

## Study in focus

### Sleep: a prescription for insight?

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“Please remember the number ‘3’. Now please remember what you had for breakfast and then, in your mind trace, the route you took to get to work this morning. What was the number you were asked to remember? The majority of readers will correctly respond ‘3’ and simultaneously note that this memorization task did not require a night of sleep, or even a catnap, for accurate recall.” From this trivial memory experiment, we can surmise that some memory processes are indeed independent of sleep. It is hard, however, to ignore the increase in recent studies reporting both sleep-dependent learning and sleep-enhanced learning.

#### Sleep-enhanced insight gain: both declarative and nondeclarative learning?

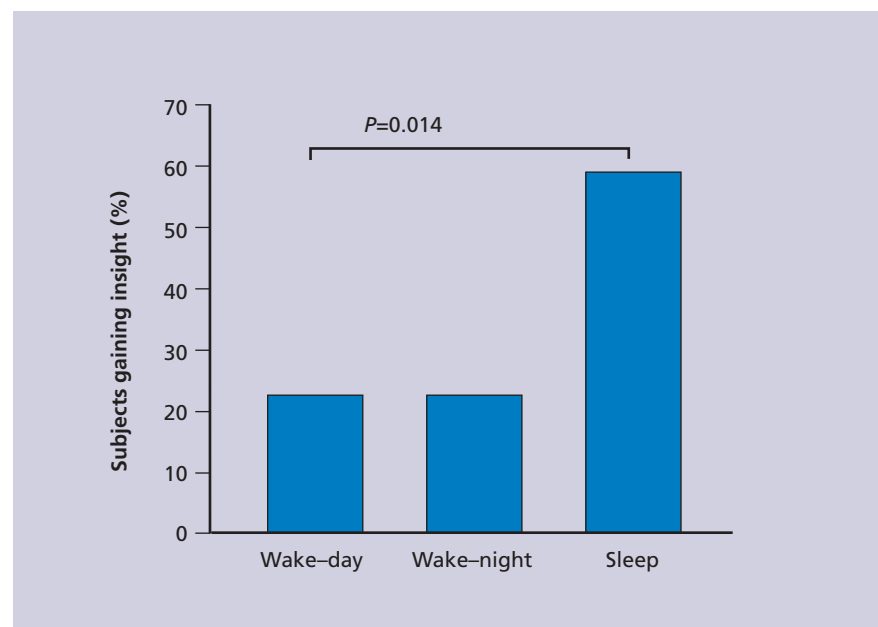
A paper by Wagner et al., published in the January edition of *Nature* 2004, demonstrated a unique relationship between sleep and learning in the form of insight gain.<sup>1</sup> Wagner et al. reported that post-training, nocturnal sleep significantly increased the proportion of participants who gained insight into a hidden rule of the trained task. Participants were tested on the Number Reduction Task (NRT) before and after one of the following:

- a night of sleep
- a night of sleep deprivation
- a full day of waking.

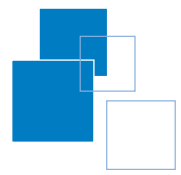
The NRT may be accurately performed using two possible methods. The first is an explicitly presented, brute force method whereby subjects apply two simple rules across seven steps to determine the final answer. The second requires divining the hidden structure of the task thereby allowing ‘solvers’ to leap ahead to the final answer after

only two steps. Insight was determined as the moment participants were able to jump to a final answer without completing the entire trial, as well as being able to explicitly state the hidden rule. Wagner et al. found that participants who slept between tests gained significantly more insight than either of the waking groups (fig. 1).

These interesting results provoke many further questions. To begin, what is the underlying mechanism of insight gain? While not entirely consistent with the authors’ interpretation, we believe that insight may be a hybrid between the two main systems of learning and memory: declarative (explicit) and nondeclarative (implicit) memory.<sup>2,3</sup> Declarative memory



**Figure 1.** Effects of sleep and wakefulness on the occurrence of insight. Columns indicate the percentage of subjects gaining insight into the hidden rule in the three experimental conditions of the main experiment, in which subjects either slept (at night) or remained awake (at night or during the daytime) between initial training and retesting.



includes both episodic memory (comprising knowledge of personal events or episodes), and semantic knowledge (comprising knowledge of ‘facts’ about the world). All of the other memories that do not require conscious acquisition and recall are part of a collection of nondeclarative and procedural memories. These memories include information acquired during skill learning (including motor skills, perceptual skills and cognitive skills), habit formation, simple classical conditioning, priming and nonassociative learning.

The insight gain studied by Wagner et al. initially revealed itself in an implicit manner.<sup>1</sup> Then, through a slow process (enhanced by sleep), it emerged from the nondeclarative into the declarative realms as a fully assembled insight into the task structure. The authors proposed that insight gain is not a procedural learning process, since the reaction time data did not become faster with learning, which is the hallmark of procedural learning. Instead, all participants who gained insight (regardless of whether they were in the sleep or wake groups) actually showed a slowing in reaction time just prior to insight gain compared with participants who did not gain insight. “Specifically, the slowing of reaction time in solvers appears to reflect the presence of an incipient representation of the rule overlapping with that required for implicit task performance.”<sup>1</sup> Nonsolvers’ reaction time continued to decrease as their procedural skills improved without declarative awareness. Solvers, on the other hand, showed a slowing in response while insight was emerging from nondeclarative information into a declarative reportable result. The insight may, therefore, develop in a nondeclarative fashion, but the moment of ‘aha’ indicates the solidification of the information into a declarative thought. Thus, insight gain appears to contain aspects of both declarative and nondeclarative learning.

The paper by Wagner et al. represents the latest in a series of studies demonstrating links between sleep and various types of learning. Sleep has been linked to nondeclarative learning<sup>4–6</sup> and, more controversially, to declarative learning.<sup>6–8</sup> The classic method for studying the effect of sleep on learning is to investigate changes in:

- task performance after selective sleep stage deprivation
- task performance after total sleep deprivation
- in sleep parameters correlated with task improvement.

It is the combination of all three of these investigations as well as testing of multiple memory systems that will lead to a more complete picture of the influence of sleep on learning. While the results of Wagner et al. are important and informative, a more complete picture of the role sleep may play in learning (as represented here by insight gain) would be afforded by further analysis of the sleep data. For example, are there any changes in sleep parameters between the experimental and nonexperimental sleep night, or a correlation between behavioral performance and sleep parameters? What is it about sleep that may have facilitated insight? The sleep parameter information is of particular interest as recent studies indicate that individual sleep stages may play specific roles in selective types of learning.

## Specificity of sleep stages for learning

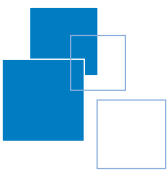
In his review of the literature on sleep and learning over the past 75 years, Smith concluded that there was little evidence for a positive effect of sleep in the consolidation of declarative material, and that the benefit of sleep was limited to procedural learning.<sup>7</sup> A possible explanation for Smith’s negative

conclusion relates to an historic overemphasis of sleep research focusing on rapid eye movement (REM) sleep. A number of recent studies suggest that task improvement relates to the interaction of the type of learning studied and specific sleep stages.<sup>6,9–11</sup>

Learning across a wide variety of tasks has been shown to depend on individually stage 2, stages 3 and 4 (which comprise slow-wave sleep [SWS]), and REM. For example, recent work by Walker et al. on a finger-tapping task demonstrated nocturnal sleep-dependent motor learning and implicated stage 2 as the relevant sleep stage.<sup>9</sup>

Multiple studies show links between SWS and declarative memory.<sup>7</sup> Plihal and Born found selective improvement in a declarative task in participants allowed only early-night sleep (SWS rich), but no improvement in a procedural learning task, whereas selective procedural learning was found in participants allowed only late-night sleep (REM rich) and no improvement in the declarative memory task.<sup>6</sup> Bodizs et al. made direct recordings of human hippocampal activity in epileptic patients and found that the relative spectral power of SWS was positively correlated with visual memory performance according to the Rey–Osterrieth Complex Figure Test, a declarative visuospatial memory task.<sup>12</sup>

REM sleep has frequently been demonstrated to aid procedural learning. Animal studies have shown that, during REM sleep, hippocampal neurons fire in the same spatial and temporal patterns as during training in a learning environment.<sup>13</sup> Firing rates in hippocampal CA1 place-cells exposed to their place field in previous waking experience were increased during subsequent REM sleep, as compared with firing rates of unexposed cells.<sup>14</sup> Further, investigations of the ‘REM window’ (a period of time after procedural



training when rats show increased amounts of REM and during which REM deprivation leads to diminished retention)<sup>15</sup> report that the REM window is specific to exposure to learning rather than mere stress, and the REM window can be modulated by increasing task demands.<sup>7</sup> In humans, similar results have been shown regarding REM sleep and a variety of nondeclarative tasks.<sup>5,16,17</sup> Performance improvements on a visual texture discrimination task have also been shown to require REM sleep.<sup>4</sup>

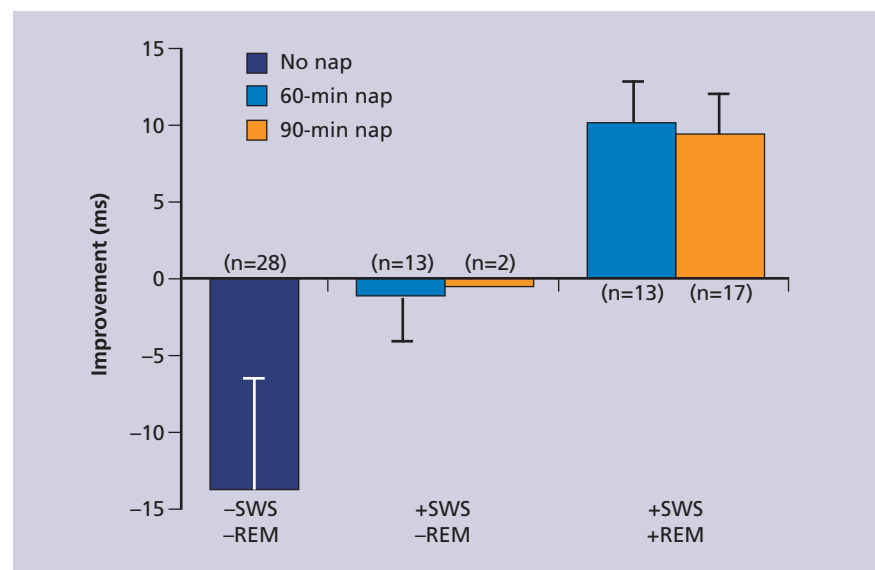
Stickgold and colleagues later showed that improvement in the texture discrimination task used by Karni et al. was dependent on both SWS and REM.<sup>4,11</sup> Stickgold et al. demonstrated that improvement in performance in the texture discrimination task occurred only after a full night's sleep.<sup>11</sup> By examining the effect of particular sleep stages on learning, Stickgold and coworkers noted a relationship between overnight improvement, and both SWS and REM sleep. Specifically, improvement correlated with the product of the amount of SWS in the early part of the night and REM in the last part of the night. Stickgold et al. proposed a two-step model for sleep-dependent learning, in which SWS and REM have independent and sequential roles in the process of consolidation.

The question of whether both SWS and REM are necessary for nondeclarative learning or whether only REM is necessary may be resolved by considering a different model of sleep-dependent learning. One possible model holds that learning is composed of multiple processes for which specific sleep stages are necessary. For example, Poe et al. suggest that the process of learning novel information may require a concomitant process of forgetting familiar information, and that both learning and forgetting are driven by REM sleep.<sup>18</sup> Poe and colleagues found that hippo-

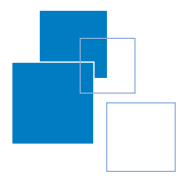
campal place-cell firing patterns to novel stimuli are replayed during REM sleep, but that the firing patterns experience a gradual phase shift during REM from being in phase with the peak of the theta cycle on the first day of training to being in phase with the trough of the theta cycle on the seventh day of training. The authors interpret these results as a learning process whereby as novel information becomes familiar and new information comes on line, REM sleep aids in the process of forgetting the familiar to make room for the novel.

A similar hypothesis is that learning new information requires a preliminary stage of clearing neural circuitry before learning can occur, similar to clearing a desktop before new work begins. Such a clearing mechanism may require SWS. Mednick et al. recently reported that repeated within-day testing on the same texture discrimination task mentioned previously showed significant decreases in performance across the day.<sup>19</sup> This deterioration in perceptual processing increased regardless of subject

motivation or task difficulty. Mednick et al. found that a midday nap rich in SWS reversed perceptual deterioration and restored performance to the best level of the day.<sup>19</sup> Along with napping, switching the position of the target in the visual field also reversed perceptual deterioration, as this assigned a new set of neurons to the task of target discrimination. Importantly, naps with SWS did not produce learning, only a clearing of deterioration. But, a nap including both SWS and REM actually led to an improvement in performance equivalent to that following a full night of sleep (fig. 2).<sup>10</sup> These data may indicate two sequential stages of learning. The first stage of learning, driven by SWS, clears the neuronal circuitry of deterioration. The second REM-dependent stage of learning induces long-term changes in neural circuitry manifesting in improved task performance. In contrast with the forgetting hypothesis that implicates REM sleep, the clearing hypothesis proposes that individual processes are dependent on specific sleep stages.



**Figure 2.** Performance improvement with a nap including rapid eye movement (REM) and slow-wave sleep (SWS). Same-day improvement scores were recorded in subjects who had no nap, a 60-minute nap, or a 90-minute nap, and then divided by the presence or absence of REM and SWS. The no-nap group shows deterioration at 19:00 hours from baseline test at 09:00 hours. The 60-minute and 90-minute nap groups with SWS and no REM show no deterioration, but no improvement. The 60-minute and 90-minute nap groups with SWS and REM show significant improvement at 19:00 hours.



## Complexity and specificity markers for sleep-dependent learning

In summary, by placing the results of Wagner et al. in the overall picture emerging concerning the influence of sleep on learning, a number of observations can be made. The primary observation is that not all memories require sleep, but the more complex and elaborate the information to be learned, the more likely sleep will be required for consolidation. Thus, similar to the 'REM' window reported in rats, neuronal replay of waking experience during sleep, specifically REM sleep, may be modulated by increasing task demands for human learning, though this has not been tested. For example, remembering the number '3' over a 10-minute interval may be a simple enough exercise requiring a minimal assembly of cooperative neuron firing, whereas assembling of an abstract, hidden pattern may require a complex distributed network of neurons.

The second observation is that not all sleep is equal, such that a division of labor exists between the various sleep stages and the specifics of what we learn. Numerous studies mentioned above have investigated a variety of learning tasks and found relationships between disparate tasks and specific sleep stages. Future research focusing on this division of labor in the different sleep stages with specific types of learning may be a fruitful direction to increase understanding of both sleep and learning and memory systems.

### Key messages for the primary care physician

- Sleep has been linked both to nondeclarative learning and declarative learning.
- Individual sleep stages may play specific roles in selective types of learning.
- SWS- and REM-dependent stages of sleep are implicated in the processes of learning and clearing the neural circuitry ('forgetting').

#### After reading this article you should be able to:

- 1) Understand which specific sleep stages are linked to motor and procedural learning, and to declarative memory
- 2) Identify methods that are commonly used to investigate the effect of sleep on learning

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