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Memory Consolidation in Sleep: Dream or Reality

Review

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We discuss several lines of evidence refuting the hypothesis that procedural or declarative memories are processed/consolidated in sleep. One of the strongest arguments against a role for sleep in declarative memory involves the demonstration that the marked suppression or elimination of REM sleep in subjects on antidepressant drugs or with brainstem lesions produces no detrimental effects on cognition. Procedural memory, like declarative memory, undergoes a slow, time-dependent period of consolidation. A process has recently been described wherein performance on some procedural tasks improves with the mere passage of time and has been termed "enhancement." Some studies, but not others, have reported that the consolidation/enhancement of perceptual and motor skills is dependent on sleep. We suggest that consolidation or enhancement, initiated in waking with task acquisition, could in some instances extend to sleep, but sleep would serve no unique role in these processes. In sum, there is no compelling evidence to support a relationship between sleep and memory consolidation.

Introduction

The issue of memory consolidation in sleep, long dormant, is currently a lively topic in the sleep field and, seemingly, in the neurosciences in general. It would appear that current interest in this topic stems in part from the possible intersection of two important processes—memory consolidation and the functions of sleep.

If a link between sleep and memory were to be demonstrated, the ramifications could be far reaching, possibly extending to lifestyle changes involving a redistribution/reorganization of sleep-waking states, favoring sleep. Recent claims that sleep beneficially affects cognition suggest that sleep may be an important, untapped route to learning and perhaps should be utilized for that purpose. Robert Stickgold suggested that sleep may be as important, or even more so, than traditional factors in determining intelligence or academic success. Based on his findings (Stickgold et al., 2000a) of improved performance on a perceptual discrimination task following sleep, Stickgold remarked (Blakeslee, 2000) that "The study challenges expectations and prejudices about what makes a smart student. How well Harvard undergrads do the next day on a retest does not depend on what prep school they went to, their SAT scores or how hard they tried. Rather, it mostly depends on how well they slept."

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We present a wide spectrum of evidence that refutes the position that sleep serves a role in the processing or consolidation of memory. The following main topics will be covered: (1) early work in this area—a brief history; (2) some important general considerations on this topic; (3) REM sleep deprivation studies in animals; (4) cognitive capacities of humans with greatly suppressed or absent REM sleep; (5) recent human studies on procedural memory and sleep; (6) the "replay" of patterns of neural activity of waking in subsequent sleep in animals; (7) "other factors" that dispute a role for sleep in memory processing; and (8) a proposed function for sleep.

A Revisiting of This Issue

Although possibly not recognized outside of the sleep field, the role of sleep in memory processing is not a new issue, but is one that was thoroughly examined in the 1960s to 1970s. There was a wealth of research in animals, and to a lesser extent in humans, devoted to this topic (for review, see McGrath and Cohen, 1978; Horne and McGrath, 1984; Smith, 1985; Horne, 1988). Current interest represents a second wave. Most of the early work in this area in both animals and humans examined the effects of REM sleep deprivation on previously learned material. As later discussed in detail, the results of numerous studies on this subject, involving various manipulations across species, were divided. There were as many reports that failed to describe a link between sleep and memory as there were those that claimed such a relationship (Horne and McGrath, 1984; Horne, 1988; Vertes and Eastman, 2000a, 2000b).

Several authors have chronicled this early work, but none more comprehensively than James Horne (Horne and McGrath, 1984; Horne, 1988, 2000). Following a review of this work, Horne (1988) concluded: "Findings from REM sleep deprivation studies are not convincing enough to warrant there being any vital association between REM sleep and memory or other aspects of the learning and forgetting process in the adult mammal." And further, "In view of the attention paid to REM sleep and dreaming, and the importance given to this form of sleep by many people, REM sleep deprivation in human adults is surprisingly uneventful—it can even be of benefit to people suffering from certain forms of depression."

There was a marked decline in research in this area beginning about the mid-1970s, undoubtedly reflecting the fact that, on balance, the early work failed to convincingly demonstrate a relationship between sleep and memory. As most would agree, we are now in a period of revival—sleep and memory consolidation is again a very topical issue.

Interestingly, this revival may have been sparked by a report by Francis Crick—an eminent scientist but seemingly removed from the sleep field. In 1983, Crick and Mitchison published a theoretical paper in *Nature* entitled "The Function of Dream Sleep" in which they put forth the intriguing idea that the primary function of dream sleep (or REM sleep) was to purge unwanted or extraneous memories during sleep—or, in their terms,

"reverse learning." In a well-crafted (and subsequently oft-quoted) synthesis of their position, they stated that "We dream in order to forget." From a historical perspective, it is surprising that Crick and Mitchison's theory attracted few adherents.

It is evident that we do not support the notion that sleep serves a role in the processing of information—either to store or erase it. Of the two contrasting views, however, we feel that Crick and Mitchison's position (reverse learning) is more compelling than its counterpart (memory consolidation in sleep). In brief, based on neural net models, Crick and Mitchison (1983) proposed that as information is continuously stored in cortical networks, these networks become overloaded, resulting in the development of "parasitic modes" that need to be removed. This is accomplished in REM sleep by a process of reverse learning. Although the model leaves much unanswered, it is consistent with well-recognized properties of dreams as bizarre/unreal events (unstable networks) that are probably best forgotten (reverse learning). Crick and Mitchison's message seems to be that we remember few of our dreams, and thankfully so. Or, in their words, "In this model, attempting to remember one's dreams should perhaps not be encouraged, because such remembering may help to retain patterns of thought which are better forgotten. These are the very patterns the organism was attempting to damp down." Although Crick and Mitchison's theory did not generate much enthusiasm in the sleep field, it refocused attention on the possible involvement of sleep in cognitive functions.

The most immediate impetus, however, to the resurgence of interest in sleep-memory consolidation came from two complementary articles that appeared in *Science* in 1994: one by Wilson and McNaughton (1994) in rats and the other by Karni et al. (1994) in humans. Wilson and McNaughton (1994) reported that ensembles of hippocampal "place" cells tend to repeat patterns of waking activity in subsequent episodes of slow wave sleep, while Karni et al. (1994) showed that improvement on a visual task in humans was dependent upon REM sleep. The two studies supported the position that memories are consolidated in sleep.

General Considerations Relevant to the Current Debate

In the following, we discuss some general issues that we believe are relevant to the current debate on the role of sleep in memory consolidation, namely that (1) there is no correspondence between the cognitive content of waking and sleep, making it unlikely that sleep serves to consolidate waking experiences; (2) sleep is an amnesiac state, rendering it a very poor candidate for memory processing; and (3) by all accounts, sleep is involved in procedural but not in declarative memory, thereby narrowing the debate to the role of sleep in procedural memory.

Mismatch between the Cognitive Content of Waking and Sleep

The mental/cognitive content of sleep (SWS/REM) is dreams (Nielsen, 2000). Dreams are the sole window to the cognitive processes of sleep. The hypothesis that sleep serves a role in memory consolidation would be more appealing if dreams reproduced waking experiences (or even approximately so), but they do not.

More than 100 years ago, Freud (1900) considered the possibility that dreams/sleep may serve a role in memory processing, but he dismissed it. Freud speculated that "It might perhaps occur to us that the phenomenon of dreaming could be reduced entirely to that of memory: dreams, it might be supposed, are a manifestation of a reproductive activity which is at work even in the night and which is an end in itself." Continuing, "But views of this sort are inherently improbable owing to the manner in which dreams deal with the material to be remembered. Strümpell rightly points out that dreams do not reproduce experiences. They take one step forward, but the next step in the chain is omitted, or appears in altered form, or is replaced by something entirely extraneous. Dreams yield no more than *fragments* of reproductions; and this is so general a rule that theoretical conclusions may be based on it."

Freud states the obvious. It is not unreasonable to suggest that dreams (or sleep) "could be reduced entirely to that of memory" or may represent "a reproductive activity which is at work even in the night," but this view is "inherently improbable" owing to the fact that "dreams do not reproduce [waking] experiences." In a sense, case closed.

More recently, Owen Flanagan (2000) expressed a similar view, stating: "since we rarely dream about what we need to remember, the hypothesis that dreams themselves serve any memory enhancing function appears unwarranted."

It would seem that most proponents of the sleep-memory consolidation hypothesis (S-MC) would agree that waking experiences are not faithfully reproduced in dreams or committed to memory through dreams. However, in a twist of logic that we find difficult to understand, it appears that adherents to this view would acknowledge that material that reaches consciousness in sleep (dreams) is not stored, while at the same time holding that material that never reaches consciousness (whatever its nature) is somehow magically processed and consolidated in sleep.

The S-MC position seems to require two parallel systems (seemingly sharing the same neural substrates) involved in the processing of waking material in sleep: a "sleep conscious" system (dreams) that distorts and imprecisely codes waking events and a "sleep unconscious" system that faithfully records and stores waking events. If the latter system exists, it is surprising that it has so far escaped detection.

Sleep Is an Amnesiac State

It is well recognized that the contents of sleep are poorly remembered. This suggests that structures responsible for the encoding and storage of information in waking are suppressed or absent in sleep. This was pointed out by Hobson et al. (1998), stating: "The loss of memory in REM sleep makes dreaming consciousness much more difficult to recall than waking consciousness. This phenomenological deficit logically implies a physiological deficit: some functional process, present and responsible for memory in waking, is absent, or at least greatly diminished, in REM sleep."

Insights into the amnesiac quality of sleep are provided by recent functional imaging studies in humans

identifying patterns of brain activity in sleep/REM sleep. Although differences exist among reports, a fairly consistent pattern of brain activity in REM has emerged from these studies. Some important findings are as follows: (1) the pontine reticular formation is highly active in REM sleep; (2) primary sensory areas (e.g., striate cortex for the visual system) are inactive in REM, whereas sensory association regions are very active in REM sleep; (3) limbic and paralimbic regions, including the lateral hypothalamus, the amygdala and anterior cingulate, and parahippocampal cortices are intensely activated in REM; and (4) widespread regions of the frontal cortex, including the lateral orbital and dorsolateral prefrontal cortices, show marked reductions in activity in REM sleep (Maquet et al., 1996; Braun et al., 1997, 1998; Nofzinger et al., 1997).

This general pattern of activity in REM has been viewed as a "closed system" (Braun et al., 1998), essentially, an internal network disconnected from normal inputs and outputs. For instance, the suppression of activity in the primary visual cortex (input) is consistent with the well-characterized sensory blockade of REM sleep, whereas the deactivation of the prefrontal cortex (output) parallels the failure of dreams to influence executive systems for behavior. In essence, patterns of brain activity in sleep are quite consistent with what would be expected of the "dreaming brain"; that is, internally generated images removed from reality are processed and manipulated in sleep and then quickly discarded. More specifically, internal (mainly visual) images are fed to the limbic system, where they become incorporated into dreams, but due to the suppression of activity of the prefrontal cortex, these dream scenarios are not permanently stored, nor do they influence behavior. Commenting on the effects of dampened prefrontal cortical activity on memory in sleep, Jones (1998) stated that this produces "an attenuation of processes important in episodic and working memory and perhaps explaining why, unless awakened from a dream, a sleeping person has no memory of the dream."

To conclude, the brain is in a non-memory encoding mode in sleep/REM sleep, which accounts for the amnesiac quality of dreams—and importantly, in our view, amnesia for all cognitive contents of sleep. As indicated above, we find great difficulty with the position that acknowledges, on the one hand, that material reaching awareness in sleep (dreams) is lost to memory (reflecting a nonencoding mode of the brain in sleep), while on the other hand claiming that material that never reaches consciousness is faithfully processed and committed to memory during sleep.

Sleep Is Not Involved in Declarative Memory

It is well documented that there are two main classes of memory: declarative and procedural memory (Cohen, 1984; Squire and Cohen, 1984; Eichenbaum and Cohen, 2001). Declarative (or explicit) memory consists of general factual knowledge of the world and its inhabitants (facts, events, people, places, etc.) and has two recognized subclasses, semantic memory (impersonal facts) and episodic memory (personal or autobiographical facts and experiences) (Tulving, 1972, 1984). Procedural (implicit) memory, on the other hand, has been described as "how to" memory and largely involves the unconscious acquisition and utilization of perceptual and motor skills.

In a previous report (Vertes and Eastman, 2000a), we reviewed a large body of literature showing that the major classes of antidepressant drugs (monoamine oxidase inhibitors, tricyclic antidepressants, and selective serotonin reuptake inhibitors) suppress REM sleep, but despite this marked suppression of sleep, these compounds, on the whole, have no adverse effects on learning and memory (also see below). In response, Stickgold (2000) remarked that these findings were not unexpected in that subjects were tested for declarative memory and this type of memory is not processed/consolidated in sleep. According to Stickgold, "Since all proponents of REM-dependent memory consolidation agree that REM is not involved in declarative memories, such as those formed in paired associates training, the failure to observe REM-dependent consolidation may simply reflect the testing of a memory system that is not REM-dependent."

In like manner, following a recent review of memory processing and sleep in humans, Smith (2001) similarly concluded that REM sleep is not involved in declarative memory. He described six of seven studies showing no increases in the amounts of REM sleep following learning and seven of seven studies demonstrating that REM deprivation did not disrupt declarative learning/memory and concluded that "REM sleep is not involved with consolidation of declarative material."

With few exceptions (Fenn et al., 2003), all recent human experimentation in this field has employed procedural tasks—either perceptual (Karni et al., 1994; Gais et al., 2000; Stickgold et al., 2000a, 2000b) or motor/visuomotor tasks (Maquet et al., 2000, 2003; Fischer et al., 2002; Walker et al., 2002, 2003a, 2003b). This concentration on procedural learning appears to reflect the current view that sleep is involved in procedural but not in declarative memory (Stickgold, 2000; Smith and Rose, 2000; Smith, 2001).

Sleep Suppression/Elimination in Animals and Humans: Effects on Memory Processing and Consolidation

Animal Studies

There is a long history of research on the role of sleep on cognition in animals that peaked in the 1960s to 1970s. Several reviews have been devoted to this topic (McGrath and Cohen, 1978; Horne and McGrath, 1984; Smith, 1985, 1996; Horne, 1988). The effects of sleep on memory in animals have commonly been assessed using sleep/REM sleep deprivation techniques; that is, training animals to criteria on tasks, depriving them of sleep (SWS, REM, or both), and then retesting them on the tasks.

Studies involving sleep deprivation techniques in animals have been equally divided, favoring, or not favoring, a role for sleep in memory consolidation. Although several factors have undoubtedly contributed to the mixed results, one of the most important appears to be the general state of the animals in these reports. It is widely acknowledged that the animals (mostly rodents) in many of these studies were compromised due to the severe methods used to deprive them of sleep.

The most commonly used deprivation procedure has been the "flower pot" method. In brief, animals are placed on top of a small pedestal (usually a small inverted flower pot) sitting in a larger jar containing water. As animals enter sleep/REM sleep, they lose postural tone (atonia), partially or fully slip from the pedestal into the water, and awaken. Controls are placed on larger diameter pedestals or are allowed normal sleep in their home cages.

Although the flower pot (or pedestal) technique is an effective means of depriving animals of sleep, it is known to produce several secondary effects that are very stressful to animals, including isolation, heat loss, and muscle fatigue. Accordingly, as a group, these effects have been referred to as the "stress factor" associated with this method of deprivation (Fishbein and Gutwein, 1977; Horne and McGrath, 1984; Coenen and van Luijtelaar, 1985). It has been proposed that "stress," rather than the loss of sleep per se, largely accounted for the learning impairments in many of these studies. Specifically, it has been argued that impairments with sleep deprivation were not true learning/memory deficits but merely performance deficits; that is, animals were simply unable to perform the required task(s) due, in large part, to the physically debilitating effects of the deprivation.

There have been attempts to separate learning from performance deficits (or control for the stress factor), principally (1) by using less-stressful sleep deprivation techniques, such as the multiple platform, pendulum, or the disk-over-water techniques (van Hulzen and Coenen, 1980, 1982; van Luijtelaar and Coenen, 1986; Rechtschaffen and Bergmann, 1995; Rechtschaffen, 1998); and/or (2) by allowing animals to recover from the effects of deprivation before testing them. In both instances, these procedures have been shown to produce minimal or no disruption of learning/memory—or considerably less than seen without them (Fishbein, 1970, 1971; van Hulzen and Coenen, 1982).

In effect, then, the stress associated with the use of the pedestal technique has confounded the findings of many of the animal studies. Born and Gais (2000) (supporters of the sleep-memory consolidation hypothesis) recently addressed this, stating that "There are obvious flaws of REM sleep suppression paradigms that do not allow for any conclusion, either pro or contra the REM sleep-memory hypothesis." Horne (1988), following a review of this literature, similarly concluded that "In sum, and in relation to the memory consolidation hypothesis for REM sleep, I find the field of REM sleep deprivation and learning in animals unconvincing."

Human Studies

Studies examining the effects of sleep deprivation on memory processing in humans are considerably less numerous than those with animals, but like reports in animals, the results have been mixed—and if anything, on balance, they show no relationship between sleep and memory consolidation (for review, see Horne, 1988; Vertes and Eastman, 2000a; Smith, 2001). These reports generally involve depriving subjects of a single night, or at most a couple of nights, of sleep. Although these studies are informative, it appears that a clearer understanding of the role of sleep in memory processing may be gained from an examination of the cognitive functioning of individuals that lack sleep/REM sleep. The effects of the marked suppression or elimination of sleep (mainly REM sleep) on memory processing/consolidation are discussed below.

Brainstem Lesions

Although large lesions of the brainstem generally result in coma or death (Cairns, 1952), there are a few documented cases of individuals who have survived these lesions with normal faculties intact. They were conscious, ambulatory, and verbally communicative—and importantly, they lacked REM sleep (Osorio and Daroff, 1980; Lavie et al., 1984; Valldeoriola et al., 1993). Osorio and Daroff (1980) described two such patients and reported that, aside from minor neurological deficits, they led normal lives. They stated that "Our two patients are the first awake and ambulatory humans in whom total absence of REM sleep has been demonstrated. These REM deprived patients behaved entirely appropriately and were by no means psychotic." The "psychotic" reference alludes to the early notion, subsequently dispelled (Vogel, 1975), that long-term REM deprivation produces psychosis.

Lavie et al. (1984) described the interesting case of a man who at the age of 20 suffered damage to the pontine region of the brainstem from shrapnel from a gunshot wound. Following the injury, the man was comatose for 10 days, remained in critical condition for another 2 weeks, and then recovered. An examination of his patterns of sleep at the age of 33 revealed a virtual absence of REM sleep. Despite this, the man led a normal life. Following the injury, he completed college, then law school, and at the time of the study was a practicing attorney.

Although no systematic attempt was made to examine the cognitive capacities of these patients, the virtual total loss of REM sleep did not seem to result in any apparent cognitive deficits.

Antidepressant Drugs

It is well recognized that virtually all major antidepressant drugs suppress REM sleep, i.e., the monoamine oxidase inhibitors (MAOIs), the tricyclic antidepressants (TCAs), and the selective serotonin reuptake inhibitors (SSRIs).

Of the three classes of antidepressants, the MAOIs have the most pronounced REM-suppressive actions, virtually completely (or completely) eliminating REM sleep for months to years (Wyatt et al., 1969, 1971a, 1971b; Kupfer and Bowers, 1972; Dunleavy and Oswald, 1973). Although not systematically examined, the general cognitive status of individuals on MAOIs has been described in several case reports. Richard Wyatt, a pioneer in this field, reported that various MAOIs, while strongly suppressing REM sleep, did not noticeably alter behavior. For instance, in a study of narcoleptics, Wyatt et al. (1971b) reported that phenelzine completely abolished REM sleep in five patients for periods of 14–226 days without obvious complications. They stated: "The complete drug-induced suppression of REM sleep in these patients is longer and more profound than any previously described"; and yet, "No adverse psychological effects were noted during the period of total rapid-eye-movement suppression."

Several other studies have similarly reported that MAOIs profoundly suppress (or eliminate) REM sleep

without observable cognitive or motor dysfunctions (Akindele et al., 1970; Georgotas et al., 1983, 1989; Raskin et al., 1983).

Unlike the MAOIs, the TCAs and SSRIs do not eliminate REM sleep, but profoundly suppress it by 75%–85% in the short term (days) and 30%–50% in the long term (weeks to years). Since the newer antidepressants, particularly SSRIs, are in such widespread use, considerably more attention has been paid to their possible effects on cognitive functions. Several reviews have been devoted to this topic (Thompson and Trimble, 1982; Deptula and Pomara, 1990; Thompson, 1991; Knegtering et al., 1994; Amado-Boccara et al., 1995).

As a group, the TCAs have no adverse actions on memory (Thompson and Trimble, 1982; Deptula and Pomara, 1990; Thompson, 1991; Amado-Boccara et al., 1995). A notable exception is amitriptyline, which is known to affect memory, but does so through its sedative and anti-cholinergic actions (Curran et al., 1988; Spring et al., 1992). By contrast, several other TCAs, including doxepin, desipramine, nortriptyline, amoxapine, protriptyline, maprotiline, and chlorimipramine have virtually no detrimental effects on memory (Liljequist et al., 1974; Pishkin et al., 1978; Linnoila et al., 1983; McNair et al., 1984; Curran et al., 1988; Georgotas et al., 1989; Allain et al., 1992).

As is well recognized, SSRIs are currently the preferred treatment for depression. Unlike the TCAs, the SSRIs have no sedative or anti-cholinergic actions. The SSRIs have been extensively examined, with no evidence of adverse actions on motor or cognitive functions (Saletu et al., 1980; Linnoila et al., 1983; Lamping et al., 1984; Curran and Lader, 1986; Hindmarch and Bhatti, 1988; Saletu and Grunberger, 1988; Hindmarch et al., 1990; Spring et al., 1992; Kerr et al., 1992, 1993; Fairweather et al., 1993, 1996; Geretsegger et al., 1994). For instance, an early review (Thompson, 1991) concluded that "Newer compounds devoid of antimuscarinic effects, particularly the serotonin reuptake inhibitors, if not sedative, have not been associated with memory impairment"; while a more recent one (Amado-Boccara et al., 1995) similarly stated: "antidepressants which inhibit serotonin reuptake seem to have no deleterious cognitive effects."

It appears, then, that the marked suppression or complete loss of REM sleep in humans with brainstem lesions or antidepressant drugs has no detrimental effect on cognitive functions.

Commenting on this, Stickgold (2000) remarked that this was not surprising, for the memories generally examined in these cases were working memory and declarative memory, which would not be expected to be altered by a disruption of REM sleep. Stickgold stated: "It is not surprising that simple cognitive and psychomotor memory tests fail to show any obvious impairment of performance after administration of drugs that disrupt REM sleep. These tests classically measure working memory and declarative memory systems that we would not expect to be affected by REM deprivation. We know of no cases in which anyone, for example, tested the effects of these drugs on complex perceptual procedural learning."

Although it is possible that antidepressants, while not affecting declarative processes, may disrupt procedural memory, the evidence is lacking. As discussed, the widespread use of antidepressants has prompted a close examination of their possible side effects, not only cognitive but motor. With few exceptions, most of the commonly used antidepressants have little or no adverse actions on motor functions—indirectly indicating a lack of an effect on procedural memory.

Memory Consolidation, Procedural Memory, and Sleep

Memory consolidation refers to the process of the conversion of information from initially "labile" states to more enduring forms, largely resistant to interference. Nadel and Moscovitch (1997) described memory consolidation as the "neural processing that occurs after information is initially registered which contributes to its permanent storage in memory."

Two types of memory consolidation have been described: short-term consolidation requiring minutes to hours and long-term processes that could stretch for years or a lifetime (Squire, 1987; McGaugh, 2000; Eichenbaum and Cohen, 2001; Dudai, 1989, 2004). Dudai (2004) has aptly designated these two types of memory consolidation as "synaptic" and "systems" consolidation, reflecting localization at the neuronal or systems level.

The demonstration that the storage of information could be disrupted shortly after acquisition by several factors (electroconvulsive shock, protein synthesis inhibition) focused attention on early events that transform traces from labile to stable states (Squire et al., 1975; Davis and Squire, 1984). These processes have now been well characterized and basically involve a series of molecular and cellular events that culminate in gene activation, protein synthesis, and synaptic restructuring (Bailey et al., 1996; Martin et al., 2000; Kandel, 2001; Dubnau et al., 2003; Lamprecht and LeDoux, 2004).

Systems consolidation, on the other hand, refers to long-term processes extending for months to years that secure older memories, presumably by shifting their locus of storage from the hippocampus to the neocortex (Squire and Alvarez, 1995; Eichenbaum et al., 1996; Rempel-Clower et al., 1996; McGaugh, 2000; Eichenbaum and Cohen, 2001). "Systems consolidation" largely developed from observations of memory dysfunctions of H.M. and other patients with extensive damage to the medial temporal lobes. As is well documented, H.M. suffered a total anterograde amnesia and a temporally graded retrograde amnesia involving a nearly complete memory loss dating back to about 11 years prior to surgery, but relatively intact memories before that time (Scoville and Milner, 1957; Corkin, 1984).

"Consolidation" has been used ambiguously in the sleep literature to denote a rather ill-defined sleep-associated mechanism that serves to consolidate waking experiences. It has essentially been used operationally to refer to sleep-dependent processes that produce greater gains in performance with sleep than without it. Only recently have attempts been made (Graves et al., 2001) to relate sleep-dependent consolidation to processes well characterized at the synaptic or systems level.

Although not discussed in these terms, sleep-depen-

dent consolidation would appear to be a variant of synaptic consolidation—primarily for two reasons. In the first instance, sleep-dependent consolidation is a short-term event; major changes are observed within 24 hr postacquisition and progressively decline thereafter (Smith, 1985, 1996). Second, as discussed, sleep is selectively involved in the consolidation of procedural memories, and being procedural, would not seem to involve temporal lobe structures associated with the long-term storage and reorganization of information—or systems consolidation. As Dudai (2004) recently noted: "At the time of this writing, no evidence is available for more prolonged consolidation of skill."

Procedural Memory and Time-Dependent Consolidation

As indicated, procedural memory is one of the two major classes of memory and is characterized as "how to" memory, the essentially unconscious acquisition and storage of perceptual and motor skills. Until fairly recently, procedural memory was not thought to be governed by the same principles as declarative memory, including short-term consolidation over time. In a series of studies, however, Shadmehr and colleagues (Brashers-Krug et al., 1996; Shadmehr and Brashers-Krug, 1997; Donchin et al., 2002) reported that human motor learning, like other types of learning, undergoes a process of consolidation. Specifically, they showed that the learning of a motor task (reaching movements with planar manipulandum) was significantly disrupted when a second task followed the first by 5 or 60 min, but not when the two tasks were separated by more than 4 hr. They concluded that motor skills are "consolidated" over an approximately 4–6 hr period, comparable to the consolidation of declarative memories. They stated: "Previous studies in humans and other primates have found this time-dependent disruption of consolidation only in explicit memory tasks which rely on brain structures of the medial temporal lobe. Our results indicate that motor memories, which do not depend on the medial temporal lobe, can be transformed by a similar process of consolidation" (Brashers-Krug et al., 1996).

In line with the foregoing, Muellbacher et al. (2002) demonstrated that transcranial magnetic stimulation of the primary motor cortex (M1) disrupted performance on a motor task (finger movements) when applied immediately following training, but not when given 6 hr after acquisition.

If, as indicated above, motor learning involves a period of consolidation lasting about 4–6 hr, it is not unreasonable to surmise that this process, initiated with task acquisition in waking, could continue into sleep in a time-dependent manner. In this sense, then, (procedural) consolidation *would* (or could) take place during sleep. This could account for the beneficial effects of sleep on procedural learning in some studies. Importantly, however, this would be a time-dependent, and not state-dependent, process that begins with acquisition in waking and could, in some instances, extend to sleep. An obviously important difference between state- and time-dependent mechanisms is that changes in state (e.g., sleep to waking) would not alter the process; that is, awakenings from sleep would not disrupt time-dependent consolidation begun in waking.

In this regard, Shadmehr and associates (Donchin et al., 2002) recently demonstrated time (but not state) dependency on an arm reaching task (see above). They trained two groups of subjects on the task, and following training, one group was allowed normal sleep and the other was sleep deprived, and then both groups were tested on the next day. There was no difference in performance of the sleep- and non-sleep-deprived subjects on the task, indicating a time-dependent and not a state-dependent process of consolidation. They addressed inconsistencies between their findings and earlier ones suggesting that sleep serves a special role in procedural consolidation, stating: "A number of studies have found a role for sleep in consolidation of certain kinds of perceptual skills. In those studies, sleep, and not simply the passage of time, has been shown to be required for changes in performance between the end of training and test of recall." By contrast, "we found no significant effect of sleep on performance."

Until recently, "consolidation" in the sleep literature was used in the classic sense of referring to processes that strengthen labile traces—with straightforward predictions. In this sense, learned material of waking would reside in a temporarily unstable state requiring the stabilization/consolidation of sleep. Accordingly, normal sleep would "consolidate" waking experiences, maintaining levels of performance, whereas alterations of sleep would disrupt consolidation, leading to poorer performance.

Seemingly lost in the current debate is the fact that the term "consolidation" (at least for recent human sleep studies) has taken on a very different meaning; that is, rather than referring to a stabilization of learning, it is used to signify *improvements* in learning—or gains in performance with sleep.

In an initial report, which became the prototype for others that followed, Karni and Sagi (1993) showed that the mere passage of time improved performance on a perceptual learning task. The task involved identifying the orientation of three diagonal lines (arranged horizontally or vertically) embedded in a background of horizontal lines. The stimulus (target and background elements) was presented briefly (10 ms) in one quadrant of the visual field followed by a blank screen and then a masking pattern (100 ms). The interval between the onset of the stimulus and onset of the mask (stimulus-to-mask onset asynchrony [SOA]) was varied, and the measure of performance was an 80% correct identification (threshold SOA) of the stimulus (horizontal or vertical lines) at a set interval. The index of improved performance was a decrease in threshold SOA (Karni and Sagi, 1993; Karni et al., 1994). Karni and Sagi (1993) reported that subjects showed no improvement on the task immediately after training but marked improvement 8–10 hr following training.

In a follow-up examination of the effects of sleep on this perceptual task, Karni et al. (1994) described gains in performance over a normal night of sleep, but none when REM sleep (but not SWS) was eliminated, and they concluded that consolidation in sleep "is strongly dependent on REM sleep." Interestingly, Karni et al. (1994) drew attention to differences between their paradigm and earlier ones, pointing out that they examined improvements in learning (and not loss), whereas previ-

ous studies assessed the effects of sleep on the retention of material, or the rate of forgetting.

As discussed, in an initial report, Karni and Sagi (1993) demonstrated improved learning over time during waking, and in a follow-up study (Karni et al., 1994), improvements over time during sleep (and during waking), raising the question as to the similarity/differences of the processes in the two states. This was clarified by Karni (1995) stating: "Indeed our results suggest that REM sleep is not a unique brain state for memory processing in adults—normal skill (procedural) learning does occur during the waking state. Our somewhat counter-intuitive finding was, however, that much of this improvement happens not during or immediately after practice but rather 8–10 hr after a training session has ended, suggesting a slow, latent process of learning." And further, "The issue of whether experienced-triggered brain changes, presumably occurring during sleep (for which REM sleep is needed) are qualitatively different from the neural mechanisms subserving waking state consolidation remains open. Nevertheless, one would expect that systematic deprivation of REM sleep would not be very detrimental to skill learning in general because normal consolidation should occur during the waking state."

In effect, then, as discussed for consolidation as stabilization, consolidation as enhancement (improvement) appears to be state independent. Enhancement would be expected to occur 8–10 hr following training, independent of state.

Although Karni described comparable enhancement on the perceptual task in waking and sleep, subsequent studies (Stickgold et al., 2000a, 2000b; Gais et al., 2000) using this same task reported significant gains in performance (enhancement) during sleep, but failed to demonstrate the same degree of improvement during waking as shown by Karni and associates (Karni and Sagi, 1993; Karni et al., 1994). It was also the case that studies differed with respect to the role served by different states of sleep in consolidation, reporting, for instance, that consolidation/enhancement occurs during REM sleep (Karni et al., 1994), during SWS (early sleep dominated by SWS) (Gais et al., 2000), or both (amount of SWS in the first quartile of the night + amount of REM sleep in the last quartile of the night) (Stickgold et al., 2000a). The source of these differences remains unclear, but resolving them is undoubtedly important, particularly the extent to which performance improves during waking on the task.

There has been a recent shift in research paradigms in this area from perceptual learning to motor learning. Avi Karni (with Leslie Ungerleider) developed a motor task, which like Karni's perceptual discrimination task, has subsequently been adopted by others. The task consists of a sequence of four finger movements (excluding the thumb), with one sequence (e.g., 4-1-3-2-4) serving as the trained sequence and another as the untrained or control sequence. The measure of improved performance is a reduction in errors (accuracy) and an increase in speed. Karni et al. (1998) reported that (1) 10–20 min of daily practice on the task produced large gains in performance that reached asymptote in 3 weeks; and (2) germane to present issues, brief training on the task (six 40 s spaced sessions) resulted in improvement (enhancement) on the task 24 hr after training—similar to that described for perceptual learning. According to the authors, limited training on the task not only produced gains during the sessions but also initiated delayed improvement, indicating that "some gains require time to become effective and continue to develop after motor practice has ended."

Although these investigators (Karni et al., 1998) described changes in performance 24 hr after training, this interval was apparently not chosen to assess the effects of sleep on the task. No mention was made of sleep. They instead (Ungerleider et al., 2002) noted the similarity between their findings and earlier ones on perceptual and motor learning and concluded: "These results, and those of Karni and Sagi (1993), thus point to a window of about 6 hr for consolidation to occur."

The effects of sleep on performance on the finger tapping task have subsequently been examined using sleep deprivation (Fischer et al., 2002) and non-sleep deprivation (Walker et al., 2002, 2003a) techniques. Walker et al. (2003a) reported that training subjects in the morning (10:00 AM) and then testing them at three successive 4 hr intervals throughout the day resulted in linear increases in performance, but gains in performance during waking were significantly less than with overnight sleep.

Using a deprivation procedure, Fischer et al. (2002) trained four groups of subjects on the finger tapping task—two groups in the evening (10:00 PM) and two in the morning (10:00 AM) and then tested each group 8 hr later. One pair of each group was sleep deprived and the other received normal sleep, resulting in the following four groups: nighttime waking (sleep deprivation), nighttime sleep (as normal), daytime waking (as normal), and daytime sleep (not normal). They described greater gains in performance (speed on the task) over intervals of sleep (nighttime and daytime) than waking (nighttime and daytime).

Similar to differences in stages of sleep contributing to perceptual learning, overnight improvement on the finger tapping task was variously attributed to stage two SWS (Walker et al., 2002) and to REM sleep (Fischer et al., 2002).

While the foregoing studies showed that sleep contributes to overnight improvement on the task, they also importantly demonstrated that effects are not restricted to sleep but also occur during waking. In the Walker et al. (2003a) report, changes in waking were progressive but marginally statistically significant (see their Figure 2A), whereas for Fischer et al. (2002), improvements in waking were highly statistically significant (daytime waking group). These findings, combined with those on perceptual learning (Karni and Sagi, 1993; Karni et al., 1994), thus point to a time-dependent process of improvement on some perceptual and motor skills during both waking and sleep.

Although enhancement may prove to be a significant mechanism for the slow, time-dependent reorganization of procedural skills, it is important to note, as discussed by Walker et al. (2003a), that gains in performance with the passage of time (in waking or sleep) are very small compared to those found with practice on a task. Specifically, Walker et al. (2003a) reported that the performance of subjects receiving repeated practice on the finger tapping task (Karni et al., 1998) was "far in excess

of values achieved by subjects in this study" (i.e., values due to enhancement in sleep). In addition, while enhancement has been described for the finger tapping task, it has not been demonstrated for other motor tasks (Donchin et al., 2002; Goedert and Willingham, 2002). For instance, Donchin et al. (2002) trained subjects over three sessions on an arm reaching task (see above), tested them 24 hr later, and reported that performance *declined* on 24 hr retest from peak performance on the third session of training (i.e., lack of enhancement).

Unresolved Issues

To summarize, procedural memories, like declarative memories, consolidate over time (time dependent). This process begins with task initiation, and if not disrupted by competing tasks, proceeds unabated until completion, generally in 4–8 hr. Consolidation (as stabilization) appears to be state independent; that is, once initiated (in waking) it proceeds continuously through waking and possibly into sleep. Sleep, however, serves no unique role in procedural consolidation. A process of enhancement has recently been described for some perceptual and motor skills consisting of *improvements* in performance with the passage of time without further practice on a task. Enhancement has been shown to occur during both waking and sleep, but reportedly to a much greater degree in sleep than waking for some tasks in some studies.

To a large extent, the current debate on the role of sleep in memory consolidation appears to revolve around the question of whether enhancement is unique to sleep or is more pronounced in sleep than in waking. In the following, we briefly address some unresolved issues/questions on enhancement.

1. Is enhancement a general phenomenon of perceptual/motor learning? To date, enhancement has been demonstrated for one perceptual skill (perceptual discrimination task) and one motor task (finger tapping task). As a relatively new phenomenon, enhancement has not been widely examined. As discussed, however, Donchin et al. (2002) described consolidation (as stabilization) for an arm reaching task but were unable to show enhancement with this same task. The tasks to which enhancement applies need to be determined.

2. If enhancement were to be demonstrated for other tasks, would it differ in degree across behavioral states as reported for the perceptual discrimination and finger tapping tasks in some studies?

3. What is the contribution of enhancement to improvements in skill learning? As noted above, Walker et al. (2003a) reported that gains in performance with the passage of time (enhancement) on the finger tapping task were very small compared to those found with repeated practice on the task. This raises the question of the overall contribution of enhancement, relative to rehearsals, in the mastery of skills. For example, certain professions (concert musicians, professional athletes) require finely tuned motor skills that develop with years (or a lifetime) of practice. What is the relative contribution of practice to enhancement in the development of the skills required for these professions—or the common skills of daily life?

4. What mechanisms may be responsible for enhancement in sleep—or waking? In a recent review, Walker (2004) discussed several processes that could account for enhancement in sleep, including sleep spindles, PGO waves (Datta, 2000), levels of transmitters/neuromodulators, and immediate early gene expression. For example, he pointed out that "during REM sleep, there is a significant increase in cholinergic tone, which has been considered to play a role in sleep-dependent plasticity." But continuing, Walker (2004) indicated that it is probably premature to attribute the possible beneficial effects of sleep on memory (enhancement) to any one or group of factors, including transmitter levels, stating that "direct evidence implicating post-sleep behavioral learning associated with changes in neurotransmitter concentration during either NREM or REM sleep remains scarce." It also is quite likely that general properties of sleep, rather than sleep mechanisms per se, may be responsible for the reported greater degree of enhancement in sleep than waking in some studies; that is, less interference from competing behaviors in sleep than waking for some tasks. In this regard, Gottselig et al. (2004) recently reported that subjects showed the same degree of improvement on an auditory sequence task following periods of restful waking or sleep and attributed improvement in both instances to the lack of interference from competing events.

5. Finally, what stage(s) of sleep is critical for enhancement? As discussed, findings conflict regarding the specific stages of sleep involved in consolidation/enhancement; reports have variously implicated SWS, REM sleep, or both in these processes. This needs to be resolved.

"Replay" of Patterns of Neural Activity of Waking in Subsequent Sleep in Animals

A process commonly referred to as "replay" has recently been described wherein patterns of neural activity in waking are repeated in subsequent episodes of sleep (Pavlides and Winson, 1989; Wilson and McNaughton, 1994; Skaggs and McNaughton, 1996; Kudrimoti et al., 1999; Nadasdy et al., 1999; Hirase et al., 2001; Louie and Wilson, 2001; Hoffman and McNaughton, 2002; Lee and Wilson, 2002). Replay has been mainly, but not solely, demonstrated in the hippocampus and is thought to represent a reactivation, and hence consolidation, of hippocampally dependent memories in sleep. Although replay supports the view that sleep consolidates memories by rehearsing or replaying them in sleep, it is important to note that replay is not restricted to sleep, but has been shown to occur equally in (quiet) waking and sleep in rats (Kudrimoti et al., 1999) and primates (Hoffman and McNaughton, 2002). Although first described for sleep (Pavlides and Winson, 1989; Wilson and McNaughton, 1994), replay is not specific to sleep. In addition, there is no evidence that replay serves to secure or consolidate memories (Benington and Frank, 2003). It is very possible that neural circuits that are repeatedly or strongly activated in waking would, consequently, be those most likely to show rebound activation in subsequent sleep—or in waking. This reactivation would not necessarily consolidate replayed traces but may merely reflect their previous activation.

Although replay appears to be a reliable phenomenon for rats, the possibility exists that replay in sleep is unique to lower animals and has no counterpart in hu-

mans. For example, sequences of hippocampal activity corresponding to movements through a maze may be repeated during sleep in rats, whereas our hippocampal activity during sleep would poorly replicate routes taken to the grocery store and back—as seems to be the case. In effect, replay in sleep was lost with evolution.

As developed below, we view replay in animals as a process analogous to the episodic transfer of information from waking to sleep in humans (Fosse et al., 2003). As will be discussed, the amount of material transferred from waking to sleep, however, in both animals and humans, appears to be quite small and unlikely serves a mnemonic function.

As mentioned, Freud (1900) initially considered, but then dismissed, the notion that sleep serves a role in memory consolidation. This was based, in large part, on the mismatch between the cognitive content of waking and sleep; that is, other than brief intrusions of daytime material into sleep (day residue), waking experiences are not replicated in sleep. Although this is well recognized, surprisingly few studies have systematically examined the transfer of waking material into sleep (Dement et al., 1965; Fosse et al., 2003).

In the most thorough study to date, Fosse et al. (2003) examined the correspondence between waking experiences and dream reports of 29 subjects over a 14 day period, focusing on locations, actions, objects, characters, themes, and emotions. Of a total of 299 dream reports of SWS/REM sleep, only 5 (1.4%) were judged to be highly similar to waking events and qualified as strong candidates for the transfer of episodic memories from waking to sleep. Fosse et al. (2003) thus concluded that "sleep has no role in episodic memory consolidation"; and further that "reactivation of episodic memories appears to be actively blocked during sleep."

Schwartz (2003) recently drew attention to the seeming discrepancy between the small amount (1%–2%) of episodic material transferred from waking to sleep in humans and the presumably significant repetition of patterns of waking activity in sleep in animals—or replay.

In effect, replay in animals suggests that patterns of neural activity in the hippocampus/cortex are similar during waking and sleep, whereas the human data would indicate very dissimilar patterns during these two states, as shown by the pronounced mismatch between the episodic content of waking and sleep—only 1%–2% overlap.

The typical procedure for assessing replay in animals is to compare patterns of unit activity during well-trained tasks (task) of waking to patterns in sleep preceding (presleep) and following (postsleep) the task. The measure of "reactivation" is a greater similarity of patterns of activity in postsleep to task than presleep to task. Although not always the case, animals generally receive concentrated training on a familiar task which is followed immediately (or at least without intervening experiences) by sleep. These conditions favor reactivation—and certainly legitimately so.

Even under these circumstances, however, effects are quite small, i.e., percentages of reactivated patterns of hippocampal activity in sleep from waking (for review, see Benington and Frank, 2003). For instance, Nadasdy et al. (1999) reported that 87 of 1716 (5%) sequences of hippocampal unit activity (triplets) were common to presleep and task (see above) compared to 160 of 1716 (9%) common to postsleep and task. Although this represented a statistically significant change from pre- to postsleep, the difference (4%) was not robust. In like manner, using a method of explained variance (McNaughton et al., 2003), Kudrimoti et al. (1999) reported that ~15% of the variance of ensemble activity (unit pairs) in the hippocampus during waking in rats could be explained by changes in postsleep relative to presleep.

Although these values (4%–15%) are higher than shown for episodic transfer in humans (1%–2%), it is important to again note that these studies generally involved well-trained tasks in confined environments. Transfer is reduced in unrestricted settings. For instance, McNaughton and colleagues (J.L. Gerrard et al., 2001, Soc. Neurosci., abstract Volume *27*, p. 1698) examined reactivation (replay) in sleep of two groups of rats: one group repeatedly circled a small tract (1–2 m), and the other group spent an equivalent amount of time exploring a long corridor (2 m × 13 m), rarely revisiting the same locations. They demonstrated that reactivation/replay was significantly less in the open environment than in the restricted environment, leading them to conclude that "repetition facilitates trace reactivation." The foregoing suggests that reactivation decreases as the environment expands, such that reactivation for rats in their natural habitat would be quite low, possibly approaching episodic transfer in humans of 1%–2%.

In summary, a small percentage (1%–2%) of waking experiences transfer from waking to sleep in humans. Freud termed this the "day-residue" which can be incorporated into dreams. A similar phenomenon has been described in animals—the replay of ensembles of neural activity of waking in subsequent sleep. Although the precise relationship between replay in animals and episodic transfer in humans remains to be determined, there are parallels: the two processes appear to be of the same magnitude, involve the same structures, and apparently do not produce lasting changes.

Other Factors

If sleep serves to consolidate experiences, it might be expected that species with the greatest cognitive demands would have the most sleep—or a direct relationship would be found between percentages of sleep/REM sleep and degree of cortical development (encephalization). Siegel (2001) recently demonstrated, however, that no such relationship exists. Humans do not exhibit exceptionally high amounts of REM sleep but rather place intermediate among species in amounts of REM sleep and total sleep. Presumably, the most important factor in determining amounts of sleep/REM sleep is the degree of maturity at birth—animals mature at birth have low amounts of REM, while those immature at birth have high amounts of REM sleep (Zepelin, 1989, 2000; Siegel et al., 1999).

Importantly, levels of sleep/REM sleep do not covary with encephalization or intelligence. The egg-laying platypus, a primitive mammal with a lisencephalic cortex, has the highest recorded amounts of REM sleep (8 hr/day) (Siegel et al., 1999), whereas whales and dolphins, which by all accounts are very intelligent species, have the lowest levels of REM sleep (about 15 min/day) (Zepe-

lin, 2000; Siegel, 2001). It could be argued that the quality (or efficiency) of REM and not the quantity is the critical factor in determining its role in consolidation (e.g., humans can do more with less sleep). The sleep of higher organisms, however, does not appear to exhibit any unique characteristics that would set it apart from that of lower organisms, i.e., render it more efficient. For instance, the sleep architecture of cats and humans is remarkably similar, though differing with respect to amounts of REM and total sleep: 3.2 hr and 15.9 hr, respectively, for cats, and 1.9 hr and 8.0 hr for humans (Zepelin, 1989, 2000).

With recent advances in gene expression profiling, several reports have demonstrated that a host of genes is differentially expressed in waking and sleep (for review, see Tononi and Cirelli, 2001). In initial studies, Tononi, Cirelli, and colleagues (Cirelli et al., 1996; Cirelli and Tononi, 1998, 2000a) reported that important "plasticity-related" genes are more highly expressed in waking than in sleep in rats, such as phosphorlyated CRE binding protein (P-CREB), Arc, BDNF, and nerve growth factor-induced A (NGFI-A). In a subsequent analysis of ~10,000 genes, they found that only 0.5% were differentially expressed across behavioral states but emphasized that those showing greater expression in waking than sleep constituted important functional categories (Cirelli and Tononi, 2000b). These included immediate early genes (IEGs) and transcription factors, genes related to energy metabolism, chaperones/heat shock proteins, growth factors/adhesion molecules, vesicle and synapse-related genes, neurotransmitter/hormone receptors, neurotransmitter transporters, and various enzymes.

The finding that genes associated with energy metabolism and transmitter functions are more highly expressed in waking than sleep supports other measures indicating that the brain (or cortex) is very "activated" in waking relative to sleep (SWS), while the further demonstration that IEGs and transcription factors (plasticity-related genes) are selectively upregulated in waking suggests that needs for information processing are high in waking and low (or absent) in sleep. Or, according to Cirelli and Tononi (2000a), this would indicate that "molecular changes associated with the establishment of long term changes take place during waking and much less or not at all during sleep."

What Is the Function of Sleep/REM Sleep?

Although the proposal that sleep serves a role in memory consolidation (Jenkins and Dallenbach, 1924) predates the discovery of REM sleep, the discovery of REM (Aserinsky and Kleitman, 1953) undoubtedly provided a major boost to the view that sleep (or REM sleep) serves to process information. In effect, the identification of a sleep state with properties similar to wakefulness reinforced the notion that the function(s) of REM overlapped with those of waking, including information processing.

Although it is commonly believed that REM sleep is analogous to wakefulness, the two states are, in fact, very different. Aside from an activated forebrain (hippocampus and allo/neocortex), waking and REM share few properties. There is no counterpart in waking to various events of REM, including uncontrolled horizontal movement of the eyes, random contractions of various muscle groups, PGO waves, and profound muscle atonia (Vertes, 1984). In many ways, REM is more similar to slow wave sleep than to waking. Unlike waking, both SWS and REM are unconscious states in which normal sensory input and motor output are blocked. In addition, REM is imbedded in SWS (all transitions to REM are through SWS) and dreams are present in both sleep states.

In accord with others (Benington and Heller, 1995; Berger and Phillips, 1995), we believe that the primary function of sleep is restitution for the brain/CNS, and within this context, the role of REM sleep is to prepare the brain for recovery from sleep. As previously discussed in detail (Vertes, 1986), we hold that the foremost function of REM sleep is to provide periodic endogenous stimulation to the brain, which serves to maintain minimum requisite levels of CNS activity throughout sleep. REM is the mechanism used by the brain to ensure and promote recovery from sleep. The brain is strongly depressed in SWS, particularly in delta sleep, and incapable of tolerating long continuous periods of relative suppression. REM serves the critical function of periodically activating the brain during sleep without awakening the organism or disturbing the continuity of sleep.

Our theory is consistent with sleep state organization, the main elements of which are that (1) the percentage of REM sleep is very high in early infancy (about 50% of total sleep time) and declines sharply at 2–3 months of age; (2) sleep continuously cycles from light to deep sleep and back to lighter stages of sleep as the cycle repeats itself; and (3) REM sleep is quite evenly distributed throughout sleep (occurring about every 90 min) and the duration of REM periods become progressively longer throughout sleep.

Regarding this organization, we suggest that the high percentage of REM sleep in neonates serves to offset equally high amounts of SWS in newborns (see also Benington and Heller, 1994); that sleep cyclically alternates between light and deep sleep to prevent the brain from dwelling too long in deep SWS; and that the progressively longer periods of REM throughout sleep serve to prime the brain for a return to consciousness as waking approaches. In summary, SWS and REM sleep serve complementary functions: SWS is restorative for the brain (and possibly the body), whereas REM sleep ensures smooth transitions between SWS and waking.

Summary and Conclusions

Although there appears to be fairly widespread support for the notion that memories are processed/consolidated offline in sleep, there is not sufficient evidence for it. Early work in animals and humans failed to establish a link between sleep and learning/memory, and no compelling evidence has emerged from recent studies to support such a relationship.

The consensus position is that sleep serves no role in declarative memory; that is, no role in memory for facts and events—or the type of memory commonly referred to by the terms "memory" or "remembering." The lack of involvement of sleep in declarative processes is supported by the demonstration that the marked suppression or complete loss of REM sleep in

human subjects on antidepressant drugs or with brainstem lesions has no detrimental effects on learning/memory. In addition, the recent demonstration that only a very small amount of declarative/episodic material transfers from waking to sleep in humans (about 1%–2%) indicates that an exceedingly small percentage of waking experiences are even available for consolidation in sleep.

Attention has recently focused on the role of sleep in the consolidation of procedural memory in humans. Two processes have been described: consolidation and enhancement. Consolidation refers to the slow, time-dependent transformation of procedural material from labile to secure forms, largely resistant to interference—analogous to processes shown for declarative memories. Consolidation (as stabilization) begins with task initiation, and unless disrupted by competing events, proceeds continuously through waking and possibly into sleep in a time-dependent manner. There is no indication that sleep serves a unique role in the consolidation of procedural skills. Disruptions of sleep do not alter procedural consolidation.

A process of enhancement has recently been described for some perceptual and motor skills, consisting of *improvements* in performance with the mere passage of time without further practice on a task. Unlike consolidation (as stabilization), some recent studies have reported that sleep serves a special role in enhancement; that is, enhancement is selective for sleep—or more pronounced in sleep than in waking.

Although enhancement may prove to be an important mechanism in procedural learning/memory, this remains to be determined. As discussed, as a relatively new phenomenon, enhancement has been demonstrated for some procedural tasks but not for others, has been shown to be more pronounced in sleep than waking in some studies but not in others, and importantly appears to contribute little to the learning of procedural skills relative to practice on tasks.

In summary, there is simply not enough evidence, or evidence of sufficient weight, to maintain that one of the functions of sleep is memory consolidation.

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