

COGNITIVE NEUROSCIENCE

COMMENTARY

Rhythms of sleep: orchestrating memory consolidation (Commentary on Clemens *et al.*)



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During sleep, consolidation of declarative memory is thought to be mediated by a ‘dialogue’ between hippocampal and neocortical networks, promoting the reorganization of recent memory traces (Buzsaki, 1996; Clemens *et al.*, 2005). Consistent with this hypothesis, several rodent studies have established a temporal relationship between 12 and 15 Hz cortical sleep spindle oscillations and high-frequency ripple bursts originating in the hippocampus (Clemens *et al.*, 2006, 2007, 2011). Both spindles and ripples are thought to facilitate synaptic plasticity and the consolidation of memory. An accumulating body of evidence indicates that network-level ‘reactivation’ of recent experience occurs during ripple bursts in rodents (Ji & Wilson, 2007; Marshall & Born, 2007), while human studies demonstrate that spindle activity during post-learning sleep predicts enhanced retention of recently learned material (Siapas & Wilson, 1998; Sirota *et al.*, 2003; Schabus *et al.*, 2004; O’Neill *et al.*, 2010). Nevertheless, the dynamics underlying a potential role for spindle–ripple interactions in cortical plasticity remain largely unknown.

In their new study, Clemens *et al.* (2011); (this issue) report the first human data examining millisecond-timescale temporal interactions between hippocampal ripples and cortical sleep spindles. Intracranial EEG data were acquired in epilepsy patients from implanted parahippocampal foramen ovale electrodes, which the authors have previously established as sensitive for detecting 80–140 Hz ripple bursts similar to those described in the hippocampus proper (Sirota & Buzsaki, 2005). Clemens *et al.* (2011) demonstrate a correlation between spindles and hippocampal ripples on two distinct timescales. First, in line with the findings of prior studies (Sirota & Buzsaki, 2005; Clemens *et al.*, 2006, 2007, 2011), ripple activity was increased during the ± 1 s window surrounding spindles. More significantly, however, Clemens and colleagues also found that ripple bursts were tightly phase-locked to the ‘troughs’ of the individual oscillations comprising a spindle (at which time neuronal excitation presumably reaches a maximum), with ripple activity reaching a peak just a few milliseconds prior to each trough. This phase-locking of ripples to spindle troughs on a millisecond timescale has been reported in only one prior study [in rodents (Clemens *et al.*, 2007)], and is relevant to elucidating mechanisms of sleep-dependent plasticity for several reasons. Firstly, coordinated activity on this timescale cannot be explained via a generic influence of the < 1 Hz cortical slow oscillation, known to group sleep rhythms on the multi-second timescale (Steriade, 2003; Tamminen *et al.*, 2010), suggesting there may be a particular functional significance for these more precisely timed interactions between ripples and spindles. Secondly, this observation supports the longstanding suggestion that hippocampal output during ripple bursts induces plasticity in cortical targets: as ripples are associated with the ‘reactivation’ of specific recent memory traces, timing their expression to maximally excitatory phases of a spindle could optimally facilitate hippocampus-mediated cortical plasticity.

Interestingly, Clemens *et al.* (2011) found that ripple activity consistently peaks just *prior* to spindle troughs. In contrast, Sirota *et al.* (2003) reported that both ripples and CA1 unit activity peaked approximately 50 ms after spindle troughs in rodents, speculating that neocortical activity exerted a modulating influence on hippocampal networks, triggering the expression of ripples. The present findings may prompt some renewed discussion about the causal direction of this particular hippocampal–cortical interaction, as some models of sleep-dependent memory consolidation favor the notion that hippocampal memory reactivation during ripple bursts should exert a driving influence on mechanisms of plasticity in the cortex rather than *vice versa*. Regardless of such remaining questions, these observations by Clemens and colleagues add an important level of nuance to our understanding of oscillatory brain dynamics underlying sleep-dependent memory consolidation in humans, providing further evidence that the functional significance of sleep spindles lies in their facilitation of hippocampus-mediated cortical plasticity during sleep.

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