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Old Brains Come Uncoupled in Sleep: Slow Wave-Spindle Synchrony, Brain Atrophy, and Forgetting

Highlights

- Precise coupling of NREM slow waves and spindles dictates memory consolidation
- Aging impairs slow wave-spindle coupling, leading to overnight forgetting
- Age-related atrophy in mPFC predicts the failure of such coupling and thus memory

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In Brief

Helfrich et al. demonstrate that the precise coupling between sleeping brainwaves, called slow waves and spindles, supports memory retention. However, this brainwave coupling during sleep is impaired in older adults due to loss of tissue in the medial frontal lobe, resulting in next-day forgetting.

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Old Brains Come Uncoupled in Sleep: Slow Wave-Spindle Synchrony, Brain Atrophy, and Forgetting

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SUMMARY

The coupled interaction between slow-wave oscillations and sleep spindles during non-rapid-eye-movement (NREM) sleep has been proposed to support memory consolidation. However, little evidence in humans supports this theory. Moreover, whether such dynamic coupling is impaired as a consequence of brain aging in later life, contributing to cognitive and memory decline, is unknown. Combining electroencephalography (EEG), structural MRI, and sleep-dependent memory assessment, we addressed these questions in cognitively normal young and older adults. Directional cross-frequency coupling analyses demonstrated that the slow wave governs a precise temporal coordination of sleep spindles, the quality of which predicts overnight memory retention. Moreover, selective atrophy within the medial frontal cortex in older adults predicted a temporal dispersion of this slow wave-spindle coupling, impairing overnight memory consolidation and leading to forgetting. Prefrontal-dependent deficits in the spatiotemporal coordination of NREM sleep oscillations therefore represent one pathway explaining age-related memory decline.

INTRODUCTION

The precise temporal coordination of non-rapid-eye-movement (NREM) sleep oscillations has been proposed to support the long-term consolidation of memory (Diekelmann and Born, 2010; Walker and Stickgold, 2006). Within these theoretical frameworks, temporal interactions between cortical slow oscillations (SOs; <1.25 Hz), sleep spindles (~12–16 Hz), and hippocampal ripples (~80–100 Hz) form a hierarchy that allows for information transformation necessary for long-term memory retention (Diekelmann and Born, 2010; Frankland and Bontempi, 2005; Latchoumane et al., 2017; Rasch and Born, 2013; Staresina et al., 2015). In particular, the depolarizing "up-states" of the SOs are proposed to facilitate sleep spindle and ripple expression, with hippocampal ripples being temporally nested into spindle troughs (Rasch and Born, 2013; Staresina et al., 2015). The coupling of these NREM oscillations is thought to support intrinsically timed information transfer across several spatiotemporal scales underlying long-term memory (Diekelmann and Born, 2010).

There is, however, limited empirical evidence supporting this oscillatory interaction model of hippocampal memory consolidation. Non-invasive brain stimulation findings have demonstrated that boosting SO power can indirectly co-modulate sleep spindle activity (Ladenbauer et al., 2017; Marshall et al., 2006), while SO-spindle coupling during a nap in young adults tracks offline memory retention (Niknazar et al., 2015). Yet, the mechanistic relationship of SO-spindle synchrony and how this determines the success or failure of overnight hippocampal-dependent memory consolidation remains unknown, as does the causal necessity of brain regions in supporting coupled NREM oscillation dynamics and memory benefit.

Regarding the latter, there is growing evidence that aging markedly disrupts sleep and overnight memory consolidation (Mander et al., 2017). If sleep oscillatory coupling is compromised in older adults, what is it about the aging brain that degrades interactive synchrony of NREM oscillations, thereby leading to memory impairment? This question is of special relevance as it may reveal a currently under-appreciated mechanism (impaired SO-spindle coupling) that contributes to memory decline in later life and, if identified, would define a novel therapeutic target for clinical intervention (Ladenbauer et al., 2017).

Here, we address these unanswered questions by combining structural MRI, polysomnography with full-head (19 channel) scalp electroencephalography (EEG), and the assessment of sleep-dependent hippocampal memory in young and older adults. We specifically tested the hypothesis that the precise temporal coupling of cortical NREM SOs and spindles, as predicted by theoretical models, facilitates overnight memory retention in young adults and whether older adults have a temporal un-coupling of these oscillations, leading to impaired overnight