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Current Opinion in Neurobiology

Parsing the role of sleep in memory processing

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It would be nice if we could talk about sleep and memory as if there were only one type of memory and one type of sleep. But this is far from the case. Sleep and memory each comes in many forms, and furthermore, memories can go through multiple forms of post-encoding processing that must be individually addressed. Finally, sleep stages *per se* do not affect memories. Rather, the neuromodulatory and electrophysiological events that characterize these sleep stages must mediate sleep-dependent memory processing. In this review, we attempt to parse out the relative contributions and interactions of these often frustratingly complex systems.

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Current Opinion in Neurobiology 2013, **23**:847–853

This review comes from a themed issue on **Circadian rhythm and sleep**

Edited by **Clifford Saper** and **Amita Sehgal**

For a complete overview see the Issue and the Editorial

Available online 22nd April 2013

0959-4388/$ – see front matter,

http://dx.doi.org/10.1016/j.conb.2013.04.002

Parsing off-line memory processing

Three separate issues must be addressed in discussing how memories are processed after their initial encoding; first, the type of memory; second, the type of processing; and third, the time course of the processing. Figure 1a shows the standard taxonomy of human memory [1]. While originally based on conceptual differences among memories, these categories are largely subserved by distinct anatomical brain regions. Thus, declarative memories are hippocampally dependent [2], at least initially (e.g. [3]), while procedural memories are hippocampally independent, instead relying heavily on the striatum [4,5].

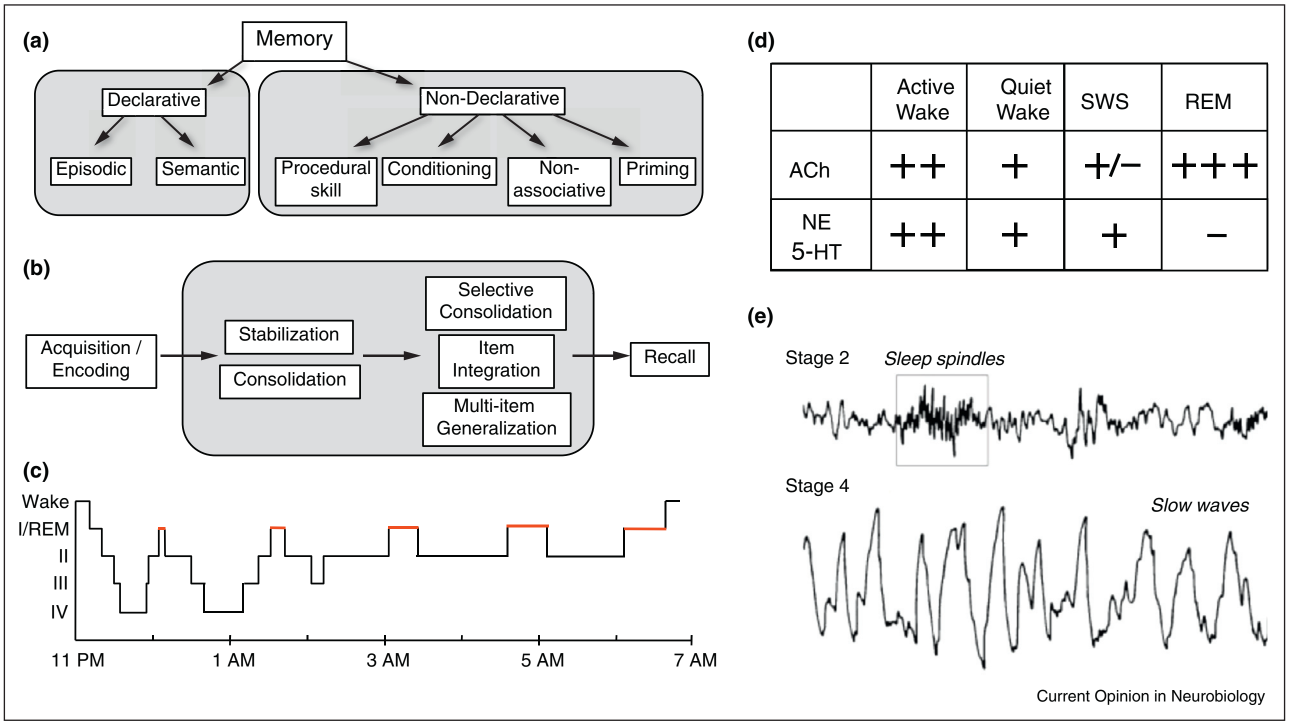
Less clear is the extent of post-encoding memory processing (Figure 1b). That some form of post-encoding processing occurs has been clear since the work of Müller and Pilzecker in 1900 [6], who introduced the concept of memory 'consolidation' as a form of post-encoding memory processing that turned an initially labile memory into a permanent form. These findings led to a dichotomization of memories. There was an initial, labile form of memory that could be disrupted by electroconvulsive shock or protein synthesis inhibitors, and a consolidated form, into which the labile form was normally converted within a matter of hours [7]. But even these supposedly permanent memories could often be disrupted by hippocampal lesions after even longer post-encoding intervals — up to 2–5 days in rats [8], 4–8 weeks in primates [9] and years, perhaps even decades, in humans [10].

Beyond consolidation, several additional forms of post-encoding memory processing can take place. These can result in absolute improvements in procedural task performance, or qualitative changes in declarative memories. These will be discussed more fully below, as they are often sleep-dependent changes. But they include selective item consolidation, where only some studied items are selected for retention; item integration, where new memories are integrated into preexisting networks of associated memories; and multi-item generalizations, where gist and rules are extracted from a set of newly formed memories, and where false memories can be generated.

All of these modifications of an initially encoded memory occur over time. Some forms are complete within 2–4 hours, while others may extend across the life of the organism. Recognition of the full sweep of this time course makes the term 'consolidation' feel inadequate, certainly for describing the sum of these processes, and perhaps even for describing the initial 'consolidation' described by Müller and Pilzecker [6] and those who followed. Indeed, the permanence of these consolidated memories has been shown to be a misnomer. 'Consolidated' memories can be returned to a labile state simply by reactivating them. Once relabilized, they must be 'reconsolidated' by a process that requires protein synthesis [11], and in the absence of such reconsolidation, the memory can be lost. Thus, memory consolidation may only hold a memory from the time of its consolidation until it is next recalled, when consolidation must occur anew.

We have begun to refer to this collection of post-encoding processes as memory 'evolution' [12••]. We use this term to highlight two aspects of post-encoding processing. First, the changes that occur over time shape the memory into a form that can be quite different from its original form, but which has evolved into a form that optimally serves the projected future needs of the organism. Thus, some memories are most useful if kept distinct from others and in their original form, while others are most useful when combined with others and subsumed under

Figure 1



Sleep and memory. Sleep-dependent memory processing depends on **(a)** the type of memory being processed, **(b)** the stage or form of processing, **(c)** the sleep stage in which processing occurs, **(d)** the neuromodulatory regulation of that sleep stage, and **(e)** the unique electrophysiological activities found in specific sleep stages.

an overarching rule that succinctly describes all of the original memories. The second reason we use the term evolution is to highlight the fact that memories continue to change over time, molded by new experiences and new needs.

Parsing the forms of memory processing

Any discussion of sleep and memory requires that we understand what types of memories and memory processes are under consideration. But the state dependency of these processes can be summarized by stating that, with the exception of the rapid (2–4 hours) consolidation that provides the initial stabilization of the memory, there is evidence that each of these forms of memory processing occurs preferentially, if not exclusively, during sleep.

Memory stabilization and enhancement

While the initial consolidation of memories occurs independent of sleep–wake states, sleep can produce additional stabilization and even absolute enhancement. For declarative memories, subjects who memorize a list of word pairs are more susceptible to interference from subsequently learned related word pairs if the interference training comes after a day of wakefulness than if it comes after a night of sleep [13,14]. Enhanced memory following sleep, relative to wake, has also been seen for word pairs [15], as well as for the details within stories [16] and even nonsense syllables [17]. But in these studies, what is seen is *less memory deterioration* across sleep than across wake, rather than an absolute improvement in memory after sleep. Such absolute improvement has only been seen for procedural learning, where competing processes of forgetting are often not present. Such absolute improvement following sleep, but not following daytime wake, has been seen for motor [18,19], visual [20] and auditory [21] learning tasks, as well as more complex procedural learning tasks, such as the Tower of Hanoi [22] or the probabilistic weather prediction task [23]. The absence of absolute performance enhancement for declarative memories suggests that there is forgetting of these memories across both wake and sleep that exceeds any enhancements of memory during sleep.

Selective item consolidation

More recently, it has become clear that not all memories benefit from sleep. In some cases, this has been seen as the selective retention of emotional material over neutral, whether pictures [24], emotional texts [25], or simply emotional portions of pictures [26]. In other cases, sleep selectively benefits newly formed memories that are expected to have future relevance [27•] or for which subsequent recall will be rewarded [28], even when these