng P, Lei X, Yu J. Age-related differences in sleep-based memory consolidation: a meta-analysis. **Neuropsychologia** 97: 46–55, 2017. doi:10.1016/j.neuropsychologia.2017.02.001.

1189. Hornung OP, Danker-Hopfe H, Heuser I. Age-related changes in sleep and memory: commonalities and interrelationships. **Exp Gerontol** 40: 279–285, 2005. doi:10.1016/j.exger.2005.02.001.

1190. Xu L, Jiang CQ, Lam TH, Zhang WS, Cherny SS, Thomas GN, Cheng KK. Sleep duration and memory in the elderly Chinese: longitudinal analysis of the Guangzhou Biobank Cohort Study. **Sleep** 37: 1737–1744, 2014. doi:10.5665/sleep.4162.

1191. Calev H, Spampinato LM, Press VG, Meltzer DO, Arora VM. Prevalence of impaired memory in hospitalized adults and associations with in-hospital sleep loss. **J Hosp Med** 10: 439–445, 2015. doi:10.1002/jhm.2364.

1192. Cavuoto MG, Ong B, Pike KE, Nicholas CL, Bei B, Kinsella GJ. Better objective sleep quality in older adults with high subjective memory decline. **J Alzheimers Dis** 53: 943–953, 2016. doi:10.3233/JAD-160187.

1193. Kang SH, Yoon IY, Lee SD, Kim T, Lee CS, Han JW, Kim KW, Kim CH. Subjective memory complaints in an elderly population with poor sleep quality. **Aging Ment Health** 21: 532–536, 2017. doi:10.1080/13607863.2015.1124839.

1194. Tsapanou A, Gu Y, O'Shea DM, Yannakoulia M, Kosmidis M, Dardiotis E, Hadjigeorgiou G, Sakka P, Stern Y, Scarmeas N. Sleep quality and duration in relation to memory in the elderly: initial results from the Hellenic Longitudinal Investigation of Aging and Diet. **Neurobiol Learn Mem** 141: 217–225, 2017. doi:10.1016/j.nlm.2017.04.011.

1195. Rana BK, Panizzon MS, Franz CE, Spoon KM, Jacobson KC, Xian H, Ancoli-Israel S, Lyons M, Kremen WS. Association of sleep quality on memory-related executive functions in middle age. **J Int Neuropsychol Soc** 24: 67–76, 2018. doi:10.1017/S1355617717000637.

1196. Manousakis JE, Scovelle AJ, Rajaratnam SM, Naismith SL, Anderson C. Advanced circadian timing and sleep fragmentation differentially impact on memory complaint subtype in subjective cognitive decline. **J Alzheimers Dis** 66: 565–577, 2018. doi:10.3233/JAD-180612.

1197. Wilckens KA, Tudorascu DL, Snitz BE, Price JC, Aizenstein HJ, Lopez OL, Erickson KI, Lopresti BJ, Laymon CM, Minhas D, Mathis CA, Buysse DJ, Klunk WE, Cohen AD. Sleep moderates the relationship between amyloid beta and memory recall. **Neurobiol Aging** 71: 142–148, 2018. doi:10.1016/j.neurobiolaging.2018.07.011.

1198. Gamaldo AA, Wright RS, Aiken-Morgan AT, Allaire JC, Thorpe RJ, Whitfield KE. The association between subjective memory complaints and sleep within older African American adults. **J Gerontol B Psychol Sci Soc Sci** 74: 202–211, 2019. doi:10.1093/geronb/gbx069.

1199. Hokett E, Duarte A. Age and race-related differences in sleep discontinuity linked to associative memory performance and its neural underpinnings. **Front Hum Neurosci** 13: 176, 2019. doi:10.3389/fnhum.2019.00176.

1200. Hokett E, Arunmozhi A, Campbell J, Verhaeghen P, Duarte A. A systematic review and meta-analysis of individual differences in naturalistic sleep quality and episodic memory performance in young and older adults. **Neurosci Biobehav Rev** 127: 675–688, 2021. doi:10.1016/j.neubiorev.2021.05.010.

1201. Manousakis JE, Nicholas C, Scovelle AJ, Naismith SL, Anderson C. Associations between sleep and verbal memory in subjective cognitive decline: a role for semantic clustering. **Neurobiol Learn Mem** 166: 107086, 2019. doi:10.1016/j.nlm.2019.107086.

1202. Yeh AY, Pressler SJ, Algase D, Struble LM, Pozehl BJ, Berger AM, Giordani BJ. Sleep-wake disturbances and episodic memory in older adults. **Biol Res Nurs** 23: 141–150, 2021. doi:10.1177/1099800420941601.

1203. Siddarth P, Thana-Udom K, Ojha R, Merrill D, Dzierzewski JM, Miller K, Small GW, Ercoli L. Sleep quality, neurocognitive performance, and memory self-appraisal in middle-aged and older adults with memory complaints. **Int Psychogeriatr** 33: 703–713, 2021. doi:10.1017/S1041610220003324.

1204. Cruz T, García L, Álvarez MA, Manzanero AL. Sleep quality and memory function in healthy ageing. **Neurologia (Engl Ed)** 37: 31–37, 2022. doi:10.1016/j.nrleng.2018.10.024.

1205. Mary A, Bastin C, Lina JM, Rauchs G. Editorial: The impact of age-related changes in brain network organization and sleep on memory. **Front Aging Neurosci** 14: 1049278, 2022. doi:10.3389/fnagi.2022.1049278.

1206. Kroeger D, Vetrivelan R. To sleep or not to sleep—effects on memory in normal aging and disease. **Aging Brain** 3: 100068, 2023. doi:10.1016/j.nbas.2023.100068.

1207. Wei Y, Luo M, Mai X, Feng L, Tang T, Yang D, Krishnan GP, Bazhenov M. The role of age-related sleep EEG changes in memory decline: experiments and computational modeling. **Annu Int Conf IEEE Eng Med Biol Soc** 2023: 1–4, 2023. doi:10.1109/EMBC40787.2023.10340681.

1208. Voumvourakis KI, Sideri E, Papadimitropoulos GN, Tsantzali I, Hewlett P, Kitsos D, Stefanou M, Bonakis A, Giannopoulos S, Tsivgoulis G, Paraskevas GP. The dynamic relationship between the glymphatic system, aging, memory, and sleep. **Biomedicines** 11: 2092, 2023. doi:10.3390/biomedicines11082092.

1209. Hamel A, Mary A, Rauchs G. Sleep and memory consolidation in aging: a neuroimaging perspective. **Rev Neurol (Paris)** 179: 658–666, 2023. doi:10.1016/j.neurol.2023.08.003.

1210. Skourti E, Simos P, Zampetakis A, Koutentaki E, Zaganas I, Alexopoulou C, Vgontzas A, Basta M. Long-term associations between objective sleep quality and quantity and verbal memory performance in normal cognition and mild cognitive impairment. **Front Neurosci** 17: 1265016, 2023. doi:10.3389/fnins.2023.1265016.

1211. Mander BA, Winer JR, Walker MP. Sleep and human aging. **Neuron** 94: 19–36, 2017. doi:10.1016/j.neuron.2017.02.004.

1212. Conte F, Arzilli C, Errico BM, Giganti F, Iovino D, Ficca G. Sleep measures expressing 'functional uncertainty' in elderlies' sleep. **Gerontology** 60: 448–457, 2014. doi:10.1159/000358083.

1213. Kales A, Wilson T, Kales JD, Jacobson A, Paulson MJ, Kollar E, Walter RD. Measurements of all-night sleep in normal elderly persons: effects of aging. **J Am Geriatr Soc** 15: 405–414, 1967. doi:10.1111/j.1532-5415.1967.tb02072.x.

1214. Landolt HP, Dijk DJ, Achermann P, Borbély AA. Effect of age on the sleep EEG: slow-wave activity and spindle frequency activity in young and middle-aged men. **Brain Res** 738: 205–212, 1996. doi:10.1016/S0006-8993(96)00770-6.

1215. Ohayon MM, Carskadon MA, Guilleminault C, Vitiello MV. Meta-analysis of quantitative sleep parameters from childhood to old age in healthy individuals: developing normative sleep values across the human lifespan. **Sleep** 27: 1255–1273, 2004. doi:10.1093/sleep/27.7.1255.

1216. Foley DJ, Vitiello MV, Bliwise DL, Ancoli-Israel S, Monjan AA, Walsh JK. Frequent napping is associated with excessive daytime sleepiness, depression, pain, and nocturia in older adults: findings from the National Sleep Foundation '2003 Sleep in America' poll. **Am J Geriatr Psychiatry** 15: 344–350, 2007. doi:10.1097/01.JGP.0000249385.50101.67.

1217. Redline S, Kirchner HL, Quan SF, Gottlieb DJ, Kapur V, Newman A. The effects of age, sex, ethnicity, and sleep-disordered breathing on sleep architecture. **Arch Intern Med** 164: 406–418, 2004. doi:10.1001/archinte.164.4.406.

1218. Rosinvil T, Bouvier J, Dubé J, Lafrenière A, Bouchard M, Cyr-Cronier J, Gosselin N, Carrier J, Lina JM. Are age and sex effects on sleep slow waves only a matter of electroencephalogram amplitude? **Sleep** 44: zsaa186, 2021. doi:10.1093/sleep/zsaa186.

1219. Carrier J, Viens I, Poirier G, Robillard R, Lafortune M, Vandewalle G, Martin N, Barakat M, Paquet J, Filipini D. Sleep slow wave changes during the middle years of life. **Eur J Neurosci** 33: 758–766, 2011. doi:10.1111/j.1460-9568.2010.07543.x.

1220. Dubé J, Lafortune M, Bedetti C, Bouchard M, Gagnon JF, Doyon J, Evans AC, Lina JM, Carrier J. Cortical thinning explains changes in sleep slow waves during adulthood. **J Neurosci** 35: 7795–7807, 2015. doi:10.1523/JNEUROSCI.3956-14.2015.

1221. Landolt HP, Borbély AA. Age-dependent changes in sleep EEG topography. **Clin Neurophysiol** 112: 369–377, 2001. doi:10.1016/S1388-2457(00)00542-3.

1222. Mander BA, Rao V, Lu B, Saletin JM, Lindquist JR, Ancoli-Israel S, Jagust W, Walker MP. Prefrontal atrophy, disrupted NREM slow waves and impaired hippocampal-dependent memory in aging. **Nat Neurosci** 16: 357–364, 2013. doi:10.1038/nn.3324.

1223. Dijk DJ, Beersma DG, van den Hoofdakker RH. All night spectral analysis of EEG sleep in young adult and middle-aged male subjects. **Neurobiol Aging** 10: 677–682, 1989. doi:10.1016/0197-4580(89)90004-3.

1224. Gao C, Scullin MK. Longitudinal trajectories of spectral power during sleep in middle-aged and older adults. **Aging Brain** 3: 100058, 2023. doi:10.1016/j.nbas.2022.100058.

1225. De Gennaro L, Ferrara M. Sleep spindles: an overview. **Sleep Med Rev** 7: 423–440, 2003. doi:10.1053/smrv.2002.0252.

1226. Ujma PP, Konrad BN, Simor P, Gombos F, Körmendi J, Steiger A, Dresler M, Bódizs R. Sleep EEG functional connectivity varies with age and sex, but not general intelligence. **Neurobiol Aging** 78: 87–97, 2019. doi:10.1016/j.neurobiolaging.2019.02.007.

1227. Mander BA, Rao V, Lu B, Saletin JM, Ancoli-Israel S, Jagust WJ, Walker MP. Impaired prefrontal sleep spindle regulation of hippocampal-dependent learning in older adults. **Cereb Cortex** 24: 3301–3309, 2014. doi:10.1093/cercor/bht188.

1228. Martin N, Lafortune M, Godbout J, Barakat M, Robillard R, Poirier G, Bastien C, Carrier J. Topography of age-related changes in sleep spindles. **Neurobiol Aging** 34: 468–476, 2013. doi:10.1016/j.neurobiolaging.2012.05.020.

1229. Rauchs G, Schabus M, Parapatics S, Bertran F, Clochon P, Hot P, Denise P, Desgranges B, Eustache F, Gruber G, Anderer P. Is there a link between sleep changes and memory in Alzheimer's disease? **Neuroreport** 19: 1159–1162, 2008. doi:10.1097/WNR.0b013e32830867c4.

1230. van Cauter E, Leproult R, Plat L. Age-related changes in slow wave sleep and REM sleep and relationship with growth hormone and cortisol levels in healthy men. **JAMA** 284: 861–868, 2000. doi:10.1001/jama.284.7.861.

1231. Scarpelli S, D'Atri A, Bartolacci C, Mangiaruga A, Gorgoni M, De Gennaro L. Oscillatory EEG activity during REM sleep in elderly people predicts subsequent dream recall after awakenings. **Front Neurol** 10: 985, 2019. doi:10.3389/fneur.2019.00985.

1232. McKillop LE, Vyazovskiy VV. Sleep and ageing: from human studies to rodent models. **Curr Opin Physiol** 15: 210–216, 2020. doi:10.1016/j.cophys.2020.03.004.

1233. Dijk DJ, Duffy JF, Riel E, Shanahan TL, Czeisler CA. Ageing and the circadian and homeostatic regulation of human sleep during forced desynchrony of rest, melatonin and temperature rhythms. **J Physiol** 516: 611–627, 1999. doi:10.1111/j.1469-7793.1999.0611v.x.

1234. Borbély AA. A two process model of sleep regulation. **Hum Neurobiol** 1: 195–204, 1982.

1235. Münch M, Knoblauch V, Blatter K, Schröder C, Schnitzler C, Kräuchi K, Wirz-Justice A, Cajochen C. The frontal predominance in human EEG delta activity after sleep loss decreases with age. **Eur J Neurosci** 20: 1402–1410, 2004. doi:10.1111/j.1460-9568.2004.03580.x.

1236. Dijk DJ, Groeger JA, Stanley N, Deacon S. Age-related reduction in daytime sleep propensity and nocturnal slow wave sleep. **Sleep** 33: 211–223, 2010. doi:10.1093/sleep/33.2.211.

1237. Vienne J, Spann R, Guo F, Rosbash M. Age-related reduction of recovery sleep and arousal threshold in *Drosophila*. **Sleep** 39: 1613–1624, 2016. doi:10.5665/sleep.6032.

1238. Panagiotou M, Vyazovskiy VV, Meijer JH, Deboer T. Differences in electroencephalographic non-rapid-eye movement sleep slow-wave characteristics between young and old mice. **Sci Rep** 7: 43656, 2017. doi:10.1038/srep43656.

1239. McKillop LE, Fisher SP, Cui N, Peirson SN, Foster RG, Wafford KA, Vyazovskiy VV. Effects of aging on cortical neural dynamics and local sleep homeostasis in mice. **J Neurosci** 38: 3911–3928, 2018. doi:10.1523/JNEUROSCI.2513-17.2018.

1240. Soltani S, Chauvette S, Bukhtiyarova O, Lina JM, Dubé J, Seigneur J, Carrier J, Timofeev I. Sleep-wake cycle in young and older mice. **Front Syst Neurosci** 13: 51, 2019. doi:10.3389/fnsys.2019.00051.

1241. Paulose JK, Wang C, O'Hara BF, Cassone VM. The effects of aging on sleep parameters in a healthy, melatonin-competent mouse model. **Nat Sci Sleep** 11: 113–121, 2019. doi:10.2147/NSS.S214423.

1242. Saper CB, Fuller PM, Pedersen NP, Lu J, Scammell TE. Sleep state switching. **Neuron** 68: 1023–1042, 2010. doi:10.1016/j.neuron.2010.11.032.

1243. Luppi PH, Peyron C, Fort P. Not a single but multiple populations of GABAergic neurons control sleep. **Sleep Med Rev** 32: 85–94, 2017. doi:10.1016/j.smrv.2016.03.002.

1244. Lim AS, Ellison BA, Wang JL, Yu L, Schneider JA, Buchman AS, Bennett DA, Saper CB. Sleep is related to neuron numbers in the ventrolateral preoptic/intermediate nucleus in older adults with and without Alzheimer's disease. **Brain** 137: 2847–2861, 2014. doi:10.1093/brain/awu222.

1245. Kessler BA, Stanley EM, Frederick-Duus D, Fadel J. Age-related loss of orexin/hypocretin neurons. **Neuroscience** 178: 82–88, 2011. doi:10.1016/j.neuroscience.2011.01.031.

1246. Hunt NJ, Rodriguez ML, Waters KA, Machaalani R. Changes in orexin (hypocretin) neuronal expression with normal aging in the human hypothalamus. **Neurobiol Aging** 36: 292–300, 2015. doi:10.1016/j.neurobiolaging.2014.08.010.

1247. Kasanuki K, Iseki E, Kondo D, Fujishiro H, Minegishi M, Sato K, Katsuse O, Hino H, Kosaka K, Arai H. Neuropathological investigation of hypocretin expression in brains of dementia with Lewy bodies. **Neurosci Lett** 569: 68–73, 2014. doi:10.1016/j.neulet.2014.03.020.

1248. Lim AS, Fleischman DA, Dawe RJ, Yu L, Arfanakis K, Buchman AS, Bennett DA. Regional neocortical gray matter structure and sleep fragmentation in older adults. **Sleep** 39: 227–235, 2016. doi:10.5665/sleep.5354.

1249. Varga AW, Ducca EL, Kishi A, Fischer E, Parekh A, Koushyk V, Yau PL, Gumb T, Leibert DP, Wohlleber ME, Burschtin OE, Convit A, Rapoport DM, Osorio RS, Ayappa I. Effects of aging on slow-wave sleep dynamics and human spatial navigational memory consolidation. **Neurobiol Aging** 42: 142–149, 2016. doi:10.1016/j.neurobiolaging.2016.03.008.

1250. Fogel S, Vien C, Karni A, Benali H, Carrier J, Doyon J. Sleep spindles: a physiological marker of age-related changes in gray matter in brain regions supporting motor skill memory consolidation. **Neurobiol Aging** 49: 154–164, 2017. doi:10.1016/j.neurobiolaging.2016.10.009.

1251. Fjell AM, Sørensen Ø, Amlien IK, Bartrés-Faz D, Brandmaier AM, Buchmann N, et al. Poor self-reported sleep is related to regional cortical thinning in aging but not memory decline-results from the Lifebrain consortium. **Cereb Cortex** 31: 1953–1969, 2021. doi:10.1093/cercor/bhaa332.

1252. Aly M, Moscovitch M. The effects of sleep on episodic memory in older and younger adults. **Memory** 18: 327–334, 2010. doi:10.1080/09658211003601548.

1253. Abichou K, La Corte V, Hubert N, Orriols E, Gaston-Bellegarde A, Nicolas S, Piolino P. Young and older adults benefit from sleep, but not from active wakefulness for memory consolidation of what-where-when naturalistic events. **Front Aging Neurosci** 11: 58, 2019. doi:10.3389/fnagi.2019.00058.

1254. Cherdieu M, Reynaud E, Uhlrich J, Versace R, Mazza S. Does age worsen sleep-dependent memory consolidation? **J Sleep Res** 23: 53–60, 2014. doi:10.1111/jsr.12100.

1255. Mary A, Schreiner S, Peigneux P. Accelerated long-term forgetting in aging and intra-sleep awakenings. **Front Psychol** 4: 750, 2013. doi:10.3389/fpsyg.2013.00750.

1256. Scullin MK, Fairley J, Decker MJ, Bliwise DL. The effects of an afternoon nap on episodic memory in young and older adults. **Sleep** 40: zsx035, 2017. doi:10.1093/sleep/zsx035.

1257. Kawai M, Schneider LD, Linkovski O, Jordan JT, Karna R, Pirog S, Cotto I, Buck C, Giardino WJ, O'Hara R. High-resolution spectral sleep analysis reveals a novel association between slow oscillations and memory retention in elderly adults. **Front Aging Neurosci** 12: 540424, 2020. doi:10.3389/fnagi.2020.540424.

1258. Backhaus J, Born J, Hoeckesfeld R, Fokuhl S, Hohagen F, Junghanns K. Midlife decline in declarative memory consolidation is correlated with a decline in slow wave sleep. **Learn Mem** 14: 336–341, 2007. doi:10.1101/lm.470507.

1259. Scullin MK. Sleep, memory, and aging: the link between slow-wave sleep and episodic memory changes from younger to older adults. **Psychol Aging** 28: 105–114, 2013. doi:10.1037/a0028830.

1260. Baran B, Mantua J, Spencer RM. Age-related changes in the sleep-dependent reorganization of declarative memories. **J Cogn Neurosci** 28: 792–802, 2016. doi:10.1162/jocn_a_00938.

1261. Mander BA, Marks SM, Vogel JW, Rao V, Lu B, Saletin JM, Ancoli-Israel S, Jagust WJ, Walker MP. β-amyloid disrupts human NREM slow waves and related hippocampus-dependent memory consolidation. **Nat Neurosci** 18: 1051–1057, 2015. doi:10.1038/nn.4035.

1262. Isotalus HK, Carr WJ, Blackman J, Averill GG, Radtke O, Selwood J, Williams R, Ford E, McCullagh L, McErlane J, O'Donnell C, Durant C, Bartsch U, Jones MW, Muñoz-Neira C, Wearn AR, Grogan JP, Coulthard EJ. L-DOPA increases slow-wave sleep duration and selectively modulates memory persistence in older adults. **Front Behav Neurosci** 17: 1096720, 2023. doi:10.3389/fnbeh.2023.1096720.

1263. Westerberg CE, Mander BA, Florczak SM, Weintraub S, Mesulam MM, Zee PC, Paller KA. Concurrent impairments in sleep and memory in amnestic mild cognitive impairment. **J Int Neuropsychol Soc** 18: 490–500, 2012. doi:10.1017/S135561771200001X.

1264. Osorio-Forero A, Cherrad N, Banterle L, Fernandez LM, Lüthi A. When the locus coeruleus speaks up in sleep: recent insights, emerging perspectives. **Int J Mol Sci** 23: 5028, 2022. doi:10.3390/ijms23095028.

1265. Champetier P, André C, Weber FD, Rehel S, Ourry V, Laniepce A, Lutz A, Bertran F, Cabé N, Pitel AL, Poisnel G, de la Sayette V, Vivien D, Chételat G, Rauchs G. Age-related changes in fast spindle clustering during non-rapid eye movement sleep and their relevance for memory consolidation. **Sleep** 46: zsac282, 2023. doi:10.1093/sleep/zsac282.

1266. Ladenbauer J, Ladenbauer J, Külzow N, Flöel A. Memory-relevant nap sleep physiology in healthy and pathological aging. **Sleep** 44: zsab002, 2021. doi:10.1093/sleep/zsab002.

1267. Muehlroth BE, Sander MC, Fandakova Y, Grandy TH, Rasch B, Shing YL, Werkle-Bergner M. Precise slow oscillation-spindle coupling promotes memory consolidation in younger and older adults. **Sci Rep** 9: 1940, 2019. doi:10.1038/s41598-018-36557-z.

1268. Muehlroth BE, Sander MC, Fandakova Y, Grandy TH, Rasch B, Lee Shing Y, Werkle-Bergner M. Memory quality modulates the effect of aging on memory consolidation during sleep: reduced maintenance but intact gain. **Neuroimage** 209: 116490, 2020. doi:10.1016/j.neuroimage.2019.116490.

1269. Seeck-Hirschner M, Baier PC, Weinhold SL, Dittmar M, Heiermann S, Aldenhoff JB, Göder R. Declarative memory performance is associated with the number of sleep spindles in elderly women. **Am J Geriatr Psychiatry** 20: 782–788, 2012. doi:10.1097/JGP.0b013e31823033da.

1270. Sonni A, Spencer RM. Sleep protects memories from interference in older adults. **Neurobiol Aging** 36: 2272–2281, 2015. doi:10.1016/j.neurobiolaging.2015.03.010.

1271. Schredl M, Weber B, Leins ML, Heuser I. Donepezil-induced REM sleep augmentation enhances memory performance in elderly, healthy persons. **Exp Gerontol** 36: 353–361, 2001. doi:10.1016/s0531-5565(00)00206-0.

1272. Hornung OP, Regen F, Danker-Hopfe H, Schredl M, Heuser I. The relationship between REM sleep and memory consolidation in old age and effects of cholinergic medication. **Biol Psychiatry** 61: 750–757, 2007. doi:10.1016/j.biopsych.2006.08.034.

1273. Mazzoni G, Gori S, Formicola G, Gneri C, Massetani R, Murri L, Salzarulo P. Word recall correlates with sleep cycles in elderly subjects. **J Sleep Res** 8: 185–188, 1999. doi:10.1046/j.1365-2869.1999.00154.x.

1274. Xie X, Xu Y, Wang R, Lei X, Yu J. Wake after sleep onset time moderated age-related emotional memory bias. **Exp Aging Res** 48: 362–372, 2022. doi:10.1080/0361073X.2021.1985359.

1275. Jones BJ, Schultz KS, Adams S, Baran B, Spencer RM. Emotional bias of sleep-dependent processing shifts from negative to positive with aging. **Neurobiol Aging** 45: 178–189, 2016. doi:10.1016/j.neurobiolaging.2016.05.019.

1276. Rodheim K, Kainec K, Noh E, Jones B, Spencer RM. Emotional memory consolidation during sleep is associated with slow oscillation-spindle coupling strength in young and older adults. **Learn Mem** 30: 237–244, 2023. doi:10.1101/lm.053685.122.

1277. Wilson JK, Baran B, Pace-Schott EF, Ivry RB, Spencer RM. Sleep modulates word-pair learning but not motor sequence learning in healthy older adults. **Neurobiol Aging** 33: 991–1000, 2012. doi:10.1016/j.neurobiolaging.2011.06.029.

1278. Spencer RM, Gouw AM, Ivry RB. Age-related decline of sleep-dependent consolidation. **Learn Mem** 14: 480–484, 2007. doi:10.1101/lm.569407.

1279. Backhaus W, Kempe S, Hummel FC. The effect of sleep on motor learning in the aging and stroke population - a systematic review. **Restor Neurol Neurosci** 34: 153–164, 2016. doi:10.3233/RNN-150521.

1280. Peters KR, Ray L, Smith V, Smith C. Changes in the density of stage 2 sleep spindles following motor learning in young and older adults. **J Sleep Res** 17: 23–33, 2008. doi:10.1111/j.1365-2869.2008.00634.x.

1281. King BR, Saucier P, Albouy G, Fogel SM, Rumpf JJ, Klann J, Buccino G, Binkofski F, Classen J, Karni A, Doyon J. Cerebral activation during initial motor learning forecasts subsequent sleep-facilitated memory consolidation in older adults. **Cereb Cortex** 27: 1588–1601, 2017. doi:10.1093/cercor/bhv347.

1282. Vien C, Boré A, Boutin A, Pinsard B, Carrier J, Doyon J, Fogel S. Thalamo-cortical white matter underlies motor memory consolidation via modulation of sleep spindles in young and older adults. **Neuroscience** 402: 104–115, 2019. doi:10.1016/j.neuroscience.2018.12.049.

1283. Mander BA, Zhu AH, Lindquist JR, Villeneuve S, Rao V, Lu B, Saletin JM, Ancoli-Israel S, Jagust WJ, Walker MP. White matter structure in older adults moderates the benefit of sleep spindles on motor memory consolidation. **J Neurosci** 37: 11675–11687, 2017. doi:10.1523/JNEUROSCI.3033-16.2017.

1284. Tucker M, McKinley S, Stickgold R. Sleep optimizes motor skill in older adults. **J Am Geriatr Soc** 59: 603–609, 2011. doi:10.1111/j.1532-5415.2011.03324.x.

1285. Vecsey CG, Park AJ, Khatib N, Abel T. Effects of sleep deprivation and aging on long-term and remote memory in mice. **Learn Mem** 22: 197–202, 2015. doi:10.1101/lm.036590.114.

1286. Yuan RK, Lopez MR, Ramos-Alvarez MM, Normandin ME, Thomas AS, Uygun DS, Cerda VR, Grenier AE, Wood MT, Gagliardi CM, Guajardo H, Muzzio IA. Differential effect of sleep deprivation on place cell representations, sleep architecture, and memory in young and old mice. **Cell Rep** 35: 109234, 2021. doi:10.1016/j.celrep.2021.109234.

1287. Rahman A, Languille S, Lamberty Y, Babiloni C, Perret M, Bordet R, Blin OJ, Jacob T, Auffret A, Schenker E, Richardson J, Pifferi F, Aujard F. Sleep deprivation impairs spatial retrieval but not spatial learning in the non-human primate grey mouse lemur. **PLoS One** 8: e64493, 2013. doi:10.1371/journal.pone.0064493.

1288. Rahman A, Lamberty Y, Schenker E, Cella M, Languille S, Bordet R, Richardson J, Pifferi F, Aujard F. Effects of acute administration of donepezil or memantine on sleep-deprivation-induced spatial memory deficit in young and aged non-human primate grey mouse lemurs (*Microcebus murinus*). **PLoS One** 12: e0184822, 2017. doi:10.1371/journal.pone.0184822.

1289. Malkani RG, Zee PC. Brain stimulation for improving sleep and memory. **Sleep Med Clin** 17: 505–521, 2022. doi:10.1016/j.jsmc.2022.06.013.

1290. Salfi F, D'Atri A, Tempesta D, De Gennaro L, Ferrara M. Boosting slow oscillations during sleep to improve memory function in elderly people: a review of the literature. **Brain Sci** 10: 300, 2020. doi:10.3390/brainsci10050300.

1291. Westerberg CE, Florczak SM, Weintraub S, Mesulam MM, Marshall L, Zee PC, Paller KA. Memory improvement via slow-oscillatory stimulation during sleep in older adults. **Neurobiol Aging** 36: 2577–2586, 2015. doi:10.1016/j.neurobiolaging.2015.05.014.

1292. Ladenbauer J, Külzow N, Passmann S, Antonenko D, Grittner U, Tamm S, Flöel A. Brain stimulation during an afternoon nap boosts slow oscillatory activity and memory consolidation in older adults. **Neuroimage** 142: 311–323, 2016. doi:10.1016/j.neuroimage.2016.06.057.

1293. Papalambros NA, Santostasi G, Malkani RG, Braun R, Weintraub S, Paller KA, Zee PC. Acoustic enhancement of sleep slow oscillations and concomitant memory improvement in older adults. **Front Hum Neurosci** 11: 109, 2017. doi:10.3389/fnhum.2017.00109.

1294. Papalambros NA, Weintraub S, Chen T, Grimaldi D, Santostasi G, Paller KA, Zee PC, Malkani RG. Acoustic enhancement of sleep slow oscillations in mild cognitive impairment. **Ann Clin Transl Neurol** 6: 1191–1201, 2019. doi:10.1002/acn3.796.

1295. Navarrete M, Schneider J, Ngo HV, Valderrama M, Casson AJ, Lewis PA. Examining the optimal timing for closed-loop auditory stimulation of slow-wave sleep in young and older adults. **Sleep** 43: zsz315, 2020. doi:10.1093/sleep/zsz315.

1296. Zeller CJ, Wunderlin M, Wicki K, Teunissen CE, Nissen C, Züst MA, Klöppel S. Multi-night acoustic stimulation is associated with better sleep, amyloid dynamics, and memory in older adults with cognitive impairment. **Geroscience** 46: 6157–6172, 2024. doi:10.1007/s11357-024-01195-z.

1297. Estrada C, Fernández-Gómez FJ, López D, Gonzalez-Cuello A, Tunez I, Toledo F, Blin O, Bordet R, Richardson JC, Fernandez-Villalba E, Herrero MT. Transcranial magnetic stimulation and aging: Effects on spatial learning and memory after sleep deprivation in *Octodon degus*. **Neurobiol Learn Mem** 125: 274–281, 2015. doi:10.1016/j.nlm.2015.09.011.

1298. Estrada C, López D, Conesa A, Fernández-Gómez FJ, Gonzalez-Cuello A, Toledo F, Tunez I, Blin O, Bordet R, Richardson JC, Fernandez-Villalba E, Herrero MT. Cognitive impairment after sleep deprivation rescued by transcranial magnetic stimulation application in *Octodon degus*. **Neurotox Res** 28: 361–371, 2015. doi:10.1007/s12640-015-9544-x.

1299. Eggert T, Dorn H, Sauter C, Nitsche MA, Bajbouj M, Danker-Hopfe H. No effects of slow oscillatory transcranial direct current stimulation (tDCS) on sleep-dependent memory consolidation in healthy elderly subjects. **Brain Stimul** 6: 938–945, 2013. doi:10.1016/j.brs.2013.05.006.

1300. Paßmann S, Külzow N, Ladenbauer J, Antonenko D, Grittner U, Tamm S, Flöel A. Boosting slow oscillatory activity using tDCS during early nocturnal slow wave sleep does not improve memory consolidation in healthy older adults. **Brain Stimul** 9: 730–739, 2016. doi:10.1016/j.brs.2016.04.016.

1301. Schneider J, Lewis PA, Koester D, Born J, Ngo HV. Susceptibility to auditory closed-loop stimulation of sleep slow oscillations changes with age. **Sleep** 43: zsaa111, 2020. doi:10.1093/sleep/zsaa111.

1302. Wunderlin M, Zeller CJ, Senti SR, Fehér KD, Suppiger D, Wyss P, Koenig T, Teunissen CE, Nissen C, Klöppel S, Züst MA. Acoustic stimulation during sleep predicts long-lasting increases in memory performance and beneficial amyloid response in older adults. **Age Ageing** 52: afad228, 2023. doi:10.1093/ageing/afad228.

1303. Johnson BP, Scharf SM, Verceles AC, Westlake KP. Sensorimotor performance is improved by targeted memory reactivation during a daytime nap in healthy older adults. **Neurosci Lett** 731: 134973, 2020. doi:10.1016/j.neulet.2020.134973.

1304. Cordi MJ, Schreiner T, Rasch B. No effect of vocabulary reactivation in older adults. **Neuropsychologia** 119: 253–261, 2018. doi:10.1016/j.neuropsychologia.2018.08.021.

1305. Nicolas J, Carrier J, Swinnen SP, Doyon J, Albouy G, King BR. Targeted memory reactivation during post-learning sleep does not enhance motor memory consolidation in older adults. **J Sleep Res** 33: e14027, 2024. doi:10.1111/jsr.14027.

1306. Peter-Derex L, Yammine P, Bastuji H, Croisile B. Sleep and Alzheimer's disease. **Sleep Med Rev** 19: 29–38, 2015. doi:10.1016/j.smrv.2014.03.007.

1307. Wang C, Holtzman DM. Bidirectional relationship between sleep and Alzheimer's disease: role of amyloid, tau, and other factors. **Neuropsychopharmacology** 45: 104–120, 2020. doi:10.1038/s41386-019-0478-5.

1308. Bishir M, Bhat A, Essa MM, Ekpo O, Ihunwo AO, Veeraraghavan VP, Mohan SK, Mahalakshmi AM, Ray B, Tuladhar S, Chang S, Chidambaram SB, Sakharkar MK, Guillemin GJ, Qoronfleh MW, Ojcius DM. Sleep deprivation and neurological disorders. **Biomed Res Int** 2020: 5764017, 2020. doi:10.1155/2020/5764017.

1309. Colvonen PJ, Straus LD, Acheson D, Gehrman P. A review of the relationship between emotional learning and memory, sleep, and PTSD. **Curr Psychiatry Rep** 21: 2, 2019. doi:10.1007/s11920-019-0987-2.

1310. Kirov R, Brand S. Sleep problems and their effect in ADHD. **Expert Rev Neurother** 14: 287–299, 2014. doi:10.1586/14737175.2014.885382.

1311. Scarpelli S, Gorgoni M, D'Atri A, Reda F, De Gennaro L. Advances in understanding the relationship between sleep and attention deficit-hyperactivity disorder (ADHD). **J Clin Med** 8: 1737, 2019. doi:10.3390/jcm8101737.

1312. Kotagal S, Broomall E. Sleep in children with autism spectrum disorder. **Pediatr Neurol** 47: 242–251, 2012. doi:10.1016/j.pediatrneurol.2012.05.007.

1313. Cipolli C, Mazzetti M, Plazzi G. Sleep-dependent memory consolidation in patients with sleep disorders. **Sleep Med Rev** 17: 91–103, 2013. doi:10.1016/j.smrv.2012.01.004.

1314. Perlis ML, Posner D, Riemann D, Bastien CH, Teel J, Thase M. Insomnia. **Lancet** 400: 1047–1060, 2022. doi:10.1016/S0140-6736(22)00879-0.

1315. Perlis ML, Pigeon WR, Grandner MA, Bishop TM, Riemann D, Ellis JG, Teel JR, Posner DA. Why treat insomnia? **J Prim Care Community Health** 12: 21501327211014084, 2021. doi:10.1177/21501327211014084.

1316. Shochat T, Umphress J, Israel AG, Ancoli-Israel S. Insomnia in primary care patients. **Sleep** 22, *Suppl* 1: S359–S365, 1999.

1317. Baglioni C, Regen W, Teghen A, Spiegelhalder K, Feige B, Nissen C, Riemann D. Sleep changes in the disorder of insomnia: a meta-analysis of polysomnographic studies. **Sleep Med Rev** 18: 195–213, 2014. doi:10.1016/j.smrv.2013.04.001.

1318. Bonnet MH, Arand DL. EEG arousal norms by age. **J Clin Sleep Med** 03: 271–274, 2007. doi:10.5664/jcsm.26796.

1319. Huang L, Zhou J, Li Z, Lei F, Tang X. Sleep perception and the multiple sleep latency test in patients with primary insomnia. **J Sleep Res** 21: 684–692, 2012. doi:10.1111/j.1365-2869.2012.01028.x.

1320. Perlis ML, Giles DE, Mendelson WB, Bootzin RR, Wyatt JK. Psychophysiological insomnia: the behavioural model and a neurocognitive perspective. **J Sleep Res** 6: 179–188, 1997. doi:10.1046/j.1365-2869.1997.00045.x.

1321. Perlis ML, Merica H, Smith MT, Giles DE. Beta EEG activity and insomnia. **Sleep Med Rev** 5: 363–374, 2001. doi:10.1053/smrv.2001.0151.

1322. Besset A, Villemin E, Tafti M, Billiard M. Homeostatic process and sleep spindles in patients with sleep-maintenance insomnia: effect of partial (21 h) sleep deprivation. **Electroencephalogr Clin Neurophysiol** 107: 122–132, 1998. doi:10.1016/S0013-4694(98)00048-0.

1323. Bastien CH, St-Jean G, Turcotte I, Morin CM, Lavallée M, Carrier J. Sleep spindles in chronic psychophysiological insomnia. **J Psychosom Res** 66: 59–65, 2009. doi:10.1016/j.jpsychores.2008.05.013.

1324. Bonnet MH, Arand DL. Hyperarousal and insomnia: state of the science. **Sleep Med Rev** 14: 9–15, 2010. doi:10.1016/j.smrv.2009.05.002.

1325. Riemann D, Spiegelhalder K, Feige B, Voderholzer U, Berger M, Perlis M, Nissen C. The hyperarousal model of insomnia: a review of the concept and its evidence. **Sleep Med Rev** 14: 19–31, 2010. doi:10.1016/j.smrv.2009.04.002.

1326. Feige B, Baglioni C, Spiegelhalder K, Hirscher V, Nissen C, Riemann D. The microstructure of sleep in primary insomnia: an overview and extension. **Int J Psychophysiol** 89: 171–180, 2013. doi:10.1016/j.ijpsycho.2013.04.002.

1327. Maes J, Verbraecken J, Willemen M, De Volder I, van Gastel A, Michiels N, Verbeek I, Vandekerckhove M, Wuyts J, Haex B, Willemen T, Exadaktylos V, Bulckaert A, Cluydts R**.** Sleep misperception, EEG characteristics and autonomic nervous system activity in primary insomnia: a retrospective study on polysomnographic data. **Int J Psychophysiol** 91: 163–171, 2014. doi:10.1016/j.ijpsycho.2013.10.012.

1328. Salas RE, Galea JM, Gamaldo AA, Gamaldo CE, Allen RP, Smith MT, Cantarero G, Lam BD, Celnik PA**.** Increased use-dependent plasticity in chronic insomnia. **Sleep** 37: 535–544, 2014. doi:10.5665/sleep.3492.

1329. van Someren EJ**.** Brain mechanisms of insomnia: new perspectives on causes and consequences. **Physiol Rev** 101: 995–1046, 2021. doi:10.1152/physrev.00046.2019.

1330. Choi A, Kim B, Labriola E, Wiest A, Wang Y, Smith J, Shin H, Jin X, An I, Hong J, Antila H, Thomas S, Bhattarai JP, Beier K, Ma M, Weber F, Chung S**.** Circuit mechanism underlying fragmented sleep and memory deficits in 16p11.2 deletion mouse model of autism. **iScience** 27: 111285, 2024. doi:10.1016/j.isci.2024.111285.

1331. Perlis ML, Jungquist C, Smith MT, Posner D**.** *Cognitive Behavioral Treatment of Insomnia*. Springer-Verlag, 2005.

1332. Wardle-Pinkston S, Slavish DC, Taylor DJ**.** Insomnia and cognitive performance: a systematic review and meta-analysis. **Sleep Med Rev** 48: 101205, 2019. doi:10.1016/j.smrv.2019.07.008.

1333. Chunhua X, Jiacui D, Xue L, Kai W**.** Impaired emotional memory and decision-making following primary insomnia. **Medicine (Baltimore)** 98: e16512, 2019. doi:10.1097/MD.0000000000016512.

1334. Wassing R, Schalkwijk F, Lakbila-Kamal O, Ramautar JR, Stoffers D, Mutsaerts HJ, Talamini LM, van Someren EJ**.** Haunted by the past: old emotions remain salient in insomnia disorder. **Brain** 142: 1783–1796, 2019. doi:10.1093/brain/awz089.

1335. Pérusse AD, De Koninck J, Pedneault-Drolet M, Ellis JG, Bastien CH**.** REM dream activity of insomnia sufferers: a systematic comparison with good sleepers. **Sleep Med** 20: 147–154, 2016. doi:10.1016/j.sleep.2015.08.007.

1336. Feige B, Nanovska S, Baglioni C, Bier B, Cabrera L, Diemers S, Quellmalz M, Siegel M, Xeni I, Szentkiralyi A, Doerr J-P, Riemann D**.** Insomnia—perchance a dream? Results from a NREM/REM sleep awakening study in good sleepers and patients with insomnia. **Sleep** 41: 10.1093/sleep/zsy032, 2018. doi:10.1093/sleep/zsy032.

1337. Cellini N**.** Memory consolidation in sleep disorders. **Sleep Med Rev** 35: 101–112, 2017. doi:10.1016/j.smrv.2016.09.003.

1338. Goerke M, Müller NG, Cohrs S**.** Sleep-dependent memory consolidation and its implications for psychiatry. **J Neural Transm (Vienna)** 124: 163–178, 2017. doi:10.1007/s00702-015-1476-3.

1339. Backhaus J, Junghanns K, Born J, Hohaus K, Faasch F, Hohagen F**.** Impaired declarative memory consolidation during sleep in patients with primary insomnia: influence of sleep architecture and nocturnal cortisol release. **Biol Psychiatry** 60: 1324–1330, 2006. doi:10.1016/j.biopsych.2006.03.051.

1340. Nissen C, Kloepfer C, Feige B, Piosczyk H, Spiegelhalder K, Voderholzer U, Riemann D**.** Sleep-related memory consolidation in primary insomnia. **J Sleep Res** 20: 129–136, 2011. doi:10.1111/j.1365-2869.2010.00872.x.

1341. Griessenberger H, Heib DP, Lechinger J, Luketina N, Petzka M, Moeckel T, Hoedlmoser K, Schabus M**.** Susceptibility to declarative memory interference is pronounced in primary insomnia. **PLoS One** 8: e57394, 2013. doi:10.1371/journal.pone.0057394.

1342. Goerke M, Cohrs S, Rodenbeck A, Grittner U, Sommer W, Kunz D**.** Declarative memory consolidation during the first night in a sleep lab: the role of REM sleep and cortisol. **Psychoneuroendocrinology** 38: 1102–1111, 2013. doi:10.1016/j.psyneuen.2012.10.019.

1343. Nissen C, Kloepfer C, Nofzinger EA, Feige B, Voderholzer U, Riemann D**.** Impaired sleep-related memory consolidation in primary insomnia—a pilot study. **Sleep** 29: 1068–1073, 2006. doi:10.1093/sleep/29.8.1068.

1344. Cellini N, de Zambotti M, Covassin N, Sarlo M, Stegagno L**.** Impaired off-line motor skills consolidation in young primary insomniacs. **Neurobiol Learn Mem** 114: 141–147, 2014. doi:10.1016/j.nlm.2014.06.006.

1345. Seo J, Moore KN, Gazecki S, Bottary RM, Milad MR, Song H, Pace-Schott EF**.** Delayed fear extinction in individuals with insomnia disorder. **Sleep** 41: zsy095, 2018. doi:10.1093/sleep/zsy095.

1346. Seugnet L, Dissel S, Thimgan M, Cao L, Shaw PJ**.** Identification of genes that maintain behavioral and structural plasticity during sleep loss. **Front Neural Circuits** 11: 79, 2017. doi:10.3389/fncir.2017.00079.

1347. Sharma R, Sahota P, Thakkar MM**.** Severe and protracted sleep disruptions in mouse model of post-traumatic stress disorder. **Sleep** 41: 10.1093/sleep/zsy003, 2018. doi:10.1093/sleep/zsy003.

1348. MacFarlane J, Morin CM, Montplaisir J**.** Hypnotics in insomnia: the experience of zolpidem. **Clin Ther** 36: 1676–1701, 2014. doi:10.1016/j.clinthera.2014.09.017.

1349. Niknazar M, Krishnan GP, Bazhenov M, Mednick SC**.** Coupling of thalamocortical sleep oscillations are important for memory consolidation in humans. **PLoS One** 10: e0144720, 2015. doi:10.1371/journal.pone.0144720.

1350. Zhang J, Yetton B, Whitehurst LN, Naji M, Mednick SC**.** The effect of zolpidem on memory consolidation over a night of sleep. **Sleep** 43: zsaa084, 2020. doi:10.1093/sleep/zsaa084.

1351. Simon KC, Whitehurst LN, Zhang J, Mednick SC**.** Zolpidem maintains memories for negative emotions across a night of sleep. **Affect Sci** 3: 389–399, 2022. doi:10.1007/s42761-021-00079-1.

1352. Carbone J, Bibián C, Reischl P, Born J, Forcato C, Diekelmann S**.** The effect of zolpidem on targeted memory reactivation during sleep. **Learn Mem** 28: 307–318, 2021. doi:10.1101/lm.052787.120.

1353. Fairweather DB, Kerr JS, Hindmarch I**.** The effects of acute and repeated doses of zolpidem on subjective sleep, psychomotor performance and cognitive function in elderly volunteers. **Eur J Clin Pharmacol** 43: 597–601, 1992. doi:10.1007/BF02284957.

1354. Monti JM**.** Effect of zolpidem on sleep in insomniac patients. **Eur J Clin Pharmacol** 36: 461–466, 1989. doi:10.1007/BF00558070.

1355. Angus WR, Romney DM**.** The effect of diazepam on patients' memory. **J Clin Psychopharmacol** 4: 203–206, 1984.

1356. Gamble MC, Katsuki F, McCoy JG, Strecker RE, McKenna JT**.** The dual orexinergic receptor antagonist DORA-22 improves the sleep disruption and memory impairment produced by a rodent insomnia model. **Sleep** 43: zsz241, 2020. doi:10.1093/sleep/zsz241.

1357. Schabus M, Heib DP, Lechinger J, Griessenberger H, Klimesch W, Pawlizki A, Kunz AB, Sterman BM, Hoedlmoser K**.** Enhancing sleep quality and memory in insomnia using instrumental sensorimotor rhythm conditioning. **Biol Psychol** 95: 126–134, 2014. doi:10.1016/j.biopsycho.2013.02.020.

1358. Dudysová D, Janků K, Piorecký M, Hantáková V, Orendáčová M, Piorecká V, Štrobl J, Kliková M, Ngo HV, Kopřivová J. Closed-loop auditory stimulation of slow-wave sleep in chronic insomnia: a pilot study. **J Sleep Res** 33: e14179, 2024. doi:10.1111/jsr.14179.

1359. You S, Lv T, Qin R, Hu Z, Ke Z, Yao W, Zhao H, Bai F. Neuro-navigated rTMS Improves sleep and cognitive impairment via regulating sleep-related networks' spontaneous activity in AD spectrum patients. **Clin Interv Aging** 18: 1333–1349, 2023. doi:10.2147/CIA.S416992.

1360. Schwartz S, Clerget A, Perogamvros L. Enhancing imagery rehearsal therapy for nightmares with targeted memory reactivation. **Curr Biol** 32: 4808–4816.e4, 2022. doi:10.1016/j.cub.2022.09.032.

1361. van der Heijden AC, van den Heuvel OA, van der Werf YD, Talamini LM, van Marle HJF. Sleep as a window to target traumatic memories. **Neurosci Biobehav Rev** 140: 104765, 2022. doi:10.1016/j.neubiorev.2022.104765.

1362. Reed T, Cohen Kadosh R. Transcranial electrical stimulation (tES) mechanisms and its effects on cortical excitability and connectivity. **J Inherit Metab Dis** 41: 1123–1130, 2018. doi:10.1007/S10545-018-0181-4.

1363. Yavari F, Jamil A, Mosayebi Samani M, Vidor LP, Nitsche MA. Basic and functional effects of transcranial electrical stimulation (tES)—an introduction. **Neurosci Biobehav Rev** 85: 81–92, 2018. doi:10.1016/j.neubiorev.2017.06.015.

1364. Liu A, Vöröslakos M, Kronberg G, Henin S, Krause MR, Huang Y, Opitz A, Mehta A, Pack CC, Krekelberg B, Berényi A, Parra LC, Melloni L, Devinsky O, Buzsáki G. Immediate neurophysiological effects of transcranial electrical stimulation. **Nat Commun** 9: 5092, 2018. doi:10.1038/s41467-018-07233-7.

1365. Bland NS, Sale MV. Current challenges: the ups and downs of tACS. **Exp Brain Res** 237: 3071–3088, 2019. doi:10.1007/s00221-019-05666-0.

1366. Fröhlich F. Experiments and models of cortical oscillations as a target for noninvasive brain stimulation. **Prog Brain Res** 222: 41–73, 2015. doi:10.1016/bs.pbr.2015.07.025.

1367. Jamil A, Nitsche MA. What effect does tDCS have on the brain? Basic physiology of tDCS. **Curr Behav Neurosci Rep** 4: 331–340, 2017. doi:10.1007/s40473-017-0134-5.

1368. Lafon B, Henin S, Huang Y, Friedman D, Melloni L, Thesen T, Doyle W, Buzsáki G, Devinsky O, Parra LC, A Liu A. Low frequency transcranial electrical stimulation does not entrain sleep rhythms measured by human intracranial recordings. **Nat Commun** 9: 949, 2018. doi:10.1038/s41467-017-01045-x.

1369. Vöröslakos M, Takeuchi Y, Brinyiczki K, Zombori T, Oliva A, Fernández-Ruiz A, Kozák G, Kincses ZT, Iványi B, Buzsáki G, Berényi A. Direct effects of transcranial electric stimulation on brain circuits in rats and humans. **Nat Commun** 9: 483, 2018. doi:10.1038/s41467-018-02928-3.

1370. Binder S, Rawohl J, Born J, Marshall L. Transcranial slow oscillation stimulation during NREM sleep enhances acquisition of the radial maze task and modulates cortical network activity in rats. **Front Behav Neurosci** 7: 220, 2013. doi:10.3389/fnbeh.2013.00220.

1371. Binder S, Berg K, Gasca F, Lafon B, Parra LC, Born J, Marshall L. Transcranial slow oscillation stimulation during sleep enhances memory consolidation in rats. **Brain Stimul** 7: 508–515, 2014. doi:10.1016/j.brs.2014.03.001.

1372. Cellini N, Shimizu RE, Connolly PM, Armstrong DM, Hernandez LT, Polakiewicz AG, Estrada R, Aguilar-Simon M, Weisend MP, Mednick SC, Simons SB. Short duration repetitive transcranial electrical stimulation during sleep enhances declarative memory of facts. **Front Hum Neurosci** 13: 123, 2019. doi:10.3389/fnhum.2019.00123.

1373. Johnson JM, Durrant SJ. The effect of cathodal transcranial direct current stimulation during rapid eye-movement sleep on neutral and emotional memory. **R Soc Open Sci** 5: 172353, 2018. doi:10.1098/rsos.172353.

1374. Del Felice A, Magalini A, Masiero S. Slow-oscillatory transcranial direct current stimulation modulates memory in temporal lobe epilepsy by altering sleep spindle generators: a possible rehabilitation tool. **Brain Stimul** 8: 567–573, 2015. doi:10.1016/j.brs.2015.01.410.

1375. Prehn-Kristensen A, Munz M, Göder R, Wilhelm I, Korr K, Vahl W, Wiesner CD, Baving L. Transcranial oscillatory direct current stimulation during sleep improves declarative memory consolidation in children with attention-deficit/hyperactivity disorder to a level comparable to healthy controls. **Brain Stimul** 7: 793–799, 2014. doi:10.1016/j.brs.2014.07.036.

1376. Ambrus GG, Pisoni A, Primaßin A, Turi Z, Paulus W, Antal A. Bi-frontal transcranial alternating current stimulation in the ripple range reduced overnight forgetting. **Front Cell Neurosci** 9: 374, 2015. doi:10.3389/fncel.2015.00374.

1377. Jones AP, Bryant NB, Robert BM, Mullins TS, Trumbo MCS, Ketz NA, Howard MD, Pilly PK, Clark VP. Closed-loop tACS delivered during slow-wave sleep reduces retroactive interference on a paired-associates learning task. **Brain Sci** 13: 468, 2023. doi:10.3390/brainsci13030468.

1378. Ketz N, Jones AP, Bryant NB, Clark VP, Pilly PK. Closed-loop slow-wave tACS improves sleep-dependent long-term memory generalization by modulating endogenous oscillations. **J Neurosci** 38: 7314–7326, 2018. doi:10.1523/JNEUROSCI.0273-18.2018.

1379. Jones AP, Choe J, Bryant NB, Robinson CS, Ketz NA, Skorheim SW, Combs A, Lamphere ML, Robert B, Gill HA, Heinrich MD, Howard MD, Clark VP, Pilly PK. Dose-dependent effects of closed-loop tACS delivered during slow-wave oscillations on memory consolidation. **Front Neurosci** 12: 867, 2018. doi:10.3389/fnins.2018.00867.

1380. Lustenberger C, Boyle MR, Alagapan S, Mellin JM, Vaughn BV, Fröhlich F. Feedback-controlled transcranial alternating current stimulation reveals a functional role of sleep spindles in motor memory consolidation. **Curr Biol** 26: 2127–2136, 2016. doi:10.1016/j.cub.2016.06.044.

1381. Garside P, Arizpe J, Lau CI, Goh C, Walsh V. Cross-hemispheric alternating current stimulation during a nap disrupts slow wave activity and associated memory consolidation. **Brain Stimul** 8: 520–527, 2015. doi:10.1016/j.brs.2014.12.010.

1382. Bueno-Lopez A, Eggert T, Dorn H, Danker-Hopfe H. Slow oscillatory transcranial direct current stimulation (so-tDCS) during slow wave sleep has no effects on declarative memory in healthy young subjects. **Brain Stimul** 12: 948–958, 2019. doi:10.1016/j.brs.2019.02.012.

1383. Sahlem GL, Badran BW, Halford JJ, Williams NR, Korte JE, Leslie K, Strachan M, Breedlove JL, Runion J, Bachman DL, Uhde TW, Borckardt JJ, George MS. Oscillating square wave transcranial direct current stimulation (tDCS) delivered during slow wave sleep does not improve declarative memory more than sham: a randomized sham controlled crossover study. **Brain Stimul** 8: 528–534, 2015. doi:10.1016/j.brs.2015.01.414.

1384. Ruch S, Fehér K, Homan S, Morishima Y, Mueller SM, Mueller SV, Dierks T, Grieder M. Bi-temporal anodal transcranial direct current

stimulation during slow-wave sleep boosts slow-wave density but not memory consolidation. **Brain Sci** 11: 410, 2021. doi:10.3390/brainsci11040410.

1385. Savic B, Müri R, Meier B**.** A single session of prefrontal cortex transcranial direct current stimulation does not modulate implicit task sequence learning and consolidation. **Brain Stimul** 10: 567–575, 2017. doi:10.1016/j.brs.2017.01.001.

1386. Baselgia S, Kasten FH, Herrmann CS, Rasch B, Paβmann S**.** No benefit in memory performance after nocturnal memory reactivation coupled with theta-tACS. **Clocks Sleep** 6: 211–233, 2024. doi:10.3390/clockssleep6020015.

1387. Koo PC, Mölle M, Marshall L**.** Efficacy of slow oscillatory-transcranial direct current stimulation on EEG and memory—contribution of an inter-individual factor. **Eur J Neurosci** 47: 812–823, 2018. doi:10.1111/ejn.13877.

1388. Marshall L, Binder S**.** Contribution of transcranial oscillatory stimulation to research on neural networks: an emphasis on hippocampo-neocortical rhythms. **Front Hum Neurosci** 7: 614, 2013. doi:10.3389/fnhum.2013.00614.

1389. Barham MP, Enticott PG, Conduit R, Lum JA**.** Transcranial electrical stimulation during sleep enhances declarative (but not procedural) memory consolidation: evidence from a meta-analysis. **Neurosci Biobehav Rev** 63: 65–77, 2016. doi:10.1016/j.neubiorev.2016.01.009.

1390. Bergmann TO, Groppa S, Seeger M, Mölle M, Marshall L, Siebner HR**.** Acute changes in motor cortical excitability during slow oscillatory and constant anodal transcranial direct current stimulation. **J Neurophysiol** 102: 2303–2311, 2009. doi:10.1152/jn.00437.2009.

1391. Bergmann TO, Mölle M, Schmidt MA, Lindner C, Marshall L, Born J, Siebner HR**.** EEG-guided transcranial magnetic stimulation reveals rapid shifts in motor cortical excitability during the human sleep slow oscillation. **J Neurosci** 32: 243–253, 2012. doi:10.1523/JNEUROSCI.4792-11.2012.

1392. Kuhn M, Maier JG, Wolf E, Mainberger F, Feige B, Maywald S, Bredl A, Michel M, Sendelbach N, Normann C, Klöppel S, Eckert A, Riemann D, Nissen C**.** Indices of cortical plasticity after therapeutic sleep deprivation in patients with major depressive disorder. **J Affect Disord** 277: 425–435, 2020. doi:10.1016/j.jad.2020.08.052.

1393. Massimini M, Ferrarelli F, Esser SK, Riedner BA, Huber R, Murphy M, Peterson MJ, Tononi G**.** Triggering sleep slow waves by transcranial magnetic stimulation. **Proc Natl Acad Sci USA** 104: 8496–8501, 2007. doi:10.1073/pnas.0702495104.

1394. Centorino MB, Bajor LA, Gootam PK, Nakase-Richardson R, Kozel FA**.** The relationship of transcranial magnetic stimulation with sleep and plasticity. **J Psychiatr Pract** 26: 434–443, 2020. doi:10.1097/PRA.0000000000000506.

1395. Ma Y**.** Application of noninvasive brain stimulation for sleep quality enhancement and cognitive improvement. **Stud Health Technol Inform** 308: 556–561, 2023. doi:10.3233/SHTI230884.

1396. Luber B, Steffener J, Tucker A, Habeck C, Peterchev AV, Deng ZD, Basner RC, Stern Y, Lisanby SH**.** Extended remediation of sleep deprived-induced working memory deficits using fMRI-guided transcranial magnetic stimulation. **Sleep** 36: 857–871, 2013. doi:10.5665/sleep.2712.

1397. Martinez-Cancino DP, Azpiroz-Leehan J, Jimenez-Angeles L, Garcia-Quintanar A, Santana-Miranda R**.** Effects of high frequency rTMS on sleep deprivation: a pilot study. **Annu Int Conf IEEE Eng Med Biol Soc** 2016: 5937–5940, 2016. doi:10.1109/EMBC.2016.7592080.

1398. Zheng X, Wang R, Ma B, Zhang J, Qian X, Fang Q, An J**.** rTMS reduces spatial learning and memory deficits induced by sleep deprivation possibly via suppressing the expression of kynurenine 3-monooxygenase in rats. **Behav Brain Res** 456: 114704, 2024. doi:10.1016/j.bbr.2023.114704.

1399. Galea JM, Albert NB, Ditye T, Miall RC**.** Disruption of the dorsolateral prefrontal cortex facilitates the consolidation of procedural skills. **J Cogn Neurosci** 22: 1158–1164, 2010. doi:10.1162/jocn.2009.21259.

1400. Breton J, Robertson EM**.** Dual enhancement mechanisms for overnight motor memory consolidation. **Nat Hum Behav** 1: 111, 2017. doi:10.1038/s41562-017-0111.

1401. Di Biase L, Falato E, Di Lazzaro V**.** Transcranial focused ultrasound (tFUS) and transcranial unfocused ultrasound (tUS) neuromodulation: from theoretical principles to stimulation practices. **Front Neurol** 10: 549, 2019. doi:10.3389/fneur.2019.00549.

1402. Ramachandran S, Niu X, Yu K, He B**.** Transcranial ultrasound neuromodulation induces neuronal correlation change in the rat somatosensory cortex. **J Neural Eng** 19: 056002, 2022. doi:10.1088/1741-2552/ac889f.

1403. Wang T, Wang X, Tian Y, Gang W, Li X, Yan J, Yuan Y**.** Modulation effect of low-intensity transcranial ultrasound stimulation on REM and NREM sleep. **Cereb Cortex** 33: 5238–5250, 2023. doi:10.1093/cercor/bhac413.

1404. Dong S, Xie Z, Yuan Y**.** Transcranial ultrasound stimulation modulates neural activities during NREM and REM depending on the stimulation phase of slow oscillations and theta waves in the hippocampus. **Cereb Cortex** 33: 8956–8966, 2023. doi:10.1093/cercor/bhad174.

1405. Leminen MM, Virkkala J, Saure E, Paajanen T, Zee PC, Santostasi G, Hublin C, Müller K, Porkka-Heiskanen T, Huotilainen M, Paunio T**.** Enhanced memory consolidation via automatic sound stimulation during non-REM sleep. **Sleep** 40: zsx003, 2017. doi:10.1093/sleep/zsx003.

1406. Zeller CJ, Züst MA, Wunderlin M, Nissen C, Klöppel S**.** The promise of portable remote auditory stimulation tools to enhance slow-wave sleep and prevent cognitive decline. **J Sleep Res** 32: e13818, 2023. doi:10.1111/jsr.13818.

1407. Ong JL, Lo JC, Chee NI, Santostasi G, Paller KA, Zee PC, Chee MW**.** Effects of phase-locked acoustic stimulation during a nap on EEG spectra and declarative memory consolidation. **Sleep Med** 20: 88–97, 2016. doi:10.1016/j.sleep.2015.10.016.

1408. Krugliakova E, Volk C, Jaramillo V, Sousouri G, Huber R**.** Changes in cross-frequency coupling following closed-loop auditory stimulation in non-rapid eye movement sleep. **Sci Rep** 10: 10628, 2020. doi:10.1038/s41598-020-67392-w.

1409. Ruch S, Schmidig FJ, Knüsel L, Henke K**.** Closed-loop modulation of local slow oscillations in human NREM sleep. **Neuroimage** 264: 119682, 2022. doi:10.1016/j.neuroimage.2022.119682.

1410. Leach S, Krugliakova E, Sousouri G, Snipes S, Skorucak J, Schühle S, Müller M, Ferster ML, Da Poian G, Karlen W, Huber R**.** Acoustically evoked K-complexes together with sleep spindles boost verbal declarative memory consolidation in healthy adults. **Sci Rep** 14: 19184, 2024. doi:10.1038/s41598-024-67701-7.

1411. Weigenand A, Mölle M, Werner F, Martinetz T, Marshall L**.** Timing matters: open-loop stimulation does not improve overnight consolidation of word pairs in humans. **Eur J Neurosci** 44: 2357–2368, 2016. doi:10.1111/ejn.13334.

1412. Fehér KD, Omlin X, Tarokh L, Schneider CL, Morishima Y, Züst MA, Wunderlin M, Koenig T, Hertenstein E, Ellenberger B, Ruch S, Schmidig F, Mikutta C, Trinca E, Senn W, Feige B, Klöppel S, Nissen C. Feasibility, efficacy, and functional relevance of automated auditory closed-loop suppression of slow-wave sleep in humans. **J Sleep Res** 32: e13846, 2023. doi:10.1111/jsr.13846.

1413. Ngo HV, Seibold M, Boche DC, Mölle M, Born J. Insights on auditory closed-loop stimulation targeting sleep spindles in slow oscillation up-states. **J Neurosci Methods** 316: 117–124, 2019. doi:10.1016/j.jneumeth.2018.09.006.

1414. Harrington MO, Ngo HV, Cairney SA. No benefit of auditory closed-loop stimulation on memory for semantically-incongruent associations. **Neurobiol Learn Mem** 183: 107482, 2021. doi:10.1016/j.nlm.2021.107482.

1415. Henin S, Borges H, Shankar A, Sarac C, Melloni L, Friedman D, Flinker A, Parra LC, Buzsaki G, Devinsky O, Liu A. Closed-loop acoustic stimulation enhances sleep oscillations but not memory performance. **eNeuro** 6: ENEURO.0306-19.2019, 2019. doi:10.1523/ENEURO.0306-19.2019.

1416. Baxter BS, Mylonas D, Kwok KS, Talbot CE, Patel R, Zhu L, Vangel M, Stickgold R, Manoach DS. The effects of closed-loop auditory stimulation on sleep oscillatory dynamics in relation to motor procedural memory consolidation. **Sleep** 46: zsad206, 2023. doi:10.1093/sleep/zsad206.

1417. Aksamaz S, Mölle M, Akinola EO, Gromodka E, Bazhenov M, Marshall L. Single closed-loop acoustic stimulation targeting memory consolidation suppressed hippocampal ripple and thalamo-cortical spindle activity in mice. **Eur J Neurosci** 59: 595–612, 2024. doi:10.1111/ejn.16116.

1418. Wunderlin M, Züst MA, Fehér KD, Klöppel S, Nissen C. The role of slow wave sleep in the development of dementia and its potential for preventative interventions. **Psychiatry Res Neuroimaging** 306: 111178, 2020. doi:10.1016/j.pscychresns.2020.111178.

1419. Wunderlin M, Züst MA, Hertenstein E, Fehér KD, Schneider CL, Klöppel S, Nissen C. Modulating overnight memory consolidation by acoustic stimulation during slow-wave sleep: a systematic review and meta-analysis. **Sleep** 44: zsaa296, 2021. doi:10.1093/sleep/zsaa296.

1420. Grimaldi D, Papalambros NA, Zee PC, Malkani RG. Neurostimulation techniques to enhance sleep and improve cognition in aging. **Neurobiol Dis** 141: 104865, 2020. doi:10.1016/j.nbd.2020.104865.

1421. Malkani RG, Zee PC. Brain stimulation for improving sleep and memory. **Sleep Med Clin** 15: 101–115, 2020. doi:10.1016/j.jsmc.2019.11.002.

1422. Scholes S, Santisteban JA, Zhang Y, Bertone A, Gruber R. Modulation of slow-wave sleep: implications for psychiatry. **Curr Psychiatry Rep** 22: 52, 2020. doi:10.1007/s11920-020-01175-y.

1423. Diep C, Ftouni S, Manousakis JE, Nicholas CL, Drummond SPA, Anderson C. Acoustic slow wave sleep enhancement via a novel, automated device improves executive function in middle-aged men. **Sleep** 43: zsz197, 2020. doi:10.1093/sleep/zsz197.

1424. Harrington MO, Cairney SA. Sounding it out: auditory stimulation and overnight memory processing. **Curr Sleep Med Rep** 7: 112–119, 2021. doi:10.1007/s40675-021-00207-0.

1425. Debellemanière E, Pinaud C, Schneider J, Arnal PJ, Casson AJ, Chennaoui M, Galtier M, Navarrete M, Lewis PA. Optimising sounds for the driving of sleep oscillations by closed-loop auditory stimulation. **J Sleep Res** 31: e13676, 2022. doi:10.1111/jsr.13676.

1426. Jourde HR, Merlo R, Brooks M, Rowe M, Coffey EB. The neurophysiology of closed-loop auditory stimulation in sleep: a magnetoencephalography study. **Eur J Neurosci** 59: 613–640, 2024. doi:10.1111/ejn.16132.

1427. Navarrete M, Arthur S, Treder MS, Lewis PA. Ongoing neural oscillations predict the post-stimulus outcome of closed loop auditory stimulation during slow-wave sleep. **Neuroimage** 253: 119055, 2022. doi:10.1016/j.neuroimage.2022.119055.

1428. Wei Y, Krishnan GP, Marshall L, Martinetz T, Bazhenov M. Stimulation augments spike sequence replay and memory consolidation during slow-wave sleep. **J Neurosci** 40: 811–824, 2020. doi:10.1523/JNEUROSCI.1427-19.2019.

1429. Mushtaq M, Marshall L, Ul Haq R, Martinetz T. Possible mechanisms to improve sleep spindles via closed loop stimulation during slow wave sleep: a computational study. **PLoS One** 19: e0306218, 2024. doi:10.1371/journal.pone.0306218.

1430. Bayer L, Constantinescu I, Perrig S, Vienne J, Vidal PP, Mühlethaler M, Schwartz S. Rocking synchronizes brain waves during a short nap. **Curr Biol** 21: R461–R462, 2011. doi:10.1016/j.cub.2011.05.012.

1431. Schreiner T, Staresina BP. Sleep: rock and swing versus toss and turn. **Curr Biol** 29: R86–R88, 2019. doi:10.1016/j.cub.2018.12.035.

1432. Kompotis K, Hubbard J, Emmenegger Y, Perrault A, Mühlethaler M, Schwartz S, Bayer L, Franken P. Rocking promotes sleep in mice through rhythmic stimulation of the vestibular system. **Curr Biol** 29: 392–401.e4, 2019. doi:10.1016/j.cub.2018.12.007.

1433. Choi SH, Kwon HB, Jin HW, Yoon H, Lee MH, Lee YJ, Park KS. Weak closed-loop vibrational stimulation improves the depth of slow-wave sleep and declarative memory consolidation. **Sleep** 44: zsaa285, 2021. doi:10.1093/sleep/zsaa285.

1434. Schouten DI, Pereira SIR, Tops M, Louzada FM. State of the art on targeted memory reactivation: Sleep your way to enhanced cognition. **Sleep Med Rev** 32: 123–131, 2017. doi:10.1016/j.smrv.2016.04.002.

1435. Carbone J, Diekelmann S. An update on recent advances in targeted memory reactivation during sleep. **npj Sci Learn** 9: 31, 2024. doi:10.1038/s41539-024-00244-8.

1436. Vargas IM, Schechtman E, Paller KA. Targeted memory reactivation during sleep to strengthen memory for arbitrary pairings. **Neuropsychologia** 124: 144–150, 2019. doi:10.1016/j.neuropsychologia.2018.12.017.

1437. Zwaka H, Bartels R, Gora J, Franck V, Culo A, Götsch M, Menzel R. Context odor presentation during sleep enhances memory in honeybees. **Curr Biol** 25: 2869–2874, 2015. doi:10.1016/j.cub.2015.09.069.

1438. Bendor D, Wilson MA. Biasing the content of hippocampal replay during sleep. **Nat Neurosci** 15: 1439–1444, 2012. doi:10.1038/nn.3203.

1439. Tamminen J, Mebude M. Reinstatement of odour context cues veridical memories but not false memories. **Memory** 27: 575–579, 2019. doi:10.1080/09658211.2018.1513041.

1440. Witkowski S, Noh S, Lee V, Grimaldi D, Preston AR, Paller KA. Does memory reactivation during sleep support generalization at the cost of memory specifics? **Neurobiol Learn Mem** 182: 107442, 2021. doi:10.1016/j.nlm.2021.107442.

1441. Batterink LJ, Paller KA. Sleep-based memory processing facilitates grammatical generalization: evidence from targeted memory reactivation. **Brain Lang** 167: 83–93, 2017. doi:10.1016/j.bandl.2015.09.003.

1442. Zhao X, Chen PH, Chen J, Sun H. Manipulated overlapping reactivation of multiple memories promotes explicit gist abstraction. **Neurobiol Learn Mem** 213: 107953, 2024. doi:10.1016/j.nlm.2024.107953.

1443. Sifuentes Ortega R, Peigneux P. Does targeted memory reactivation during SWS and REM sleep have differential effects on mnemonic discrimination and generalization? **Sleep**, 47: zsae114, 2024. doi:10.1093/sleep/zsae114.

1444. Seibold M, Rasch B, Born J, Diekelmann S. Reactivation of interference during sleep does not impair ongoing memory consolidation. **Memory** 26: 377–384, 2018. doi:10.1080/09658211.2017.1329442.

1445. Ashton JE, Cairney SA, Gaskell MG. No effect of targeted memory reactivation during slow-wave sleep on emotional recognition memory. **J Sleep Res** 27: 129–137, 2018. doi:10.1111/jsr.12542.

1446. Denis D, Payne JD. Targeted memory reactivation during nonrapid eye movement sleep enhances neutral, but not negative, components of memory. **eNeuro** 11: ENEURO.0285-23.2024, 2024. doi:10.1523/ENEURO.0285-23.2024.

1447. Lehmann M, Schreiner T, Seifritz E, Rasch B. Emotional arousal modulates oscillatory correlates of targeted memory reactivation during NREM, but not REM sleep. **Sci Rep** 6: 39229, 2016. doi:10.1038/srep39229.

1448. Pereira SI, Tsimpanouli ME, Hutchison I, Schneider J, Anderson IM, McFarquhar M, Elliott R, Lewis PA. Cueing emotional memories during slow wave sleep modulates next-day activity in the orbitofrontal cortex and the amygdala. **Neuroimage** 253: 119120, 2022. doi:10.1016/j.neuroimage.2022.119120.

1449. Xia T, Chen D, Zeng S, Yao Z, Liu J, Qin S, Paller KA, Torres Platas SG, Antony JW, Hu X. Aversive memories can be weakened during human sleep via the reactivation of positive interfering memories. **Proc Natl Acad Sci USA** 121: e2400678121, 2024. doi:10.1073/pnas.2400678121.

1450. Hu X, Antony JW, Creery JD, Vargas IM, Bodenhausen GV, Paller KA. Cognitive neuroscience. Unlearning implicit social biases during sleep. **Science** 348: 1013–1015, 2015. doi:10.1126/science.aaa3841.

1451. Xia T, Antony JW, Paller KA, Hu X. Targeted memory reactivation during sleep influences social bias as a function of slow-oscillation phase and delta power. **Psychophysiology** 60: e14224, 2023. doi:10.1111/psyp.14224.

1452. Schönauer M, Geisler T, Gais S. Strengthening procedural memories by reactivation in sleep. **J Cogn Neurosci** 26: 143–153, 2014. doi:10.1162/jocn_a_00471.

1453. Johnson BP, Scharf SM, Verceles AC, Westlake KP. Use of targeted memory reactivation enhances skill performance during a nap and enhances declarative memory during wake in healthy young adults. **J Sleep Res** 28: e12832, 2019. doi:10.1111/jsr.12832.

1454. Rihm JS, Diekelmann S, Born J, Rasch B. Reactivating memories during sleep by odors: odor specificity and associated changes in sleep oscillations. **J Cogn Neurosci** 26: 1806–1818, 2014. doi:10.1162/jocn_a_00579.

1455. Bar E, Marmelshtein A, Arzi A, Perl O, Livne E, Hizmi E, Paz R, Sobel N, Dudai Y, Nir Y. Local targeted memory reactivation in human sleep. **Curr Biol** 30: 1435–1446.e5, 2020. doi:10.1016/j.cub.2020.01.091.

1456. Cairney SA, Sobczak JM, Lindsay S, Gaskell MG. Mechanisms of memory retrieval in slow-wave sleep. **Sleep** 40: zsx114, 2017. doi:10.1093/sleep/zsx114.

1457. Schreiner T, Rasch B. Boosting vocabulary learning by verbal cueing during sleep. **Cereb Cortex** 25: 4169–4179, 2015. doi:10.1093/cercor/bhu139.

1458. Wilhelm I, Schreiner T, Beck J, Rasch B. No effect of targeted memory reactivation during sleep on retention of vocabulary in adolescents. **Sci Rep** 10: 4255, 2020. doi:10.1038/s41598-020-61183-z.

1459. Forcato C, Klinzing JG, Carbone J, Radloff M, Weber FD, Born J, Diekelmann S. Reactivation during sleep with incomplete reminder cues rather than complete ones stabilizes long-term memory in humans. **Commun Biol** 3: 733, 2020. doi:10.1038/s42003-020-01457-4.

1460. Gao C, Fillmore P, Scullin MK. Classical music, educational learning, and slow wave sleep: a targeted memory reactivation experiment. **Neurobiol Learn Mem** 171: 107206, 2020. doi:10.1016/j.nlm.2020.107206.

1461. Neumann F, Oberhauser V, Kornmeier J. How odor cues help to optimize learning during sleep in a real life-setting. **Sci Rep** 10: 1227, 2020. doi:10.1038/s41598-020-57613-7.

1462. Klinzing JG, Kugler S, Soekadar SR, Rasch B, Born J, Diekelmann S. Odor cueing during slow-wave sleep benefits memory independently of low cholinergic tone. **Psychopharmacology (Berl)** 235: 291–299, 2018. doi:10.1007/s00213-017-4768-5.

1463. Cairney SA, Lindsay S, Sobczak JM, Paller KA, Gaskell MG. The benefits of targeted memory reactivation for consolidation in sleep are contingent on memory accuracy and direct cue-memory associations. **Sleep** 39: 1139–1150, 2016. doi:10.5665/sleep.5772.

1464. Creery JD, Oudiette D, Antony JW, Paller KA. Targeted memory reactivation during sleep depends on prior learning. **Sleep** 38: 755–763, 2015. doi:10.5665/sleep.4670.

1465. Fuentemilla L, Miró J, Ripollés P, Vilà-Balló A, Juncadella M, Castañer S, Salord N, Monasterio C, Falip M, Rodríguez-Fornells A. Hippocampus-dependent strengthening of targeted memories via reactivation during sleep in humans. **Curr Biol** 23: 1769–1775, 2013. doi:10.1016/j.cub.2013.07.006.

1466. Diekelmann S, Biggel S, Rasch B, Born J. Offline consolidation of memory varies with time in slow wave sleep and can be accelerated by cuing memory reactivations. **Neurobiol Learn Mem** 98: 103–111, 2012. doi:10.1016/j.nlm.2012.07.002.

1467. Batterink LJ, Creery JD, Paller KA. Phase of spontaneous slow oscillations during sleep influences memory-related processing of auditory cues. **J Neurosci** 36: 1401–1409, 2016. doi:10.1523/JNEUROSCI.3175-15.2016.

1468. Ngo HV, Staresina BP. Shaping overnight consolidation via slow-oscillation closed-loop targeted memory reactivation. **Proc Natl Acad Sci USA** 119: e2123428119, 2022. doi:10.1073/pnas.2123428119.

1469. Abdellahi ME, Koopman AC, Treder MS, Lewis PA. Targeting targeted memory reactivation: characteristics of cued reactivation in sleep. **Neuroimage** 266: 119820, 2023. doi:10.1016/j.neuroimage.2022.119820.

1470. Wang JY, Heck KL, Born J, Ngo HV, Diekelmann S. No difference between slow oscillation up- and down-state cueing for memory consolidation during sleep. **J Sleep Res** 31: e13562, 2022. doi:10.1111/jsr.13562.

1471. Joensen BH, Harrington MO, Berens SC, Cairney SA, Gaskell MG, Horner AJ. Targeted memory reactivation during sleep can induce forgetting of overlapping memories. **Learn Mem** 29: 401–411, 2022. doi:10.1101/lm.053594.122.

1472. Oyarzún JP, Morís J, Luque D, de Diego-Balaguer R, Fuentemilla L. Targeted memory reactivation during sleep adaptively promotes the strengthening or weakening of overlapping memories. **J Neurosci** 37: 7748–7758, 2017. doi:10.1523/JNEUROSCI.3537-16.2017.

1473. Diekelmann S, Büchel C, Born J, Rasch B. Labile or stable: opposing consequences for memory when reactivated during waking and sleep. **Nat Neurosci** 14: 381–386, 2011. doi:10.1038/nn.2744.

1474. Shanahan LK, Gjorgieva E, Paller KA, Kahnt T, Gottfried JA. Odor-evoked category reactivation in human ventromedial prefrontal cortex during sleep promotes memory consolidation. **eLife** 7: e39681, 2018. doi:10.7554/eLife.39681.

1475. Wang B, Antony JW, Lurie S, Brooks PP, Paller KA, Norman KA. Targeted memory reactivation during sleep elicits neural signals related to learning content. **J Neurosci** 39: 6728–6736, 2019. doi:10.1523/JNEUROSCI.2798-18.2019.

1476. Carbone J, Bibian C, Born J, Forcato C, Diekelmann S. Comparing targeted memory reactivation during slow wave sleep and sleep stage 2. **Sci Rep** 14: 9057, 2024. doi:10.1038/s41598-024-59696-y.

1477. Göldi M, van Poppel EA, Rasch B, Schreiner T. Increased neuronal signatures of targeted memory reactivation during slow-wave up states. **Sci Rep** 9: 2715, 2019. doi:10.1038/s41598-019-39178-2.

1478. Sánchez-Corzo A, Baum DM, Irani M, Hinrichs S, Reisenegger R, Whitaker GA, Born J, Sitaram R, Klinzing JG. Odor cueing of declarative memories during sleep enhances coordinated spindles and slow oscillations. **Neuroimage** 287: 120521, 2024. doi:10.1016/j.neuroimage.2024.120521.

1479. Berkers RM, Ekman M, van Dongen EV, Takashima A, Barth M, Paller KA, Fernández G. Cued reactivation during slow-wave sleep induces brain connectivity changes related to memory stabilization. **Sci Rep** 8: 16958, 2018. doi:10.1038/s41598-018-35287-6.

1480. Wick A, Rasch B. Targeted memory reactivation during slow-wave sleep vs. sleep stage N2: no significant differences in a vocabulary task. **Learn Mem** 30: 192–200, 2023. doi:10.1101/lm.053683.122.

1481. Leong CW, Leow JW, Grunstein RR, Naismith SL, Teh JZ, D'Rozario AL, Saini B. A systematic scoping review of the effects of central nervous system active drugs on sleep spindles and sleep-dependent memory consolidation. **Sleep Med Rev** 62: 101605, 2022. doi:10.1016/j.smrv.2022.101605.

1482. Doghramji K, Jangro WC. Adverse effects of psychotropic medications on sleep. **Psychiatr Clin North Am** 39: 487–502, 2016. doi:10.1016/j.psc.2016.04.009.

1483. Hall-Porter JM, Schweitzer PK, Eisenstein RD, Ahmed HA, Walsh JK. The effect of two benzodiazepine receptor agonist hypnotics on sleep-dependent memory consolidation. **J Clin Sleep Med** 10: 27–34, 2014. doi:10.5664/jcsm.3352.

1484. Meléndez J, Galli I, Boric K, Ortega A, Zuñiga L, Henríquez-Roldán CF, Cárdenas AM. Zolpidem and triazolam do not affect the nocturnal sleep-induced memory improvement. **Psychopharmacology (Berl)** 181: 21–26, 2005. doi:10.1007/s00213-005-2228-0.

1485. Bomalaski MN, Claflin ES, Townsend W, Peterson MD. Zolpidem for the treatment of neurologic disorders: a systematic review. **JAMA Neurol** 74: 1130–1139, 2017. doi:10.1001/jamaneurol.2017.1133.

1486. Becker LA, Penagos H, Flores FJ, Manoach DS, Wilson MA, Varela C. Eszopiclone and zolpidem produce opposite effects on hippocampal ripple density. **Front Pharmacol** 12: 792148, 2021. doi:10.3389/fphar.2021.792148.

1487. Wamsley EJ, Shinn AK, Tucker MA, Ono KE, McKinley SK, Ely AV, Goff DC, Stickgold R, Manoach DS. The effects of eszopiclone on sleep spindles and memory consolidation in schizophrenia: a randomized placebo-controlled trial. **Sleep** 36: 1369–1376, 2013. doi:10.5665/sleep.2968.

1488. Mylonas D, Baran B, Demanuele C, Cox R, Vuper TC, Seicol BJ, Fowler RA, Correll D, Parr E, Callahan CE, Morgan A, Henderson D, Vangel M, Stickgold R, Manoach DS. The effects of eszopiclone on sleep spindles and memory consolidation in schizophrenia: a randomized clinical trial. **Neuropsychopharmacology** 45: 2189–2197, 2020. doi:10.1038/s41386-020-00833-2.

1489. Feld GB, Wilhelm I, Ma Y, Groch S, Binkofski F, Mölle M, Born J. Slow wave sleep induced by GABA agonist tiagabine fails to benefit memory consolidation. **Sleep** 36: 1317–1326, 2013. doi:10.5665/sleep.2954.

1490. Zhang Y, Gruber R. Can slow-wave sleep enhancement improve memory? A review of current approaches and cognitive outcomes. **Yale J Biol Med** 92: 63–80, 2019.

1491. Nemeth DP, Quan N. Modulation of neural networks by interleukin-1. **Brain Plast** 7: 17–32, 2021. doi:10.3233/BPL-200109.

1492. Wadhwa M, Kumari P, Chauhan G, Roy K, Alam S, Kishore K, Ray K, Panjwani U. Sleep deprivation induces spatial memory impairment by altered hippocampus neuroinflammatory responses and glial cells activation in rats. **J Neuroimmunol** 312: 38–48, 2017. doi:10.1016/j.jneuroim.2017.09.003.

1493. Zhang M, Zhang M, Kou G, Li Y. The relationship between gut microbiota and inflammatory response, learning and memory in mice by sleep deprivation. **Front Cell Infect Microbiol** 13: 1159771, 2023. doi:10.3389/fcimb.2023.1159771.

1494. Zhu B, Dong Y, Xu Z, Gompf HS, Ward SAP, Xue Z, Miao C, Zhang Y, Chamberlin NL, Xie Z. Sleep disturbance induces neuroinflammation and impairment of learning and memory. **Neurobiol Dis** 48: 348–355, 2012. doi:10.1016/j.nbd.2012.06.022.

1495. Krueger JM, Majde JA. Microbial products and cytokines in sleep and fever regulation. **Crit Rev Immunol** 37: 291–315, 2017. doi:10.1615/CritRevImmunol.v37.i2-6.70.

1496. Rockstrom MD, Chen L, Taishi P, Nguyen JT, Gibbons CM, Veasey SC, Krueger JM. Tumor necrosis factor alpha in sleep regulation. **Sleep Med Rev** 40: 69–78, 2018. doi:10.1016/j.smrv.2017.10.005.

1497. Schmidt EM, Linz B, Diekelmann S, Besedovsky L, Lange T, Born J. Effects of an interleukin-1 receptor antagonist on human sleep, sleep-associated memory consolidation, and blood monocytes. **Brain Behav Immun** 47: 178–185, 2015. doi:10.1016/j.bbi.2014.11.012.

1498. Besedovsky L, Schmidt EM, Linz B, Diekelmann S, Lange T, Born J. Signs of enhanced sleep and sleep-associated memory processing following the anti-inflammatory antibiotic minocycline in men. **J Psychopharmacol** 31: 204–210, 2017. doi:10.1177/0269881116658991.

1499. Wadhwa M, Prabhakar A, Ray K, Roy K, Kumari P, Jha PK, Kishore K, Kumar S, Panjwani U. Inhibiting the microglia activation improves the spatial memory and adult neurogenesis in rat hippocampus during 48 h of sleep deprivation. **J Neuroinflammation** 14: 222, 2017. doi:10.1186/s12974-017-0998-z.

1500. Ugalde-Muñiz P, Hernández-Luna MG, García-Velasco S, Lugo-Huitrón R, Murcia-Ramírez J, Martínez-Tapia RJ, Noriega-Navarro R, Navarro L. Activation of dopamine D2 receptors attenuates neuroinflammation and ameliorates the memory impairment induced by rapid eye movement sleep deprivation in a murine model. **Front Neurosci** 16: 988167, 2022. doi:10.3389/fnins.2022.988167.

1501. Skilling QM, Eniwaye B, Clawson BC, Shaver J, Ognjanovski N, Aton SJ, Zochowski M**.** Acetylcholine-gated current translates wake neuronal firing rate information into a spike timing-based code in non-REM sleep, stabilizing neural network dynamics during memory consolidation. **PLoS Comput Biol** 17: e1009424, 2021. doi:10.1371/journal.pcbi.1009424.

1502. Nghiem TA, Tort-Colet N, Górski T, Ferrari U, Moghimyfiroozabad S, Goldman JS, Teleńczuk B, Capone C, Bal T, Di Volo M, Destexhe A**.** Cholinergic switch between two types of slow waves in cerebral cortex. **Cereb Cortex** 30: 3451–3466, 2020. doi:10.1093/cercor/bhz320.

1503. Dias I, Levers MR, Lamberti M, Hassink GC, van Wezel R, Le Feber J**.** Consolidation of memory traces in cultured cortical networks requires low cholinergic tone, synchronized activity and high network excitability. **J Neural Eng** 18: 10.1088/1741–12552/abfb3f, 2021. doi:10.1088/1741-2552/abfb3f.

1504. Inayat S, Qandeel, Nazariahangarkolaee M, Singh S, McNaughton BL, Whishaw IQ, Mohajerani MH**.** Low acetylcholine during early sleep is important for motor memory consolidation. **Sleep** 43: zsz297, 2020. doi:10.1093/sleep/zsz297.

1505. Rasch B, Gais S, Born J**.** Impaired off-line consolidation of motor memories after combined blockade of cholinergic receptors during REM sleep-rich sleep. **Neuropsychopharmacology** 34: 1843–1853, 2009. doi:10.1038/npp.2009.6.

1506. Goerke M, Cohrs S, Rodenbeck A, Kunz D**.** Differential effect of an anticholinergic antidepressant on sleep-dependent memory consolidation. **Sleep** 37: 977–985, 2014. doi:10.5665/sleep.3674.

1507. Kjaerby C, Andersen M, Hauglund N, Untiet V, Dall C, Sigurdsson B, Ding F, Feng J, Li Y, Weikop P, Hirase H, Nedergaard M**.** Memory-enhancing properties of sleep depend on the oscillatory amplitude of norepinephrine. **Nat Neurosci** 25: 1059–1070, 2022. doi:10.1038/s41593-022-01102-9.

1508. Groch S, Wilhelm I, Diekelmann S, Sayk F, Gais S, Born J**.** Contribution of norepinephrine to emotional memory consolidation during sleep. **Psychoneuroendocrinology** 36: 1342–1350, 2011. doi:10.1016/j.psyneuen.2011.03.006.

1509. Durán E, Pandinelli M, Logothetis NK, Eschenko O**.** Altered norepinephrine transmission after spatial learning impairs sleep-mediated memory consolidation in rats. **Sci Rep** 13: 4231, 2023. doi:10.1038/s41598-023-31308-1.

1510. Zhang Z, Ferretti V, Güntan İ, Moro A, Steinberg EA, Ye Z, Zecharia AY, Yu X, Vyssotski AL, Brickley SG, Yustos R, Pillidge ZE, Harding EC, Wisden W, Franks NP**.** Neuronal ensembles sufficient for recovery sleep and the sedative actions of α2 adrenergic agonists. **Nat Neurosci** 18: 553–561, 2015. doi:10.1038/nn.3957.

1511. Zhang C, Huang L, Xu M**.** Dopamine control of REM sleep and cataplexy. **Neurosci Bull** 38: 1617–1619, 2022. doi:10.1007/s12264-022-00925-7.

1512. Fraigne JJ, Luppi PH, Mahoney CE, DeLuca R, Shiromani PJ, Weber F, Adamantidis A, Peever J**.** Dopamine neurons in the ventral tegmental area modulate rapid eye movement sleep. **Sleep** 46: zsad024, 2023. doi:10.1093/sleep/zsad024.

1513. Toth BA, Chang KS, Fechtali S, Burgess CR**.** Dopamine release in the nucleus accumbens promotes REM sleep and cataplexy. **iScience** 26: 107613, 2023. doi:10.1016/j.isci.2023.107613.

1514. Hasegawa E, Li Y, Sakurai T**.** Regulation of REM sleep in mice: the role of dopamine and serotonin function in the basolateral amygdala. **Neurosci Res** 200: 28–33, 2024. doi:10.1016/j.neures.2023.09.003.

1515. Späth-Schwalbe E, Uthgenannt D, Voget G, Kern W, Born J, Fehm HL**.** Corticotropin-releasing hormone-induced adrenocorticotropin and cortisol secretion depends on sleep and wakefulness. **J Clin Endocrinol Metab** 77: 1170–1173, 1993. doi:10.1210/jcem.77.5.8077308.

1516. Bennion KA, Mickley Steinmetz KR, Kensinger EA, Payne JD**.** Eye tracking, cortisol, and a sleep vs. wake consolidation delay: combining methods to uncover an interactive effect of sleep and cortisol on memory. **J Vis Exp** 88: 51500, 2014. doi:10.3791/51500.

1517. Born J, Wagner U**.** Memory consolidation during sleep: role of cortisol feedback. **Ann NY Acad Sci** 1032: 198–201, 2004. doi:10.1196/annals.1314.020.

1518. Payne JD, Nadel L**.** Sleep, dreams, and memory consolidation: the role of the stress hormone cortisol. **Learn Mem** 11: 671–678, 2004. doi:10.1101/lm.77104.

1519. Wagner U, Degirmenci M, Drosopoulos S, Perras B, Born J**.** Effects of cortisol suppression on sleep-associated consolidation of neutral and emotional memory. **Biol Psychiatry** 58: 885–893, 2005. doi:10.1016/j.biopsych.2005.05.008.

1520. Wagner U, Born J**.** Memory consolidation during sleep: interactive effects of sleep stages and HPA regulation. **Stress** 11: 28–41, 2008. doi:10.1080/10253890701408822.

1521. Rimmele U, Besedovsky L, Lange T, Born J**.** Emotional memory can be persistently weakened by suppressing cortisol during retrieval. **Neurobiol Learn Mem** 119: 102–107, 2015. doi:10.1016/j.nlm.2015.01.010.

1522. Hallschmid M**.** Intranasal insulin. **J Neuroendocrinol** 33: e12934, 2021. doi:10.1111/jne.12934.

1523. Hallschmid M**.** Intranasal insulin for Alzheimer's disease. **CNS Drugs** 35: 21–37, 2021. doi:10.1007/s40263-020-00781-x.

1524. Ritze Y, Kern W, Ebner E-M, Jahn S, Benedict C, Hallschmid M**.** Metabolic and cognitive outcomes of subchronic once-daily intranasal insulin administration in healthy men. **Front Endocrinol (Lausanne)** 9: 663, 2018. doi:10.3389/fendo.2018.00663.

1525. Born J, Lange T, Kern W, McGregor GP, Bickel U, Fehm HL**.** Sniffing neuropeptides: a transnasal approach to the human brain. **Nat Neurosci** 5: 514–516, 2002. doi:10.1038/nn849.

1526. Benedict C, Hallschmid M, Hatke A, Schultes B, Fehm HL, Born J, Kern W**.** Intranasal insulin improves memory in humans. **Psychoneuroendocrinology** 29: 1326–1334, 2004. doi:10.1016/j.psyneuen.2004.04.003.

1527. Ramasubbu K, Ramanathan G, Venkatraman G, Rajeswari VD**.** Sleep-associated insulin resistance promotes neurodegeneration. **Mol Biol Rep** 50: 8665–8681, 2023. doi:10.1007/s11033-023-08710-z.

1528. Feld GB, Wilhem I, Benedict C, Rüdel B, Klameth C, Born J, Hallschmid M**.** Central nervous insulin signaling in sleep-associated memory formation and neuroendocrine regulation. **Neuropsychopharmacology** 41: 1540–1550, 2016. doi:10.1038/npp.2015.312.

1529. Dudai Y**.** The neurobiology of consolidations, or, how stable is the engram? **Annu Rev Psychol** 55: 51–86, 2004. doi:10.1146/annurev.psych.55.090902.142050.

1530. Malenka RC, Bear MF**.** LTP and LTD: an embarrassment of riches. **Neuron** 44: 5–21, 2004. doi:10.1016/j.neuron.2004.09.012.

1531. Gais S, Rasch B, Wagner U, Born J**.** Visual-procedural memory consolidation during sleep blocked by glutamatergic receptor antagonists. **J Neurosci** 28: 5513–5518, 2008. doi:10.1523/JNEUROSCI.5374-07.2008.

1532. Feld GB, Lange T, Gais S, Born J. Sleep-dependent declarative memory consolidation–unaffected after blocking NMDA or AMPA receptors but enhanced by NMDA coagonist D-cycloserine. **Neuropsychopharmacology** 38: 2688–2697, 2013. doi:10.1038/npp.2013.179.

1533. Alizadeh Asfestani M, Braganza E, Schwidetzky J, Santiago J, Soekadar S, Born J, Feld GB. Overnight memory consolidation facilitates rather than interferes with new learning of similar materials-a study probing NMDA receptors. **Neuropsychopharmacology** 43: 2292–2298, 2018. doi:10.1038/s41386-018-0139-0.

1534. Feld GB, Bergmann TO, Alizadeh-Asfestani M, Stuke V, Wriede JP, Soekadar S, Born J. Specific changes in sleep oscillations after blocking human metabotropic glutamate receptor 5 in the absence of altered memory function. **J Psychopharmacol** 35: 652–667, 2021. doi:10.1177/02698811211005627.

1535. Cordi MJ, Schlarb AA, Rasch B. Deepening sleep by hypnotic suggestion. **Sleep** 37: 1143–1152, 2014. doi:10.5665/sleep.3778.

1536. Cordi MJ, Hirsiger S, Mérillat S, Rasch B. Improving sleep and cognition by hypnotic suggestion in the elderly. **Neuropsychologia** 69: 176–182, 2015. doi:10.1016/j.neuropsychologia.2015.02.001.

1537. Beck J, Cordi MJ, Rasch B. Hypnotic suggestions increase slow-wave parameters but decrease slow-wave spindle coupling. **Nat Sci Sleep** 13: 1383–1393, 2021. doi:10.2147/NSS.S316997.

1538. Besedovsky L, Cordi M, Wißlicen L, Martínez-Albert E, Born J, Rasch B. Hypnotic enhancement of slow-wave sleep increases sleep-associated hormone secretion and reduces sympathetic predominance in healthy humans. **Commun Biol** 5: 747, 2022. doi:10.1038/s42003-022-03643-y.

1539. Elkins G, Padilla VJ, Otte J, Sanford K, Benge J, Stevens A, Scullin M, Corlett CE, Ekanayake V. Hypnosis intervention for sleep disturbances in individuals with mild cognitive impairment: a randomized pilot study. **Int J Clin Exp Hypn** 72: 16–28, 2024. doi:10.1080/00207144.2023.2279672.

1540. Chamine I, Atchley R, Oken BS. Hypnosis intervention effects on sleep outcomes: a systematic review. **J Clin Sleep Med** 14: 271–283, 2018. doi:10.5664/jcsm.6952.

1541. Cordi MJ, Rasch B. Hypnotizability may relate to interoceptive ability to accurately perceive sleep depth: an exploratory study. **Int J Clin Exp Hypn** 70: 385–402, 2022. doi:10.1080/00207144.2022.2130068.

1542. Cordi MJ, Rossier L, Rasch B. Hypnotic suggestions given before nighttime sleep extend slow-wave sleep as compared to a control text in highly hypnotizable subjects. **Int J Clin Exp Hypn** 68: 105–129, 2020. doi:10.1080/00207144.2020.1687260.

1543. Cordi MJ, Rasch B. Systematic decrease of slow-wave sleep after a guided imagery designed to deepen sleep in low hypnotizable subjects. **J Sleep Res** 30: e13168, 2021. doi:10.1111/jsr.13168.