Overnight alchemy: sleep-dependent memory evolution

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Diekelmann and Born offer an elegant and convincing overview of evidence supporting the role of sleep in the consolidation of newly acquired memories (The memory function of sleep. *Nature Rev. Neurosci.* **11**, 114–126 (2010))[1]. An increasing awareness of memory stages that move beyond classical consolidation (for example, see REF. 2), a process concerned with the veridical preservation of stored information, highlights the internal contradictions of a system that, on the one hand, seeks to preserve memories in their original form and, on the other hand, allows them to evolve into more generalized representations of the world in which we live.

Although there is considerable evidence that slow-wave sleep (SWS) facilitates the consolidation, and thus the preservation, of newly formed episodic memories[3], emerging data suggest that sleep, and in some cases rapid eye movement (REM) sleep, can play an important part in the extraction of generalized informational schemas from individual experiences[4–6]. This is an alternative view to that proposed by Diekelmann and Born[1], which examines systems — followed by synaptic — consolidation across the night.

Here, we focus on the integrative stage of memory processing[3,7], beyond consolidation. Without implying that any of these stages is uniquely linked to a specific brain state, we review evidence for the proposal that sleep, and REM sleep in particular, supports three specific but not mutually exclusive forms of memory integration: first, the unitization of recently acquired related items; second, the assimilation of recently encoded items into networks of more remote items; and third, the abstraction of general rules from existing information stores, a process that leads to the construction of novel, higher-level schemas (FIG. 1).

Unitization

The human brain is remarkably efficient at combining temporally and conceptually distinct memories into 'unitized' constructs, especially during sleep. For example, overnight unitization has been observed in a sequential finger-tapping motor skill task[8] in which subjects learn to type numerical sequences, such as 4-1-3-2-1-3-2-1-4. During initial learning, subjects seem to break the sequence into 'chunks' (for example, 413-21-3214), separated by brief pauses. But following a night of sleep, the sequence becomes unitized and is typed without pauses (that is, 413213214). Similar unitization has been observed in a transitive-inference task[9] in which subjects are explicitly taught the relationships between pairs of elements from a 5-element set and then, 12 hours later, are asked to infer the relationships between novel pairs of elements. Although all subjects show improved performance, those tested after a night of sleep (as opposed to others trained in the morning and tested that evening) showed a disproportionate 25% advantage in correctly inferring the most distant relationships. Such findings emphasize the ability of sleep to link separate yet related items, producing useful and efficient unitized representations and conceptual schemas.

Assimilation

The human brain also integrates new memories into pre-existing networks of related information, a process referred to as assimilation[10]. Such assimilation might be optimized during REM sleep. Subjects can solve 30% more anagram word puzzles following awakenings from REM sleep than after non-REM (NREM) awakenings[11]. Similarly, following awakenings from REM sleep (but not after awakenings from NREM sleep or during waking), normally weakly related word pairs produce more semantic priming than do strongly related pairs[12]. A more specific example of assimilation is the incorporation of newly learned spoken words into pre-existing lexical memory stores, measured by the ability of a new word to compete with well-known, phonemically related words during auditory

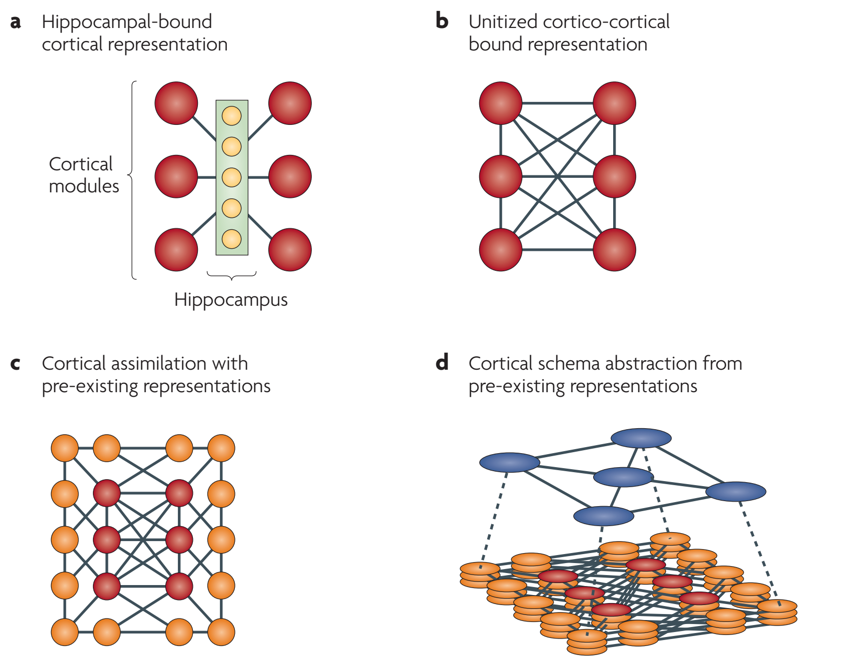

Figure 1 | **Evolving stages of episodic memory representations. a** | During initial encoding, the hippocampus binds neocortical elements (shown in red) of the episodic experience. During subsequent sleep, new representations of the experience are formed. **b** | Unitized memory representations result from new cortical connections between recently learned, related items, the products of which (shown as conjoined items) are often applicable beyond the bound elements. **c** | Assimilated representations result from new associations formed between recent, possibly unitized, experiences (shown in red) and pre-existing, semantically related memory networks (shown in orange). **d** | Abstracted representations (generalized schemas) result from the discovery of a commonality among newly acquired or pre-existing unitized and assimilated representations, and represent new information not previously identified or stored. Such abstraction reflects the distillation of multiple representations and the creation of a novel representation defining a statistical law or 'grammar', built from, yet distinct from, the pre-existing associative networks.

word recognition. A night of sleep, but not an equivalent time spent awake, supports such assimilation[13].

Abstraction

Assimilation presupposes the existence of conceptual schemas into which new information can be assimilated. The 'abstraction' of such schemas from raw information can also benefit from sleep. Infants exposed to an artificial grammar consisting of nonsense three-syllable 'words' display awareness of the abstracted grammatical rules embedded in the stimuli following a nap, but not after an equivalent time period awake[14]. Similarly, a night of sleep more than doubles the likelihood that subjects will discover a hidden rule for solving a class of mathematical problems[15]. Such building of rule abstraction may also benefit specifically from REM sleep. Several studies using the 'Wff N Proof' logic task[16] (a probabilistic learning task[17]) and the remote-associates task[18] all implicate REM sleep in the abstraction of patterns and rules from large numbers of stimulus trials.

Rethinking sleep and memory

Beyond preserving or strengthening item memories, sleep seems to facilitate the 'offline' assimilation and generalization of these individual memories in a manner that optimizes their potential usefulness for dealing with events in the future. Such integrative models of memory processing have been suggested before in various contexts[3,4,7,19].

What we hope to add to this discussion is the functional distinction between these stages. We propose that a first post-encoding stage, which might occur preferentially during SWS, consolidates new episodic item memories while keeping individual memory representations separate and distinct. By contrast, a second, potentially REM-dependent, stage supports the integration of these and older memories into rich associative networks, mapping our past and predicting our future, a process requiring a cooperative systems-level transformation of memories. It is this second stage of memory integration that extracts, abstracts and generalizes recently consolidated item memories in a process that might be linked to the production of dreams. Several aspects of REM physiology support its role in such integrative functions. These include reduced levels of noradrenaline and increased levels of acetylcholine[5], minimal hippocampal outflow to the cortex[20], cortico-cortical processing in association areas without contribution from dorsolateral prefrontal regions[21], and dominance of theta wave carrier oscillations, facilitating associative linking throughout disparate cortical areas[22].

Although the first stage of item memory consolidation might occur across a single night, or even during a single period of SWS, effective integration of these memories probably takes several NREM–REM cycles or multiple nights before optimal representations are complete. Indeed, these memory-processing demands might be one evolutionary factor that has shaped the canonical human NREM–REM cycle, and within it, the shift from SWS to REM dominance across the night. Eventually, veridical representations of most episodic item memories probably decay (maybe actively so during sleep), leaving only the abstracted, generalized meaning of accumulated experiences. Perhaps it is no surprise that we are never told to "stay awake on a problem".

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