Links between the brain and body during sleep: implications for memory processing

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Sleep is intimately related to memory processes. The established view is that the transformation of experiences into long-term memories is linked to sleep-related CNS function. However, there is increasing evidence that the autonomic nervous system (ANS), long recognized to modulate cognition during waking, can impact memory processing during sleep. Here, we review human research that examines the role of autonomic activity and sleep in memory formation. We argue that autonomic activity during sleep may set the stage for the CNS dynamics associated with sleep and memory stability and integration. Further, we consider how the link between ANS activity and polysomnographic markers of sleep may help elucidate both healthy and pathological cognitive aging in humans.

Forming lasting memories is a combined outcome of wake and sleep processing
The solace of our memories, the comfort of extracting relevant information from the past to assist in navigating the present, is one of the defining elements of human experience and is critical to adaptive survival in an ever-changing world. Understanding how lasting memories are formed continues to be among the forefront pursuits in neuroscience, particularly as the percentage of adults showing age-related memory deficits steadily rise.

Various theories have proposed how both wake and sleep experiences contribute to lasting memory representations. Specifically, many of these theories posit that during wake, we encounter stimuli that the brain interprets, with input and feedback from the ANS [1]. The autonomic inputs during wake modulate the salience of initial memory traces [2,3]. Our brains, then, leverage the neural conditions during sleep (e.g., minimal external inputs and synchronized neuronal firing) to further process encountered information [4]. This is believed to occur through sleep-dependent neuronal replay and the redistribution of learned information from short-term to long-term stores in the brain [5,6].

As individuals age, truncated sleep, nighttime awakenings, and increased rigidity in peripheral physiology becomes the norm [7], setting the stage for age-dependent memory decline, and in some cases – pathological memory decline (e.g., in Alzheimer’s disease and related dementias) [8]. Research efforts have narrowed in on the changes in the brain from wake to sleep and across different sleep stages to explain these memory deficits. These inquiries have unearthed compelling evidence pointing to electroencephalographic features that predict memory outcomes [9] and may be relevant to age-dependent memory losses. However, much of the existing research has overlooked the fact that sleep, like memory, is a phenomenon of both the brain and the body. Critically, shifts in the CNS during sleep are synchronized with predictable fluctuations in the ANS. Given that ANS and CNS linkage during wake modulates memory outcomes, could considering ANS activity during sleep further elucidate the relationship between sleep and memory processes?
Here, we review the sleep and memory literatures with a concerted focus on how the relationship between the ANS and CNS supports each phenomenon. We discuss the critical, and often overlooked, importance of ANS excitation and fluctuations across wake and sleep to stabilize memory in the CNS and discuss theoretical considerations that will assist in a greater understanding of the relationship among the ANS, sleep, and memory.

**Sleep supports declarative memory processing**

Declarative (i.e., explicit) memories, those that can be deliberately brought to awareness (e.g., recalling a friend’s birthday), and nondeclarative (implicit) memories, those for which recall requires little conscious effort (e.g., riding a bike; typing), rely on neural activity in specific brain structures. Specifically, declarative memory generally relies on processing in the hippocampus and neocortex, where implicit memory involves the cerebellum and striatum, among other brain regions [10–12]. Declarative memories are further divided into episodic, memories for events tied to a temporal context and place (e.g., what jeans you wore yesterday), and semantic, memories for general information (e.g., Selma is a town in Alabama, USA). Declarative memories are the focus of this review, due to the established literature connecting sleep and ANS processes to declarative memory formation. Yet, it is important to note that ANS and sleep processes may play a role in nondeclarative memory formation as well [13,14], though there is less convergence and fewer existing studies from which to draw conclusions [15].

Declarative memories are established through the interplay of three phases: encoding, consolidation, and retrieval, with each requiring a set of cellular-, molecular-, and systems-level alterations [16]. Encoding, or the uptake of information from external or internal events, is a rapid process enabled by the activation of cell assemblies in both the hippocampus and neocortex [17,18]. Partially overlapping cell assemblies in the hippocampus allow for learning to trigger new cell firing as well as to engage other cells associated in detecting features of the nascent memory at the time of learning (e.g., cells firing in response to stimuli that identify an environmental context are also firing for details of the experience you had in that context) [19,20].

After encoding, a process of consolidation ensues – the transformation of labile encoded experiences into stable, long-term neural representations. Consolidation optimally occurs during states when there are few competing processes that would demand new learning [21,22]. It is believed that during consolidation, neurons replay encoding firing patterns in the hippocampus and the neocortex, which facilitates the distribution (and potentially transfer) of the memory trace to neocortical regions and striatal networks that are relevant to the stimuli [23–25]. Sleep has been implicated in this consolidation process. During sleep, it is thought that slow wave oscillations (0.5–4 Hz), sleep spindles (12–16 Hz), and ripples (140–180 Hz; not detectable in human electroencephalogram) are indicators of neural dynamics that integrate new memories by linking hippocampal and thalamocortical circuits. The repeated reactivation of learned stimuli is facilitated by slow, synchronized cell firing that originates in the prefrontal circuits. The thalamocortical spindles and the hippocampal ripples are then connected by slow wave oscillations providing a temporal context for the consolidation and neuronal replay process [26]. Importantly, replay also provides for biased consolidation, with traces that are replayed more often being more readily maintained [27].

Lastly, retrieval is the reactivation of stored representations. Retrieval processes involve both external and internal cues, influenced by the availability/integrity of the information and accessibility to the information after being cued [28,29]. Traces of memory (engrams) are likely not stored in isolation but intertwined with several contextual cues [30], and as a result, retrieval processes engage a broad host of neural structures. This includes the hippocampus, the prefrontal cortex, which guides top-down selection of information, and the parietal cortex, which mediates
attention-driven retrieval efforts [16]. Importantly, the act of retrieving a memory can return a memory trace to its more labile form [31,32]. In this labile state, the memory can again be updated, or transformed, and undergo further consolidation, also referred to as reconsolidation.

In sum, the systems that support memory are dynamic and interactive, facilitating the formation of memory traces that are stable, yet malleable. The malleability of our memories makes them susceptible to influences that can either change, enhance, or degrade them [33]. In the next section, we discuss the ANS as one of the important moderators of memory formation.

The ANS and memory
The ANS is part of the PNS. It regulates various physiological processes, including heart rate, blood pressure, respiration, and digestion. It contains three primary divisions: the sympathetic, parasympathetic, and enteric nervous systems. The sympathetic and parasympathetic systems work antagonistically, synergistically, and independently to gather information from sensory organs and coordinate responses to internal and external demands [33,34]. The sympathetic nerves are primarily responsible for energy mobilization (e.g., via enhanced metabolism, blood oxygenation), whereas the parasympathetic system predominates during rest, with the coordination between the activity of the two systems often working to restore and maintain homeostasis [33]. Both the sympathetic and parasympathetic nervous systems interact with the CNS, and in particular, the central autonomic network (CAN) [34,35]. The CAN is a set of CNS structures, including the locus coeruleus (LC), hypothalamus, amygdala, dorsomedial prefrontal cortices, hippocampus, and thalamus, that, indirectly or directly, receive inputs from and modulate output to the ANS. In mammals, under physiological conditions, both the parasympathetic and sympathetic systems are tonically active, with efferent pathways extending from the brain stem and hypothalamus to all major peripheral organs (e.g., heart, lungs, stomach, pancreas, small and large intestines, and liver). These far-reaching and dense projections allow each ANS to quickly up- or downregulate their inputs to peripheral tissues at any time, ultimately providing for quick physiological changes (e.g., sweating, increased heart rate) in response to behavioral demands (e.g., running) [35].

Much of the afferent communication from the ANS to the CNS is through the vagus nerve, the longest autonomic nerve in the body. Roughly 75% of the fibers in the vagus nerve are afferents, which mostly project to the nucleus of the solitary tract (NTS) in the brain stem and then to various regions of the CAN [36–38]. The afferent fibers of the vagus nerve signal information about the sensory environment and autonomic response to the CNS [38]. Early lesion studies helped elucidate the role the vagus nerve may play in modulating biological process important for memory functions [39–41]. More recently, studies have linked vagal nerve activity to plasticity markers in the hippocampus [42,43]. Together, these studies implicate that the vagus nerve may play a role in adaptive memory formation.

The vagus nerve and memory formation
Studies have determined that during wakefulness, the vagus nerve’s input to the CNS can benefit memory performance. Transcutaneous vagal nerve stimulation (tVNS), a noninvasive method that stimulates vagal afferents through the skin, has also been deemed valuable in examining memory benefits [44,45]. These stimulation techniques often target auricular vagal afferents, which can be accessed through the left ear [45]. In one study, 30 adults (average age 60 years old) were exposed to tVNS versus sham for 17 min peri-encoding and performed better on a face–name association task [46]. These memory-enhancing effects likely reflect, at least in part, the vagus nerve’s role in processing arousing information. In response to internal or external arousing events, a cascade of endogenous hormones is released into the periphery. Adrenaline, one of
the known peripheral modulators of hippocampal memory, exerts some of its effect via the β-adrenergic receptors present on the vagus nerve. The vagus then projects to the brain stem and higher order memory-modulating centers, like the hippocampus, to influence early memory formation [47]. In fact, vagal nerve stimulation in rodents has been shown to increase adrenergic activity in the brain stem and facilitate long-term potentiation in the hippocampus [47,48]. Further, afferent vagal stimulation can increase cholinergic activity in the neocortex and modulate GABA-A and B receptor activity in the hippocampus [49,50]. Pathways involving neocortical cholinergic networks and hippocampal GABA activity have each been tied to memory modulation in the CNS [51,52].

While there are accruing data on the cognitive effects of ANS manipulation, most studies examining the influence of vagal activity on human cognition have relied on heart rate variability (HRV), a noninvasive method that examines the variability between individual R peaks (which reflect ventricular depolarization) in the QRS complex of electrocardiogram (ECG). Heart rate reflects the dual innervation of both sympathetic and parasympathetic systems; however, a spectral analysis of the ECG signal can parse and extract components of heart rate indicative of various underlying autonomic sources. The three main oscillatory features that are typically extracted are the very low-frequency (0.004–0.04 Hz) component, the low-frequency component (0.04–0.15 Hz), and the high-frequency (HF) component (0.15–0.40 Hz). The interpretation of the very low- and low-frequency components is debated [53]. HF HRV has been argued to reflect the vagally mediated effects of respiration on heart rate, and it has been linked to memory performance [54–59]. HRV has also been tied to cognitive skills important for long-term memory outcomes. For example, individuals with higher resting HF HRV show better attention and executive function – cognitive skills that interact with memory formation [60–63].

So far, the work we have reviewed considers the relationship between the ANS and memory after intervals of wake. Importantly, the ANS continues to communicate with the CNS during sleep (Box 1). Until recently, interdependencies between the ANS, sleep, and memory went largely overlooked (Box 2). As discussed in the following sections, emerging evidence indicates that ANS sleep dynamics also influence memory outcomes.

**Sleep, ANS, and memory: recent findings**

A series of recent studies have examined the role of ANS activity in sleep-dependent memory outcomes. In one such study, the impact of vagal activity during sleep on working memory – the active, short-term storage, processing, and manipulation of information – was examined [64]. Previous studies have demonstrated that sleep-deprived individuals perform worse on working memory tasks compared with those who are well-rested [65,66]. Studies have also suggested that post-training sleep benefits working memory performance gains compared with wakefulness [67,68]. In these studies, training adult participants on an n-back task (i.e., individuals judge whether an individual item is the same as an item presented previously in a sequence) over several sessions improved accuracy of performance, but only if the interval between training sessions included nocturnal sleep or a nap in comparison with daytime periods of wakefulness [67–69]. However, the sleep-related physiological processes that promote such enhancement remained to be addressed. In a recent study, researchers explored whether HF HRV during sleep accounted for the sleep-associated gains in working memory [70]. Young adult participants were tested, in the morning and evening, on an operation span task in which a trial consisted of subjects maintaining and manipulating a set of letters interspersed with simple math equation distractors. During the intertest period, subjects either experienced a nap or wake during which time polysomnography and electrocardiography was used to assess sleep features
Recent studies have examined whether ECG and EEG coupling during sleep may be important for memory processing. This research builds upon studies that have found heart rate acceleration and HF HRV during slow wave sleep (SWS), but not wake, was a significant predictor of working memory improvement [70]. An alternative interpretation of these results to consider, though, is that HF HRV represents an additional marker of sleep depth, as other electrophysiological indicators associated with sleep quality were not examined [e.g., eye movements/minute of rapid eye movement (REM) or spectral power during sleep].

Researchers have also investigated whether HF HRV during sleep facilitates improvement in long-term memory. In one study, researchers used the remote association task [71], in which distinct memory manipulations (implicit vs. explicit) have been shown to rely on REM sleep [14]. This study aimed to examine the relative impact of electroencephalographic and HRV variables on performance gains. Here, electroencephalographic parameters (e.g., minutes in SWS and REM and sleep spindles) and HF HRV in SWS and REM sleep accounted for a significant amount of the variance in performance (73% of explained variance). This was more than when sleep variables were modeled alone (46% of explained variance). In this study, HF HRV during REM sleep emerged as the strongest predictor of performance. Further, REM duration was negatively associated with memory performance (and not correlated with HF HRV). Sleep spindles, another traditional memory indicator of non-REM (NREM) sleep, were also not a significant predictor after REM HF HRV was included in statistical models, and the two variables were not correlated. Together, these data imply that ANS and electroencephalographic features of sleep combine to better predict memory dynamics than traditional sleep indicators alone. These findings, together with the working memory findings, provide new, yet compelling evidence that CNS and ANS activity during both NREM and REM may synergistically support the physiological dynamics underlying sleep’s support for memory processing.

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Box 2. NREM and REM sleep support memory

Sleep’s role in memory processes has been thoroughly documented, including observations that features of NREM sleep are linked to sleep-dependent neuronal replay. Leading theories suggest that the temporal framework curated by processes reflected in the hippocampal ripple, thalamic spindle, and neocortical slow oscillation likely facilitates the transfer of a hippocampal memory trace to neocortical regions [114,120–123]. In humans, increases in slow waves generated in frontal brain regions were shown to be further accompanied by spontaneous memory reactivation [114]. Moreover, studies have demonstrated that neocortical activation during NREM sleep can influence hippocampal slow wave ripples and memory replay [123]. Precise timing of these thalamocortical interactions increases the likelihood that related memory traces will reach the neocortex at the same time, boosting the potential for memory stabilization [114,120–123]. Indeed, sleep rich in spindles timed at the up phase of the slow wave has been linked to behavioral improvements in declarative memory [124,125]. For example, studies that have artificially increased temporal coupling, using acoustic stimulation (e.g., playing a tone during learning and again during sleep), or pharmacological intervention [125] have found improvements in declarative memory [126].

The roles of REM sleep in the context of memory outcomes are less clear, with some conflicting observations. Some studies have reported increased number and density of REMs, as well as higher theta power after learning [127–130]. The neural conditions that underlie REM sleep, of increased transient neural firing in the neocortex and hippocampus [16], traditionally linked this brain state to ‘wake-like’ plasticity. These REM neural conditions—the lack of external inputs and sensory information—lead to hypotheses that characterized REM as an especially associative state with unique benefits for nonhippocampal-dependent, procedural [131] and perceptual memories [9,131], implicit associative processing [14,71], and emotional memory consolidation [132]. Features of REM sleep, including minutes in REM [93] and REM theta frequency [134], are linked to memory processes. Specifically, the increased ACh levels coupled with diminished noradrenaline and serotonin in the hippocampus support maintenance and induction of long-term potentiation during REM, indirectly affecting synaptic plasticity [138]. REM, compared with NREM sleep, has also been hypothesized as a better time for synaptic reorganization due to the higher cholinergic tone [136]. However, much of REM’s role in memory has come into question through studies of selective REM deprivation, either behaviorally or pharmacologically. Some of these studies have shown REM deprivation reduces procedural memory, memory for emotional word pairs, and story learning. However, others have reported no impact of REM deprivation on a range of memory tasks (see for review [137]). In an optogenetics study in mice targeting REM oscillations [134], the authors inhibited GABAergic neurons implicated in the generation of REM-dependent hippocampal theta oscillations, selectively during REMs, and found that in addition to reduced theta during REM sleep, the manipulation impaired spatial object recognition memory and fear-conditioned contextual memory. This study provides compelling evidence of a causal relationship between REM neural dynamics and postsleep memory. Examining the implications of the findings to humans, as well as deeper investigation into REM’s role in long-term memory processes, will require further studies.

often occurs directly after K-complexes in the EEG [72] and increases in slow oscillation amplitude and HF HRV, concomitantly, during sleep after acoustic stimulation [72]. This suggests that cardiac and brain electrical oscillations may be associated and that sleep neural activity may be better understood if the corresponding cardiac activity is also taken into consideration [73]. Recent studies have approached these research questions by using highly precise temporal modeling techniques to identify decreases in heart rate, or heart rate bursts (e.g., lasting 3–5 s), during NREM sleep in healthy, young adults [74,75]. This work demonstrated that decreases in heart rate are consistently preceded by increases in slow oscillations and spindle power in the EEG and directly followed by increases in HF HRV. These coupled events, termed autonomic/central events (ACEs), occur in a 20-s window and are better at predicting postsleep improvement in declarative memory than sleep or cardiac activity occurring outside of the temporal window. Specifically, slow oscillation density, spindle density, and HR burst density during N2 sleep as well as baseline HF HRV failed to significantly predict declarative memory outcomes in these experiments. By contrast, a model including ACEs significantly predicted memory performance, with ACE-related slow oscillations and HF power during N2 sleep emerging as robust predictors. ACE sigma power was also significantly correlated with memory performance outcomes. A similar finding was observed with respect to working memory before and after a nap in young adults [64,70]. Here, individuals performed significantly better on a working memory task after a nap and ACE-related slow wave activity during N3 predicted working memory performance improvement. Together, these studies suggest that considering both the CNS and ANS during sleep, as well as their temporal coupling, may further illuminate sleep’s role for memory.
processes. These relationships could reflect a third, yet common mechanism driving cortical EEG and cardiac indicators, or alternatively represent a unique brain–heart link. Further studies are needed to examine these interpretations.

**Sleep, ANS, and memory: theoretical considerations and future directions**

**ANS–CNS coordination across wake and sleep may be one key to unlocking the neural basis of stable memories**

How might the activity of the ANS during sleep provide insights into sleep-dependent memory processing? First, it is important to consider the role the ANS plays in regulating the purposeful use of metabolic resources across both wake and sleep states. This is dependent on the cyclic relationships between sympathetic and parasympathetic activity. During wake, activation of the ANS and changes in the CNS work to enhance attention to external stimuli and facilitate the processing of arousing information. The ANS is involved in ‘tagging’ novel and arousing information via sympathetic cardiac responses, typically indexed as increases in heart rate and/or blood pressure (Figure 1, Key figure). This change in sympathetic nerve activity is associated with activation of two endocrine systems, the hypothalamic–pituitary–adrenomedullary (HPA) and the sympathetic adrenomedullary (SAM) axes, that cause adrenal hormone release. Activation of the SAM axis instigates the release of epinephrine by adrenergic fibers in the periphery, whereas activation of the HPA axis triggers the release of cortisol. The adrenergic effects are quickly transmitted to the NTS in the brain stem via the vagus nerve’s release of norepinephrine (NE) [76]. The brain stem then communicates with CNS structures, including the LC and the amygdala, where dense adrenergic circuitry with the hippocampus and neocortex allow the LC and amygdala to exert modulatory influence over initial memory storage [1,76–78]. Other neuromodulators, specifically acetylcholine (ACh) in the hippocampus, have been hypothesized to suppress feedback networks in the hippocampus and neocortex during encoding and prevent interference from stored information. As evidence of this modulatory influence, inducing stress directly before learning boosts memory recall [2,47,80,81]. Memory proficiency is also linked to measures of sympathetic activation (and/or parasympathetic withdrawal) [2,82,83]. In sum, arousing experiences during wake directly before or during encoding can enhance memory by triggering a cascade of events that starts with the sympathetic nervous system and culminates in modulation of memory circuitry in the CNS.

During NREM sleep, these ‘tagged’ events now need to be consolidated but under different neural and metabolic conditions. Now, feedback networks between the hippocampus and neocortex become critical for replay and transfer [84–87]. Specifically, at sleep onset, all ANS activity plummets, with greater decreases in sympathetic versus parasympathetic activity, leaving parasympathetic/vagal output to dominate the ANS projections to the brain stem [71] (Figure 1). These reductions in excitatory sympathetic inputs in the periphery are mimicked in the CNS where adrenergic neurotransmission is also reduced throughout NREM sleep compared with waking [88,89]. The reduction in ACh in the hippocampus is also prevalent and is hypothesized to release the hippocampus from cholinergic suppression allowing for communication within the hippocampus and between the hippocampus and the neocortex [89]. Activation of sympathetic inputs, or increased vagal withdrawal, beyond normal levels expected during NREM or REM sleep may disrupt sleep-related consolidation processes, leading to less stable long-term memories. Indeed, increasing sympathetic activity directly before sleep, via an acute stress task, reduces HF HRV during NREM sleep [90]. However, the impact on postsleep memory performance has yet to be formally examined. We would hypothesize that increases in sympathetic arousal during sleep would disrupt the vagal/parasympathetic conditions that underlie CNS consolidation, and as a result, there would be increased cortical arousal, poorer sleep continuity, and increased forgetting of information learned prior to sleep. Further, the loss of
sleep-dependent vagal dominance could also set the stage for poorer next-day attention, memory encoding, and may be one pathway linking sleep to long-term cognitive impairments.

Considering the memory boosting impacts of both daytime arousal and the stabilizing effort of NREM sleep, timed correctly, these processes may work together to support memory formation. The encoding “tag” associated with the release of arousal-related neuromodulators (e.g., NE, cortisol) near new learning (and likely not near sleep) has been suggested to help select memory events for extraordinary processing during sleep [86]. This has been supported by a number of studies as well as a recent meta-analysis suggesting sleep (both NREM and REM) preferentially enhances emotional memory consolidation [91–93]. This framework shares aspects with our proposal outlined earlier that persistent sympathetic arousal (or vagal withdrawal) near sleep would...
work against the consolidation conditions optimized during sleep. Future studies considering ANS modulation (e.g., cardiac, hormonal) during sleep are necessary to better understand links between these dynamics.

During REM sleep, there is a powerful increase in cholinergic activity in the hippocampus, which is paired with a parallel increase in phasic sympathetic and vagal activity compared with NREM sleep (Figure 1). Septo-hippocampal cholinergic projections are widespread in the hippocampus releasing ACh in postsynaptic sites [94,95]. Increased ACh release, combined with diminished amounts of NE, supports REM-related long-term potentiation [95]. Studies in animal models have shown that vagal nerve stimulation results in an enhanced release of ACh. A recent study has shown that stimulating the vagus nerve in non-human primates can result in changes in local field potentials in the prefrontal, sensorimotor, and parietal cortices during sleep [96]. Specifically, local field potentials in cortical regions after electrical stimulation of the vagus were larger during both NREM and REM sleep compared with cortical changes after vagal stimulation during active or quiet wake states. The REM-dependent increase in ACh has led to the characterization of REM sleep as a highly plastic brain state able to support neural reorganization and integration (Figure 1) [16,97]. This is consistent with research suggesting REM sleep may be an important time for associative memory enhancement as well as insight and creativity [14,71]. However, little research has explored the interdependence between these central and autonomic profiles during REM.

**ANS and cognitive aging**

Recent research efforts have highlighted the potential role of sleep in accelerated cognitive aging. One line of research has tied the reduced clearance and accumulation of amyloid and tau proteins to disturbed sleep and sleep loss [98,99]. The accumulation of these proteins can precipitate memory impairments as seen, for instance, in dementia and age-related cognitive decline [101,102]. Complementary research has shown that poor and disordered sleep exacerbates memory losses associated with age-related cognitive pathology. These findings suggest that successful treatment of sleep disruption may delay the onset of mild cognitive impairment, and sleep treatments are now emerging as a promising therapeutic target to mitigate Alzheimer’s disease symptomology in those with comorbid sleep disorders and Alzheimer’s disease [103–106]. These promising research trajectories may benefit from including sleep autonomic activity in their considerations.

During aging, responses of the ANS tend to become more rigid and less flexible [107–109]. In the context of memory processing, one could speculate that this leads to altered ANS communication with the CNS and reduced ‘tagging’ of relevant information during encoding. There is also a significant dampening of vagal activity [108,109], which has been tied to cognitive loss with aging [109,110]. Autonomic dysregulation during sleep could also set the stage for sympathetic hyperarousal, which would likely result in fragmented, less restorative sleep [111]. This may impede memory processes and could even explain some of the variance in normal age-related cognitive losses. Exploring these sleep–ANS interdependencies in aging remains an important venue for future work.

A clearer understanding of the role of the ANS during sleep may also provide insights into the use of adaptive memory strategies during aging. It has been argued that older adults often show a positive memory bias compared with younger adults [112]. For example, when asked to recall a series of negative, neutral, or positive pictures or words, older adults tend to remember neutral and positive stimuli better than negative ones, unlike their younger counterparts who display a negative memory bias, presumably fueled by ANS tagging and biased CNS processing. The
The adaptive nature of these affective memory biases has been theoretically discussed and attributed to psychological shifts in perspective, with older adults valuing positive information which precipitates preferential memory processing [113]. This may imply a decoupling of the ANS and memory with aging, or perhaps even a differential relationship between sleep and affective processing. Disentangling the mechanisms of these memory changes is a fruitful target for future work (see Outstanding questions).

Concluding remarks

Strong empirical evidence supports sleep’s role in memory formation; however, the underlying mechanisms are not well delineated. While much of the prior literature has focused on the CNS, emerging data support the influence of the ANS in this context, with recent data highlighting, for instance, the impact of cardiac fluctuations on postsleep memory performance. Integration of the role of ANS signaling as well as its coupling with the CNS into current sleep–memory frameworks may lead to a better understanding of the sleeping brain’s role in memory processing. These insights could also pave the path to novel interventions to improve memory and slow age-related memory decline. More research to carefully map the role of the ANS during sleep and its impact on memory is warranted.

Author contributions

L.N.W. wrote the first draft of the manuscript. All authors provided critical revisions and approved the final version for submission.

Declaration of interests

The authors declare no competing interests in relation to this work.

Resources


References


Outstanding questions

To what extent do autonomic inputs impact each phase of the memory process – encoding, consolidation, and retrieval?

What are the ways that cardiac–brain coupling informs arousal-dependent tags of information? How do these autonomic tags bias sleep-dependent consolidation?

How do memory-related neuromodulators (e.g., NE, ACH) shift in response to vagal inputs during sleep? Can vagal-dependent shifts in memory-related neuromodulators illuminate ANS-CNS pathways important for memory stabilization and integration?

What are the mechanistic pathways linking autonomic shifts during sleep to age-related memory declines? Can studies of ANS dysregulation be extended to examine sleep’s role in pathological aging?


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