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The case against memory consolidation in REM sleep

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Abstract: We present evidence disputing the hypothesis that memories are processed or consolidated in REM sleep. A review of REM deprivation (REMD) studies in animals shows these reports to be about equally divided in showing that REMD does, or does not, disrupt learning/memory. The studies supporting a relationship between REM sleep and memory have been strongly criticized for the confounding effects of very stressful REM deprivation techniques. The three major classes of antidepressant drugs, monoamine oxidase inhibitors (MAOIs), tricyclic antidepressants (TCAs), and selective serotonin reuptake inhibitors (SSRIs), profoundly suppress REM sleep. The MAOIs virtually abolish REM sleep, and the TCAs and SSRIs have been shown to produce immediate (40–85%) and sustained (30–50%) reductions in REM sleep. Despite marked suppression of REM sleep, these classes of antidepressants on the whole do not disrupt learning/memory. There have been a few reports of patients who have survived bilateral lesions of the pons with few lingering complications. Although these lesions essentially abolished REM sleep, the patients reportedly led normal lives. Recent functional imaging studies in humans have revealed patterns of brain activity in REM sleep that are consistent with dream processes but not with memory consolidation. We propose that the primary function of REM sleep is to provide periodic endogenous stimulation to the brain which serves to maintain requisite levels of central nervous system (CNS) activity throughout sleep. REM is the mechanism used by the brain to promote recovery from sleep. We believe that the cumulative evidence indicates that REM sleep serves no role in the processing or consolidation of memory.

Keywords: antidepressant drugs, brain stem lesions; dreams; functional imaging; memory consolidation; REM deprivation; REM sleep; theta rhythm

1. Introduction

Although its origin is difficult to establish precisely, the view that memories are processed and consolidated in sleep, or specifically in REM sleep, dates back at least to the report of Jenkins and Dallenbach (1924) claiming that human recall improves following an intervening period of sleep. There was intense interest in the possible role of sleep in memory in the late 1960s to the 1980s as evidenced by the wealth of scientific papers on animals (and to lesser extent on humans) devoted to this issue. The position that memories are consolidated in REM has been championed by, among others, Pearlman (Pearlman 1971; 1978; 1979; Pearlman & Becker 1973), Fishbein (Fishbein 1970; 1971; Fishbein & Gutwein 1977; Gutwein & Fishbein 1980a; 1980b); Hennevin and colleagues (Bloch et al. 1979; Hars et al. 1985; Hennevin et al. 1995b; Leconte et al. 1974), and Smith (1985; 1995; 1996; Smith & Butler 1982; Smith & Kelly 1988; Smith & Lapp 1991; Smith & Rose 1996; 1997).

There was a marked decline in the number of studies devoted to this area beginning about the mid-1980s. As discussed below, the principal reason for this fall-off was that on balance the early work failed to convincingly demonstrate a relationship between sleep and memory. There were as many studies that failed to describe a link between sleep and memory as those that claimed such a relationship (Horne 1988; Horne & McGrath 1984; McGrath & Cohen 1978; Smith 1985).

There has been a renewed interest in the role of sleep and memory stemming in part from two complementary articles that appeared in *Science* in 1994: one by Wilson and McNaughton (1994) on rats and the other by Karni et al.

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(1994) on humans. In a follow-up to a study by Pavlides and Winson (1989), Wilson and McNaughton (1994) reported that ensembles of hippocampal "place" cells tend to repeat patterns of activity of waking in subsequent episodes of slow wave sleep (SWS). Karni et al. (1994) showed that improvement on a visual task in humans depended on REM sleep. The two studies supported the view that memories are consolidated in sleep. It is interesting to note that, propelled by these reports, this area reached national public attention in the United States when Jonathan Winson and Matt Wilson appeared on the Charlie Rose television program explaining and promoting their shared belief that sleep is vital for memory consolidation.

This area has recently received a further boost from Allan Hobson and colleagues who have recently come out in favor of the hypothesis that memories are consolidated in REM sleep (Stickgold et al. 2000b). This recent position seems very much at odds with their earlier proposal, termed the activation-synthesis hypothesis (Hobson 1988b; Hobson & McCarley 1977), claiming that dreams (the cognitive component of REM sleep) represent the best cognitive fit (synthesis) to the undifferentiated and random action (activation) of the brain stem on the forebrain, and as such would have little value to the organism and presumably would not need to be remembered.

As indicated by our title, we do not subscribe to the view that memories are consolidated in REM sleep. This target article evolved from an earlier piece by Vertes (1995) which appeared as part of a series in *Sleep Research Society Bulletin* on the topic of sleep and memory. In the same series, Hennevin et al. (1995a), supporters of a role for sleep in memory consolidation, acknowledged why others may be skeptical of this position. They stated:

> The hypothesis of memory processing in sleep has always had to face criticism both from people working in the field of sleep, who predominantly consider that sleeping serves more basic biological functions, and from people in the field of learning and memory, who do not easily accept the idea that information processing can take place in a non-conscious state.

As researchers involved in both sleep (Vertes 1984; 1990) and memory work (Vertes 1986a; Vertes & Kocsis 1997), we remain skeptical on both counts, largely for the reasons put forth by Hennevin et al. (1995a); that is, sleep involves basic biological functions and memory requires consciousness.

2. Background

Memory consolidation refers to neural processing that occurs after information is initially registered, which contributes to its permanent storage in memory (Nadel & Moscovitch 1997). As mentioned, several reports appeared in the 1970s exploring the possible role of sleep in memory consolidation. These studies were of two basic types: (1) examinations of potential increases in REM sleep following heightened experiences in waking; and (2) examinations of the effects of REM sleep deprivation on previously learned tasks. A number of reviews (Dujardin et al. 1990; Fishbein & Gutwein 1977; Horne 1988; Horne & McGrath 1984; McGrath & Cohen 1978; Pearlman 1979; Smith 1985), including recent ones (Hennevin et al. 1995b; Rechtschaffen 1998; Smith 1995; 1996), have been devoted to the topic of sleep and memory. The following is not intended as a review of this area, but rather is meant to serve as a general background and critical assessment of some important issues involving sleep and memory.

2.1. Effects of heightened experiences of waking on subsequent REM sleep

The rationale behind this set of studies is as follows: If REM serves to consolidate learning/memory, then exposure to enhanced learning situations or enriched environments in waking should result in increases in REM to process and consolidate these experiences. We will only briefly discuss this work for we do not believe that it represents a particularly powerful test of the REM consolidation hypothesis owing, among other things, to confounding effects of natural variations in REM sleep and the difficulty of establishing, at least for animals, that enriched experiences represent a significant departure from normal routines. Additionally, there is a certain degree of circularity in this position, in that enhanced learning experiences in waking presumably trigger increases in REM to consolidate them, yet they only become "learning experiences" after being processed and consolidated in REM sleep.

The findings of several reports in animals and humans using this paradigm have been mixed. In general, the majority of studies in animals have reported that heightened learning experiences or enriched conditions in waking produce increases in the amount of REM sleep (Horne 1988; Horne & McGrath 1984; McGrath & Cohen 1978; Smith 1985); on the whole, human studies have not shown this to be the case (Allen et al. 1972; Bowe-Anders et al. 1974; Horne 1976; Horne & Walmsley 1976; Zimmerman et al. 1978).

Horne and McGrath (1984) have raised objections to the animal work, pointing out, for instance, that in many of these reports: (1) increases in REM appeared to be an "artifact" of an overall increase in total sleep time (TST); that is, the proportion of REM to TST was not increased (Gutwein & Fishbein 1980a; 1980b; Kiyono et al. 1981; Krech et al. 1962; Mirmiran et al. 1982; Tagney 1973;); and (2) control animals were generally confined to impoverished environments, raising the possibility that differences between control and experimental animals involved decreases in REM (reflecting decreases in TST) for controls rather than increases for the experimental animals (Gutwein & Fishbein 1980a; 1980b; Krech et al. 1962; Tagney 1973).

McGrath and Cohen (1978) reviewed 15 studies in humans examining the effects of enhanced waking experiences on REM sleep (nondeprivation studies) and reported a lack of effect in 10 of the 15 reports. They concluded: "nondeprivation studies employing humans seemingly provide little support for a relationship between REM sleep and learning."

2.2. REM deprivation (REMD) studies in animals

REM deprivation (REMD) studies in animals and humans are of two types: prior REMD and post (or subsequent) REMD, reflecting whether the REM deprivation period precedes (prior) or follows (post) the learning situation.

2.2.1. Post-REMD studies. Specifically, the post-REMD procedure involves training animals to criterion on a task(s), depriving them of REM sleep for varying periods of time, and then retesting them on the task(s). If REM is critical

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for learning/memory, REMD should severely disrupt these functions; and if REM is not critical, REMD should have no effect on learning/memory.

The most widely used technique for depriving animals of REM sleep is the water tank (or pedestal) technique. In brief, animals are placed on top of a small pedestal (usually a small inverted flower pot) that is surrounded by water. As animals enter REM sleep, they lose postural tone (atonia), partially or fully slip from the pedestal into the water, and awaken. The procedure is thought to fairly selectively deprive animals of REM sleep. Controls are placed on larger diameter pedestals or allowed normal sleep in their home cages.

It is widely acknowledged that the pedestal technique introduces several spurious and uncontrolled variables that are generally recognized to confound results obtained with this method; these include isolation, wetness, heat loss, high levels of stress, muscle fatigue, and a significant loss of slow wave sleep as well as REM (Coenen & van Luijtelaar 1985; Ellman et al. 1978; Fishbein & Gutwein 1977; Grahnstedt & Ursin 1985; Horne & McGrath 1984; Kovalzon & Tsibulsky 1984; Youngblood et al. 1997). The pedestal technique is a severe method for REMD; alternatives are presently used such as the multiple platform and pendulum techniques (van Hulzen & Coenen 1980; 1982; van Luijtelaar & Coenen 1986) as well as the recently developed disk-over-water method of Rechtschaffen and Bergmann (Rechtschaffen 1998; Rechtschaffen & Bergmann 1995).

It appears that the problems inherent in the pedestal technique have significantly clouded findings obtained with it. In fact, Bill Fishbein, an advocate of the REM consolidation hypothesis, recently acknowledged (Fishbein 1995) that he abandoned REMD work in mice because he was not able to respond adequately to criticisms leveled at the technique. He stated that he could not

> have anticipated all the flack that I received, in the years to come, about the "stress factor" produced by the mouse-on-the pedestal technique. I spent a great deal of time trying to prove that there was no stress factor. Despite my efforts to design experiments in a way that training and retention testing were not confounded by the pedestal procedure, it became clear that no matter what control experiment I did, I was never going to convince everyone. Eventually this controversy led me to completely abandon the REM deprivation procedure and look instead at the effects of learning on REM enhancement.

With the caveat, then, that many of the REMD studies supporting a role for REM in memory consolidation may lack validity based on the use of the pedestal technique, a review of the REMD work in animals shows studies to be about equally divided among those showing that REMD disrupted learning/memory (Fishbein 1971; Leconte et al. 1974; Pearlman & Becker 1973; 1974; Smith & Butler 1982; Smith & Kelly 1988) and those showing that this was not the case (Albert et al. 1970; Dodge & Beatty 1980; Joy & Prinz 1969; Miller et al. 1971; Shiromani et al. 1979; Sloan 1972; van Hulzen & Coenen 1979).

As discussed above, it is generally acknowledged that depriving animals of REM sleep with the pedestal technique or other means is debilitating. This has led to the view that the impairments seen following REMD are not true learning/memory deficits but merely performance deficits; that is, animals are simply unable to perform the required task(s), in large part owing to the physically debilitating effects of the deprivation. Attempts to separate learning from performance deficits primarily by looking at short term versus long term effects of REMD have largely shown that impairments are short term or, in effect, performance deficits (Fishbein 1970; 1971; van Hulzen & Coenen 1982).

For example, Fishbein (1971) trained groups of mice on a passive avoidance task, deprived them of REM sleep for 1, 3, 5, or 7 days using the pedestal technique, and then retested them on the task 30 min, 3 h, and 24 h following removal from the pedestal. The results showed that: (1) mice deprived of REM for 1 day showed no impairments at any of the three retest intervals (i.e., 30 min, 3 h, or 24 h) and (2) mice deprived for 3, 5, or 7 days showed marked deficits when retested at 30 min and 3 h but no impairments when retested at 24 h. In essence, mice deprived of REM for 3, 5, or 7 days were very impaired on short term but not on long term retest (i.e., 24 h), indicating that deficits were most likely performance and not learning/memory deficits.

2.2.2. Prior REMD studies. A number of reports (Bueno et al. 1994; Danguir & Nicolaidis 1976; Fishbein 1970; Hartmann & Stern 1972; Linden et al. 1975; Sagales & Domino 1973; Stern 1971; van Hulzen & Coenen 1982; Venkatkrishna-Bhatt et al. 1978) have shown that depriving animals of REM sleep prior to training (prior REMD) impairs acquisition/learning on a variety of tasks. These studies, however, do not seem to test the REM consolidation hypothesis since the deprivation period precedes training/acquisition and there is no potential carryover of information pre to post REMD as in the post-REMD design.

Aside from their intended purpose, we suggest that the prior REMD studies support the position that the deficits seen in post-REMD reports were performance and not memory deficits. With both paradigms (prior and post REMD) animals are impaired to similar degrees on the same types of tasks. In the post-REMD paradigm, however, the claim is made that deficits involve the inability of animals to use information learned prior to deprivation, as a direct result of the loss of REM; that is, animals perform poorly following REM deprivation because without REM they are unable to process, store, and utilize information acquired before deprivation to meet the demands of the task – a memory deficit. Although impairments are similar with the prior REMD paradigm, the claim could not be made that this involves a memory dysfunction. We suggest that in both cases the impairments are mainly performance deficits due in large part to the debilitating effects of deprivation procedures. The following report (van Hulzen & Coenen 1982) is consistent with this view.

van Hulzen and Coenen (1982) deprived two groups of rats of REM sleep for three days – one group with the pedestal (or water tank) technique and the other with the less stressful pendulum technique. Immediately following deprivation, both groups were trained on a two-way shuttle avoidance task (acquisition) and then retested six days later. Rats deprived with the pedestal technique showed severe impairments in acquisition but not on retest; those deprived by the pendulum method showed no deficits on acquisition or retest.

The results show that prior REMD by a stressful technique (pedestal), as opposed to a more moderate procedure (pendulum), affects immediate performance, while neither procedure impairs performance/learning when rats are fully

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recovered from REMD – that is, six days after deprivation. The findings suggest that stress (or other factors) associated with REMD and not necessarily the loss of a particular stage of sleep is largely responsible for the disruptive effects of REMD. This was indicated by the authors when they stated:

> shuttle box avoidance performance [was found] to be severely disrupted following 72 hrs of PS [paradoxical sleep] deprivation by means of the water tank technique. Similar effects could not be replicated in using the pendulum technique. Therefore, the possibility that these phenomena are not due to PS deprivation per se must seriously be considered. (van Hulzen & Coenen 1982)

2.2.3. Summary and conclusions. A review of REMD studies in animals shows that they are about equally divided in showing that REMD does or does not disrupt learning/memory. As developed above, it has been argued that reports claiming that REMD disrupts learning/memory are confounded by the use of very stressful deprivation procedures. It appears that stress (and associated factors) rather than the loss of sleep/REM sleep is responsible for the learning/memory deficits seen in these studies. While these reports are open to other interpretations, there appears to be no alternative explanation for studies that fail to show that REMD disrupts learning/memory.

Following a comprehensive review of the REMD literature, Horne (1988) concluded:

> The memory consolidation theories for REM sleep function are having increasing difficulty in handling REM sleep deprivation findings, as it is clear from both animal and human studies that even the longest periods of deprivation do not incapacitate memory, and at best only produce modest decrements.

And further, "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."

2.3. REM windows

Carlyle Smith, a foremost advocate of the REM consolidation hypothesis and a major contributor to this area, has put forth and provided supporting evidence for the existence of "REM windows"; that is, specific segments of REM sleep that are enhanced following learning and corresponding segments which when disrupted (REMD) impair learning/memory. According to the proposal, memories are selectively consolidated during the period of the REM windows (for review, see Smith 1985; 1995; 1996).

The REMD studies of Smith and coworkers focusing on REM windows appear subject to some of the same problems as other REMD studies, foremost of which is the inability to adequately control for the stress factor associated with the use of the pedestal technique for REMD. However, in defense of Smith and colleagues it should be noted that their work is less vulnerable to this criticism because their REMD periods are generally short, about 4–12 h.

On the other hand, there are difficulties with "REM windows" not encountered by other REMD studies. Of significant concern is the shifting nature of the REM window. As readily acknowledged by Smith (1985; 1996), the precise location of the window in REM varies widely, dependent on such factors as species and even strain of animals, the nature of the training tasks, and the number and distribution (concentrated or dispersed) of training trials per session and/or per day. For instance, in separate reports, the times (post training) of the "REM window(s)" were: 9–12 and 17–20 h (Smith & Butler 1982), 48–72 h (Smith & Kelly 1988), 53–56 h (Smith & MacNeill 1993), 5–8 h (Smith & Rose 1996), and 1–4 h (Smith & Rose 1997). In fact, the last two studies (Smith & Rose 1996; 1997) involved virtually identical conditions (place learning with rats on the Morris water maze) yet the window shifted from 5–8 h in the earlier report to 1–4 h in the later one. Apparently, the only difference was a change from distributed (Smith & Rose 1996) to massed trials (Smith & Rose 1997).

It appears that REM windows (at least as defined for animals) are not present in humans. Smith and Lapp (1991) examined patterns of REM sleep (potential windows) in college students following an intense learning experience (post exams) compared to baseline periods (summer vacation), and reported that aside from an increase in the total number of (rapid) eye movements in test versus control conditions (most prominent in the fifth REM period), there were no changes in sleep/REM sleep under the two conditions. They stated: "No other REM-related measure (minutes of REM sleep, % REM sleep or latency from stage 2 onset to any of the five REM periods) was found to be significant. Further, there were no changes in any of the other sleep parameters measured" (Smith & Lapp 1991).

Finally, although there is some suggestion from recent work in humans that information is differentially processed in distinct phases of SWS and/or REM sleep (Plihal & Born 1997; Stickgold et al. 2000b), to our knowledge "REM windows" has not been independently demonstrated outside of the laboratory of Smith and colleagues (see Smith 1996). It seems that this potentially important phenomenon would be considerably strengthened if confirmed in other laboratories.

2.4. REMD studies in humans: Early reports

Compared to their numbers on animals, relatively few reports on humans have examined the effects of REMD on learning/memory. In contrast to the case with animals in which reports were about equally divided among those showing, or not, that REMD affects learning, the majority of studies in humans have described minimal or no effects of REM deprivation on learning/memory (Castaldo et al. 1974; Chernik 1972; Ekstrand et al. 1971; Lewin & Glaubman 1975; Muzio et al. 1972). If anything, complex tasks (Empson & Clarke 1970; Tilley & Empson 1978), as opposed to simple tasks (Castaldo et al. 1974; Chernik 1972), appear to be affected by REMD.

Following a review of early REMD studies in humans, Horne (1988) concluded:

> It is clear that, given before or after learning, REM sleep deprivation does not lead to any greater learning impairment on simple tasks, but difficult tasks are more affected. Whilst these latter findings can reach statistical significance, the effects are still relatively small, and not convincing enough to support any theory that REM sleep has a crucial role to play in the consolidation of memory.

2.5. REM sleep and memory consolidation in humans: Recent reports

Karni and Sagi (1993) initially showed that improved performance on a perceptual learning task required the pas-

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sage of time; that is, subjects showed no improvement immediately following training but marked improvement 8–10 h following training. As discussed below, they have extended their original findings to sleep: performance was shown to improve not only with an intervening period of waking but also of sleep (Karni et al. 1994).

The task involved identifying the orientation of three diagonal lines (arranged either horizontally or vertically) embedded in a background of horizontal lines. The stimulus (target and background elements) was presented briefly (10 msec) in one quadrant of the visual field followed by a blank screen and then a patterned mask (100 msec). 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 & Sagi 1993; Karni et al. 1994).

In the sleep study, Karni et al. (1994) trained subjects on the task and then tested them after a normal night of sleep, sleep without SWS, or sleep without REM. They described significantly improved performance following a normal night of sleep as well as sleep that included REM but not SWS (SWS deprivation condition), but no gains in performance in the absence of REM sleep (REM deprivation condition). Karni et al. (1994) concluded that learning of this perceptual skill was a slow latent process requiring consolidation over time. The period of consolidation could be in waking or sleep, but if in sleep, it required REM sleep not SWS.

Using the identical visual display, Stickgold et al. (2000b) recently reported, like Karni et al. (1994), that subjects exhibited marked improvement on the task following sleep. Specifically, they reported: (1) no improvement on the task over the course of waking; (2) no improvement unless subjects obtained at least 6 h of sleep; (3) improved performance proportional to the total amount of sleep after 6 h of sleep; and (4) improved performance proportional to the amount of SWS in the first quartile of the night (SWS1) and to the amount of REM in the last quartile (REM4). They proposed that learning was a two-step process requiring both SWS (SWS1) and REM (REM4).

Although there are parallels between the two sets of findings (Karni et al. 1994; Karni & Sagi 1993; Stickgold et al. 2000b), there are several pronounced differences. A major difference involves the performance of subjects during waking. As discussed above, Karni and Sagi (1993) originally showed and subsequently confirmed (Karni et al. 1994) that performance significantly improved over time during waking. By contrast, Stickgold et al. (2000b) reported no improvement during post training waking behavior, even after 12 h, commenting: "12 hours of wake behavior was inadequate to produce reliable improvement while as little as 9 hours of sleep reliably produced improved performance."

Additional differences were as follows: (1) Stickgold et al. (2000b) demonstrated a direct relationship between improved performance and total amounts of SWS, particularly SWS1, whereas Karni et al. (1994) showed that depriving subjects of SWS did not alter performance; and (2) Stickgold et al. (2000b) reported that a minimum amount of sleep (6 h) was required for improved performance, and after 6 h gains were proportional to the total amount of sleep; neither was the case in the report by Karni et al. (1994). Until these discrepancies are resolved, it is difficult to evaluate the reliability of the findings using this perceptual learning paradigm.

2.6. Theta rhythm and REM sleep

In a variation of the REM consolidation hypothesis, Jonathan Winson has proposed and provided supporting documentation for the position that certain types of memory, specifically memories that are critical for the survival of the species, are selectively processed and consolidated in REM sleep (Pavlides & Winson 1989; Winson 1985; 1990; 1993). The theta rhythm of the hippocampus figures prominently in this proposal (Greenstein et al. 1988; Pavlides et al. 1988; Winson 1972; 1978).

Winson (1972) reviewed the behavioral correlates of the theta rhythm of waking in several species and showed that theta was selectively present during certain behaviors characterized as species-specific behaviors that are critical for survival; for example, exploration in rats, defensive behaviors in rabbits, and predation in cats. In addition, theta is present throughout REM sleep (Vanderwolf 1969).

A number of recent reports (including those of Winson and colleagues) have shown that theta is directly involved in mnemonic functions of the hippocampus (for review, Vertes & Kocsis 1997). For example, it has been demonstrated that: (1) long term potentiation (LTP) is optimally elicited in the hippocampus with stimulation at theta frequency (i.e., 5–7 Hz or pulses separated by 170–200 msec) (Diamond et al. 1988; Greenstein et al. 1988; Larson & Lynch 1986; 1988; Larson et al. 1986; Leung et al. 1992; Rose & Dunwiddie 1986; Staubli & Lynch 1987); (2) stimulation delivered in the presence but not in the absence of theta potentiates population responses in the hippocampus (Bramham & Srebro 1989; Huerta & Lisman 1993; Pavlides et al. 1988); and (3) discrete medial septal (MS) lesions that abolish theta produce severe learning/memory deficits, as do MS lesions with unexplored effects on the hippocampal EEG (Berger-Sweeney et al. 1994; Dutar et al. 1995; Hagan et al. 1988; Hepler et al. 1985; Kesner et al. 1986; Leutgeb & Mizumori 1999; M'Harzi & Jarrard 1992; Mizumori et al. 1990; Poucet et al. 1991; Shen et al. 1996; Stackman & Walsh 1995; Walsh et al. 1996; Winson 1978).

In brief, then, Winson's position is that theta serves to encode survival-enhancing information during waking and to consolidate this information during REM sleep. In this scheme, theta is essential for the acquisition of skills for survival.

The primary focus of the research of the senior author is the theta rhythm of the hippocampus. In fact, the senior author was introduced to this area by Jonathan Winson and remains enormously grateful for the opportunity to learn from him. As is evident, however, we do not share Winson's view that theta is instrumental in consolidating memories in REM sleep.

We believe that the case is strong for the involvement of theta in mnemonic functions of waking but not of REM sleep (Vertes 1986a; Vertes & Kocsis 1997). This seeming discrepancy was recently addressed by Fishbein (1996) stating, "Robert Vertes has published a variety of studies that would lead one to assume he would be a leading champion of the theory of memory consolidation in REM sleep. Despite his important contributions he does not believe the collected evidence supports it."

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Our position is that theta of REM is a by-product of the intense activation of the pontine region of the brainstem in REM sleep; theta merely reflects this activation and as such may not have any functional significance in REM or at least not the same functional significance as in waking. In a series of studies (Kocsis & Vertes 1994; 1997; Vertes 1979; 1981; 1988; 1992; Vertes & Martin 1988), we have shown that the theta rhythm is generated by a system of connections from the pontine reticular formation (PRF) to the septum-hippocampus. In brief, cells of nucleus pontis oralis of PRF fire tonically with theta and transfer this tonic barrage to the supramammillary nucleus of the hypothalamus where it is converted into a rhythmical pattern of discharge and then relayed to the GABAergic/cholinergic pacemaking cells of the medial septum to drive theta (Vertes & Kocsis 1997).

As previously described (Datta 1995; Jones 1991; Steriade & McCarley 1990a; Vertes 1984; 1990), pontine and lower mesencephalic regions of the brainstem contain discrete populations of cells that control individual events of REM sleep; when activated together these cell groups trigger each of the major indices of REM sleep (cortical EEG desynchronization, hippocampal theta, muscle atonia, PGO spikes, rapid eye movements, myoclonic twitches, and cardiorespiratory fluctuations), and hence the REM state. Part of this orchestration of activity of the pontine RF in REM involves excitation of nucleus pontis oralis and consequently theta. As argued above, theta of REM may simply reflect a highly activated brainstem in REM, and thus bear little functional relationship to its role in waking.

The presence of similar electrophysiological events in waking and sleep does not indicate that they serve the same (or even similar) physiological and/or behavioral function(s). For example, the cortical EEG desynchronization of waking and REM by no means signifies identical processes in the two states; that is, the EEG desynchronization of waking is associated with diverse sensory, motor, emotional, and cognitive processes that are notably absent in REM sleep.

As indicated, we favor the position that theta is critically involved in memory processing functions of waking (Vertes 1986a; Vertes & Kocsis 1997). Specifically, we propose that theta serves to gate and/or encode information reaching the hippocampus simultaneously with it from various external sources (e.g., the entorhinal cortex). In the awake state, the "information arriving with theta" is governed by the behavioral situation (context); that is, the sum of internal and external events relatively time locked to theta. If theta were involved in memory processing functions in REM, it should, in a similar manner, gate information to the hippocampus in that state. Unlike waking, however, in which the information reaching the hippocampus is dictated by behavioral circumstances, there appears to be no mechanism in REM for the selection and orderly transfer of information to the hippocampus from other sources. If the transfer of information in REM is not orderly, or is essentially chaotic, it would seem that there would be no functional value in consolidating or "remembering" this information. In effect, dream-like material might be presented to the hippocampus in REM, but there would be no purpose in storing or consolidating it during REM. This may be the reason that dreams (or other cognitive material of REM) are so poorly remembered.

In sum, the theta rhythm is present in waking and REM; we believe that theta serves a mnemonic function in waking but not in REM sleep.

3. REM sleep and antidepressant drugs

It is well recognized that virtually all major antidepressant drugs suppress REM sleep (for review, Vogel et al. 1990) and it has, in fact, been proposed that the clinical efficacy of these drugs largely derives from their suppressant effects on REM sleep (Vogel 1975; 1983). The major classes of antidepressant drugs are the monoamine oxidase inhibitors (MAOIs), the tricyclic antidepressants (TCAs), and the recently developed and widely used selective serotonin reuptake inhibitors (SSRIs). A review of the actions of several members of these classes of antidepressants shows that they profoundly suppress REM sleep.

3.1. Monoamine oxidase inhibitors (MAOIs)

Of the antidepressants, the MAOIs have the strongest suppressive action on REM sleep. A number of early reports using normal and patient populations showed that MAOIs virtually completely (or completely) suppressed REM sleep for weeks to several months. In an initial study, Wyatt et al. (1969) reported that the MAOIs, isocarboxazid, pargyline hydrochloride, and mebanazine, reduced REM from about 20–25% of TST to 9.7, 8.6, and 0.4% of TST, respectively, and that in one subject REM was virtually eliminated for two weeks.

In a subsequent report in anxious-depressed patients, Wyatt et al. (1971b) described the remarkable findings that the MAOI, phenelzine (Nardil), given at therapeutic doses, completely abolished REM sleep in six patients for periods of 14 to 40 days. There was a gradual decline in amounts of REM sleep for the first two weeks on the drug and a total loss of REM after 3–4 weeks. In a complementary study with narcoleptic patients, Wyatt et al. (1971a) reported that phenelzine completely abolished REM in five of seven patients for the following lengths of time: 14, 19, 93, 102, and 226 days. They stated that: "The complete drug-induced suppression of REM sleep in these patients is longer and more profound than any previously described"; and further that "no adverse psychological effects were noted during the period of total rapid-eye-movement suppression."

Several other studies have similarly shown that MAOIs essentially abolish REM sleep. Akindele et al. (1970) reported that phenelzine completely eliminated REM sleep in four subjects (one normal and three depressed) for 2 to 8 weeks, and addressing possible behavioral consequences stated that, "Far from this leading to disastrous effects on mental functions, as some might have proposed, clinical improvement began." Kupfer and Bowers (1972) showed that phenelzine abolished REM in seven of nine patients, and drastically suppressed it in remaining patients from predrug values of 23.1 and 24.8% of TST to 1.4 and 0.5% of TST, respectively. Finally, Dunleavy and Oswald (1973) reported that phenelzine eliminated REM in 22 depressed patients.

If REM sleep were involved in memory consolidation, it would seem that the total loss of REM with MAOIs for periods of several months to a year (Dunleavy & Oswald 1973; Kupfer & Bowers 1972; Wyatt et al. 1969; 1971a; 1971b) would affect memory. As indicated above, the loss of REM

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did not appear to be associated with any noticeable decline in cognitive functions in these largely patient populations. These studies, however, made no systematic attempt to assess the effects of MAOIs on cognition.

Other reports, however, have examined the actions of MAOIs, primarily phenelzine, on cognition/memory and described an essential lack of impairment (Georgotas et al. 1983; 1989; Raskin et al. 1983; Rothman et al. 1962). For example, Raskin et al. (1983) observed no adverse effects of phenelzine on a battery of 13 psychomotor and cognitive tasks in a heterogeneous population of 29 depressed patients. Similarly, Georgotas et al. (1983; 1989) reported that elderly depressed patients given phenelzine for 2 to 7 weeks showed no alteration in several measures of cognitive function, and concluded that the lack of adverse effects with phenelzine suggests that it is preferable to TCAs (see below) in the treatment of depression in the geriatric population.

3.2. Tricyclic antidepressants (TCAs) and selective serotonin reuptake inhibitors (SSRIs)

As discussed below, virtually all of the commonly used TCAs and SSRIs significantly suppress REM sleep, but unlike the MAOIs, do not eliminate it. Also, the TCAs and SSRIs appear to exert immediate suppressive effects on REM (within the first few days of treatment); by contrast, the MAOIs produce maximal effects on REM about 2–3 weeks following the start of treatment.

An early report by Dunleavy et al. (1972) in normal subjects analyzed the effects on sleep of six TCAs and showed that four of them (imipramine, desipramine, chlorimipramine, and doxepin) markedly depressed REM, beginning with the first night of administration. Chlorimipramine had the strongest suppressive effect on REM sleep, producing a complete loss of REM for the first three nights and an approximate 50% reduction in REM for the remaining four weeks of the study.

Several subsequent examinations of the actions on sleep of these and other TCAs (amitriptyline, amoxapine, nortriptyline, imipramine, maprotiline, clomipramine) have demonstrated that, as a class, TCAs produce an immediate 40–70% reduction in REM and sustained 30–50% decreases in REM sleep (Brebbia et al. 1975; Hartmann & Cravens 1973; Kupfer et al. 1979; 1982; 1991; 1994; Mendlewicz et al. 1991; Nicholson & Pascoe 1986; Passouant et al. 1975; Roth et al. 1982; Shipley et al. 1984; Staner et al. 1995; Ware et al. 1989). Of the TCAs, clomipramine appears to be the strongest REM-suppressant (Passouant et al. 1975; Sharpley & Cowen 1995; Thase 1998).

The SSRIs, like the TCAs, produce an initial marked reduction in REM sleep that slightly abates with time. Examinations of the effects on sleep of several SSRIs (indalpine, fluvoxamine, fluoxetine [Prozac], paroxetine, and zimelidine) show that on average they produce an initial reduction in REM of 40–85% and long term decreases of 30–50% (Kupfer et al. 1991; Nicholson & Pascoe 1986; 1988; Nicholson et al. 1989; Oswald & Adam 1986; Saletu et al. 1991; Sharpley et al. 1996; Shipley et al. 1984; Staner et al. 1995; Vasar et al. 1994; Vogel et al. 1990).

In general, the SSRIs exert stronger suppressive effects on REM than do the TCAs. Staner et al. (1995) compared the actions on sleep of long term treatment with paroxetine (SSRI) and amitriptyline (TCA) in depressed patients, and showed a 42% reduction in REM with paroxetine compared to a 30% reduction with amitriptyline. Similar findings have been described in other comparisons of these classes of antidepressants (Kupfer et al. 1991; Nicholson & Pascoe 1986).

Although the TCAs and SSRIs do not completely eliminate REM sleep, they significantly suppress it by as much as 75–85% in the short term (days) and 40–50% in the long term (weeks/months). As discussed for the MAOIs, if memories are consolidated in REM sleep, it would seem that the sustained reductions in REM with TCAs/SSRIs would alter memory.

There is a substantial literature describing the effects of TCAs and SSRIs on cognitive functions in normal and depressed subjects, including several reviews devoted to the topic (Amado-Boccara et al. 1995; Deptula & Pomara 1990; Knegtering et al. 1994; Thompson 1991; Thompson & Trimble 1982). Because these classes of antidepressants are in such widespread use, it is obviously important to know if they disrupt motor/cognitive functioning.

3.2.1. The effects of TCAs on cognition/memory. Although there is conflicting evidence, mainly related to the diverse procedures used to evaluate the effects of antidepressants on cognition (Amado-Boccara et al. 1995; Deptula & Pomara 1990; Thompson & Trimble 1982), the general consensus is that some TCAs, primarily amitriptyline, impair memory, but most have minor or no effects on memory (for review, Amado-Boccara et al. 1995; Deptula & Pomara 1990; Thompson 1991; Thompson & Trimble 1982). Virtually all TCAs have some sedative and anticholinergic actions (Hardman et al. 1996), and if cognitive dysfunctions are present with TCAs they reportedly involve these properties (Curran et al. 1988; Deptula & Pomara 1990; Spring et al. 1992; Thompson 1991).

A number of studies have shown that amitriptyline disrupts memory – whether given acutely or long term, to the depressed or nondepressed, and across all age groups (Branconnier et al. 1982; Curran et al. 1988; Lamping et al. 1984; Linnoila et al. 1983; Spring et al. 1992; Warot et al. 1996). For instance, Spring et al. (1992) compared the effects of a four-week treatment with amitriptyline and clovoxamine (an SSRI) on psychomotor and memory tests in depressed outpatients, and reported that amitriptyline, despite alleviating depression, significantly impaired performance on the memory tasks. Clovoxamine, on the other hand, had no adverse effects of psychomotor/cognitive performance (see also below).

Spring et al. (1992) attributed the disruptive effects of amitriptyline on cognition to its anticholinergic actions, noting that, in general, anticholinergics (e.g., scopolamine) disrupt memory (Caine et al. 1981; Drachman & Leavitt 1974). They stated: "The decline in memory performance associated with amitriptyline apparently reflects the relatively high anticholinergic action of the drug, rather than a deficiency in its antidepressant action." And further, "Among the tricyclics, amitriptyline has the most pronounced anticholinergic effects, and would, therefore be expected to have the most adverse effect on memory."

Consistent with this interpretation, Curran et al. (1988) compared the effects on memory of four antidepressants (amitriptyline, trazodone, viloxazine, and protriptyline) that varied with respect to their sedative and anticholinergic properties, and showed that the sedating compounds

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(amitriptyline and trazodone) but not the nonsedating ones (viloxazine and protriptyline) impaired performance on a battery of memory tests, and that disruptive effects were considerably greater with amitriptyline (an anticholinergic) than with trazodone (no anticholinergic properties) (Gershon & Newton 1980).

In contrast to amitriptyline, most other TCAs have minimal or no adverse effects on memory/cognition. In a well-designed study, Peselow et al. (1991) examined the effects on learning/memory of a four-week treatment with the TCA imipramine (Tofranil) with 50 depressed outpatients, and reported that imipramine improved memory in these patients. Although the improvement in memory was attributed to the clinical efficacy of the compound (not to a memory-enhancing function for imipramine), Peselow et al. (1991) clearly demonstrated, as have several others (Amin et al. 1980; Friedman et al. 1966; Glass et al. 1981; Henry et al. 1973; Raskin et al. 1983; Rothman et al. 1962) that imipramine did not impair memory – even though imipramine is a powerful REM suppressant (Kupfer et al. 1994; Ware et al. 1989). For instance, Kupfer et al. (1994) showed that imipramine produced sustained 35–40% reductions in REM sleep for three years in depressed patients.

Finally, several other TCAs (doxepin, desipramine, nortriptyline, amoxapine, protriptyline, maprotiline, and chlorimipramine) that also suppress REM sleep reportedly produce little or no detrimental effects on memory (Allain et al. 1992; Curran et al. 1988; Georgotas et al. 1989; Liljequist et al. 1974; Linnoila et al. 1983; McNair et al. 1984; Pishkin et al. 1978).

3.2.2. The effects of SSRIs on cognition/memory. As is well recognized, SSRIs are very widely used and currently the most prescribed treatment for depression. As a group the SSRIs do not appear to alter cognitive functions. For instance, there is no indication that any of the following SSRIs have any detrimental effects on psychomotor/cognitive functions in normal or patient populations: fluvoxamine, zimeldine, clovoxamine (an SSRI and partial noradrenergic reuptake inhibitor), sertraline, paroxetine, or fluoxetine (Curran & Lader 1986; Fairweather et al. 1993; 1996; Geretsegger et al. 1994; Hindmarch & Bhatti 1988; Hindmarch et al. 1990; Lamping et al. 1984; Linnoila et al. 1983; Saletu & Grunberger 1988; Saletu et al. 1980; Spring et al. 1992).

Kerr et al. (1992) recently examined the actions of paroxetine, alone or in combination with alcohol, on several psychomotor/cognitive tests in elderly nondepressed subjects with the goal of determining whether SSRIs, unlike compounds with anticholinergic and/or sedative effects, may alter cognitive functions. They speculated that SSRIs "are unlikely to have detrimental cognitive and psychomotor effects because of their unique pharmacological profile," and noted further that "patients often report that treatment with SSRIs leaves them feeling more able to think clearly." It was shown that paroxetine not only had no adverse effects on psychomotor and cognitive functions, but that it slightly ameliorated performance deficits produced by alcohol (Kerr et al. 1992).

Comparisons of the actions of amitriptyline and SSRIs on psychomotor/cognitive performance in healthy or depressed subjects (Curran & Lader 1986; Fairweather et al. 1993; Lamping et al. 1984; Linnoila et al. 1983; Spring et al. 1992) have demonstrated that amitriptyline but not SSRIs produced significant impairments. Lamping et al. (1984) reported that even though amitriptyline and clovoxamine gave rise to comparable relief from depression, the two antidepressants differentially affected memory; that is, "an impairment of memory after chronic amitriptyline administration, as contrasted with an improvement in memory after chronic administration of clovoxamine." Spring et al. (1992) described virtually the identical findings using the same two compounds.

Finally, an early review of this area (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. Furthermore, a few more recent studies suggest that these drugs may exert a beneficial influence on memory processes in memory-impaired individuals"; while a recent review (Amado-Boccara et al. 1995) similarly concluded that: "antidepressants which inhibit serotonin reuptake seem to have no deleterious cognitive effects."

3.2.3. Summary of the effects of antidepressants on cognition/memory. In summary, (1) MAOIs virtually abolish REM sleep but have no adverse effects on cognition/memory. (2) TCAs suppress REM by 30–70%. While amitriptyline, a strong anticholinergic and sedative compound, disrupts memory, most other TCAs produce minimal, or generally no, disruptive effects of cognitive/memory. (3) SSRIs suppress REM sleep by 40–85% but do not alter memory or other cognitive functions.

4. Brain stem lesions and REM sleep in humans

Although sizeable lesions at rostral, mesencephalic levels of the brainstem often result in persistent coma or death (Cairns 1952), those located more caudally within the pons are less severe and have been shown to give rise to a condition termed the "locked-in" syndrome. As originally described by Plum and Posner (1966), patients with this syndrome are fully conscious, alert, and responsive, but are quadriplegic and mute. Most of the patients retain the ability to make eye movements and very limited facial/head movements and some can communicate by small facial gestures. For instance, Feldman (1971) described a case of a woman with this syndrome who learned to communicate by Morse code using eye blinks and jaw movements.

A number of reports have examined sleep-wake profiles of these patients, and probably not surprisingly, have shown that most of them (or at least those with bilateral pontine lesions) completely lack REM sleep (Chase et al. 1968; Cummings & Greenberg 1977; Markand & Dyken 1976). For instance, Markand and Dyken (1976) reported that REM sleep was entirely absent in five of seven patients with the "locked-in" syndrome; SWS was present in essentially normal amounts. From case reports, the mental capacities of these patients, including memory for events and people, appear to be intact.

Although rare, there have been a few reports of patients with bilateral pontine lesions who are conscious, ambulatory, and verbally communicative (Lavie et al. 1984; Osorio & Daroff 1980; Valldeoriola et al. 1993). It appears that the lesions in these patients are less extensive than those with the locked-in syndrome. Nonetheless, like patients with the locked-in syndrome, they lack REM sleep (Osorio & Daroff 1980; Valldeoriola et al. 1993). Osorio and Daroff (1980)

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described two such patients. Both of them showed similar sleep deficiencies, the most prominent of which was a complete loss of REM sleep. It was further pointed out that aside from minor neurological deficits, the patients led normal lives. The authors stated: "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 twenty suffered damage to the pontine region of the brainstem from shrapnel fragments from a gunshot wound. Following the injury, the man was comatose for 10 days, remained in critical condition for another two weeks and then recovered. An examination of his patterns of sleep at the age of 33 revealed that he essentially lacked REM sleep; that is, REM was absent on most nights and averaged 2.25% of TST on the other nights. Similar to the study by Osorio and Daroff (1980), Lavie et al. (1984) reported that despite the virtually total loss of REM sleep, the man led a normal life. For instance, following the injury the man 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.

5. Functional imaging studies of brain activity in REM sleep

Recent functional imaging studies of human brain activity in REM sleep reveal patterns of activity that are consistent with dream processes but not with memory consolidation.

The mental/cognitive content of REM sleep is dreams. Although dreams are not restricted to REM, they are unquestionably a prominent feature of REM sleep. Dreams are the sole window to cognitive processes of REM sleep. Although the function(s) of dreams have been, and continue to be, strongly debated (see Revonsuo, this issue), a generally agreed-upon feature of dreams is that they are poorly remembered. Similar to its function, diverse explanations have been put forth to account for the amnesic quality of dreams.

Foulkes and coworkers (Foulkes 1982a; 1985; 1999; Foulkes & Fleisher 1975; Foulkes et al. 1989), leading proponents of the view that dreams are a meaningful extension of waking mental life, have suggested that the reason dreams are so easily forgotten is that the brain in REM sleep is in a reflective mode (akin to reminiscing about, or reflecting on, events during waking) rather than in an encoding mode. An important difference, however, between the reflections of dreams and waking is that during waking one can rapidly switch from the reflective to the encoding mode to integrate and possibly store information. This cannot readily be done in REM sleep and as a result the reflections/reminiscences of REM (dreams) are lost to memory (Foulkes 1985; Foulkes & Fleisher 1975).

At the opposite end of the spectrum to the position of Foulkes and others (Domhoff 1969; 1996; Domhoff & Schneider 1998; Hall & Van de Castle 1966; Van de Castle 1994) that dreams are logical and meaningful, Hobson and colleagues (Hobson 1988b; Hobson et al. 1998b) have argued that dreams can be defined by such characteristics as hallucinosis, bizarreness, delusion, and confabulation and have likened dreams to the "delirium of organic brain disease"(Hobson 1997b). Hobson et al. (1998b) have proposed a purely physiological explanation for the amnesia of REM, pointing to the likely correspondence between memory loss and underlying physiological changes in REM, 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."

Independent of theories of dreams, recent functional imaging studies in humans during sleep have revealed patterns of activity in REM that appear to reflect dream processes, including its amnesic quality. Although differences exist among reports (Braun et al. 1997; 1998; Maquet et al. 1996; Nofzinger et al. 1997), a fairly consistent pattern of brain activity in REM sleep in humans 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; by contrast, extrastriate (visual) regions (as well as other sensory association sites) are very active in REM; (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 (Braun et al. 1997; 1998; Maquet et al. 1996; 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 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, whereas the deactivation of the prefrontal cortex (output) parallels the failure of dreams to influence executive systems for behavior. With respect to the latter, Braun et al. (1997) stated: "REM sleep may constitute a state of generalized brain activity with the specific exclusion of executive systems which normally participate in the highest order analysis and integration of neural information."

In effect (and not unexpectedly), the brain in REM sleep mirrors the dreaming brain; that is, internally generated visual images are fed to (or recruited by) the limbic system. They are then incorporated into dreams but due to the suppression of activity of the prefrontal cortex dream scenarios are not often recorded and generally do not influence waking behavior. In this regard, in an article on the neural basis of consciousness, Jones (1998) commented that the recent demonstration in imaging studies (Braun et al. 1997; Maquet et al. 1996) that activity in the frontal cortex is depressed in REM suggests "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."

Finally, if dream material is so readily forgotten in REM sleep (reflecting the state of the brain in REM), it seems

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unlikely that other mental phenomena that are not incorporated into dreams would be processed and permanently stored during REM sleep.

In summary, the pattern of brain activity in REM sleep is consistent with dreams but inconsistent with the orderly evaluation, organization, and storage of information which is the domain of attentive, waking consciousness.

6. A proposed function for REM sleep

It appears that the active state of the brain during REM has fueled claims that REM sleep is involved in complex, higher order functions, including memory (for review, Rechtschaffen 1998).

It is tempting to speculate, as several theories do, that magical processes occur during REM sleep; that is, that during the unconscious state of REM sleep some programmed or purposeful reordering of mental events occurs so that a nightly replay of daytime events during REM enhances the storage or consolidation of these events. In contrast to the view that the effects of REM extend beyond sleep to influence waking activities, we propose that REM can be entirely understood within the context of sleep without invoking mental phenomena or quasi-conscious processes (for review, Vertes 1986b). REM is a state of sleep; as such, it would seem that attempts to describe its function should look to sleep and not to waking.

As described in detail in our earlier theoretical paper (see Vertes 1986b), we propose that the primary 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. We argued that 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 subject or disturbing the continuity of sleep. By analogy, the process of induction and recovery from general anesthesia is a delicate one requiring the special skills of highly trained medical professionals. The brain performs a very similar function daily and seemingly flawlessly. REM is an integral part of this process.

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 minutes) and the duration of REM periods become progressively longer throughout sleep.

Regarding this organization, we would suggest that the high percentage of REM sleep in neonates serves to offset equally high amounts of SWS in newborns (see also, Benington & 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. With respect to the latter, the disorientation experienced on sudden, unexpected awakenings from sleep (middle of the night), compared to natural awakening, may reflect an inadequate preparation of the brain for waking due to incomplete REM.

In line with the foregoing, reductions in REM, seen particularly with antidepressants, are generally accompanied by a reorganization of sleep; that is, marked increases in light SWS and corresponding decreases in deep SWS as well as frequent awakening (Cohen et al. 1982; Kupfer et al. 1989; 1991; Nicholson & Pascoe 1988; Saletu et al. 1983; 1991; Schenk et al. 1981; Shipley et al. 1984; Staner et al. 1995; Wyatt et al. 1971b). For the SSRIs, this has been referred to as the "alerting" effect on sleep of these antidepressants (Kupfer et al. 1989; 1991; Nicholson & Pascoe 1988; Saletu et al. 1983; 1991; Schenk et al. 1981; Shipley et al. 1984; Staner et al. 1995).

In accord with others (Benington & Heller 1995; Berger & Phillips 1995), we believe that the general purpose of sleep is restitution/recuperation for the CNS, and within this context, the primary function of REM sleep is to prepare the brain/CNS for recovery from sleep.

7. Conclusions

We believe that the evidence reviewed in this report disputes the claim that REM sleep serves a role in the consolidation of memory. Numerous studies have shown that depriving animals of REM sleep has no effect on learning/memory. Although other reports have shown that REM deprivation (REMD) disrupts memory, many of them have been questioned based on the use of the stressful pedestal technique for REMD leading to the view that reported deficits were performance and not learning/memory deficits. The majority of REM deprivation studies in humans have failed to show that REMD disrupts memory. Perhaps the strongest evidence against the memory consolidation hypothesis comes from the demonstration that antidepressant drugs or brain stem lesions profoundly suppress, or eliminate, REM sleep, yet neither appears to alter memory/cognitive functions. Finally, recent imaging studies in humans during sleep have described patterns of activity that are consistent with dreams, including their amnesic quality, but inconsistent with the orderly processing, evaluation, and storage of information that characterizes waking consciousness. In conclusion, we believe that the weight of evidence, as reviewed herein, fails to support a role for REM sleep in the processing or consolidation of memory.

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