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Science. Author manuscript; available in PMC 2022 January 15.

Published in final edited form as:

Science. 2001 November 02; 294(5544): 1058–1063. doi:10.1126/science.1063049.

The REM Sleep–Memory Consolidation Hypothesis

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Abstract

It has been hypothesized that REM (rapid eye movement) sleep has an important role in memory consolidation. The evidence for this hypothesis is reviewed and found to be weak and contradictory. Animal studies correlating changes in REM sleep parameters with learning have produced inconsistent results and are confounded by stress effects. Humans with pharmacological and brain lesion–induced suppression of REM sleep do not show memory deficits, and other human sleep-learning studies have not produced consistent results. The time spent in REM sleep is not correlated with learning ability across humans, nor is there a positive relation between REM sleep time or intensity and encephalization across species. Although sleep is clearly important for optimum acquisition and performance of learned tasks, a major role in memory consolidation is unproven.

The function and meaning of dreams have always been a source of mystery and fascination. Some ancient civilizations saw dreams as a way to divine the future or visit with long-departed ancestors. At the beginning of the last century they were viewed as mechanisms for wish fulfillment, as expressions of archetypal symbols, and as the “royal road to the unconscious.” Since the discovery of REM sleep, the state in which vivid dreams most frequently occur (1), measurement of the physiological parameters of REM sleep and their correlation with dream reports has been possible. Early work led to the suggestion that REM sleep was necessary to prevent waking hallucinations and mental illness, an initially popular idea that was refuted by subsequent work (2). The physiological correlates of REM sleep have been found to exist in nearly all mammals, bringing the tools of basic neuroscience to bear on this state.

In the modern era, a literature examining the links between REM sleep and learning has arisen. The interest in this field was heightened by a publication (3) hypothesizing that the function of REM sleep was the forgetting of unneeded memory traces, reviving an idea that had been previously advanced by others (4, 5). Much new theoretical and experimental work on REM sleep and learning followed. As a result, the prior ideas about a central role for REM sleep in motivation and psychological well-being have now been largely displaced in the popular consciousness by the purported REM sleep–learning link. A recent news article

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in *Science* declared that “neuroscientists have long known that memory consolidation goes on during sleep” (6).

This article reviews the evidence linking REM sleep to memory consolidation. The much smaller literature suggesting that non-REM sleep has a central role in memory consolidation is also considered; an excellent review on this subject has recently appeared, with extensive commentary (7).

In humans, learning can occur at the beginning of the waking period and be preserved 16 hours later, before sleep begins. Under duress, it is possible to go for 40 or more hours without sleep and still be able to disgorge information acquired at the beginning of the sleepless period, despite many intervening distractions. Thus, when we are considering a role for sleep in human memory consolidation, we are referring to a possible role in the longer term encoding of information and optimization of its recall, not a requirement of sleep for recalling events of the prior day.

The massed training, or cramming, that most of us have done during sleepless nights in our student years is not an efficient way to retain a good understanding of any subject matter. However, the well-known inefficiency of this procedure for both rote and skill learning is not by itself evidence for the role of sleep in learning as much as for the necessity of maintaining attention and integrating and practicing new material and skills over an extended period of time (8–10).

A mix of positive and negative results in human studies has led many sleep-learning researchers to suggest that REM sleep may not be important for certain kinds of memory, such as what has been termed “explicit” or “declarative” memory. This includes rote memory, language memory, and (depending on the precise definition offered) certain aspects of conceptual memory. REM sleep would thus be excluded from having any substantial role in much of what is considered to be unique in human intellectual capacity. It is “procedural” memory, defined as performance on perceptual and perceptuo-motor skills, that is claimed to be impaired by sleep disruption (11–13). However, other researchers suggest that REM sleep has a key role in language or emotional learning (14–16).

Evidence relevant to the REM sleep–memory consolidation hypothesis is of three general types. The first is evidence that learning causes an increase in REM sleep duration. The second consists of evidence that memory processing occurs during REM sleep. The third comes from deprivation studies suggesting that if REM sleep is prevented, memories are not consolidated. Each type of evidence is considered below.

Evidence for Increased REM Sleep Duration with Learning

The idea that REM sleep duration should increase with learning is based on the hypothesis that increased learning will require increased memory consolidation and hence more REM sleep time. Animal learning studies can require the subject to learn a new task in a controlled situation, but it is unclear whether such a manipulation consistently increases the total amount of learning that occurs. One can assume that an animal is continuously learning, albeit not at the behest of the experimenter. There is no guarantee that the novelty of a

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new experimental situation will produce a substantial overall increase in learning, unless one assumes that minimal learning occurs in the home cage situation where the animal interacts with its conspecifics and others who handle it, anticipates food and water changes, and responds to sensory stimuli.

Even if the novelty of the learning situation is assumed to produce a marked increase in the quantity of learning, it will not produce this effect alone. It is quite likely that stress associated with shock avoidance (used in many REM sleep–learning studies), frustration involved in appetitive reinforcement paradigms, and other emotional aspects of the situation will have a major impact on the animal. The assumption that levels of stress are not correlated (positively or negatively) with the nature of the learning task and with the animal's success at the task is unproven and unexplored in most of these studies. This issue is particularly worrisome because it has been shown that moderate stress, in the absence of any imposed learning task, can produce a marked increase in REM sleep (17, 18), whereas higher levels of stress disrupt sleep. The inability to measure and separate stress and other emotional variables readily from learning makes it difficult to determine which of these, if any, are affecting subsequent REM sleep.

Smith (19, 20) has closely examined the issue of REM sleep increase after learning. Using rats, he found that such increases occurred at different times after the imposed learning task. Increases in non-REM sleep relative to baseline were also seen in many of these studies. In some experiments the REM sleep increase occurred immediately after training. More frequently it appeared to occur with some delay, in some cases 36 hours or more after training. In one avoidance task, REM sleep increases were seen from 1 to 4 hours, 9 to 12 hours, and 21 to 24 hours after training, but not at other times. In other studies, the "REM sleep window" was said to last more than 15 days. These REM sleep windows were said to depend "upon the type of task, strain of animal and number of training trials per session" used and to vary even with the particular vendor that supplied animals of the same strain (19, 21). Because in many of these studies the window is defined post hoc, it is unclear how replicable this phenomenon is.

A REM sleep enhancement phenomenon has also been sought in human studies. Some of these studies have used prism glasses that distort the visual world. Such glasses perform a 90° rotation or inversion of the subject's view. Over a period of days, subjects learn to adjust to these glasses. Because adjustment to these changes affects most aspects of waking behavior, requires the alteration of rapid eye movements, and is quite difficult, it would be the type of paradigm thought to involve REM sleep most strongly. An initial abstract in 1970 concluded that such an experience produced an increase in REM sleep (22), but a more thorough study using a similar paradigm found no such increase (23). Further work by the authors of the original abstract confirmed the absence of an effect (24), as did three additional studies using a variety of visual distortions (25). Another study using a somewhat different spatial rearrangement did find a small effect, with REM sleep increasing from 19% to 22% of total sleep time (26). These same authors noted a small increase in REM sleep during language learning, a type of task that others have concluded does not require REM sleep (27).

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Smith and Lapp (16), recording sleep in students after an intensive exam period, reported no change in REM sleep time, but they did find an increase in the density of REM sleep eye movements, in contrast with findings of increased REM sleep time in most “successful” learning studies in rats (19). REM sleep eye movement density is considered an index of the intensity of REM sleep. The control group for the human exam study consisted of students with financial problems that prevented them from taking their exams, so that they were not “involved in any major learning situation.” Apart from the fact that the major finding of REM sleep increases after learning was not replicated in this study, the work illustrates some of the pitfalls of sleep-learning studies. It is difficult, especially in humans, to devise a proper control group, equate stress levels, and equalize other sleep-disturbing factors. Initial conditions that depress baseline sleep amounts may cause an apparent increase in REM sleep parameters during the experimental period. The “high-learning” group may not actually differ from the control group in the total amount of learning taking place. From these studies, it is difficult to draw a conclusion about the existence of any change in the amount of REM sleep in humans after learning.

Another way to explore the possibility of a causal link between learning and REM sleep time in humans is to correlate amounts of REM sleep with learning ability as measured by the intelligence quotient or similar measures. Early work in mentally retarded individuals and patients with degenerative brain syndromes suggested that REM sleep amounts were correlated with intelligence level in some groups (28–30). In contrast, no relation was found between IQ and REM sleep duration in retarded subjects in a more recent study (31). As all of these researchers point out, a correlation between REM sleep and intelligence may result from the independent effects of brain damage or impaired brain development on both intellectual function and REM sleep, rather than from a causal relation between REM sleep reduction and learning ability. Damage to many areas of the brain can depress REM sleep time (32, 33). A more persuasive test of this relation would be to correlate REM sleep parameters with intelligence in a normal population. In a study examining a large sample of normal children whose measured intelligence spanned a wide range, no relation between REM sleep amounts and intelligence was found (34). A similar study comparing high-IQ and average-IQ students also found no difference in REM sleep time (actually somewhat lower in the high-IQ group) (35).

A different approach to assessing the relation between REM sleep and intelligence is to examine the enormous variation in amount of REM sleep across mammals. Contrary to what might be expected, humans do not exhibit unusually high amounts of REM sleep, calculated either in hours per 24-hour period or as a percentage of sleep time. Figure 1 presents examples of species with high and low amounts of REM sleep. In general, animals that are born relatively mature, such as the guinea pig and marine mammals, have low amounts of REM sleep, whereas animals born relatively immature, such as the platypus, ferret, and armadillo, have high amounts of REM sleep throughout their lives (36, 37). Animals with high amounts of REM sleep are not those generally considered to be the most intelligent. The egg-laying platypus is one of most primitive mammals and has a lisencephalic cerebral cortex, yet it has the highest amount of REM sleep yet observed (36). Humans have moderate amounts of REM sleep, in line with what would be predicted purely on the basis of their relative maturity at birth. Whales and dolphins—which have the largest

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brains on Earth, some of the highest brain/body weight ratios, and intellectual abilities otherwise found only in humans and the great apes (38)—have very little REM sleep. Some whale and dolphin species may have no REM sleep at all (39). The putative REM sleep episodes seen in whales and dolphins, which are of short duration, are noteworthy for their relatively low frequency of eye movements and twitches compared to that in other mammals—that is, the REM sleep that may be present is of low intensity. Over all species examined, the correlation between encephalization and REM sleep amount (hours per day) is low but significantly negative, and there is no correlation between encephalization and REM sleep as a percentage of total sleep time (37).

Evidence for the Expression of Learning Processes During REM Sleep

Several investigators have sought evidence to support the hypothesis that memory consolidation is occurring during sleep. The replay of neuronal activity seen during prior learning episodes might be evidence for mnemonic processes. However, a replay of neuronal events in subsequent REM sleep epochs might not be part of consolidation. Indeed, such replay might be involved in genetically programmed neuronal development, may have a role in the extinction of memory traces (3–5), or may have no role in neuronal plasticity at all.

Recordings from the motor cortex analog of zebra finches (40) detected neuronal activity patterns in sleep similar to those present during waking singing, suggesting that a genetic readout (41) of species-specific bird-song may be taking place. In this study, the nature of the sleep state (REM versus non-REM) in which these patterns were present was not identified. The idea that REM sleep has a role in genetic programming of behavior during neuronal development is supported by the relatively high amounts of REM sleep in early life in mammals (42).

Two recent papers have studied unit activity in the hippocampus of rats during REM sleep in a search for evidence of mnemonic processes. The first (43) studied the firing of groups of neurons in the hippocampus, a structure known to be important in memory consolidation. The cells recorded were selectively active during waking in relation to the physical location of the animal within its environment. Prior work has shown that long-term potentiation in the hippocampus is most reliably induced when impulses arrive at peaks in the theta rhythm. Conversely, stimulation at the theta trough can undo the facilitation of a previously potentiated synapse. The authors compared the activity of “place cells” active in familiar places of the environment with those of place cells active in newly exposed portions of the environment. They found that each of these two categories of cells had differing phase relations to the theta rhythm in waking as compared to REM sleep. These findings suggested to the authors that REM sleep was exerting mnemonic functions, perhaps by strengthening memory traces linked to recent experience while eroding traces linked to more remote memories.

Another study (44) examined more extensive samples of activity in hippocampal cells in rats and compared discharge patterns during REM sleep to those during training on a circular track. By expanding and contracting the duration of the REM sleep samples and using a sliding template to identify matches, it was concluded that a replay of waking hippocampal

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activity occurred during REM sleep. However, this “replay” was found primarily in REM sleep episodes occurring immediately before the daily learning trials, not in those occurring in the hours immediately after learning. The authors interpreted this as reflecting a replay of training sessions that occurred 1 day earlier, although there is no persuasive evidence for this interpretation. It is unclear why this “replay” was not seen in REM sleep occurring subsequent to the behavioral episode. Furthermore, when these animals were exposed to a novel training task, no replay was detected in any subsequent REM sleep period. These data do not appear to support the consolidation hypothesis.

If waking events to be consolidated are replayed in sleep, one might expect not only a replay of unit activity patterns but also a reactivation of the correlated mental experience. We have access to such experiences in humans who are awakened from REM sleep. A few recent papers have examined dream reports in subjects undergoing an intensive presleep learning experience. In one such paper, fewer than 10% of dream reports contained any reference to a task just learned, and many of the dreams that referred to the learned task occurred after consolidation had occurred, not before (45). Language immersion learning and visual field inversion produced “relatively few direct incorporations of the learning material” into reported dreams (46). A review of the literature found that few dreams are linked to recent experiences, including new experiences that are subsequently remembered. The dream reports that do incorporate experiences from the prior day or two are rarely a “replay” of events or learned tasks. Instead, they are more likely to be linked to the situation in which the learning occurred or the emotions correlated with the learning experience (47, 48).

Evidence for the Blockade of Memory Formation in the Absence of REM Sleep

The consolidation hypothesis requires that memory formation be prevented or impaired if REM sleep is blocked. Thus, a large number of studies have deprived animals and humans of REM sleep after training. In evaluating this literature, we are faced with a task similar to the analysis of the effects of brain lesions on behavior. If loss of a brain region does not interfere with the function of interest, we can have some confidence that this region is not required for this function. However, if the function is disrupted, we must address the question of the mechanism involved in its disruption. Is the loss due to a deficit in the sensory input triggering the behavior in question? Is it due to a deficit in the integration of necessary sensory signals? Is it due to a disruption of the motor activity mediating the behavior? Is there a general loss of arousal or a hyperarousal that interferes with the behavior of interest? Are changes in motivational factors responsible for the deficit? Or is it the formation of connections between stimulus and response that is impaired?

In a similar manner, if REM sleep deprivation does not affect memory consolidation, we can conclude that it was not required for the task examined. However, if a deficit in recall occurs, interpretation can only be made after a number of issues are examined. A problem in the interpretation of many animal studies that use REM sleep deprivation arises from the use of the so-called “platform technique.” Jouvet discovered that REM sleep was accompanied

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by a complete loss of muscle tone (49), whereas some non-REM sleep can occur without complete relaxation. This feature can be exploited to deprive animals of REM sleep (50), substituting increased waking and disrupted non-REM sleep for REM sleep. If animals, usually rats in these studies, are confined to a small platform surrounded by water, they will begin to fall into the water when they assume the maximally relaxed recumbent posture required for REM sleep. This will obviously awaken them. If a somewhat larger platform is used, REM sleep can occur. Unfortunately, the loss of REM sleep is not the only difference between animals in the two conditions. The REM sleep–deprived animal has a greater restriction on its motor activity, which can be quite stressful for a rodent (25), and stress by itself impedes memory retrieval (51). The small-platform animal also tends to get wet, which can cause hypothermia. Further, if the sizes of the platforms are not closely regulated taking into account the weights of the individual animals, both experimental and control animals (or neither) may be deprived. In most studies, polygraphic monitoring, which is necessary to confirm the success and selectivity of the deprivation technique, has not been done, although reference to prior studies may be adequate. However, given the possibility of differences among studies in rat strain and behavior, the lack of monitoring might allow problems in the selectivity of the deprivation procedure to go unnoticed. REM sleep deprivation has many motivational and behavioral effects. Hyperphagia, hyperactivity, hypersexuality, anxiety, irritability, alterations in electroconvulsive shock thresholds (52), and other changes have been reported (50, 53–56), although a few of these findings have been disputed in subsequent studies (57). These changes could interfere with recall if animals are tested in a REM sleep–deprived state, confounding experimental results.

Another interpretation issue is the phenomenon of state-dependent learning. Some work suggests that learning that occurs under certain drug conditions may not be recalled when the animal is tested in the nondrugged state. However, by reinstating the drugged state, it can be shown that memory consolidation in such animals has occurred. In a similar way, it has been shown that animals in which consolidation has taken place in a REM sleep–deprived state may not be able to retrieve the material when tested in a nondeprived state, but do have access to the consolidated information when deprived again (58).

Many animal studies have made use of the platform deprivation technique [for reviews, see (7, 19, 25)]. Some of these studies reported that REM sleep deprivation blocked consolidation, whereas others reported no effect of the procedure; still others reported improved consolidation with REM deprivation (19, 59, 60). The failure of deprivation to prevent consolidation has been attributed to the nature of the task, with some authors concluding that only more complex tasks require REM sleep for consolidation. However, inspection of the literature reveals that experimental results varied even when the same task was assigned. For example, REM sleep deprivation has been shown to block recall of “shuttle box avoidance” tasks in some studies but not in others (19, 25, 59, 60). One explanation offered for this variability has been the “REM sleep window” hypothesis discussed above. Most studies have used REM sleep deprivation immediately after learning a task, including those with positive as well as negative results. Other studies have claimed better results if one waits for a REM sleep window, although even in this situation both positive and negative results have occurred.

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A less stressful REM sleep deprivation technique was devised in which a gentle rocking motion was used to prevent REM sleep in rats (61). With this deprivation procedure, no learning deficit was seen on the same task that had been disrupted by the platform deprivation technique. This result suggests that stress, rather than REM sleep loss, was the critical variable.

Human REM sleep deprivation can be accomplished with polygraphic monitoring by awakening the subject whenever REM sleep begins. REM sleep deprivation results in more frequent attempts to enter REM sleep, but deprivation can be accomplished with as few as nine awakenings per night (59). Because in humans most REM sleep time occurs late in the sleep period, some human studies have REM or control non-REM sleep deprivation effects confounded with the circadian time of deprivation (11, 12).

Early studies of REM sleep deprivation and total sleep deprivation in humans focused on the physiological and emotional consequences of the deprivation procedure, with few reports of alterations in intellectual functioning (62). A large number of studies have shown that REM sleep deprivation does not affect learning of “intentional” tasks such as paired associate learning, verbal learning, and retention of anagrams; hence, learning researchers have focused on “procedural” learning tasks and tasks that were termed “ego threatening” (11, 60). Recently, papers by two groups of researchers have shown effects of REM sleep deprivation on a visual discrimination task that required the subject to learn to detect changes in line orientation rapidly. The first study (12) showed that REM sleep deprivation impeded learning of the task, and that non-REM sleep deprivation interfered with performance of a previously well-learned task. This study also found that improvement occurred over waking periods without intervening sleep. These results were interpreted as indicating that REM and non-REM sleep differed in their ability to maintain the rate of improvement occurring in waking. The authors did not conclude that REM sleep was necessary for memory consolidation. In the second study, by a different group (11), the same task was assigned to subjects; it was concluded that “no improvement” occurred in waking, and that therefore sleep is “absolutely required” for performance improvement. Resolution of the discrepancy in the extent of the waking consolidation found in these studies is critical to an assessment of the role of REM sleep in this task.

Monoamine oxidase (MAO) inhibitors such as phenelzine (Nardil), administered at therapeutic doses for the treatment of depression, can completely suppress REM sleep and reported dreams throughout the period of treatment, which may continue for months or years. It has specifically been noted that during this REM sleep suppression, no periods with a low-voltage electroencephalogram, no periods of muscle atonia, and no episodes of rapid eye movement appear during sleep (53). Similar but less complete suppression has been reported from tricyclic antidepressants (53). Compared to the stressful methods of deprivation often used in animal studies, this drug-induced REM sleep suppression can produce a complete loss of REM sleep for long periods of time with little apparent stress. Indeed, such drugs are widely used to reverse clinical depression.

The widespread long-term use of MAO inhibitors in humans provides a unique opportunity to determine the effects of complete REM sleep loss for long periods, and it allows access

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to subjects' introspective reports as well as the monitoring of medical professionals, family, and friends. Millions of individuals have taken or are taking these medications. This large-scale human "experiment" has not produced evidence of memory impairment, even with therapeutic doses that completely block REM sleep, but instead has produced some evidence that MAO inhibitors produce memory improvement (7, 63). In contrast, benzodiazepines, which induce sleep and are notable for their relative lack of effect on "sleep architecture" (including REM sleep time and distribution) relative to older hypnotics, have pronounced deleterious effects on memory (64, 65). If careful tests of memory function could be undertaken in humans taking MAO inhibitors in amounts sufficient to suppress REM sleep, the results would give us greater understanding of the role of REM sleep in learning. The lack of reports of memory impairment caused by these drugs (which have been on the market for more than 30 years), and the careful reports showing memory enhancement in many subjects (66), suggest that major memory deficits are unlikely to be found. However, more subtle alterations in learning might be detected and could shed light on the nature of any involvement of REM sleep in memory.

A way of reconciling the apparent lack of a major effect of MAO inhibition of REM sleep on memory with a possible requirement of REM sleep for learning would be to hypothesize that MAO inhibitors merely mask the polygraphic signs of REM sleep, and that some essential aspect of REM sleep continues, preserving its memory consolidation function. Specifically, ponto-geniculo-occipital (PGO) spikes (waves that propagate from the pons to the geniculate and cortex) and hippocampal theta waves have been hypothesized to be key elements of REM sleep involved in learning (43, 44, 67). This would be consistent with claims that REM sleep intensity (e.g., the number of phasic events such as PGO spikes, or the number or amplitude of hippocampal theta waves, per REM sleep period) is linked to the ability of REM sleep to consolidate memory, perhaps because these potentials are linked to the tetanic stimulation of important synaptic links (19, 67). It has not been possible to record PGO activity and hippocampal theta waves from humans because depth electrodes would be required. However, rapid eye movements, normally highly correlated with PGO spikes, are absent under phenelzine. A cat study using depth electrodes found complete REM sleep suppression after phenelzine administration (68).

Another approach would be to hypothesize that MAO inhibition and other monoamine-boosting drugs that severely suppress REM sleep actually substitute for the REM sleep state, performing its memory functions. MAO inhibitors act by increasing the presence of monoamines in the synaptic cleft. Tricyclic antidepressants have similar effects. Monoamines are known to suppress PGO spikes (33). These effects are opposite to the well-known reduction in monoamine release and increase in phasic events that are the fundamental characteristics of REM sleep (33). Indeed, it has been hypothesized that the cessation of monoamine release is a key function of REM sleep (69). Thus, it is clear that MAO inhibitors do not "substitute" for REM sleep at the neurotransmitter level. Furthermore, withdrawal of phenelzine and other MAO inhibitors results in a massive REM sleep rebound (53), indicating that these drugs cause a substantial REM sleep debt.

The major signs of REM sleep, including dreams, periodic muscle tone suppression, rapid eye movements, PGO spikes, and reduction in monoamine release, are all absent with MAO

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inhibition and are greatly reduced by tricyclic antidepressant drugs. A REM sleep debt is incurred by administration of these drugs. Yet these drugs are not known to have any significant deleterious effect on memory. The extensive human experience with these drugs provides strong circumstantial evidence that REM sleep is not important for learning or memory consolidation.

Animal studies have shown that lesions of the pontine tegmentum can greatly reduce or eliminate REM sleep (33, 49, 70). However, animals with such lesions have not been used in learning studies. Pontine lesions have also been shown to eliminate REM sleep in humans. Although motor function may be severely impaired in individuals with such lesions, in all reported cases, when communication has allowed assessment, intellectual function has been normal (7, 71). One individual who suffered a shrapnel injury to the brainstem has been carefully followed for more than 10 years (72). Repeated polysomnograph recordings have found little or no REM sleep. However, since the injury, this patient has been able to complete law school (with its substantial memorization requirements) and practice law. He was an editor of the logic puzzle section in a local newspaper and reports no memory problems. The findings from cases of lesion-induced REM sleep suppression are consistent with the knowledge gained from MAO suppression of REM sleep in suggesting that there is no critical role for REM sleep in learning.

The apparent lack of effects of REM sleep suppression on memory may be related to the neurochemical changes occurring during this state. In vitro and in vivo studies have shown that hippocampal post-tetanic potentiation is critically dependent on the presence of norepinephrine (73). Similarly, the alteration by experience of receptive fields in visual cortical units is facilitated by the presence of norepinephrine and blocked in the absence of this transmitter (74). One of the best documented features of REM sleep is the cessation of norepinephrine release (33). Recent work has shown that this cessation may be linked to reduced expression of phosphorylated CREB (cyclic adenosine monophosphate response element–binding protein), Arc (a growth factor– and activity-related gene), and BDNF (brain-derived neurotrophic factor); the phosphorylation of CREB and the up-regulation of Arc and BDNF are often associated with synaptic plasticity (75). The finding of reduced levels of these proteins is consistent with the above cited evidence of little effect of REM sleep deprivation on memory. It is also consistent with the rapid forgetting of dreams that are not immediately mentally rehearsed in subsequent waking.

Non-REM Sleep and Learning

Although most work on sleep and learning has explored the hypothesized role of REM sleep, some recent work has examined the possibility that non-REM sleep is important for learning and memory. This work has emphasized the possible role of synchronous discharge in reinforcing synaptic connections in the hippocampus and neocortex (76, 77). Relative to the extensive studies of the effects of selective REM sleep deprivation, there has been little work on the effects of selective non-REM sleep deprivation on memory. However, most animal studies of REM sleep deprivation reviewed above have used some form of non-REM sleep deprivation as a control procedure, and animals thus deprived have shown substantial

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learning abilities. Further work is necessary to determine whether non-REM sleep has a role in memory consolidation, although clearly non-REM sleep has a role in performance.

Conclusions

Unequal stress effects of the platform technique of REM sleep deprivation and contradictory reports using similar deprivation and learning paradigms weaken the hypothesis that REM sleep is important for memory consolidation. The absence of major memory deficits in humans with drug- or lesion-induced REM sleep suppression further under-mines the hypothesis, as does the lack of correlation between REM sleep time and learning ability in humans and across a wide range of mammals. However, sleep disruption occurring before learning will affect performance in learning tasks. This disruption is not due to the loss of sleep per se, but rather to the intrusions of sleep into waking during the learning task. In a similar way, sleep loss, because of the resulting impairment of concentration and sleep intrusions, will interfere with recall (78). Just as nutritional status, ambient temperature, level of stress, blood oxygenation, and other variables clearly affect the ability to learn, adequate sleep is vital for optimal performance in learning tasks. However, the existing literature does not indicate a major role for REM sleep in memory consolidation.

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79. I thank L. Boehmer for helpful comments on an earlier version of this manuscript. Supported by the Medical Research Service of the Department of Veterans Affairs and NIH (grants HL60296, NS14610, and MH64109).

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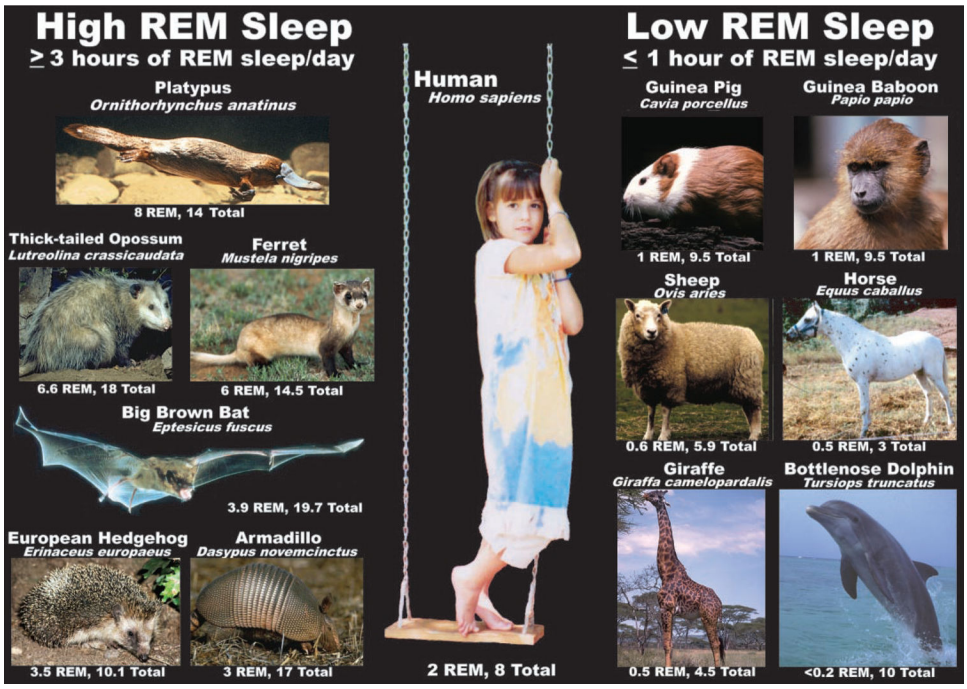

Fig. 1.

Sleep durations in representative mammals. Daily REM sleep time in mammals does not positively correlate with encephalization. The highest levels of REM sleep are seen in the platypus and the lowest in the dolphin. Despite our unique learning capabilities, human REM and non-REM sleep parameters are not unusual and are in accord with our size and level of maturity at birth relative to other mammalian species. Number of hours of REM sleep and total sleep across the 24-hour cycle are listed for each animal pictured (36, 37). [Photo credits: platypus, Tom McHugh/Photo Researchers; opossum (photo is of a Virginia opossum), Alden M. Johnson, California Academy of Sciences; ferret (photo is of a black-footed ferret), © D. Robert Franz/CORBIS; big brown bat, © 1997 Merlin Tuttle, from *Bats: Shadows in the Night*, used by permission of Crown Children's Books; hedgehog, Maurizio Lanini/CORBIS; armadillo, John and Karen Hollings-worth/U.S. Fish and Wildlife Service; human, Kristi Alderman; guinea pig, Animals Animals; guinea baboon, Mickey Gibson/Animals Animals; sheep, Barbara Wright/Animals Animals; horse, Lucie R. Alderman; giraffe, Arthur J. Emmrich, California Academy of Sciences; dolphin, Gerard Lacz/Animals Animals]