Trends in
Neurosciences

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A role for respiration in coordinating sleep oscillations and memory consolidation

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Memory consolidation is thought to rely on the interplay of sleep-related brain oscillations. Drawing on recent findings that highlight the influence of respiration on these rhythms, we outline a framework positioning respiration as pacemaker for sleep's memory function. By orchestrating the cardinal non-rapid eye movement (NREM) oscillations, namely slow oscillations, spindles, and sharp wave-ripples, respiration may coordinate the hippocampo-cortical crosstalk essential for memory consolidation.

Coupled sleep oscillations and memory consolidation

Contemporary models propose that the fundamental vehicle of memory consolidation; that is, the strengthening of episodic memories during sleep, is the reactivation of prior encoded information. Through reactivation, memory representations are transferred between the hippocampus and cortical long-term stores, transforming initially labile representations into enduring memories [1].

A central aspect of these theories is that neuronal oscillations during NREM sleep regulate memory-related information flow between distant brain areas [1,2]. Specifically, the temporal coordination between cortical slow oscillations (<1 Hz), thalamic sleep spindles (12–16 Hz) and hippocampal sharp wave-ripples (SWRs, 80–120 Hz in humans) is suggested to enable the essential communication between the hippocampus and the cortex and the strengthening of memory representations in cortical networks [1].

Recent findings have corroborated the view that the precise coupling of these canonical sleep oscillations is critical for effective memory consolidation [1,3]. The fidelity of their interactions has turned out to be a reliable predictor of the behavioral expressions of memory consolidation and to impact reactivation processes [1,3]. Conversely, even subtle disruptions in their synchrony – whether experimentally induced, disease- or age-related – impair the memory function of sleep both in humans and rodent models [1]. However, how the sleeping brain, largely isolated from external sensory input, coordinates the synchronization of these cardinal oscillations across distant networks remains a key open question [2].

Here, we briefly synthesize recent work in humans and rodents to propose a physiological framework in which respiration, a vital body rhythm, that has been shown to impact brain functioning and cognition during wakefulness [4], may serve as a pacemaker for brain-wide communication and hence memory consolidation during sleep. By modulating the emergence of slow oscillations, spindles and SWRs at their sites of origin (i.e., prefrontal cortex, thalamus, and hippocampus), respiration may facilitate their hierarchical coordination in service of memory consolidation.

Respiration impacts neural activity and cognition during wakefulness

Compelling evidence from rodent and human studies demonstrates that respiration profoundly shapes neural activity during wakefulness [5]. Breathing-entrained oscillations have been identified in both rodents and humans across various frequencies and brain areas [5–8]. Respiration has also been found to directly shape perceptual, motor, and cognitive processes in humans, typically enhancing performance during the inspiratory phase [4].

How might breathing exert its impact on neural activity and consequent cognitive function? Although the breathing rhythm originates in the preBötzinger complex within the medulla, sensory input from nasal breathing might be critical for modulating brain functions [9]. Studies in rodents have shown that mechanoreceptors in olfactory sensory neurons respond to airflow, eliciting respiration-locked oscillations in the olfactory bulb. These oscillations propagate along the olfactory pathway via the piriform and entorhinal cortices to neocortical and hippocampal regions. At downstream targets, current source density analyses revealed respiration-locked current sinks specifically in deeper layers, suggesting entrainment occurred via synaptic transmission rather than volume conduction from the olfactory bulb [2]. Although the exact mechanism by which local networks convert afferent breathing-input into local field potential (LFP) oscillations remains incompletely understood, current evidence – including single-unit recordings from the prefrontal cortex and hippocampus – indicates a higher proportion of respiration-entrained interneurons compared to pyramidal cells [2]. These results imply that respiration-locked inhibition might mediate rhythmic synchronization within local circuits, potentially driving respiratory oscillations [9]. Respiratory entrainment of local networks does not necessarily have to lead to neural synchrony at the breathing frequency or manifest in the LFP. Instead, this synchrony likely emerges from nonlinear dynamics influenced by the resonant properties of local circuits, the specific neurons recruited, and ongoing endogenous brain oscillations, which may also vary

across brain regions and vigilance states [8].

The sensory pathway proposed in the preceding text is supported by findings specifically highlighting the role of nose breathing in synchronizing neuronal oscillations and affecting memory during wakefulness in humans [6,10]. Another consideration which should be noted is that the respiratory rhythm generators in the brainstem may also contribute to the entrainment of breathing-related neural oscillations [2]; therefore, the exact mechanistic pathway through which respiration might impact brain activity remains unclear.

A role of respiration in governing sleep-related oscillations and memory reactivation

Endogenous processes during sleep are governed by internal pacemakers operating across various timescales, spanning ultradian and circadian rhythms down to the millisecond precision of sleep oscillations. The central premise of the concept outlined here is that respiration might act as one such pacemaker during NREM sleep. We propose that respiration locally modulates the emergence of slow oscillations, spindles, and SWRs during specific phases of the respiratory cycle (Figure 1), and that consequently, respiration may serve as a scaffolding rhythm, enabling the precise coordination of the cardinal NREM oscillations across distant brain regions and facilitating the relay and strengthening of reactivated memories within the hippocampo-cortical loop.

Complementary findings in mice and humans provide support for the proposed framework. Specifically, simultaneous single-unit and LFP recordings in head-fixed mice across the limbic system and prefrontal cortex revealed that respiration entrains neuronal activity in these areas, serving as a global synchronizing rhythm during NREM sleep [2]. The impact of

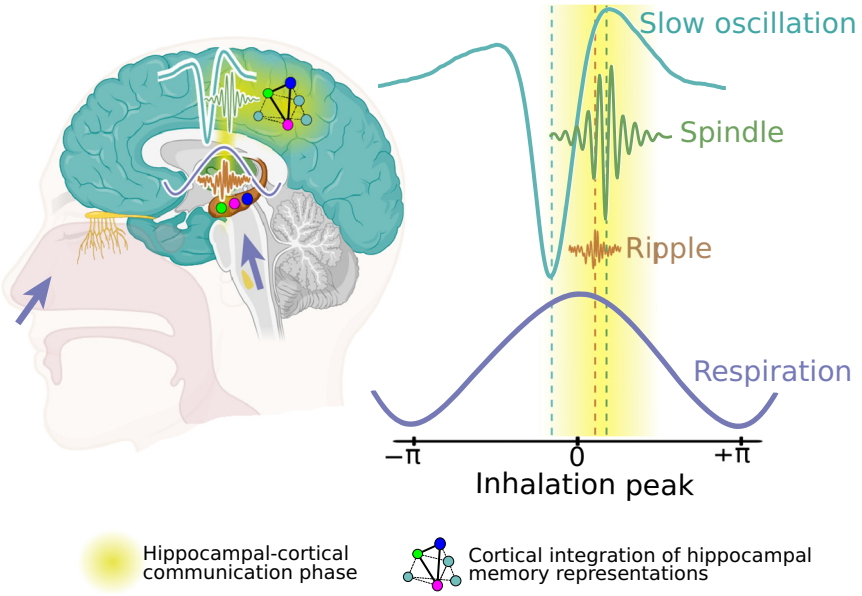

Figure 1. A respiration-centered framework for systems memory consolidation. We propose that respiration acts as a pacemaker for memory consolidation by biasing the emergence of slow oscillations, spindles, and sharp wave-ripples at specific phases of the breathing cycle [2,3]. This cross-regional calibration among sleep oscillations is thought to facilitate the relay of reactivated memories across the hippocampal–cortical loop, critical for memory consolidation. Two potential pathways for the influence of breathing on brain activity have been suggested: sensory input via the olfactory bulb (left arrow) and direct input via the respiratory rhythm center in the brainstem (right arrow) [2]. Anatomical illustrations in the figure were prepared, in part, using BioRender. Schwimmbeck, F. (2025) https://BioRender.com/o72q181.

respiration on neural activity remained intact even when input from the olfactory bulb was pharmacologically suppressed. The sustained synchronization was hypothesized to depend on a putative brain-wide corollary discharge – an efference copy of the respiratory motor signal – generated by the respiratory rhythm generators of the brainstem. While the exact pathways remain unclear, the authors suggested that the respiratory-entrained firing might be controlled either by somatostatin-expressing cells, which project from the preBötzinger complex to the thalamus, basal forebrain, and locus coeruleus (influencing cortical and hippocampal targets), or by vagal afferents. The observed entrainment not only aligned slow oscillation-related up- and down-states in the prefrontal cortex with the inhalation phase but ultimately biased hippocampal SWRs to emerge just prior to slow oscillation down-states in the cortex. Respiration also modulated prefrontal population responses to hippocampal SWRs, providing initial evidence for a putative role of respiration in coordinating cortico-hippocampal dynamics.

Extending these findings towards the multifaceted nature of sleep-related memory consolidation in humans, it was recently observed that respiration influences the emergence of NREM sleep rhythms in human participants [3,11,12]. Specifically, it was found that respiration during NREM sleep modulated both the emergence of slow oscillations and spindles in scalp EEG recordings in a sequential manner. Slow oscillation down-states were more likely to appear just before the inhalation peak, whereas sleep spindles tended to cluster just afterwards, indicating that respiration specifically influenced the likelihood of slow oscillations to group spindles. Importantly, the strength of the

coupling between respiration and slow oscillation – spindle events was tightly linked with the fidelity with which prior learned stimulus categories were reactivated during slow oscillation – spindles, establishing a functional role of respiration–brain interactions in human memory consolidation. Of note, a recent intracranial EEG study in individuals with epilepsy suggests that respiration may also affect hippocampal SWRs – the third key NREM oscillation, apart from slow oscillations and spindles – and their coupling to slow oscillations in humans [11].

While these initial studies in humans and rodents suggest that respiration might play a role in offline memory processing through its coordinating effect on sleep rhythms, causal evidence remains limited. Recent work using optogenetically induced ripples at different breathing phases enabled the study of ripple-associated hippocampal–cortical information flow dissociated from respiration, revealing that specific breathing phases amplify SWR-triggered cortical firing, boosting interregional communication efficiency [2]. Yet, the functional significance of such co-modulations for cognitive processes remains speculative. Moreover, the magnitude of the true effect of respiration, which might be catalytic rather than vital for memory consolidation, must be distinguished from concurrent physiological processes and other intrinsic pacemakers, such as cardiac or gastrointestinal rhythms. Addressing these and related questions (see Outstanding questions) could pave the way for a more comprehensive understanding of systems memory consolidation and its pathologies, extending brain-centered frameworks to encompass whole body interactions.

Acknowledgments

T.S. is supported by the Emmy Noether program of the German Research Foundation (492835154).

Declaration of interests

The authors declare no competing interests.

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https://doi.org/10.1016/j.tins.2025.02.005

References

1. Staresina, B.P. (2024) Coupled sleep rhythms for memory consolidation. *Trends Cogn. Sci.* 28, 339–351
2. Karalis, N. and Sirota, A. (2022) Breathing coordinates cortico-hippocampal dynamics in mice during offline states. *Nat. Commun.* 13, 467
3. Schreiner, T. *et al.* (2023) Respiration modulates sleep oscillations and memory reactivation in humans. *Nat. Commun.* 14, 8351
4. Brændholt, M. *et al.* (2023) Breathing in waves: understanding respiratory-brain coupling as a gradient of predictive oscillations. *Neurosci. Biobehav. Rev.* 152, 105262
5. Heck, D.H. *et al.* (2017) Breathing as a fundamental rhythm of brain function. *Front. Neural Circuits* 10, 115
6. Zelano, C. *et al.* (2016) Nasal respiration entrains human limbic oscillations and modulates cognitive function. *J. Neurosci.* 36, 12448–12467
7. Herrero, J.L. *et al.* (2018) Breathing above the brain stem: volitional control and attentional modulation in humans. *J. Neurophysiol.* 119, 145–159
8. Jung, F. (2023) Respiratory entrainment of units in the mouse parietal cortex depends on vigilance state. *Pflugers Arch.* 475, 65–76
9. Folschweiller, S. and Sauer, J.-F. (2021) Respiration-driven brain oscillations in emotional cognition. *Front. Neural Circuits* 15, 761812
10. Arshamian, A. *et al.* (2018) Respiration modulates olfactory memory consolidation in humans. *J. Neurosci.* 38 (48), 10286–10294. https://doi.org/10.1523/JNEUROSCI.3360-17.2018
11. Sheriff, A. *et al.* (2024) Breathing orchestrates synchronization of sleep oscillations in the human hippocampus. *Proc. Natl. Acad. Sci. USA* 121, e2405395121
12. Ghibaudo, V. *et al.* (2024) The timing of sleep spindles is modulated by the respiratory cycle in humans. *Clin. Neurophysiol.* 166, 252–261

Outstanding questions

To what extent does sleep-disordered breathing (e.g., obstructive sleep apnea) contribute to the compromised coupling of sleep-related oscillations in the elderly or in patients with psychiatric disorders? Could restoring normal breathing offer an interventional pathway for sustaining the memory function of sleep in these populations?

Can respiration be harnessed to enhance the impact of noninvasive brain stimulation on memory performance? For instance, could targeted memory reactivation during NREM sleep with reminder cues timed to inhalation improve later memory retention as compared to cues delivered during exhalation?

To what extent do sensory (e.g., olfactory bulb route) versus nonsensory (e.g., brainstem route) breathing-locked inputs modulate neuronal activity during sleep, and do they target the same brain regions?

Does respiration, in addition to coordinating neural rhythms during NREM sleep, also influence desynchronized, non-oscillatory (aperiodic) brain activity? Do these effects differ across sleep stages?

Given the large variation in respiration rates between mice (2–5 Hz) and humans (0.2–0.3 Hz), how can common and species-specific mechanisms explain the (congruent) influence of respiration on brain circuits across species?