

Figure 1 (Sheth). A hypothetical evolution of local brain processes as a function of behavioral state, and the effects on memory performance. Various processes (A, B, and C) combine to affect memory test performance (ordinate). With continual practice while the observer is awake, learning occurs (A), which improves performance. However, neuronal fatigue (B), which occurs hand in hand with the learning, impairs performance. During sleep, neural circuits slowly recover (C), which gives rise to "latent learning." A, B or C are transparent to the experimenter. Observed performance is some (nonlinear) combination of them.

With these ideas as a basis, I propose that two separate local brain processes are involved in the learning of a procedure or skill (see Fig. 1). Over repeated trials, the awake observer practices specifics of the procedure (A). Learning is a multifaceted process, one facet being the progressive restriction in the brain circuits that influence performance (Edelman & Tononi 2000; James 1890). I propose that while this process does not depend on sleep, a second independent process exists that does. With increasing neural specialization during learning, the circuits or synapses repeatedly engaged in the procedure adapt or fatigue (B). Synapse-specific fatigue during procedural learning is unavoidable. Repeated stimulus processing produces decreased responses in brain circuits associated with that processing – a "repetition suppression" effect (Brown & Xiang 1998; Desimone 1996; Wiggs & Martin 1998). The inefficiency in local signal transmission that arises from the synaptic fatigue or adaptation masks expression of the learning. With prolonged training on a task that involves both speed and skill, the net product of these two contravening processes, measured behaviorally, is asymptotic learning (Karni & Sagi 1991). Over still longer training periods, a decline in performance is observed (Mednick et al. 2002). Several studies (e.g., McCollough 1965) have shown that the effects of adaptation can be long lasting, particularly if a select few synapses, specific to certain stimuli or conditions and not others, are adapted.

The recovery of functions related to sensory transmission, such as the restoration of neurotransmitters or the re-formation of receptors, likely involves protein synthesis, which has its own characteristic time course, one that is longer than the time course of resource depletion in the synapse. Thus, sleep-dependent synapse-specific recovery (Fig. 1) is independent of the training in the wake state. It is, however, dependent on sleep; sleep cannot be replaced with awake resting, which fails to control internally generated activity in key brain areas, or by reversible inactivations of brain areas engaged in the consolidation, which only delays the recovery and may even shrink the critical time window during which the learnt information can be actively enhanced (target article, sect. 2.3.2.2).

Sleep is clearly not monolithic. SWS, and non-REM sleep in general, are believed to have a restorative role in brain function (Horne 1988). It is notable that there is correlational evidence for the role of non-REM sleep in memory consolidation in humans (Stage 2 sleep for motor skill learning, Walker et al. 2002; early SWS for visual discrimination skill consolidation, Gais et al. 2000; Stickgold et al. 2000b). This dovetails nicely with the idea of synapse-specific recovery. Replay of behavior-specific patterns during late REM sleep, if short-lived, may reactivate and reinforce the task-related synapses (target article, sect. 2.4.2) with minimal synaptic adaptation or fatigue.

In contrast to procedural memory, evidence that sleep improves declarative memory is inconsistent (sect. 2.2). Perhaps conclusive evidence exists but has eluded researchers, or perhaps procedural and declarative memories differ in the same respects that make the former more susceptible to sleep. Procedural learning is usually dependent on the context and modality in which the material was presented initially (Squire 1986), are "realized as cumulative changes stored within the particular neural systems engaged during learning" (Squire 1986), and typically require training for several minutes to several hours on the procedure. In contrast, declarative learning is flexible, accessible to all modalities and can be "one-shot." The weaker synaptic specificity and quicker learning of declarative as opposed to procedural learning implies less localized declarative storage, which means, by our hypothesis, less synapse specific fatigue, and smaller benefits of sleep.

In sum, two issues are critical in the present account: (1) Synaptic specificity: With greater synaptic specificity, there is greater impact of sleep on local synaptic recovery; and (2) the need for speed: On perceptual as well as motor learning tasks, perception and/or motor action must be conducted within a finite period of time for optimal performance (e.g., Stickgold et al. 2000b; Walker et al. 2002). With time constraints, inefficiency of synaptic transmission takes on even greater significance, and, because speed-accuracy tradeoffs are commonplace, the effects of sleep deprivation are observable on measures of speed as well as accuracy.

By varying each factor, this hypothesis can be experimentally verified. One possibility is to vary the degree of synapse-specific adaptation in two sets of synapses that exhibit learning during training. Visual discrimination skills that transfer to different conditions (Ahissar & Hochstein 1996; 1997) are suitable for this. Synapse-specific sleep dependent recovery will accordingly differ between the two sets. Learning following sleep loss will be impaired following sleep loss in both brain circuits, but less so in the brain circuit that learnt the procedure indirectly via transfer.

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The incredible, shrinking sleep-learning connection

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Abstract: Initial claims that REM sleep is important in the consolidation of all memories have been revised and reduced to the claim that sleep has a role only in the consolidation of procedural learning. Now, Walker hypothesizes that sleep has no role in the "stabilization phase of consolidation" but only in the "enhanced learning" phase of procedural learning. Evidence for this vague, truncated hypothesis remains as inconsistent as that for prior claims.

The idea that REM sleep is important for memory consolidation is attractive, since it would explain the vivid imagery of dreams as a repetition of the events of the prior day to enable the laying down of permanent memory traces. Unfortunately, dream reports do not support this idea. Most dreams concern emotions and activities that did not occur during prior days. Furthermore, most dreams are not subsequently recalled unless they are immediately rehearsed in waking following the dream (Rechtschaffen & Siegel 2000).

Those working on the role of sleep in human learning have modified their hypotheses to include non-REM sleep as well as REM sleep. Many studies of the relationship between human sleep and learning have focused on sleep's role in learning of word recognition and associations between words and events – tasks mimicking most of what goes on in school; this is what learning

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and memory researchers call *declarative learning*. Dr. Carlyle Smith, a leader in the sleep-memory consolidation field, after reviewing his own studies and many negative studies in the world literature, recently concluded that sleep is not important in declarative memory. He was quoted as saying "Declarative memory is such a large part of our memory that everybody would like to find [a link]. Yet no matter what I have done – I have deprived people of sleep, I have deprived people of REM sleep, I have deprived them of non-REM sleep – I have never seen any difference between people who got a good night's sleep and those who didn't" (*Los Angeles Times*, Feb. 3, 2003; see Smith 2001). Walker appears to accept this conclusion in his review, stating "a clear understanding of the role of sleep in declarative memory formation remains to be established in humans" (sect. 2.2, para. 6). However, if one accepts this conclusion, the domain of the sleep–learning connection is dramatically reduced.

In addition to redefining the role of sleep in human memory consolidation, this conclusion also has important implications for animal studies that have been used to support a role for sleep in memory consolidation. Several studies have claimed to see evidence of "replay" of neuronal activity during REM sleep or non-REM sleep. Most of these studies have seen this replay in the hippocampus (Lee & Wilson 2002; Louie & Wilson 2001; Pavlides & Winson 1989). However, it is well known that the hippocampus is critical for declarative leaning but of little importance in procedural learning (Eichenbaum 1999). Thus, even if one dismisses the technical problems with these studies (see Siegel 2001), their relevance to procedural learning and hence to the sleep-learning field is questionable.

A hallmark of sleep learning theories is the variability of hypotheses from study to study, even within studies by the same group. For example, studies of the consolidation of human procedural learning make contradictory claims, with some saying that REM but not non-REM sleep is important (De Koninck & Prevost 1991; Pearlman 1971), others stating just the reverse (Gais et al. 2000; Portnoff et al. 1966), others claiming that both sleep states are essential (Stickgold et al. 2000a), and still others making ad hoc claims, such as that "only the amount of stage 2 nonREM sleep obtained during the last quarter of the night" is important (Walker et al. 2002). The statistical reliability of such ad hoc hypotheses is questionable.

The most striking aspect of the current review is the further redefinition of the role of sleep in learning to be so limited and vague as to defy disproof. In earlier formulations, the author's colleagues indicated that memory consolidation occurs in sleep. It was emphasized that "no improvement" occurred in waking, and that therefore sleep is "absolutely required" for performance improvement (Stickgold et al. 2000b). In the current review, Walker subdivides consolidation into a "sleep-independent" process that makes memory "resistant to interference" and a "sleep-dependent" process of "enhancement." The "sleep-independent" process that makes memory "resistant to interference" sounds a lot like what learning theorists refer to simply as "consolidation." The two subdivisions of consolidation created by Walker's reformulation are difficult to separate operationally and this subdivision invites post hoc explanations of any observed effect.

Fatigue, circadian factors, and simply the passage of time have long been known to affect performance. In order to properly control for performance effects, it needs to be shown that sleep disruption produces a long term impairment of consolidation of tasks learned before the interrupted sleep, and that any decrements in performance during retesting were specific for the recently learned task. Similar tasks that had been learned previously should not be comparably affected by deprivation. It also needs to be shown that recovery from the performance decrements during learning that are known to be caused by intense practice were not creating an illusion of consolidation or "enhancement" when retesting after a recovery period. These sorts of controls have not been thoroughly and systematically done in studies claiming a role of sleep in memory consolidation (Siegel 2001; Vertes & Eastman 2000).

The scientific and popular interest in the possibility that sleep is important in memory consolidation does not derive from the hypothesis that sleep is "one of many states" in which memory consolidation occurs. If this were the case, we would be excited over the possibility that consolidation occurs during eating, drinking, and engaging in sexual behavior, and we would be exhorted to increase these activities when learning. Rather, it derives from the idea that sleep has a unique and important role in consolidation. The reformulated sleep–memory consolidation model proposed here advocates a "democratic," equal division of memory consolidation across sleep and waking states, a considerable dilution of the original idea.

Millions of humans have taken MAO inhibitors or tricyclic antidepressants, often for 10–20 years. These drugs profoundly depress or in many cases completely eliminate all detectable aspects of REM sleep. However, there is not a single report of procedural or declarative memory deficits attributable to such treatment. Similarly, well-studied individuals with permanent loss of REM sleep resulting from brain damage show normal learning abilities, including the best studied case of an individual who completed law school after his injury and was the puzzle editor of his city newspaper (Lavie et al. 1984). The "dual process" theories of learning, with both REM and nonREM sleep participating in memory consolidation, as well as REM sleep-based theories, are contradicted by these findings. Yet this literature is ignored in the current review.

It is common knowledge that sleep loss produces sleepiness and impaired concentration. Similarly, it is well established that sleep loss impairs performance of a variety of tasks in subsequent waking. Studies claiming to demonstrate an important role for sleep in memory consolidation have yet to establish that the effects they are observing are independent of these well-known phenomena.

Consolidation enhancement: Which stages of sleep for which tasks?

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Abstract: The Walker model raises a number of questions, particularly about the nature of the sleep states involved in consolidation enhancement. While REM sleep, Stage 2 sleep, and Stage 3/4 sleep have been implicated in procedural learning, we still do not understand which types of learning are involved with specific sleep states. Several possible ideas for future research are suggested.

Walker's article provides an interesting theory about the nature of procedural learning and how it relates to sleep. The theory is based primarily on the author's own work, but there are also data from other sources. The theory also relies heavily on the results of simple motor procedural or skills tasks, and the author's studies have reported on the sequential finger-tapping task. The idea that there are two basic components to motor skill learning is an interesting one. The concept of stabilization clearly seems to fit with the data that have been collected so far and the vulnerability of recently learned motor sequences in the first 6 hours after acquisition is quite interesting. However, of greater interest is the longer term second phase of consolidation enhancement, which appears to require sleep.

Involving sleep with memory systems has brought into focus the possibility that very different subsystems are at work, depending on the nature of the task. While it has been clearly demonstrated that sleep is necessary for consolidation enhancement, the particular state or states of sleep involved remains unclear. At this point, although some studies do not differentiate between sleep states, there is some information from different procedural learn-

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