Sleep the Beloved Teacher?

Recent studies of humans and rats show that neuronal firing patterns initiated by prior sensory stimulation, and even learning, can occur during sleep. But what they tell us about the functions of sleep remains unclear.

Samuel Johnson once called sleep a Gentle Tyrant. But to what end do we submit to sleep's gentle tyranny? Or, put more scientifically, what is the functional significance of sleep? This question has finally begun to be answerable. Recent studies have offered powerful suggestions about sleep's possible role in anabolic hormone release, thermoregulation and immune responsiveness [1]. All three of these possible benefits confirm folk wisdom about sleep as healer of the body, the "chief nourisher in life's feast" as Shakespeare put it. And all three can be considered to be in the bodily energy domain, as they all enhance survival by keeping the organism strong, warm and safe from invasion by microorganisms.

But is that all there is to it? What about the brain and the mind? Do they not benefit from sleep in their own special way? If Dr Johnson had read the July 29th issue of *Science*, with its reports that sleep enhances learning [2,3], he might also have called sleep a Beloved Teacher. The occurrence of dreaming had prompted speculation along these lines even before it was realized that dreaming is our conscious experience of the periodic brain activation that punctuates sleep with rapid eye movements (REMs). Indeed, if the brain is active in sleep why couldn't we be learning (as many scientists have proposed), or even actively forgetting (as Francis Crick, following David Hartley, has suggested [4])? As intuitively attractive as these hypotheses may be, it has been extremely difficult to test them. When they have been tested at all, the evidence has usually been weak, difficult to replicate, or internally contradictory. But the two *Science* reports [2,3] present exciting new evidence that memory consolidation and learning may indeed occur during sleep.

One important approach to the sleep–teach idea could be called the mnemonic criterion. If in sleep we are memorizing something experienced in waking, it should be possible to detect the same representation of external reality in neuronal activity patterns during subsequent sleep as during prior waking exposure. This is the criterion that Wilson and McNaughton's [2] study of rat hippocampal 'place-cell' activity elegantly satisfies. Following up on the earlier work of Pavlides and Winson [5], Wilson and McNaughton have not only shown that those hippocampal cells that show place-specific activity in waking are selectively activated in subsequent sleep, but that the correlation between any two co-activated place cells is similarly seen in this sleep. Other important new findings from Wilson and McNaughton's study are first, that this activation occurs in non-REM sleep as well as waking (REM sleep was not investigated), and second, that the correlation of co-activated place cells increases during the bursts of sharp electroencephalogram (EEG) waves that characterize non-REM sleep.

So it would appear that, yes, the sleeping brain does remember its previous experience, at least long enough, Wilson and McNaughton speculate, to replay it and perhaps transfer the 'memory' out of the hippocampus to the cortex. This highly specific neuronal activity in a region of the brain known to be crucial to memory and learning offers the hope of allowing us actually to watch memory and learning develop in the brain, both in waking and in sleep. Whether this sleep mnemonic actually plays a role in learning and memory remains speculation; we do not know if the rats benefited from the somnolent reiteration of their orientational data with some behavioral payoff. No doubt experimental tests of this prediction are already under way.

This behavioral-payoff criterion is precisely the subject of the very different study of Karni, Sagi and co-workers on human visual discrimination [3]. This paper is the documentation of their claim, so widely publicized two years ago, that subjects who were REM-sleep deprived failed to show the time-dependent gain in performance that could be observed if they remained awake or slept through the night undisturbed. It was as if their sleeping brain could 'learn' in REM sleep but not in non-REM sleep.

In the study of Karni and colleagues, the equivalent of Wilson and McNaughton's rats' place-cell activity is the activation of the primary visual cortex as human subjects attempt to locate unusual shapes in a dense stimulus array on a computer screen. A remarkable feature of the performance curves is that the speed with which subjects locate and identify these 'oddball' stimuli improves spontaneously in the hours after the stimulus presentation has ended, whether the subjects are awake or asleep. It is this spontaneous, time-dependent improvement in performance that is prevented by REM sleep deprivation, suggesting to the authors that REM sleep can potentiate learning by consolidating memories. In contrast, subjects did show the expected improvement if they were deprived of equivalent amounts of non-REM sleep, specifically stages III and IV. So it appears that the wake state and the REM stage of sleep can support this type of learning, but that non-REM sleep cannot.

Table 1. Comparison of two recent studies of sleep and learning.

Paper	Experimental system	Evidence for subsequent memory	Evidence for improved performance
Wilson and McNaughton [2]	Correlated firing of hippocampal place cells	**YES** during waking and non-REM sleep (not tested in REM sleep)	Not tested
Karni *et al.* [3]	Human visual discrimination learning	(Untestable)	**YES** during waking and after REM sleep **NO** after non-REM sleep

Wilson and McNaughton [2] hypothesize that the correlated firing patterns they observe reflect "coherent representations of the preceding experience (memories)". Karni *et al.* [3] describe perceptual learning as "the improvement of perceptual skills through practice", and suggest that it "may serve as a paradigm for the acquisition and retention of procedural knowledge". Both studies support the weak hypothesis that sleep is permissive to memory consolidation and learning, but neither provides evidence for or against the strong hypothesis that sleep is necessary for some types of memory consolidation and learning.

What, then, do these studies, summarized in Table 1, really tell us about sleep? Wilson and McNaughton have convincingly shown that there is a carryover, from waking to subsequent non-REM sleep, of the neuronal representation of experience. One commonsense reaction to this result might be "Oh yes, my sleep thoughts do commonly reflect my prior waking experience, especially if I have been exposed to novel and stimulating data", and it would certainly be satisfying to conclude from Wilson and McNaughton's study that the neuronal substrate of such day residues has, at least in one case, been identified. But such a conclusion may be premature.

Although Wilson and McNaughton's study clearly indicates that patterns of correlated neuronal activity induced by experience can be seen in subsequent non-REM sleep, they are also seen in subsequent waking and have not been looked for in subsequent REM sleep. Indeed, the use of the expression "reactivation of... memory traces" may be the crucial issue in the interpretation of these results. There is, alas, no evidence that the activity seen is 'reactivation', and no evidence that it represents 'memory traces'. A simpler interpretation might be that the correlated discharge, initiated by sensory stimulation, continues after the end of the stimulation, decaying as Wilson and McNaughton suggest with a time constant of about 15 minutes, regardless of the wake–sleep state of the rat. There is no evidence that activity decreased after the initial stimulation, only to become 'reactivated' in sleep; in fact, the increased activity is known to occur in subsequent waking as well. There is no evidence that the correlated firing represents a 'memory trace' in the sense of something new that is being learned, retained and made available for subsequent use. While this is by no means impossible, we must await further experiments before we can be confident in such bold and exciting interpretations.

The study by Karni's group indicates that REM sleep (but not non-REM sleep) can subserve spontaneous plasticity as effectively as waking. As the authors point out, this might be because both waking and REM share some common property that is necessary to plasticity (like the EEG activation, or acetylcholine release), or they might achieve the same result in different ways. But whether the results say more about the function of REM sleep than that of non-REM sleep is unclear. Another way to state their results is that, in the 8–10 hours after exposure, subjects 'learn' to perform better on the task unless they are in non-REM sleep. Here we run into a problem similar to that seen in the Wilson and McNaughton paper; there does not seem to be anything special about sleep *per se*. While it is indeed satisfying to demonstrate that learning can occur during sleep, the learning is only what would have occurred anyhow if the subject had not been asleep.

Over the years, numerous theories have been developed about the role of sleep in learning. One such hypothesis, supported by both of these studies, is that the learning and memory consolidation that occurs in the wake state also occurs during sleep. In other words, sleep is a permissive state, not necessary for learning, but sufficient. A stronger hypothesis, which has seemed so attractive to many researchers, and which matches the folk wisdom embodied in such concepts as putting off a decision until you've had a chance to 'sleep on it', is that there is a form of memory formation or consolidation as well as learning that occurs exclusively during sleep and that cannot occur without sleep. This hypothesis makes sleep a necessary condition for some types of learning. Unfortunately, neither Wilson and McNaughton nor Karni and his colleagues provide any evidence for or against such a hypothesis.

References

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